

# HealthMED

Journal of Society for development in new net environment in B&H

## EDITORIAL BOARD

Editor-in-chief *Mensura Kudumovic*  
Execute Editor *Mostafa Nejati*  
Associate Editor *Azra Kudumovic*  
Technical Editor *Eldin Huremovic*  
Cover design *Mirza Basic*

## Members

*Paul Andrew Bourne (Jamaica)*  
*Xiuxiang Liu (China)*  
*Nicolas Zdanowicz (Belgique)*  
*Farah Mustafa (Pakistan)*  
*Yann Meunier (USA)*  
*Forouzan Bayat Nejad (Iran)*  
*Suresh Vatsyayann (New Zealand)*  
*Maizirwan Mel (Malaysia)*  
*Budimka Novakovic (Serbia)*  
*Diaa Eldin Abdel Hameed Mohamad (Egypt)*  
*Zmago Turk (Slovenia)*  
*Bakir Mehic (Bosnia & Herzegovina)*  
*Farid Ljuca (Bosnia & Herzegovina)*  
*Sukrija Zvizdic (Bosnia & Herzegovina)*  
*Damir Marjanovic (Bosnia & Herzegovina)*  
*Emina Nakas-Icindic (Bosnia & Herzegovina)*  
*Aida Hasanovic (Bosnia & Herzegovina)*  
*Bozo Banjanin (Bosnia & Herzegovina)*

Address of the Editorial Board Sarajevo, Bolnicka BB  
phone/fax 00387 33 956 080  
healthmedjournal@gmail.com  
http://www.healthmedjournal.com

Published by DRUNPP, Sarajevo  
Volume 6 Number 3, 2012  
ISSN 1840-2291

## Sadržaj / Table of Contents

<b>Robot-assisted radical prostatectomy: A mini-health technology assessment in a teaching hospital.....</b>	<b>724</b>
<i>Silvana Barbaro, Alessandro Paudice, Serenella Scipioni, Barbara Martin, Lorena Charrier, Fabrizio Bert, Maria Michela Gianino</i>	
<b>Structuring depressive discourse: A descriptive narrative process .....</b>	<b>731</b>
<i>Luiz Carlos de Abreu, Alberto Olavo Advincula Reis, Moredesto Leite Rolim Neto, Nádia Nara Rolim Lima, Jesus de Souza Cartaxo, Elizabeth Alves Silva, Saulo Araujo Teixeira, Cícero Hedilberto Pereira Filgueiras Macedo</i>	
<b>Applying statistical process control (SPC) chart techniques to examine patient-centered performance indicators and pharmacy operational indicators using sequential control chart .....</b>	<b>736</b>
<i>Tsair-Wei Chien, Agnes LF Chan, Henry WC Leung, Ming-Ting Chou</i>	
<b>Contents of antioxidant A, E, C vitamins, Malondialdehyde (MDA), and Aminotransferases (ALT, AST) in serum professional football managers during derby matches .....</b>	<b>745</b>
<i>Sebahattin Devecioğlu</i>	
<b>Effect of Core Stability Training on patients with chronic low back pain .....</b>	<b>754</b>
<i>Wang Xueqiang, Zheng Jiejiao, Bi Xia, Liu Jing</i>	
<b>A Study on Etiologic Agents and Drug Resistance Pattern of Entropathogens Isolates from Stool Specimens of Children Less Than Five Years Old Admitted in an Iranian Hospital .....</b>	<b>760</b>
<i>Mona Mohammad Zadeh, Mohammad Rahbar, Mahnaz Saremi, Mohammad Aghazadeh, Mohammad Reza Montazer Khorasan, Mehrdad Peyrovie, Khatere Saeidi Varnamkhasti, Abdolaziz Rastegar Lari</i>	
<b>Determination of physical assessment skills used by nurses in Turkey .....</b>	<b>765</b>
<i>Zeliha Koç, Zeynep Sağlam</i>	
<b>Pre-menstrual syndrome prevalence, and correlation with carbohydrate intake in young women.....</b>	<b>774</b>
<i>Rania A Hussein, Hafiz M, Bin-Afif S, Al-Omari E, Al-Helou M</i>	
<b>A snapshot of primary care physicians educational needs regarding COPD in Crete, Greece: an exploratory case study .....</b>	<b>781</b>
<i>Nikolaos I. Kakoliris, Emmanouil K. Symvoulakis, Katerina M. Antoniou, Ilias Grammatikopoulos, Nikolaos Tzanakis, Nikolaos M. Sifakas, Christos Lionis</i>	

HealthMED journal with impact factor indexed in:

- Thomson Reuters ISI web of Science,
- Science Citation Index-Expanded,
- Scopus,
- EBSCO Academic Search Premier,
- Index Copernicus,
- getCITED, and etc.



THOMSON REUTERS



# Sadržaj / Table of Contents

<b>Discourse and bipolar disorder: Narrative therapy on northeast Brazil.....</b>	<b>787</b>
<i>Modesto Leite Rolim Neto, Alberto Olavo Advincula Reis, Luiz Carlos de Abreu, Saulo Araujo Teixeira, Cicero Hedilberto Pereira Filgueiras Macedo, Nádia Nara Rolim Lima, Jesus de Souza Cartaxo, Elizabeth Alves Silva</i>	
<b>Performance assessment indicators: How DEA and Pabon Lasso describe Iranian hospitals` performance.....</b>	<b>791</b>
<i>Ahmad Barati Marnani, Jamil Sadeghifar, Kimia Pourmohammadi, Davood Mostafaie, Masood Abolhalaj, Peivand Bastani</i>	
<b>Radioisotope Synovectomy and the role of nurses in Hemophilia care .....</b>	<b>797</b>
<i>Selmin Senol</i>	
<b>An approach for early and appropriate prediction of dengue fever using white blood cells and platelets .....</b>	<b>806</b>
<i>Wen-Pin Lai, Tsair-Wei Chien, Ming-Ting Chou</i>	
<b>Histopathological types of colonic adenomas incidence of dysplastic changes in Riyadh, Saudi Arabia .....</b>	<b>813</b>
<i>Al-Dahmash B., Saad Alkahtani I, AL-Farraj S. A., Saud A. Alarifi, AL-Eissa Mohammed Saad, Hamad Al-Yahya, Marie, M.A</i>	
<b>Pregnancy resulting from sexual abuse: Reasons alleged by Brazilian women for carrying out the abortion - Pregnancy and violence.....</b>	<b>819</b>
<i>Jefferson Drezett, Daniela Pedroso, Maria Auxiliadora Vertamatti, Hugo Macedo Junior, Marcia de Toledo Blake, Luiz Henrique Gebrim, Vitor E. Valenti, Luiz Carlos de Abreu</i>	
<b>Development of Emergency Medical Services (EMS) in Iran: Component of Transportation.....</b>	<b>826</b>
<i>Mohammadkarim Bahadori, Ramin Ravangard, Mostafa Nejati</i>	
<b>Knowledge levels of intensive care nurses regarding usage of Pulse Oximetry in a university hospital in Turkey.....</b>	<b>832</b>
<i>Dilek Yıldız, Emine İyigün, Berna Eren Fidanci</i>	
<b>Cognitive Dual-Task training improves balance function in patients with stroke .....</b>	<b>840</b>
<i>Zheng Jiejiao, Wang Xueqiang, Xu Yueying, Yang Ying, Shen Liyan, Liang Zhenwen</i>	
<b>Sleep disorders in climacteric women.....</b>	<b>846</b>
<i>Sandra Dircinha Teixeira de Araújo Moraes, Angela Maggio da Fonseca, Eli Mendes de Moraes, Vicente Renato Bagnoli, Caio Fábio Schlechta Portella, Luiz Carlos Abreu, Edmundo Chada Baracat</i>	
<b>Burdens perceived by the family caregivers of cancer patients receiving outpatient chemotherapy and family functions: a cross-sectional study .....</b>	<b>856</b>
<i>Zeynep Güneş, Hüsnüye Çalışır, Ayşe Özkan, Gülsüm Orhan</i>	
<b>Playgrounds in Novi Sad (Serbia) and their influences on children`s health and development .....</b>	<b>864</b>
<i>Milena Krkljes, Marija Jevtic</i>	
<b>Effect of quadriceps and ankle plantar flexor muscle fatigue on balance of elderly women.....</b>	<b>875</b>
<i>Fatemeh Islami, Zynolabedin Fallah, Soolmaz Mahdavi, Amin Farzaneh Hesari, Hamid Janani</i>	
<b>Comparison of efficacy of letrozole and clomiphene citrate in ovulation induction for women with polycystic ovarian syndrome.....</b>	<b>879</b>
<i>Hakan Nazik, Yakup Kumtepe</i>	
<b>Transitory tubal dysfunction during vasoactive therapy.....</b>	<b>884</b>
<i>Dejan Rancic, Olivera Dunjic, Ivana Pesic, Vesna Stojanovic</i>	
<b>Study of bacterial contamination of keyboard and mouse in a medical school computer center .....</b>	<b>889</b>
<i>Manijeh Mehdinejad, Azar Dokht Khosravi, Marjan Afzali, Ali Zarei Mahmoudabadi</i>	
<b>Age, Puberty, Sport Participation, Body Mass Index and Aerobic Capacity In Turkish Adolescents .....</b>	<b>893</b>
<i>Murat Ozsaker</i>	
<b>Patient assessment of the quality of standard and one day approach to a diagnostic of a couple infertility .....</b>	<b>900</b>
<i>Aleksandra Trninic Pjevic, Vesna Kopitovic, Artur Bjelica, Irena Bujas, Mirko Pjevic, Djordje Ilic</i>	
<b>Syntax of social life in postpartum depression: Mother-child interaction .....</b>	<b>906</b>
<i>Luiz Carlos de Abreu, Alberto Olavo Advincula Reis, Modesto Leite Rolim Neto, Nádia Nara Rolim Lima, Jesus de Souza Cartaxo, Elizabeth Alves Silva, Saulo Araujo Teixeira, Cicero Hedilberto Pereira Filgueiras Macedo</i>	
<b>Dietary and other factors as risks of hyperemesis gravidarum .....</b>	<b>910</b>
<i>Gul Kiziltan, Mendane Saka, Perim Turker, Aydan Ercan</i>	
<b>Predictive markers for one-year outcome in patients with Stemi trated with primary Percutaneous Coronary Intervention (PCI).....</b>	<b>916</b>
<i>Nebojsa Krstic, Milan Pavlovic, Goran Koracevic, Aleksandar Stojkovic, Svetlana Pavlovic</i>	
<b>The effects of group solution– focused therapy on depression and completion of treatment in patients with chronic hepatitis B.....</b>	<b>925</b>
<i>Jinous Arvand, Abdollah Shafiabadi, Mohammad Reza Falsafinejad, Mohammad Reza Zali</i>	
<b>The effects of web-based childbirth education program on activities of daily living of pregnant women.....</b>	<b>930</b>
<i>Kerziban Yenil, Ümran Sevil</i>	
<b>Sensitivity and efficiency of „silent“ phlebothrombosis early detection tests in ambulatory vascular patients.....</b>	<b>939</b>
<i>Milan Jovanovic, Aleksandra Krstic, Goran Stanojevic, Miroslav Stojanovic, Ivan Ignjatovic, Jovica Jovanovic</i>	
<b>Is spinal anesthesia really innocent? .....</b>	<b>945</b>
<i>Gökhan Açmaz, Abdullah Boztosun, Hilal Yuvaci, Aylin Inal, Iptisam Ipek Müderris</i>	
<b>Neurogenic appendicopathy in pediatric patients: A clinical and histopathological entity .....</b>	<b>950</b>
<i>Slobodan Grebeldinger, Branka Radojicic, Igor Meljnikov, Michaela Mocko-Kacanski</i>	
<b>Effects of education and exercise on pain, depression and quality of life in patients diagnosed with Fibromyalgia.....</b>	<b>962</b>
<i>Canan Demirbag, Ferdane Oguzoncul</i>	

# Sadržaj / Table of Contents

<b>Gingival enlargement induced by cyclosporine in nephrotic child</b> ..... 971 <i>Zoran Bojanic, Vladmila Bojanic, Dragan Mladenovic, Predrag Miljkovic</i>	<b>24 h Holter-monitoring of heart in diagnostics of cardiac rhythm disorders in University of Sarajevo students</b> ..... 1050 <i>Zana Pozderac, Nehru Mackic, Zumreta Kusljugic</i>
<b>Sport-Related Injuries in the Emergency Department: An analysis of 1636 cases</b> ..... 977 <i>Semih Akkaya, Mustafa Serinken, Nuray Akkaya, Özgür Karcioğlu</i>	<b>Our attitude towards the treatment of the rectal cancer</b> ..... 1062 <i>Zuvdija Kandic, Adis Kandic, Alma Kandic, Lejla Catic, Enis Kandic</i>
<b>Our experience in treatment of thoracic aortic intramural hematoma</b> ..... 983 <i>Aleksandar Mikic, Petar Djukic, Krstina Dokleštic, Slobodan Cvetkovic</i>	<b>Cardiovascular risk factors in Banovići coal mine miners</b> ..... 1067 <i>Munevera Becarevic, Esad Burgic</i>
<b>Laparoscopic management of tubal pregnancy misdiagnosed and missed by Laparotomy 35 days ago</b> ..... 988 <i>Hakan Nazik, Murat Api, Orçun Özdemir, Emre Destegül, Hasan Can Toyganözü</i>	<b>Quality of life of people with Diabetes Mellitus type 2</b> ..... 1076 <i>Nehra Mosorovic, Selmira Brkic, Sabina Nuhbegovic, Nurka Pranjic</i>
<b>Health related quality of life during pregnancy</b> ..... 990 <i>Jelena Dotlic, Milan Terzic, Slobodanka Janosevic, Dragan Babic, Momcilo Ristanovic, Tatjana Pekmezovic</i>	<b>Effects of short-term octreotide therapy on TSH adenoma with atrial fibrillation - Case report</b> ..... 1081 <i>Salih Azabagic, Amra Jakubovic Cickusic, Edin Zukic</i>
<b>Consumers' Kefir consumption: A pilot study in Turkey</b> ..... 997 <i>Saniye Bilici, Eda Köksal, Özge Küçükerdönmez, Nevin Şanlier</i>	<b>Instructions for the authors</b> ..... 1087
<b>Influence of inhaled Corticosteroids on growth in asthmatic children</b> ..... 1003 <i>Gordana Kostic, Vesna Skodric-Trifunovic, Branislav S. Gvozdenovic, Marina Petrovic, Nevenka Ilic, Mihailo I. Stjepanovic</i>	<b>Uputstvo za autore</b> ..... 1088
<b>The influence of very low calorie diet on parametres of metabolic activity of bone</b> ..... 1009 <i>Olivera Rankov, Branka Kovacev- Zavisic, Edita Stokic, Jovanka Novakovic Paro, Tijana Icin, Nemanja Kovacev</i>	
<b>Postural status and self-perception profile of children</b> .... 1016 <i>Suncica Pocek, Visnja Djordjic, Tatjana Tubic</i>	
<b>Early detection of postoperative deep vein thrombosis after general surgical procedures</b> ..... 1023 <i>Milan M. Jovanovic, Aleksandra Z. Krstic, Goran Stanojevic, Miroslav Stojanovic, Igor D. Smiljkovic, Zoran Damjanovic</i>	
<b>Lymphangioma of the spermatic cord in an elderly man: A case report</b> ..... 1033 <i>Shi Deng, Shangqing Ren, Lin Hou, Qiang Dong</i>	
<b>Postpericardiotomy syndrome as a complication of nuss procedure - Case report</b> ..... 1036 <i>Radoica Jokic, Jelena Antic, Smiljana Marinkovic, Svetlana Bukarica</i>	
<b>Complicated peritonitis in patient on Chronical Peritoneal Dialysis – Case report</b> ..... 1041 <i>Tatjana Djurdjevic-Mirkovic, Mladjan Protic, Lada Petrovic, Sinisa Mirkovic, Slavenka Vodopivec</i>	
<b>New Ruthenium Complexes with Schiff Bases as Mediators for the Low Potential Amperometric Determination of Ascorbic Acid, Part II: Voltametric and Amperometric evidence of mediation with Bromo-derivative of Tetraethylamonium dichloro-bis[N-phenyl-5-halogeno-salicylideniminato-N,O]ruthenat (III)</b> ..... 1046 <i>Emira Kahrovic, Emir Turkusic</i>	

# Robot-assisted radical prostatectomy: A mini-health technology assessment in a teaching hospital

Silvana Barbaro<sup>1</sup>, Alessandro Paudice<sup>1</sup>, Serenella Scipioni<sup>1</sup>, Barbara Martin<sup>2</sup>, Lorena Charrier<sup>2</sup>, Fabrizio Bert<sup>2</sup>, Maria Michela Gianino<sup>2</sup>

<sup>1</sup> Teaching Hospital San Giovanni Battista Turin, Italy,

<sup>2</sup> Department Of Public Health, University of Turin, Italy.

## Abstract

**Objectives:** The aim of this study is to perform a comparative costs analysis of radical retropubic prostatectomy (RRP) and robotic-assisted laparoscopic prostatectomy (RAP) for clinically localized prostate cancer and to determine whether to expand the use of RAP or to continue with conventional RRP in Teaching Hospital San Giovanni Battista Turin Italy.

**Methods:** A cohort study was carried out comprising consecutive patients undergoing radical prostatectomy. The decision of which surgical approach to use was by patient choice after a discussion of the perceived pros and cons of each alternative. No other selection criteria were routinely used. All patients were followed on a common care pathway.

Included in the assessment model were the following domains (EUnetHTA): Safety, Clinical effectiveness, Organizational aspects, Cost and economic evaluation. Data were collected from the patient's medical health record and the operating room report and data were obtained from the hospital accounting office. Two-way sensitivity analysis of RAP was performed.

**Results:** In agreement with other observations our results showed that the mean LOS for RAP-treated patients was shorter and that LOS in the ICU was longer as well as the operating time. RAP is more expensive than RRP.

**Conclusion:** In the current circumstances, increasing the use of RAP at the San Giovanni Battista Hospital does not appear expedient. This conclusion is corroborated by the sensitivity analysis which showed that RAP carries higher costs than RRP.

**Key words:** prostatectomy, robotics, economics, cost analysis, health technology assessment.

## Introduction

Retropubic radical prostatectomy (RRP) is the mainstay treatment for prostate cancer. While it remains the current standard, among the most recent alternative techniques there is robotic-assisted laparoscopic prostatectomy (RAP). Numerous studies have shown that although the operating time for RAP is longer versus RRP during the initial learning curve, the difference disappears in a larger cohort of treated cases (1-5). Furthermore, RAP has a lower complications rate and requires fewer blood transfusions.

In patients undergoing RAP, the length of hospital stay (LOS) is generally shorter. Only Nelson (6) reported similar mean LOS for RRP and RAP in their large-scale study. In a systematic review, Ficarra (7) found similar outcomes rates for function, incontinence and impotence, with only one study reporting the superiority of RAP. However, RAP has been variously shown to be more costly than RRP (8-11).

In light of available evidence, the San Giovanni Battista Teaching Hospital, Turin, Italy, wanted to determine whether to expand the use of RAP or to continue with conventional RRP. To this end, a mini-health technology assessment (HTA) was conducted to inform the hospital's general management in its decision-making procedures. The HTA was carried out from the perspective of the hospital and has included an economic evaluation with a comparative analysis of different alternatives (12).

## Methods

Included in the assessment model were the following domains (EUnetHTA) (13):

Safety in relation to: transfusion rate; major and minor complications rate; total LOS and LOS in the urology department and intensive care unit (ICU). Major complications were defined as: straight leg raising deficit; urinary fistula; cardiac and respiratory events. Minor complications were defined as: abundant urine drainage; eczematous dermatitis; urinary tract infection; surgical wound dehiscence.

Clinical effectiveness with a focus on functional abilities: impotence as a surgery-related outcome according to whether a nerve-sparing (NS) procedure was performed or not (NNS), in which case impaired functional ability was considered.

Organizational aspects as regards cooperation with other services and transfer to an ICU and LOS in the ICU in particular.

Cost and economic evaluation as measured using the following variables:

- Surgeon's and anesthesiologist's time in the operating room (in minutes);
- operating room time (in minutes);
- type and dose of anesthetic, number and types of drugs administered during hospitalization;
- LOS on the ward, LOS in the ICU if applicable;
- robot depreciation and maintenance costs.

To calculate the costs for these variables (expressed in 2008 euros), data were obtained from the hospital accounting office; specifically:

- Uro-surgeon's hourly fee: €51.6
- Anesthesiologist's hourly fee: €55.7
- Daily cost of hospitalization in a urology department equal to the resources absorbed for bed occupation and management net of resources absorbed for its use in relation to the inpatient's type of pathology: €283.22
- Daily cost of hospitalization in the ICU: €813.36
- Hourly operating room cost: €712.80

The cost of drugs was calculated taking the daily dose, duration of treatment (in days), and the purchasing price of the drug

Annual depreciation cost of the robot was €217,089.6 and the annual maintenance cost was €109,536, both divided by the number of cases treated

Ancillary service costs: analytic laboratory, radiology, pathology, blood bank, and other services (e.g., ECG, specialist examinations). These services were calculated according to the rates the region reimburses the hospital for their delivery.

A cohort study was carried out comprising consecutive patients undergoing radical prostatectomy between January 2007 and December 2008 by either RAP or RRP.

The decision of which surgical approach to use was by patient choice after a discussion of the perceived pros and cons of each alternative. No other selection criteria were routinely used.

All patients were followed on a common care pathway.

The setting was two urology departments in the same hospital, and the same two surgeons performed surgery in all patients.

Data were collected from the patient's medical health record and the operating room report. Patient-related variables were: age; Gleason score; and tumor stage. For each domain and variable, the two surgical techniques were compared to determine differences in outcome in relation to the costs that the technique carried.

Two-way sensitivity analysis of RAP was performed to determine whether and how the conclusions changed when the surgeon's and the anesthesiologist's time, the operating room time, and the case volumes were changed. The reference parameters for carrying out the analysis were retrieved from the literature. We developed a PubMed search strategy which would enable us to reach high sensitivity through MeSH terms and subheadings. All search strategies were performed on 29 November 2010. The chosen search pathway was:

Search: "Prostatectomy / methods" [MAJR] AND "Robotics"[Mesh] AND ("statistics and numerical data "[Subheading] OR "Treatment Outcome"[Mesh])

We then applied limits related to publication type (reviews) and comparative studies. Publications were included in the analysis if they stated operating time and number of RRP- and RAP-treated cases. Two reviewers assessed the abstracts for relevance; full texts of papers that appeared potentially relevant were retrieved.

The first search retrieved 33 reviews and the second 51 articles (comparative studies). Reviews

and articles were rejected if they did not report operating time and number of cases or data about RAP and RRP. In all, 17 reviews and 11 articles were selected for analysis. The following data were entered into the sensitivity analyses:

- First analysis: operating time (288 min) and number of RAP operations (n=30) as reported by Menon (4). This choice was based on the volumes of RAP operations similar to our study (30 versus 24).
- Second analysis: operating time (160 min) and number of RAP operations (n=200) as reported by Tewari (5). This choice was based on the similarities between volume and operating time for RRP (100 versus 99 cases and 163 min versus 164.8 min, respectively).
- Third analysis: the shortest operating time (130 min) retrieved from the published data (13-14) and the highest volume (Nelson, 2007, n=629) (6) of RAP which could feasibly be carried out the San Giovanni Battista Hospital.

For each of the three hypotheses and for RAP, the mean costs for the operating room and professional fees (surgeon and anesthesiologist) were recalculated since they depend on operating time, as were robot depreciation and maintenance costs since they depend on case volume. The costs and volume for RRP were kept unchanged.

### Statistical analysis

Descriptive data are shown as absolute and relative frequencies of the different modalities for categorical data and as mean  $\pm$  SD for continuous variables. Chi-square or Fisher's exact test were carried out to assess whether a significant difference could be evidenced between the RAP- and RRP-treated groups for categorical variables; continuous variables were analyzed using Student's t-test for normally distributed variables; otherwise, the Mann-Whitney test was used.

The differences in total costs between the RAP- and RRP-treated groups were assessed by fitting a multivariate model where total costs was the dependent variable and the independent variables were treatment group (RAP vs. RRP), patient age, clinical tumor stage (>3 vs.  $\leq$ 3), Gleason score ( $\geq$ 7

vs.  $\leq$ 6), major complications (presence vs. absence) and nerve-sparing procedure (no vs. yes).

The significance level was set at  $\alpha=0.05$  for all tests. All analyses were performed using Stata version 9.2 (Stata Corp., College Station, TX, USA).

### Results

Overall, the data from 123 patients (99 undergoing RRP and 24 RAP) were analyzed. Table 1 reports the patient characteristics of the two treatment groups. The mean age at surgery was  $63.8 \pm 6.4$  years; 63 patients had a Gleason score  $\geq 7$ , 11 of which had a clinical tumor stage  $> 3$ . In all, 15 patients had a clinical tumor stage  $> 3$ . Major complications occurred in 10 patients and minor complications in 13. A nerve-sparing procedure was not performed in 120 patients. The mean age and Gleason score were similar for both groups, whereas the clinical tumor stage was significantly higher in the RRP-treated group ( $P=0.004$ ).

Table 2 lists the main perioperative parameters and outcomes after surgery for both groups.

For neither technique was an association found between Gleason score  $\geq 7$  and outcome in terms of impotence (NNS) as well as for neither technique was an association found between occurrence of major complications or occurrence of major complications and NNS.

For RRP, a clinical tumor stage  $> 3$  was not associated with the occurrence of major complications nor was Gleason score associated with the occurrence of minor complications. Although the difference was not statistically significant ( $P=0.22$ ), impotence after RAP was more frequent among these patients though they had a lower clinical tumor stage than those undergoing RRP.

Compared with RRP, fewer transfusions and fewer major and minor complications were noted for RAP, although the difference was statistically significant only for the latter parameters.

There was no statistically significant difference in mean LOS; however, when the two components (LOS on the ward and in the ICU) were analyzed separately, LOS on the ward was significantly longer for the RRP-treated group ( $P<0.0001$ ). RAP required longer surgeon and anesthesiologist time, and therefore longer operating room occupation time ( $P<0.0001$ ).

Table 1. Patient characteristics

	RAP (n=24)	RRP (n=99)	P value
Mean age (yrs)	61.58±6.5	64.3±6.)	0.047
Gleason score			
≤6 – no. (%)	7 (31.8)	43 (46.7)	0.21
≥7 – no. (%)	15 (68.2)	49 (53.3)	
Clinical tumor stage			
>3 – no. (%)	0 (-)	15 (16.7)	0.040
≤3 – no. (%)	22 (100.0)	75 (83.3)	

Plus-minus values are means ±SD

Table 2. Perioperative parameters and outcomes after RAP and RRP

	RAP (n=24)	RRP (n=99)	P value
No nerve-sparing – no. (%)	21 (95.5)	79 (85.9)	0.22
Blood transfusions *	0.08±0.4	0.7±0.9	<0.001
Blood transfusion ≥1 – no. (%)	1 (4.2)	49 (49.9)	<0.001
Patients with major complications – no. (%)	1 (4.2)	9 (9.5)	0.40
Patients with minor complications – no. (%)	0 (-)	13 (13.7)	0.06
LOS *	7.0±2.6	8.1±4.9	0.11
LOS in urology ward (days) *	5.5±2.7	7.9±4.9	<0.0001
LOS in ICU (days) *	1.4±0.8	1±0†	0.33
Surgeon's time (min) *	365.8±65.9	164.8±34.6	<0.0001
Anesthesiologist's time (min) *	453.8±65.9	185.8±38.1	<0.0001
Operating room occupation time (min)**	484.3±69.6	206.0±39.7	<0.0001

LOS denotes length of stay; \*Mann-Whitney test; † 3 patients; plus-minus values are means ±SD.

Table 3. Comparison of overall costs (in euro).

	RAP (n=24)	RRP (n=99)	P value*
<b>Total surgical costs</b>	20,103.4±937.0	2,764.0±533.3	<0.0001
Operating room	5,753.4±826.4	2,447.8±471.7	<0.0001
Maintenance Robot	4,564.0±0	-	-
Depreciation Robot	9,045.4±0	-	-
Anesthesia technical costs	148.7±70.2	80.4±90.1	0.0001
Professional fees (surgeon)	317.1±57.2	142.9±29.9	<0.0001
Professional fees (anesthesiologist)	423.6±61.5	173.4±35.6	<0.0001
<b>Total hospital costs</b>	3,357.6±1,361.2	2,790.7±1,468.4	0.004
Hospital room (urology ward)	1,555.7±756.3	2,222.85±1,398.9	0.0001
Hospital room (ICU)	1,084.5±664.1	813.4±0†	0.45
Pharmacy	261.3±640.4	108.3±141.3	0.27
Blood transfusion	2.2±10.6	26.4±29.1	<0.0001
Radiology	131.2±55.4	48.3±68.5	<0.0001
Laboratory	187±56.3	142.1±43.6	0.0001
Pathology	71.7±54.0	190.6±93.0	<0.0001
Internal and external expertise	12.5±18.5	6.1±12.6	0.03
Other services (spirometry, ECG, other)	49.5±13.8	21.5±28.4	<0.0001
<b>Mean total costs (surgical + hospital)</b>	<b>23,609.7±1,730.7</b>	<b>5,635.1±1,615.3</b>	<b>&lt;0.0001‡</b>

\*Mann-Whitney test; † 3 patients; ‡ adjusted for age, clinical tumor stage, Gleason score, major complications and NNS denotes non-nerve-sparing; plus-minus values are means ±SD.

Table 4. Comparison of partial surgical costs (in euro) according to three scenarios with different case volumes and operating times

Analysis 1. RAP operating time 288 min			
	RAP (n=30)	RRP (n=99)*	Cost difference (95% CI)
Partial surgical costs	15,433.3±133.9	2,764.0±53.6	12,669.3 (12,417.7 - 12,920.9)
Analysis 2. RAP operating time 160 min			
	RAP (n=200)	RRP (n=99)*	Cost difference (95% CI)
Partial surgical costs	4,468.9±83.5	2,764.0±53.6	1,704.9 (1,474.3 - 1,935.5)
Analysis 3. RAP operating time 130 min			
	RAP (n=629)	RRP (n=99)*	Cost difference (95% CI)
Partial surgical costs	2,838.6±68.3	2,764.0±53.6	74.5 (-151.4 - +300.5)

\* same operating time and case volume for RRP as found in our study. 95% CI denotes 95% confidence interval; plus-minus values are means ±SD.

The overall costs for each item are listed in Table 3. The surgical costs, both total and by item, were significantly higher for RAP, as were hospital costs for ancillary services (radiology, analytical laboratory, internal and external expertise, and other services [spirometry, ECG, other]). In contrast, hospital room costs, probably because of higher complications rate, transfusion, and pathology examinations, were higher for RRP.

Multivariate analysis showed a statistically significant difference in total costs between RRP and RAP, with a mean cost increase of €18,106.9 for RAP versus RRP ( $P<0.0001$ ). In addition, the occurrence of major complications also impacted on costs, with a mean increase of €1,995.6 ( $P=0.002$ ).

Table 4 reports the results of the sensitivity analyses. The first analysis, which utilized Menon's data (4), showed that RAP carries a higher mean surgical cost of €12,669.3 ( $P<0.001$ ). The second analysis, which utilized Tewari's data (5), showed that RAP carries a higher cost of €1,705 ( $P<0.0001$ ). In the third analysis, which compared high case volume ( $n=629$ ) and short operating time (130 min), no statistically significant difference emerged between the two techniques.

## Discussion

In agreement with observations by Menon (4), Tewari (5), Fracalanza (2) and Ahlering (1), our results show that the mean LOS for RAP-treated patients was shorter, though the difference was not statistically significant versus RRP, and that LOS in the ICU was longer. The transfusion rate for

RAP-treated patients was significantly lower; the value we stated was lower than that reported by Krambeck (5.1%), but higher than that reported by either Tewari or Ahlering (0%) (1,3,5).

The mean operating time (surgeon's time) ranges between 127 min (Fracalanza) (2) and 214 min (Ahlering) (1) for RRP, and between 130 min (Joseph; Patel) (14,15) and 288 min (Menon) (4) for RAP. In comparison, the mean operating time for RAP at the San Giovanni Battista Hospital was higher, and that for RRP fell within the reported range (1,2,4,14,15). Unlike Menon's study (4) of 2002 (30 patients) which reported a statistically significant reduction in operating time between the first 20 and the last 10 cases, no similar trend could be found for the San Giovanni Battista Hospital data.

The percentage of non-nerve sparing procedures was found to increase in RAP even though the patients' clinical tumor stage was lower; the reason why the RAP group had lower nerve sparing might be that the surgeons were on their learning curve. Anyway, lower nerve sparing was not significantly different between RAP and RRP. While RAP was associated with lower complications rates, the difference versus RRP was statistically significant only for minor complications. Other studies reported similar findings for all complications, although, except for Tewari's study (5), the relative reduction in complications was never statistically significant.

The surgeon's costs for both techniques were lower at the San Giovanni Battista Hospital than those published in the literature. According to Lotan (9), the surgeon's cost for RAP is €1,275 (2004 dollar-euro exchange rate) and €1,203 according



to Scales (11) (2005 dollar-euro exchange rate). Similarly lower was the hourly operating room cost (€712.8 versus €955+275/hour reported in Scales and versus €734+251/half hour reported in Lotan) (9,11). The robot depreciation and maintenance costs were similar to those reported by Scales (11).

Our study has several limitations. There was a substantial difference in the surgeons' familiarity with the two techniques: RAP had only recently been introduced into surgical practice (learning-curve factor), whereas RRP was the consolidated procedure. The case volume was relatively small, especially for RAP, which could explain the longer operating time. Other studies reported much higher case volumes (Badani, 2766; Bolenz, 262; Murphy, 400; Patel, 500) (15-18).

In light of these limitations and current circumstances, increasing the use of RAP at the San Giovanni Battista Hospital does not appear expedient.

Surgeons are not currently using RAP: the San Giovanni Battista Hospital has estimated that it was more convenient to store the robot and continue with RRP. Indeed, every prostatectomy cost € 5,635.10 for RRP plus € 4,564 for the depreciation of robot: in the end the total (€ 10,199.10) is however less than the cost of RAP. This conclusion is corroborated by the sensitivity analysis which showed that RAP carries higher costs than RRP. The difference between the two techniques loses statistical significance when the operating time is 130 min and the case volume is 629; however, such a volume of radical prostatectomies at the San Giovanni is highly improbable. Hence, the following recommendations may be suggested.

The RAP system is expensive to acquire and use. Despite implicit or explicit claims that this technology is superior, its distinct advantages for most indications are currently unproven and highly operator dependent. Since too many systems are scattered in different hospitals, resulting in underutilization, the required experience is difficult to acquire for many of the surgeons using these devices.

Therefore, the surgeons should refrain from advocating the superiority of RAP as the evidence argues against such claims. Furthermore, the limited number of prostatectomies in the foreseeable future would not suffice to acquire the necessary experience or skills, even if all cases were treated by the same surgical team using RAP.

## References

1. Ahlering TE, Woo D, Eichel L, Lee DI, Edwards R, Skarecky DW. Robot-assisted versus open radical prostatectomy: a comparison of one surgeon's outcomes. *Urology*. 2004 May; 63(5):819-22.
2. Fracalanza S, Ficarra V, Cavalleri S, Galfano A, Novara G, Mangano A, Plebani M, Artibani W. Is Robotically assisted laparoscopic radical prostatectomy less invasive than retropubic radical prostatectomy? Results from a prospective, unrandomized, comparative study. *BJU Int*. 2008 May; 101(9):1145-9.
3. Krambeck AE, DiMarco DS, Rangel LJ, Bergstralh EJ, Myers RP, Blute ML, Gettman MT. Radical prostatectomy for prostatic adenocarcinoma: a matched comparison of open retropubic and robot-assisted techniques. *BJU Int*. 2009 Feb; 103(4):448-53.
4. Menon M, Tewari A, Baize B, Guillonneau B, Vallance G. Prospective comparison of radical retropubic prostatectomy and robot-assisted anatomic prostatectomy: the Vattikuti Urology Institute experience. *Urology*. 2002 Nov; 60(5):864-8.
5. Tewari A, Srivasatava A, Menon M, Members of the VIP Team. A prospective comparison of radical retropubic and robot-assisted prostatectomy: experience in one institution. *BJU Int*. 2003 Aug; 92(3):205-10.
6. Nelson B, Kaufman M, Broughton G, Cookson MS, Chang SS, Herrell SD, Baumgartner RG, Smith JA Jr.. Comparison of length of hospital stay between radical retropubic prostatectomy and robotic assisted laparoscopic prostatectomy. *J Urol*. 2007 Mar; 177(3):929-31.
7. Ficarra V, Novara G, Artibani W, Cestari A, Galfano A, Graefen M, Guazzoni G, Guillonneau B, Menon M, Montorsi F, Patel V, Rassweiler J, Van Poppel H. Retropubic, laparoscopic, and robot-assisted radical prostatectomy: a systematic review and cumulative analysis of comparative studies. *Eur Urol*. 2009 May; 55(5):1037-63.
8. Burgess SV, Atug F, Castle EP, Davis R, Thomas R. Cost analysis of radical retropubic, perineal, and robotic prostatectomy. *J Endourol* 2006; 20:827-830.
9. Lotan Y, Cadeddu JA, Gettman MT. The new economics of radical prostatectomy: cost comparison of open, laparoscopic and robot assisted techniques. *J Urol* 2004; 172:1431-1435.
10. Mouraviev V, Nosnik I, Sun L, Robertson CN, Walther P, Albala D, Moul JW, Polascik TJ. Financial comparative analysis of minimally invasive surgery to open surgery for localized prostate cancer: a single-institution experience. *Urology* 2007; 69:311-314.

11. *Scales CD Jr, Jones PJ, Eisenstein EL, Preminger GM, Albala DM. Local cost structures and the economics of robot assisted radical prostatectomy. J Urol 2005; 174:2323-2329.*
12. *Kudumovic M, Kudumovic A. Economic analysis of health. HealthMED 2008; 2:100-103*
13. *EUnetHTA Work Package 4. HTA Core Model for Medical and Surgical Interventionsv.1.0r; 2008[http://eunethta.net/Public/Work\\_Package/EUnetHTA-Project-2006-08/](http://eunethta.net/Public/Work_Package/EUnetHTA-Project-2006-08/EUnetHTA_Deliverables_project_2006-2008/) EUnetHTA\_Deliverables\_project\_2006-2008/ (accessed November 29, 2010).*
14. *Joseph JV, Rosenbaum R, Madeb R, Erturk E, Patel HR. Robotic extraperitoneal radical prostatectomy: an alternative approach. J Urol. 2006 Mar; 175(3 Pt 1):945-50; discussion 951.*
15. *Patel VR, Thaly R, Shah K. Robotic radical prostatectomy: outcomes of 500 cases. BJU Int. 2007 May; 99(5):1109-12.*
16. *Badani KK, Kaul S, Menon M. Evolution of robotic radical prostatectomy: assessment after 2766 procedures. Cancer. 2007 Nov; 110(9):1951-8.*
17. *Bolenz C, Gupta A, Hotze T, Ho R, Cadeddu JA, Roehrborn CG, Lotan Y. Cost comparison of robotic, laparoscopic, and open radical prostatectomy for prostate cancer. Eur Urol. 2010 Mar; 57(3):453-8.*
18. *Murphy DG, Kerger M, Crowe H, Peters JS, Costello AJ. Operative details and oncological and functional outcome of robotic-assisted laparoscopic radical prostatectomy: 400 cases with a minimum of 12 months follow-up. Eur Urol. 2009 Jun; 55(6):1358-66.*

*Corresponding Author*

*Maria Michela Gianino,  
Department of Public Health,  
University of Turin,  
Turin,  
Italy,  
E-mail: mariola.gianino@unito.it*

# Structuring depressive discourse: A descriptive narrative process

*Luiz Carlos de Abreu<sup>1</sup>, Alberto Olavo Advincula Reis<sup>1</sup>, Modesto Leite Rolim Neto<sup>1,2,3</sup>, Nádia Nara Rolim Lima<sup>3</sup>, Jesus de Souza Cartaxo<sup>3</sup>, Elizabeth Alves Silva<sup>3</sup>, Saulo Araujo Teixeira<sup>2</sup>, Cícero Hedilberto Pereira Filgueiras Macedo<sup>2</sup>*

<sup>1</sup> University of São Paulo, Brazil,

<sup>2</sup> Department of Medicine, University of Federal do Ceará, Brazil,

<sup>3</sup> “Suicidology” Research Group, University of Federal do Ceará, Brazil.

## Abstract

This study aimed to evaluate the importance of a descriptive narrative process of the significance involved in a depressive phenomenon. The research population consisted of 324 adult and adolescent patients of both genders, located in the central area of the city of Paraíba, for clinical and psychological health care. For surveyed patients, suffering and or psychological pain were the most common complaints. A sample of 159 patients was taken, including male and female adolescents and adults. Data were collected through a narrative interview. Shutz' procedure was used for information analysis. The obtained data offered the opportunity to review concepts, discuss life history and listen to narrative positioning episodes of manifested depression. The narratives were considered to be a determinant factor to consider inherent conflicts.

**Key words:** depression; narratives; discourse; pain; psychic illness.

## Introduction

In perspective to comprehend the inherent aspects of depressive phenomenon, we gained access to uncountable hypothesis, thesis, textual and empirical dispositions that made possible to analyze it under various points of view<sup>[1,2]</sup>. This way, to better outline this comprehension, it makes necessary to adopt well-defined criteria to evaluate and experiment it to, at the end, delimitate its peculiar unpredictable character.

The more correct criterion or profile to make possible a logical comprehension of depression is made by analysis of patient's narratives. This constitutes nowadays the most innovative and humanized tendency in methods to understand study

and formulate statements about streamlines done from histories told facing their pathology.

By living with disease, people acquire other histories to tell. This histories are not away from process of living, but are convergent to their way to see and live in the world, being a part of it. They report many lived situations which, at all, have a greater reason and change them in accessible histories to other people<sup>[3]</sup>.

Analysis of patient's narratives in manifestations of depressive phenomenon, through established parameters, fixed by significations, aims to link present and past. To depressive patient, there is just a shallow perspective of future, negative by lack of satisfaction and revenge against depressive status<sup>[4]</sup>. Comprehension about discourse of depression gives interpretation of truth games, at language spaces, what highlights the spoken aspects of disease<sup>[5]</sup>. Discursive practice is a group of anonym and historic rules, always determined in time and space, with speech function<sup>[6]</sup>.

This starting point takes us to the reflexivity about speakers that makes part of narrative about the reality of disease and about the history production belonging to this reality. Narratives, as medium to look for the truth, find at its itineraries words, actions, things, points-of-view and knowledge that come from its element of conflict. We highlight that this conflict creates a tension that organizes the events of history<sup>[7]</sup>. We also see: conflicts determine a reinvention of facts, promoting an interpretation of times and places characterized by being able to be polished, decrypted and announced by discourse.

Probably this comprehension gave some voice to anonym thinking, that remains in obscurity<sup>[8]</sup>. We believe it is necessary to rescue this moment by narrative perspective, interlacing a reflection about

untold histories, in agreement with words, a real possibility to what is unique, depressive and obscure in an enunciation. This way, people, by narrating their lives, open their discourse to allow the understanding of their meaning by other people<sup>[3]</sup>.

I should say these words while they exist. I should say them until they find me. Until they say to me - weird pain, strange missing<sup>[9]</sup>. This desire of finding time and space in what we live it overpasses the threshold of lived histories around the disease. It is one of the questions of understand them as part of social habits, incrustated of new and old words. Therefore, depression finds in words a discursive practice, forming a history of pain and/or psychic illness, through an enunciation expressed by speech.

In this exercise, said and unsaid words endanger to run the way that opens the histories, in the dynamic of events, in the movement of characters, in inquietude or illness of being<sup>[10]</sup>; over and above in what time and space delimit as truth about what deconstructs the discourse. Told histories get free from their original discursive or representative place, being contextualized<sup>[11]</sup>.

Nobody says nothing without have heard it - or being at this or that place, or being himself nothing different than himself<sup>[12]</sup>. Despite of believing in this, we would make an accretion on this exercises reconstitution, through a discursive spoken element, to comprehend the position of this discourse facing the route of truth about disease and being sick.

We believe that, by asking about said and unsaid things, depressive find the measure or interlacement between what is said, heard and read about the history. However, said things means much more than their real meaning<sup>[13]</sup>. Someway, the speech presupposes the link between the translation and the answers you search for, through nearness of words.

The words said by depressive bring with them much more meanings than they try to show. And they bring in their origins uncountable unspoken expectations, masked by discourse, at the same time it arises from the narratives translation. Disease, therefore, is based in human historicity, in human temporality, constituted by a perspective network<sup>[14]</sup>.

## Methods

We intended to understand narratives as a mechanism of social inquiry, reconstructing events

by the perspective of the informant, as much directly as possible<sup>[15]</sup>. Searching the "what" and the "who" subjects involved in the recontextualization of what provokes, when speak, an unique manner of translating the narrated situation<sup>[16]</sup>. It is fundamental, in this process, do not forget the way how subjects talk about their lives, the language used and the connections they make<sup>[17]</sup>. Approach to narratives like methods of inquiring presupposes understand them not just like an events list, but an attempt to link those events in time and sense<sup>[15]</sup>.

The surveyed population comprehended 324 people, with age starting from 10 years-old. They demanded for clinical and psychological care at two public health centers located in Paraíba, a state of northeast Brazil. The reasons of consultations were circumstances that involved pain or psychic illness. At a first moment, through medical records and case reports, a subject survey was done. Owing this information, we started to organize the sample, considering:

1. the number of visits to the healthcare unit;
2. extended pharmaceutical treatment for depression or psychopathologies;
3. history of recurrent episodes in along the same year;
4. traces of suicide ideation;
5. suicide attempts history.

Starting from this stratification, we established three criteria of inclusion in the sample, based on the tenth edition of International Classification of Diseases (ICD), from World Health Organization (WHO), according to: a) having diagnosed depression; b) having suicide ideation traces; c) having suicide attempts history.

The sample was composed by 150 individuals, including adolescents and adults of both genders, by closeness with inclusion criteria. It was a question of purposeful sampling, a selection of cases rich in information for a profound study as a standard modality<sup>[18]</sup>.

## Instruments

A narrative interview with integral recording was employed as the data collection instrument, aiming situations that encouraged and stimulated informants to narrate their history, through an im-

portant event in their lives and the social context. It is considered a unstructured, profound and specific interview<sup>[15]</sup>, contrasting different perspectives and considering the idea in which language is not neutral, but constitutes a particular cosmoview, like an exchange medium<sup>[19]</sup>.

### Data analysis

We analyzed interviews through six stages<sup>[15]</sup>:

1. particularized transcription of verbal expressions of surveyed informants;
2. text division between indexed and non-indexed material. The indexed propositions had concrete references of "who did what, when and why". The non-indexed ones considered events, values, judgments and a "life wisdom" in general ways;
3. use of indexed data for understanding correct sequence of people's events;
4. comprehension of distribution and assimilation between each one's lives;
5. comparison between individual cases, through particular context, and establishing connections.

For constructing cartographic profile of oral narratives we used the researcher triangulation strategy<sup>[18]</sup>. Three researchers read interviews, provoking the reflexivity process and posterior decrypting referential that based narratives and highlighting relevant aspects of data mapping. It is important to emphasize that all the steps regarding to ethics and bioethics in research were done.

### Results

For depressive patients, in relationship with others, the possible way to expose manifestations of disease itself is by telling and retelling their own history. The speech is interlaced with temporal events that translate the speech to the professional, who simply evaluates the symptoms according to the clinical truth that edges the patient's narrative. What is effectively said don't comes from an endless treasure of significations, but from specific conditions and possibilities<sup>[12]</sup>.

Depressive patient's discourse is necessarily composed by enunciations based on incessant search

for an answer, a truth able to explain and elucidate stereotyped questions of the world that surrounds him, in a relation of space and time. This perspective unveils the possibility to hear what is said by depressive and understand how pathology presents itself facing his personal expectations. See what a 57 year-old female patient teaches to us: "It is anguish, it is cold. I'm suffering along the year. A bad feeling kills us. Starts slowly, but gets bigger and bigger, taking your life away. It's weird and comes suddenly."

To hear what is said is much more viable, because it creates material consistence, but understand it means to outline the existence of an ordered discourse and to feel, in an axiological way, the wishes and perspectives that depression produces in its victims, the unspoken aspects of discourse.

The new is not in what is said, but in its return happening<sup>[9]</sup>. This way, the narrative, representing lived reality, highlights the habit of telling histories, outspoken, with the power patients gives them, to compose a dialogue, which outcomes depends on mutual rules of word caption.

As we can see, possibility of contemplating the unspoken words gives the comprehension that, even in normal conditions, human beings brings in its words, polished by social rules, the idea implicit on its real and subjective wishes. Depressive patient, bound to the inside and outside conflicts of disease, sends in his words the unspoken, in the most fluent and perceptive way, able to determine the most important and circumstantial points of phenomenon. If he is not heard or if he is tied in his relationship with other people, his words get masked and imprisoned in a internal storm that arises from the inside of individual. In matter-of-fact, the list of symptoms prevails; subject singularities and his life history get relegate<sup>[10]</sup>. A 38 year-old patient, user of social security system, having a history of suicide attempt, gave this confession: "Depression is like a passion fruit. Everything gets older, creating wrinkles in heart and emotion. What saves me is faith, but here comes confusion, anxiety, frustration [...] I am and old trunk with lots of memories".

In orbit of pathology, reflexivity about the narrative gives depressive patients the unique opportunity to review their concepts, share their histories and hear rational opinions by telling (once and again) episodes. For entire society, the discourse production is simultaneously controlled,

selected, organized and redistributed by some procedures that can exorcize the patients powers and dangers, block them the random happenings and mask their menacing materiality<sup>[8]</sup>.

In this direction, narratives are not mere descriptions of reality, but special producers of knowledge that, at the same time that constitutes vehicles, construct the conductors<sup>[4]</sup>. We observed that speech does not represent just the start of the speech, but the mechanism used by patients to intermeditate the sensations or the results of these sensations. A 42 year-old patient that works with steel reveals that: "Depression is like caustic soda. It corrodes everything inside. Body suffers. Everything hurts, everything pulses. And it's cold sweat." In matter-of-fact, discourse is a channel to divulcation of the wish of truth about experiences lived and shared in between pain and psychic illness.

A universal truth appears to the eyes. And is ignored, however, the need of truth, as a prodigious instrument destined to exclude all of them that, in our history, searched to outline this wish to truth and to question it against the truth<sup>[9]</sup>.

## Conclusion

The sequence of speech, in a detailed narrative review, made possible to infer that narratives can change the way people understand themselves and the others. It is a real interlace between to speak and to list thoughts, always in a dynamic that involves action, reflection and reaction.

In the same mien, it is easy and paradoxically complex to understand that the narrative comprehends a collection of meanings and interpretations of patient's psychopathology that reflexes on their clinical, social and familiar situation. Realize this fact in this narrative from a 23 year-old young woman: "Depression is like a flower that withered before become lively. It's like a dry thin branch needful of water. Silence is my greater interpreter." However, a sensible change occurs in the meaning of terms used by depressive patients. All knowledge is autobiographic<sup>[20]</sup>, because it comes from subjective perception of objective elements.

The depressive phenomenon, under the optics of narrative, determines that told and untold expressions are determinant factors to make possible the complexity of disease stabilization. Notably

when interpreter gives attention to depressive patients, trying to hear the speech and understand the meaningful silence of illness and pain. The "inter-speech" is a transition between what they say and what they need to say, so the unspoken should be considered as a basilar source on mechanisms to give cure to depressive patient.

At this moment, hearing is their escape valve, the opportunity of telling their own life history to put out their wishes and aims and give interpreter the opportunity to see different ways to stop pathology. We believe that pain needs to be changed but not forgotten. Dared, not denied<sup>[22]</sup>.

In a deeper way, narratives unveil the patients' inherent tendency to search a guideline for their discourses, to deposit the spoken and unspoken information. Fear of not being heard changes depressive into its own devil, bringing death feelings. Here, the history of life is subjugate by clinical technics.

The actions of to hear and to tell histories, is impossible to dissociate from each other to comprehend medical and popular knowledge. Evoke the speech of each patient about the disease and hear from interpreter is fundamental, in addition to hearing what, even unsaid, was interlaced in patient's words.

## References

1. Almeida Filho N, Mari JJ, Coutinho E. *Estudo Multicêntrico de morbidade psiquiátrica em áreas urbanas brasileiras (Brasília, São Paulo, Porto Alegre)*. Revista ABP-APAL 1992; 14:93-104.
2. Weissman MM, Bland RC, Canino GJ. *Cross-national epidemiology of major disorders*. 3 ed. (DSM-III). Washington DC: American Psychiatric Press; 1996.
3. Silva DGV, Mercedes T. *Narrativas como técnica de pesquisa em enfermagem*. Rev Latino-am Enfermagem, may-jun; 2002; 423-32.
4. Cunha MI. *Conta-me agora: as narrativas como alternativas pedagógicas na pesquisa e no ensino*. Rev Fac Educ jan-dec 1997;23(1-2).
5. Rabelo MC. *A construção narrativa da doença*. In: 18ª reunião da ANPOCS. Grupo de trabalho pessoa, corpo e doença. Salvador; 1994.
6. Foucault M. *L'Archéologie du savoir*. Paris: Gallimard; 1969.
7. Gancho CV. *Como analisar narrativas*. 7ª ed. São Paulo: Ática; 2003.

8. Foucault M. *L'Ordre du discours*. Paris: Gallimard; 1971.
9. Foucault M. *A ordem do discurso*. São Paulo: Loyola; 1996.
10. Peres UT. *Depressão e melancolia*. Rio de Janeiro: Jorge Zahar Editores; 2003.
11. Ricouer P. *Teoria da interpretação*. Rio de Janeiro: Edições 70; 1976.
12. Cordeiro E. *Foucault e a existência do discurso*. In: *pensamento, crítica e criação, Cadernos de Noroeste: Universidade do Minho*; 1998.
13. Foucault M. *A arqueologia do saber*. Rio de Janeiro: Forense; 1986.
14. Good BJ. *Medicine, rationality, and experience: an anthropological perspective*. Cambridge: Morgan; 1995.
15. Jovchelovitch S, Bauer MW. *Entrevista narrativa*. In: Bauer MW, Gaskell G. *Pesquisa qualitativa com texto, imagem e som: um manual prático*. Petrópolis (RJ): Vozes; 2002. p. 91.
16. Bernstein B. *The structuring of pedagogic discourse*. Londres: Routledge; 1990.
17. Spencer J. *The usefulness of qualitative methods in rehabilitation: issues of meaning of context and of change*. *Arch Phys Med Rehabil* 1993;74:119-26.
18. Nogueira-Martins MCF. *Humanização das relações assistenciais: a formação do profissional de saúde*. São Paulo: Casa do Psicólogo; 2001.
19. Farr RM. *Interviewing: the social psychology of the inter-view*. In: Fransella F, editor. *Psychology for occupational therapists*. London: Macmillan; 1982. p. 151-70.
20. Santos BS. *Um discurso sobre as ciências*. Porto: Afrontamento; 1987.
21. Solomon A. *Demônio do meio-dia: uma anatomia da depressão*. Rio de Janeiro: Objetiva; 2002.
22. Ricouer P. *Time and narrative*. Chicago: The University of Chicago Press; 1988.

*Corresponding Author*  
Luiz Carlos de Abreu  
University of São Paulo,  
Brazil,  
E-mail: luizcarlos@usp.br

# Applying statistical process control (SPC) chart techniques to examine patient-centered performance indicators and pharmacy operational indicators using sequential control chart

Tsair-Wei Chien<sup>1</sup>, Agnes LF Chan<sup>2</sup>, Henry WC Leung<sup>3</sup>, Ming-Ting Chou<sup>3</sup>

<sup>1</sup> Department of Administration, Chi Mei medical Center, Tainan, Taiwan,

<sup>2</sup> Department of Pharmacy, Chi Mei Medical Center, Tainan, Taiwan,

<sup>3</sup> Department of Cardiology, Chi Mei Medical Center, Tainan, Taiwan.

## Abstract

**Purpose:** We report the monitoring system for patient-centered performance indicators and pharmacy operational indicators that could be used locally to improve the delivery of pharmaceutical care using sequential control chart approach.

**Methods:** The patient-centered performance indicators and pharmacy operational indicators were developed and monitored routinely to ensure high quality of pharmaceutical care by using single and sequential regression analyses. The patient-centered performance indicators were developed based on medication-use indicators. A sequential control chart approach was proposed to automatically inspect the outlier at the last time point and email the respective control chart to the member for further discussion.

**Results:** A series of operational indicators and patient-centered performance indicators have been established and monitored since 1998 and adjusted each year. The results showed that patient-centered performance indicators and pharmacy operational indicators were improved each year using a sequential control chart approach.

**Conclusions:** The use of this methodology facilitated operation of pharmacy structured service appraisal system and prevented the near-missed medication errors. The program plots and mail the outlier control chart to the member focusing on a small number of key areas to be easily, quickly and clearly compared.

**Key words:** patient-centered performance indicators, pharmacy operational indicators, chart technique

## Introduction

As health care costs are consecutively increasing worldwide, health care providers (e.g., insurance companies) are being pressured to cut down costs while maintaining and improving the quality of care. Healthcare reform is also frequently a major political problem in many countries. President Obama of American United States recently achieved a 'victory' of healthcare reform in America after a prolonged and tortuous debate [1-3]. The quality of care is another important issue which has been discussing and concerning in the past decade. Health care payers, especially for a single payer nationwide healthcare system, are concerned about how the providers measure and monitor for their quality of care and clinical outcomes.

Quality improvement must be based on evidence-based research and informed through ongoing assessments of data and information [4, 5]. The use of information technology in health care is essential in substantial improvement in patient safety [6]. To attain a continuous monitor of individual performance is of importance in hospital settings implementing periodically evaluation [7].

### 1. One threshold insufficiently monitoring quality of care

In traditional, one threshold is a common way to monitor outcome of health care. As we did with profound experience in past years, the one-threshold approach is insufficiently implemented in clinical practice. It is easily and sensitively displaying either false alarm (Type I error) or false negative (Type II error) as a result of consuming cost and time when we conduct periodical evaluation of indicator management.



## 2. Control charts inefficiently evaluating quality of care

Control charts using c-chart, p-chart or np-chart to select outliers of cases beyond control limits across all time points are most common in healthcare [8-10]. However, there are so many drawbacks applying control charts in monitoring quality of care in clinical settings, such as case-by-case evaluation alike aforementioned one-threshold approach consuming cost and time to monitor, especially a bulk of count (or frequency) and ratio indicators is often combined together in a data set to require examining outlier cases. It would be tedious and cost so much time in detection using any kinds of available control charts.

## 3. Pharmaceutical care demanding an efficient and sufficient way to evaluation

Pharmaceutical care has been defined as the responsible provision of drug therapy for the purpose to achieve definite outcomes that improve a patient's quality of life. [11] The purpose of pharmaceutical care practice was to ensure that all the patients' drug therapy was indicated, effective, safe and convenient. [12] In order to achieve these outcomes, performance indicators relating to structure, process and quality of pharmaceutical care were developed. Additionally, it may provide an effective feedback on a job well done by improving their productivity and efficiency.

### *Purpose*

The study aims to illustrate an example in a pharmacy department of hospital to periodically monitor quality indicators and effectively compare quality improvement using sequential control chart. A friendly and cost-effective Excel interface to evaluate quality of care over past time points was designed and programmed.

## **Methods**

### ***Development of the PPAS and indicator management***

The PPAS, along with CQI indicators and an ongoing monitoring system, was developed in 1998. Implemented in 1999, the PPAS was linked to pharmacists' performance, and the linked sys-

tem was termed with 'CQI-PPAS'. Developing the CQI-PPAS performance appraisal system consisted of two approaches [13]: First, CQI committee was established including the pharmacy director, the indicator coordinator, and the pharmacy supervisors. CQI committee members developed the draft of departmental PPAS criteria, selected a set of CQI indicators, designed and collected the appraisal data on these indicators periodically, and then the CQI-PPAS was proposed and launched.

The draft was presented monthly at the CQI committee for review and discussion. The final draft was submitted to the vice president and president of the hospital for approval.

The selected indicators were ranked by the pharmacist supervisor according to the department's primary objectives of improving patient care and reducing costs, and the list of indicators was approved by the CQI committee of the study hospital(see Figure 1).

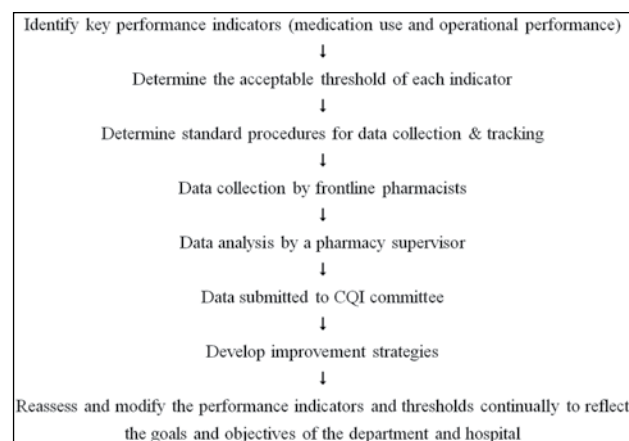


Figure 1. Procedures involved in developing a CQI indicators evaluation system

### ***To implement CQI-OPAS***

The pharmacy director met with the director of administration to stipulate the OPAS criteria and to determine the 3-step CQI-PPAS appraisal on the basis of individual pharmacist performance evaluations to achieve their CQI indicator goals.

The implement strategy of the CQI-PPAS were designed and appraised each year by a so-called sequential control chart approach to monitor performance in quality of care and to facilitate the performance of individual subsections in charge of the specific indicator.

### ***Process of CQI Indicator monitoring***

The data of all CQI indicators were collected and recorded by the frontline pharmacists. The pharmacist supervisors of five divisions of pharmacy department, (outpatient dispensing, inpatient dispensing, clinical pharmaceutical services, special compounding group (including total parenteral nutrition, chemotherapeutic compounding, and drug inventory) analyzed the data and filled it in the CQI reporting sheet. By using the traffic light appraisal, the number of each indicator was measured and compared with the number of same indicator measured in previous year. If the number of each indicator was higher than the threshold, the improvement strategies were required to propose. The CQI reporting sheet was reported to the CQI committee of pharmacy department for review and assessment each month. Since 2004, the final CQI report has been presented at the hospital's annual CQI meeting.

The pharmacist performance appraisal chart (PPAC) was used to record the CQI indicator values provided by the individual pharmacists as well as the productivity scores of individual pharmacists as reviewed by each pharmacist supervisor. Figure 1 outlines the development of CQI-PPAS process.

### ***Selecting indicators***

From 1998 to 2000, we selected a total of 18 indicators which included 13 indicators of operational process and 5 indicators of medication use. From 2001 to 2006, we continued to revise indicators of the operational process and medication use. From 2006 on, we used a total of 43 indicators, including 6 indicators for measuring the quality of drug inventory and operational processes and 37 indicators for monitoring medication use.

### ***Operational indicators***

To provide high quality patient-centered pharmaceutical care, pharmacy departments need a solid operational system. Indicators in monitoring the quality of operational activities has been listed and approved by the CQI committee of pharmacy department (Table 1). The evaluation process can be illustrated by looking at a single example, the "accuracy of dispensing of chemotherapy." The objective of using this indicator was to prevent an incorrect chemotherapeutic drugs or its dose

from being dispensed in the inpatient and outpatient pharmacy. Any errors were reported by the pharmacist who was responsible for final check on the accuracy of the prescription before distribution to patients. The pharmacist supervisor will review the report and analyze the roots and effects of the errors monthly. The CQI report sheet of dispensing errors was then entered into a CQI database and linked to the PPAS. The report was then generated monthly and discussed in the meeting of the CQI committee.

### ***Medication use indicators***

An innovative automatic monitoring system (IAMS) on medication use was implemented in the physician order entrance system (POES) in our hospital since 1998. In order to ensure patient's drug safety and reflect pharmacist's intervention effectiveness in the management of drug-related problems, we established a list of medication use indicators (Table 2) which were monitored and recorded all suspected problems on the CQI report sheet each day by clinical pharmacists and the report sheet were reviewed by the pharmacist supervision and linked to the PPAS. For example, the indicator of "Patients received warfarin without international ratio (INR) data over three months or  $INR \geq 3.0$ ." The IAMS system automatically generated an alarm/alert signal when physicians ordered warfarin for that patient. Pharmacist would follow the patients on next day of prescribing warfarin. If the physicians did not prescribe an order to check patient's INR or adjusted dosage, the clinical pharmacist would reminded them with a consultation sheet and reported on the CQI report sheet for analyses..

### ***Analysis of CQI-PPAS using sequential control chart approach***

#### ***Supplemental to one-threshold and traditional control chart approaches***

According to history information of each indicator, using control chart to detect the recent (i.e., the last time point) result in comparison with previous information is required. There are two types of data property (i.e., count and ratio) for indicators used in our periodical evaluation, whereas different variations are designed to set the control lim-

its. We programmed a routine using Excel VBA (visual basic for application) to automatically (1) detect data property; (2) compare criterion previously set using one-threshold approach; (3) yield scores of threshold classification according deviation (i.e., beyond +3 standard deviation to -3 and coded from 8 to 0, 4 as equivalence to expected value ) using control chart; (4) plot control chart and mail it to the person who is in charge of the indicator for further inspection, through which a summary report will be monthly made to examine the count distribution between operational process and medication-used indicator whether it is equal using Chi-square test with Yale adjustment for expected count less than 5.

#### *Assessing the performance through the plot of an appraisal chart*

In traditional quality control approach, a one-threshold criterion was used as a minimum acceptable performance standard or maximum allowable limit, which is an objective management irrelevant to the control limits that are yielded according to their history information across all the time points. A summary report to compare count distribution of two types of indicators equivalent or different is required. Besides, using sequential control chart to mail a plot with abnormality at the last time point will be also demonstrated helping us focusing on a small number of key areas to be easily, quickly and clearly compared.

For the control limits set by the studied pharmacy department, we determined the outlier beyond 1 standard deviation (*SD*) being emailed for further inspection and discussion. The criteria for *SDs* in c-chart (count event) and np-chart (ratio to samples, say, 100) are different, squaring averaged count is for c-chart and squaring sample size  $\times$  ratio  $\times$  (1-ratio) for np-chart.

## Results

#### *A summary report*

A summary report monthly made for investigation shown in Table 3, it is evident that there is no any difference ( $\chi^2=1.98$ ;  $p = .58$ ) in count distribution of two types of indicators at the last time point from Table 1 and 2. The only one potential outlier approaching to 95% interval confidence (CI) was

found and attributed to indicator 22 in Table 2 (i.e., anesthetic sedative induced phlebitis, cases/month).

From Table 3, it can be seen that most of indicators (95.83%) are in a range of  $\pm 1$  *SD*. Three indicators ( #8 in Table 1, #15 and #23 in Table 2) congruent to their respective expectation are identical across all the time points, indicating no variance existed.

#### *The plot of an appraisal chart*

Based on Figure 2 (c-chart), the outlier (indicator 22) beyond the criterion of 1 *SD* was plotted and automatically emailed to the person who should pay attention to the specific indicator for further inspection. With the aforementioned summary report, the superintendent will focus on the outlier and make a follow-up for a reason submission.

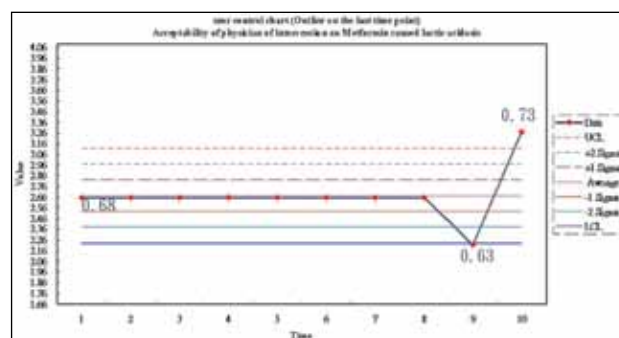


Figure 2. Outlier out of control plotted with a control chart

## Discussion

### Findings

#### *(1) Key findings*

The sequential control chart system was developed with an Excel-VBA routine which can help us alarming the indicator to be early concerned with the traditional one-threshold criterion and the supplemental sequential control chart approach.

#### *(2) What this study contributes to current knowledge*

Both summarized report and emailed outlier control chart can be integrated to quality of care in clinical settings, especially using a graphical representation with time points given us a context for understanding data. The present can only be understood and the future can only be predicted on light of the past.

Table 1. Outcomes of operational process

A: Operational process										
year	1	2	3	4	5	6	7	8	9	10
	Frequency of discrepancy between actual inventory and inventory record	frequency of discrepancy between actual use of Narcotics & record	frequency of Narcotics broken in wards	frequency of misshipments	frequency of expired drugs	No. of patients abnormal use of Narcotic drugs	(+)culture results of laminar flow area	accuracy of Dispensing of chemotherapy	frequency of missing drugs in wards	repeated dispense discontinued drugs
1998	0	0%			0	0	0	100%	0.08%	0.01%
1999	4	0.30%			0	0	0	100%	0.05%	0.01%
2000	0	0.33%	0.01%		0	0	0	100%	0.07%	0.00%
2001	1	0.36%	0.01%		0	0	3	100%	0.05%	0.00%
2002	1	0.32%	0.02%	0.00%	0	2	0	100%	0.02%	0.00%
2003	3	0.33%	0.02%	0.01%	0.12%	2	0	100%	0.02%	0.00%
2004	1	0.25%	0.02%	0.01%	0.12%	1	0	100%	0.03%	0.00%
2005	0	0.33%	0.01%	0.04%	0.12%	1	0	100%	0.03%	0.00%
2006	0	0.48%	0.03%	0.02%	0.04%	1	0	100%	0.03%	0
2007	0	0.01%	0%	0.01%	0%	1	0	100%	0.02%	0
Threshold	0	0.03%	0.03%	0.20%	0%	0%	0	100%	0.03%	0.00%
Min	<b>0</b>	<b>0.00%</b>	<b>0.00%</b>	<b>0.00%</b>	<b>0.00%</b>	<b>0.00%</b>	<b>0.00%</b>	<b>100.00%</b>	<b>0.02%</b>	<b>0.00%</b>
Mode	<b>0</b>	<b>0.33%</b>	<b>0.01%</b>	<b>0.01%</b>	<b>0.00%</b>	<b>0.00%</b>	<b>0.00%</b>	<b>100.00%</b>	<b>0.02%</b>	<b>0.01%</b>
Max	<b>4</b>	<b>0.48%</b>	<b>0.03%</b>	<b>0.04%</b>	<b>0.12%</b>	<b>200.00%</b>	<b>300.00%</b>	<b>100.00%</b>	<b>0.08%</b>	<b>0.01%</b>

Note. 1. Three parameters used by triangular distribution are Min., Mode and Max.  
 2. The three attributes of Min., Mode and Max. are used onto multidimensional scaling

Table 2. Outcome of Medication-use indicators

B: Medication-use indicators														
Years	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	Delayed patient treatment secondary to shortage of drugs	Duplicated use of drugs, %	Inappropriate indication, %	Frequency of phlebotomy timed inappropriately vs time of drug administration	Wrong dosage form, %	Vancomycin infusion rate < 15gm/min caused red neck syndrome, %	Patients receiving $\geq$ two types of oral NSAID simultaneously	Incidence of hyperglycemia TPN patients	Patients receiving Coumadin INR >3.5 after clinical pharmacist intervention	Nephrotoxicity induced by antibiotics	Inappropriate drug doses, %	Anesthetic sedative induced phlebitis, cases/month	Metformin induced lactic acidosis	Acceptability of physician intervention on Metformin caused lactic acidosis
1998		Not selected		4.70%		6.56%	0%	not selected	0	not selected	not selected			
1999		Not selected		3.95%		3.86%	0%	not selected	0	not selected	not selected			
2000		Not selected		7%		2.12%	0%	not selected	0	not selected	not selected			
2001		Not selected		2.23%		1.24%	0.01%	not selected	0	not selected	not selected			
2002	0.01%	0.00%	0.01%	2.46%	0.00%	1.12%	0.01%	35.80%	1	2.20%	0.01%	0	0	65.15%
2003	0.01%	0.00%	0.01%	2.40%	0.00%	0.21%	0.01%	32.50%	2	0.58%	0.01%	0	0	66.55%
2004	0.01%	0.00%	0.01%	2.20%	0.00%	1.02%	0%	32.40%	3	0.11%	0.00%	1	0	67.15%
2005	0.00%	0.00%	0.01%	1.82%	0.00%	0.78%	0%	30.20%	3	0%	0.00%	0	0	69.25%
2006	0.04%	0.00%	0.00%	0.78%	0.00%	0.95%	0.01%	28.00%	0	0.02%	0.01%	0	0	70.45%
2007	0.06%	0.00%	0.00%	0.68%	0.00%	2.19%	0%	30.70%	0	0%	0.00%	1	0	73.48%
Threshold	0.10%	0.01%	0.00%	$\leq$ 10%	0.00%	6%	<1%	$\leq$ 32%	<1 case/month	0.05%	0.00%	<2	0	>80%
Min	0.00%	0.00%	0.00%	0.68%	0.00%	0.21%	0.00%	28.00%	0.00%	0.00%	0.00%	0.00%	0.00%	65.15%
Mode	0.01%	0.00%	0.01%	2.00%	0.00%	1.00%	0.00%	32.00%	0.00%	0.00%	0.00%	0.00%	0.00%	60.00%
Max	0.06%	0.00%	0.01%	7.00%	0.00%	6.56%	0.01%	35.80%	300.00%	2.20%	0.01%	100.00%	0.00%	73.48%

Note. 1. Three parameters used by triangular distribution are Min., Mode and Max.

2. The three attributes of Min., Mode and Max. are used onto multidimensional scaling

Table 3. A summary report used for testing distribution of counts between two types of indicators using sequential control chart

Types of indicator	Threshold							Chi-square	prob.
	>-1 SD	Expected	<+1 SD	<+2 SD	<+3 SD	>=+3 SD	Total		
Scoring judgment:									
Operational process	7	1	2	0	0	0	10	3.15	0.68
%	70.00	10.00	20.00	0.00	0.00	0.00	100.00		
Expected	6.25	1.25	1.25	0.42	0.42	0.42	10.00		
Medication-used indicator	8	2	1	1	1	1	14		
%	57.14	14.29	7.14	7.14	7.14	7.14	100.00		
Expected	8.75	1.75	1.75	0.58	0.58	0.58	14.00		
Total	15	3	3	1	1	1	24		
%	62.50	12.50	12.50	4.17	4.17	4.17	100.00		

Note. The outlier beyond 1 SD is outlined for further inspection in the report

The control limits are set between +/- 1 SD

### (3) Implications of the results and suggested actions

We applied an Excel-VBA module to help organizations accomplish large improvements by focusing on a relatively small number of key areas to be easily, quickly and clearly compared with a graphical representation.

#### Strength of this study

The CQI-PPAS is the first system for evaluating pharmacy department performance in Taiwan. The combination of CQI indicators and pharmacist performance indicators allow managers to measure pharmacists' contribution in reduction of the risk-to-benefit ratio and the pharmacists' cognitive professional contributions [14]. In addition, PPAS enables the pharmacy department to track trends and identify strengths and weaknesses with the goal of defining and quantifying performance of key departmental functions. The CQI performance indicators integrate the clinical and technical operational activity and provide qualitative information about the range of pharmacy activities including medicine supply and pharmaceutical care contributed to individual patient care. A thoughtful performance appraisal can make employees more aware of what they need to do to receive a good performance review; it can also motivate them to achieve organizational goals [15].

The CQI-PPAS is outcome-oriented, so the evaluation system designed with an objective measurement. Pharmacists in different groups have their own CQI goals and performance expectations that differ substantially. This fosters phar-

maciest interdependence, teamwork, and cooperation. Ultimately, CQI-PPAS inspires pharmacists to be self-motivated in order to reap their self-achievement of excellent performance.

Our CQI indicator data showed continuous improvement, and pharmacists now treat patients more equitably and in a friendly manner. These results are in line with the suggestion of Bowen et al. that pharmacists with an equitable performance appraisal and feedback system treat customers more fairly [16]. The technique of statistical process control (SPC) chart can be applied to the routine utilization evaluation for a specific drug, such as Piperacillin/Tazobactam, in a hospital [17].

#### Further studies and suggestions

An integral part of the CQI concept is to have monthly reviews of the indicator values in combination with annual reviews and revisions. Monthly CQI indicator data are posted on the pharmacy's information board and website for personnel to review. For example, the "frequency of phlebotomy timed inappropriately vs. time of drug administration" was not always within the desired limit; we developed a strategy to improve the outcome rather than changing the target value for the next year. The pharmacist responsible for improvement received a positive credit performance appraisal.

The advantage of establishing a continuous quality improvement process is to minimize both medication errors [18,19] (e.g. dispensing errors, medication errors due to health care delivery system) and adverse drug events (e.g. an inappropriate vancomycin infusion). A report suggested that

between 2% to 3% of all hospital admissions in Australia may be medication related. The cost of preventable medication errors were \$350 million and \$ 17 to \$ 29 billion in Australia and the USA per year respectively[20]. Severe adverse drug event ( ADE) may also increase direct medical cost of hospital to treat ADE injured patients. By reducing such errors, the costs associated with these types of errors will also decrease [21,22]. Thus, the continuous monitoring quality improvement indicators (Table 1 &2) will indirectly reduce costs in the health care system.

### **Limitations of the study**

In establishing the performance appraisal system, we may encounter problems previously faced by other researchers. These issues include initial selection of indicators, setting acceptable performance standards, and designating an appropriate person within the department to be responsible for tracking, reporting, and improving the data [12]. Because the CQI-PPAS performance appraisal system is complex and dynamic, it requires a significant resource commitment from management and all employees within the department [23]. We therefore established our system from the top down ( i.e. from the hospital management down to the pharmacists in the pharmacy department). We selected appropriate CQI indicators according to evidence-based criteria [24, 25] and established performance appraisal criteria based on historical performance data in our pharmacy and on the group consensus for desired future performance. Maintaining the complex performance tracking system, including entering data into each tracking database and transferring it into an easy-to-read cumulative report (e.g. Table 3), did not pose any major problems.

The pharmacy director and pharmacy supervisors in the different pharmacy groups were primarily responsible for making this process more efficient and manageable. The CQI-PPAS development process was quite similar to that reported by Robert et al who proposed to define, quantify and track trends in performance levels and identified the strong and weak areas of the key function of department [12]. Furthermore, using CQI indicators that measured the standard of clinical care provided to the public was in line with hospital accreditation criteria in Taiwan [26].

There is limited data for pharmacy performance evaluation systems, and no data that is suitable for comparison with CQI-PPAS. Managing a clinical pharmacy practice and ensuring satisfactory patient care is inherently difficult: the cognitive processes and actions involved are not always easy to measure or quantify.

### **Conclusions**

This report documents our attempt to develop performance appraisal criteria linked to CQI indicators in order to monitor the performance of a clinical pharmacy as a whole and to establish an integrated system that inspires self-motivation within a pharmacy department and graphically inspects a control chart with alarm at the last one (or the last two for detecting the direction of a trend) time point. Future research is recommended to adopt the CQI-PPAS appraisal with objective and statistical theory based algorithm and technique such as single and sequential regression used in this study at pharmacy department to enhance the quality service and cost containment for health-care providers.

### **References**

1. *Brown ER. Health USA. A national health program for the United States. JAMA. 1992; 267(4):552-8.*
2. *Woolhandler S, Himmelstein DU, Angell M, Young QD; Proposal of the physicians' working group for single-payer national health insurance. JAMA. 2003; 290(6):798-805.*
3. *Manchikanti L, Hirsch JA. Obama health care for all Americans: practical implications. Pain Physician. 2009;12(2):289-304.*
4. *Moreland J, Richardson J, Chan DH, O'Neill J, Bellissimo A, Grum RM, Shanks L: Evidence-based guidelines for the secondary prevention of falls in older adults. Gerontology 2003, 49(2):93-116.*
5. *Hughes RG, Clancy CM: Nurses' role in patient safety. Journal of Nursing Care Quality 2009; 24(1), 1-4.*
6. *Bates DW, Cohen M, Leape LL, Overhage JM, Shabot MM, Sheridan T: Reducing the frequency of errors in medicine using information technology. J Am Med Assoc 2001;8(4):299-308.*

7. Chien TW, Wang WC, Lin SB, Lin CY, Guo HR, Su SB: KIDMAP, a web based system for gathering patients' feedback on their doctors. *BMC Med Res Methodol.* 2009;9:38.
8. Simpson DS, Roberts T, Walker C, Cooper KD, O'Brien F: Using statistical process control (SPC) chart techniques to support data quality and information proficiency: the underpinning structure of high-quality health care. *Quality in Primary Care* 2005; 13: 37-43.
9. VanderVeen LM: Statistical process control: a practical application for hospitals. *Journal of Healthcare Quality* 1992; 14: 20-29.
10. Chiam P, Feyi-Waboso A: The use of control charts in monitoring postcataract surgery endophthalmitis. *Eye* 2009; 23: 1028-1031.
11. Cheng T: Taiwan's new National Health Insurance program: genesis and experience so far. *Health Affairs* 2003; 22: 61-76.
12. Roberts MB, Keith MR: Implementing a performance evaluation system in a correctional managed care pharmacy. *Am J Health Syst Pharm.* 2002; 59(11):1097-104
13. Moss GL: Improving staff performance using the appraisal process. *Optometry* 2001, 72(2):126-7.
14. Angaran DM: Quality assurance to quality improvement: measuring and monitoring pharmaceutical care. *Am J Hospital Pharmacy* 1991 ; 48(9):1901-7
15. Desselle SP, Zgarrick DP: Pharmacy management, Medical / Pharmacy. *Pharmacy Management: Essentials for All Practice Settings - Published by McGraw-Hill Professional, 2004.*
16. Bowen DE, Gilliland SW, Folger R: HRM and service fairness: how being fair with employees spills over to customers. *Organizational Dynamics* 1999; 27:7-2
17. Ismail M, Iqbal Z, Hammad M, Ahsan S, Sheikh AL, Asim SM, Khan TM: Drug Utilization Evaluation of Piperacillin/Tazobactam in a Tertiary. *HealthMED* 2010, 4(4-S1):1044-1055.
18. Castle L, Franzblau-Isaac E, Paulsen J: Using Six Sigma to reduce medication errors in a home-delivery pharmacy service. *Jt Comm J Qual Patient Saf.* 2005; 31(6): 319-324
19. Chan AL: Use of Six Sigma to improve pharmacist dispensing errors at an outpatient clinic. *Am J Med Quality* 2004; 19(3):128-31.
20. Joanna Briggs Institute: Strategies to reduce medication errors with reference to older adults. *Best Practice* 2005; 9(4); 1-6.
21. US department of health and human service. Reducing and Preventing Adverse Drug Events To Decrease Hospital Costs. <http://www.ahrq.gov/qual/aderia/aderia.htm>
22. Chan AL, Lee HY, Ho CH, Cham TM, Lin SJ. (2008) Cost Evaluation of Adverse Drug Reactions in Hospitalized patients in Taiwan: A Prospective, Descriptive, Observational Study. *Curr Ther Res Clin Exp;* 69(2): 118-129.
23. Segal R. (1992). A framework for evaluating the work of pharmacists. *Top Hosp Pharm Manage.* 12(1):9-19
24. Allen SJ, Angaran DM, Balmer CM, et al.: Preliminary report of the ASHP Quality Assurance Indicators Development Group. *Am J Hosp Pharm.* 1991; 48(9):1941-7
25. Nadzam DM: Development of medication-use indicators by the Joint Commission on Accreditation of Healthcare Organizations. *Am J Hosp Pharm.,* 1991; 48(9):1925-30.
26. Taiwan Joint Commission on Hospital Accreditation. <http://www.tjcha.org.tw/index.asp>. Accessed 8 October 2008.

Corresponding author  
Ming-Ting Chou,  
Department of Cardiology,  
Chi Mei Medical Center,  
Tainan,  
Taiwan  
E-mail: [healthup@healthup.org.tw](mailto:healthup@healthup.org.tw)



# Contents of antioxidant A, E, C vitamins, Malondialdehyde (MDA), and Aminotransferases (ALT, AST) in serum professional football managers during derby matches

*Sebahattin Devecioğlu*

Firat University, Department of Physical Education and Sports School, Elazig, Turkey

## Abstract

**Aim:** Mental situations are known to induce oxidative stress in individuals subjected to intense psychological conditions. We investigated the serum Antioxidant Vitamins, Retinol (vitamin A),  $\alpha$ -tocopherol (vitamin E) and ascorbic acid (vitamin C), Malondialdehyde (MDA), alanine transaminase (ALT) and aspartate transaminase (AST) levels of Professional Football Managers during Derby Matches in the 2009-2010 season of the 2nd division of the Turkish professional soccer league in the two neighboring provinces matches (Elazığ Football Club-Malatya Football Club), which is described as a derby match.

**Method:** The serum samples of twenty club managers of Elazığ Football Club were evaluated for study. Changes in biochemical indices of oxidative damage and enzyme markers of stress were examined during a competitive football season. The main findings of the present study were that the serum Malondialdehyde and blood ALT and AST levels of this group of managers displayed differences at home and displacement.

**Results:** The participants in the two matches went through a period of heavy mental stress. In mean average values and statistical results, they showed changes in their serum MDA, ALT and AST concentrations.

**Conclusion:** In conclusion, the excessive excitement and stress can be effective on professional football manager during derby matches. The results of this study indicated that match stress affects the managers physiologically.

**Key words:** Football Manager, Vitamin, Malondialdehyde, Aminotransferase, Oxidative Stress, Psychological stress

## Introduction

In today's sports world, soccer has become a market and a huge industry with the development of science and technology. Therefore, a developing an effective management strategy is very crucial in football. In this era, administrators may not be able to meet the requirements of modern sports. Sports managers, who carry the objectives of their organizations, should be able to display effective and efficient functioning of experience, knowledge and leadership qualities to benefit their teams [1]

Certain situations trigger psychological, physiological or cognitive behavioral reactions in people. These are known as symptoms of stress [2]

While stress can motivate people to aim for the perfect, it can also cause serious illnesses or affect the performance level [3,4]

Stress is an adaptive response that prepares an organism for a threatening situation. It induces strain upon both emotional and physical endurance, and has been considered a basic factor in the aetiology of a number of diseases [5,6,7]

Stress as a concept describes the effects of psychosocial, occupational work and environmental factors on physical or mental well-being [8]

Sports clubs managers and all employees can be affected by these factors. In fact, stress and the overall quality of life and work are closely related to environmental factors [9] While occupational psychology has penetrated the world of business and sports psychologists are widely used by professional sports people, the impact of psychology based performance coaching on football management appears to remain unappreciated and undervalued [10]

There is no need to explain the stress involved in football management on the manager anymore than there is to explain the pressures in senior ma-

agement roles at board level. This includes the stress during the game as well as when working with players, staff and the board.

There is good evidence to demonstrate that coaching can be an effective intervention to help managers develop coping strategies for dealing with stress [11]

Sport management involves a variety of business related tasks in a sport context that involves interacting with others towards a goal, and the psychology of human behavior provides additional insight on these interactions [12]

Society attaches importance to the successes and failures of major sports teams. The supporters of a soccer team feel proud and happy when their team wins and they feel depressed and unhappy when their team loses. Thus, any investment decisions a fan makes may be affected by on the performance of his or her team. It has been reported that a good result in soccer affects moods or psychological well-being [13,14].

For instance, in football games tension and anxiety of an individual is at high levels. So the detection scheme features social environment and behavior from the plane of anxiety, stress, cultural diversity and socio-cultural values as effective [15]. Especially, managers live under the most stressful situations because they have to overcome various difficulties [16].

In addition, voltage, pressure, anxiety, strain and excessive stress can be defined as trouble falling all over the organism's physiological and pathological elements, which can also be defined as rough and tough action. Potential threats of the environment bring about physical and emotional response on the basis of lack of harmony among individuals. Individuals under stress suffer from excitement, constant fatigue, and high blood pressure [17]. This situation points to a serious imbalance between free radical oxidative formation and antioxidant defense mechanism, which as a result causes tissue damage and leads to formation of reduced antioxidant capacity in an individual [18,19].

The balance between formation and destruction of biological systems, oxidants' protection of cells and tissue are important in maintaining biological integrity [20].

Reactive oxygen species (ROS) are formed and degraded by all aerobic organisms, leading to either

physiological concentrations required for normal cell function or excessive quantities, the state called oxidative stress [21]. ROS-mediated oxidation of membrane lipids results in the formation of lipid peroxidation products such as malondialdehyde (MDA) [22] and isoprostanes [23]. The cellular antioxidant systems can be divided into two major groups, namely enzymatic and nonenzymatic [21]. Some nonenzymatic low molecular weight antioxidant compounds such as ascorbic acid (vitamin C),  $\alpha$ -tocopherol (vitamin E) and carotenoids are consumed and may fall below normal ranges. The determinations of enzymatic and/or nonenzymatic antioxidant levels and MDA in the samples are important for the evaluation of oxidative stress in biological systems.

Transaminases (AST and ALT) enzymes are a common mean of detecting liver damage [24,25]. Transaminases (ALT, AST), a rise in blood transaminase activities is a sensitive indicator of damage to cytoplasmic and/or mitochondrial membranes. Plasma enzyme activities rise when the membranes of only very few cells are damaged [26,27].

This study was designed to demonstrate how the oxidative stress in professional football managers are influenced during a home and opponent field derby matches.

## Materials and Methods

### *Experimental Design*

This study was conducted in the 2009-2010 season of the second division of the Turkish professional football league in the two neighboring provinces' matches (Elazığ FC-Malatya FC), which is described as a derby match. 20 professional football managers of Elazığ Football Club (FC) following the match participated in this study. Their blood samples were taken and collected in tubes without any anticoagulant before the matches at home and displacement and were centrifuged at 4500 rpm for 10 minutes and store at -85 °C until the analysis.

### *Chemicals*

The reagent 1,1,3,3-tetraethoxypropane (MDA standard) and all trans-retinol (vitamin A) were purchased from Sigma (St. Louis, MO, USA). Ascorbic acid,  $\alpha$ -tocopherol, methanol,  $\text{KH}_2\text{PO}_4$ ,  $\text{H}_3\text{PO}_4$  and  $\text{HClO}_4$  were obtained from Merck (Darmstadt, Germany).

### ***Instrumentation***

Liquid chromatographic system (Shimadzu, Kyoto, Japan) consisted of two LC-20AT pumps, a CTO-10AS VP column oven, a SPD-M20A DAD system and a RF-10AXL FLD system. The two detectors were connected in series. These apparatus were connected via a communication module (Model CBM-20A), and controlled by a Shimadzu LC Solution workstation. A Shimadzu Shim-pack vp-ODS column (150L×4.6) was used.

### **Sample Preparation and Biochemical Assays**

#### ***Determination of serum Vitamin A and E levels***

0,3 ml serum samples were transferred into polyethylene tubes and 0,3 ml ethanol was added to the tubes. After 0,3 ml n-hexane was filled into tubes for vitamins extractions, they were centrifuged. This step was repeated two times. n-hexane into tubes was evaporated under the nitrogen. Then the residues were solved in mobile phase (methanol: acetonitrile: chloroform; 47: 42: 11, v/v). Chromatograms were monitored at 326 and 296 nm (vitamin A and E respectively) and injection volume was set 50 µL. Techsphere ODS-2 packed column (5 mm particle, 250×4.6 ID) was used and flow rate was 1.0 ml min<sup>-1</sup> [28].

#### ***Determination of serum Vitamin C and MDA levels***

0,5 ml of HClO<sub>4</sub> (0,5 M) and 0,5 ml distilled water were added to an aliquot portion of serum samples [29]. Then, the samples were centrifuged at 4500 rpm for 5 minutes and supernatants were injected into HPLC system. Addition of acid was necessary to precipitate proteins and release the MDA bound to the amino groups of proteins and other amino compounds. Acid addition was also needed to maintain the stability of vitamin C.

The mobile phase was 30 mM KH<sub>2</sub>PO<sub>4</sub> -Methanol (82,5+17,5, v/v %, pH 3,6) and the flow rate was 1,2 mL min<sup>-1</sup>. Chromatograms were monitored at 250 nm and injection volume was 20 µL. A Wakosil II 5C18 RS 5µm (150×4.6 mm SS, SGE, AUS) column was used at room temperature [30].

#### ***Laboratory analysis in plasma/serum***

Serum ALT and AST activities were determined with enzymatic methods using a Roche auto

analyzer (Cobas Integra 800, Roche Diagnostics, Mannheim, Germany)

### **Statistical analysis**

Statistical analysis was performed with SPSS 15.0 for Windows software (SPSS Inc., Chicago, IL, USA). The limit of statistical significance was set at P<0.05. Results are expressed as means ±S.E.M Comparison between mean values were made by Paired Samples T test.

### **Results**

Selected components of this defense system have been reported to decrease in body fluid at stress. The values of blood are given belong to professional football managers at home and away in the tables (1, 2). The mean average values and statistical results are given in the table 3. as shown below, blood parameters are affected and changed during derby matches.

### **Discussion**

The present study demonstrated that intense psychological conditions elicit a significant response of oxidative stress biomarkers and antioxidant status indices in club managers.

Psychological stress is the consequence of the failure of an organism, human or animal, to respond appropriately to emotional or physical threats, whether actual or imagined [31]. This stress acts either positively (eustress) or negatively (distress) on the body. Previous studies have shown that psychological stress is capable of leading to dysfunctions in many organs, including the brain, gastrointestinal tract, urinary bladder and so on [32,33,34]. The performance of skeletal muscle is also affected by stress, which causes increases in muscle contraction [35].

Stress has been associated with several pathological conditions. In particular, human and animal studies have provided findings on mechanisms by which stress interferes with immune [36] Neuroendocrine [37,38] and metabolic changes [39,40]. That may increase cardiovascular risk [41,42] and psychiatric illness [43].

Oxidative stress reflects an imbalance between the production of reactive oxygen species (ROS)

Table 1. The Individual Results of Serum Parameters of Managers in Internal Field

Position	Home					
	A vitamins (µg/ml)	E vitamins (µg/ml)	C vitamins (µg/ml)	MDA (µg/ml)	AST (U/L)	ALT (U/L)
H1 Chairman	0,164	12.976	29.292	0,672	67	71
H2 Co- Chairman	0,137	9.604	26.793	0,542	25	31
H3 General Manager	0,267	15.781	30.555	0,645	37	50
H4 General Secretary and Official of Law	0,342	10.570	25.560	0,598	19	17
H5 Official of Financial	0,134	10.970	27.180	0,658	14	8
H6 Co- Chairman and Official of Financial	0,23	10.752	27.831	0,614	18	17
H7 Co- Chairman and Official of Football T.	0,191	10.388	27.354	0,658	26	35
H8 Official of Football Team Substructure	0,246	7.521	27.780	0,596	18	23
H9 Official of Media	0,321	14.254	26.412	0,654	32	48
H10 Official of Administrative and Ar-Ge	0,317	8.199	26.250	0,602	22	31
H11 Member of Board of Directors	0,443	12.900	28.533	0,611	23	19
H 12 Co- Member of Board of Directors	0,28	10.922	26.430	0,596	20	26
H13 Official of Stadium and Spectator	0,105	9.632	27.225	0,568	31	35
H14 Official of Sports Area	0,327	11.853	26.565	0,663	25	21
H15 Co-Official of Sports Area	0,179	8.786	26.946	0,548	40	28
H16 Official of Advertisement and Org.	0,268	14.310	26.307	0,656	13	44
H 17 Co-Official of Advertisement and Org.	0,322	12.303	26.187	0,602	19	22
H18 Official of Administrative	0,291	16.466	26.361	0,657	35	43
H19 Official of Administrative	0,208	9.595	26.073	0,615	18	12
H20 Official of Administrative	0,047	2.670	26.241	0,553	18	11

Table 2. The Individual Results of Serum Parameters of Managers in External Field

Position	Displacement					
	A vitamins (µg/ml)	E vitamins (µg/ml)	C vitamins (µg/ml)	MDA (µg/ml)	AST (U/L)	ALT (U/L)
D1 Chairman	0,104	11.125	27.747	0,895	57	69
D2 Co- Chairman	0,205	12.361	27.966	0,905	32	48
D3 General Manager	0,347	17.706	27.927	0,954	43	72
D4 General Secretary and Official of Law	0,172	12.050	26.289	0,856	20	19
D5 Official of Financial	0,227	12.687	26.673	0,896	18	15
D6 Co- Chairman and Official of Financial	0,123	8.349	27.705	0,856	31	29
D7 Co- Chairman and Official of Football Team	0,195	10.925	28.725	0,901	40	45
D8 Official of Football Team Substructure	0,133	6.118	28,725	0,861	33	24
D9 Official of Media	0,068	6.332	25.779	0,905	39	41
D10 Official of Administrative and Ar-Ge	0,232	6.110	26.172	0,885	25	39
D11 Member of Board of Directors	0,13	5.541	25.899	0,945	23	18
D12 Co-Member of Board of Directors	0,148	10.957	28.143	0,902	32	34
D13 Official of Stadium and Spectator	0,354	9.652	26.226	0,896	30	36
D14 Official of Sports Area	0,082	8.626	25.680	0,886	37	56
D15 Co- Official of Sports Area	0,22	12.545	33.138	0,884	20	14
D16 Official of Advertisement and Organization	0,302	13.122	28.461	0,956	53	45
D17 Co-Official of Advertisement and Organization	0,114	8.228	27.138	0,945	53	96
D18 Official of Administrative	0,314	15.611	28.326	0,868	37	39
D19 Official of Administrative	0,267	8.547	26.394	0,885	32	24
D20 Official of Administrative	0,214	8.837	27.696	0,855	33	25

Table 3. Changes in the levels of antioxidant vitamins A, E, C and lipid peroxidation product MDA and AST and ALT activities in the serum samples

N=20	A vitamins (µg/ml)	E vitamins (µg/ml)	C vitamins (µg/ml)	MDA (µg/ml)	AST (U/L)	ALT (U/L)
Home	0,241±0,02	11,023±0,70	27,094±0,27	0,615±0,13	26,000±2.75	29,600±3.50
Displacement	0,198±0.02	10,271±0.73	27,478±0.39	<b>0.897±0.13*</b>	<b>34,400±2.46*</b>	<b>39,400±4.73*</b>

Values are expressed as means ± SE; n = 20 for each match \*P < 0.05

and the system's ability to readily detoxify the reactive intermediates and/or repair the resulting damage. It plays an important role in the development of psychological stress-induced dysfunctions in many tissues; under psychological stress, the balance between oxidant and antioxidant defense systems are disturbed, which leads to oxidative damage and influences tissue function [44,45].

Researchers have demonstrated that emotional stress increases skeletal muscle performance in the presence of oxygen deficiency that results from metabolic changes caused by the sympathetic nervous system [46]. In conclusion, the present study found that psychological stress results in oxidative damage providing evidence for the possible involvement of oxidative stress.

Formation of ROS that exceed the body's antioxidant capacity has been termed oxidative stress. ROS are produced in the body as the result of normal cellular metabolism as well as through exposure to a variety of environmental (e.g., smoking, ozone, certain nutrients) and physiological (e.g., physical and mental stress) challenges [47].

Oxidative stress is known to result in several acute and chronic disorders [48,49] but the factors that induce and promote this condition are variable.

The identification of the demands endured by performers is crucial in the understanding of competition stress, as it provides insight into the factors that instigate cognitive, emotional, and behavioral responses, which, consequently, influence performance [50].

It is therefore important for researchers to consider how individuals respond in relation to the stressors experienced prior to competition. Specifically, this can be achieved by acknowledging the transactional perspective advocated by Lazarus [51,52] and the notion of emotional orientation [53,54] where the conjoining of both environmental demands and personal characteristics to generate cognitive-evaluative reactions and ascribe meaning to an encounter and subsequent emotions are considered [55].

Various researchers set different causes of stress in business life. In this context, the types of stress for McGrath [56] are as follows: organizational stress, work related stress (ray difficulty, ambiguity, and excessive workload), the role stress (conflict, ambiguity, density), behavior in stress caused by environment (the effect of a crowd and so on), stress caused by the physical environment (excessive cold or hot working environment, noise, etc.), stress arising in the social environment (conflict between individuals, private life and the stress, isolation and loneliness), an individual's self-stress (the individual's anxiety level, the detection scheme) and so on. [46]. The causes of organizational stress is classified in four groups: [57] organizational policies, an organization's structural characteristics, physical conditions and organizational processes. Ivancevich and Matteson [58]. Cartwright and others [59] have discussed the sources of stress within the scope of job characteristics and physical environmental conditions, excessive or insufficient workload, shift in working system, automation. Also, Bumin and Şengul [60] have discussed the role of the sources of stress on the behavior within an organization [61]. Allen et al. provide several important results concerning the relationship between managerial succession and organizational performance [62].

However, the link between psychological stress and oxidative stress in the football managers has not been identified in previous studies.

A study related to how managers are affected by oxidative stress during the football matches is rarely documented in the literature. This work was carried out in order to verify the investigation of the stress experienced by football administrators and to clarify the contribution of reactive oxygen species (ROS).

When we look at it in terms of physical activity, exercise is characterized by an increase in oxygen consumption in the whole body. This leads to a decrease in antioxidant levels that could promote both

an increase in the markers of lipoprotein peroxidation and damage to the erythrocyte membrane with consequent modification of membrane fluidity. For example, professional soccer players can have significantly higher values in different markers of oxidative stress because undergoing a regular and adequate training show improved antioxidant status [63].

Most studies on oxidative stress and antioxidant status following exercise have used endurance exercise protocols [64,65,66]. Because the physiological load of intermittent exercise, such as soccer, differs from continuous steady-state exercise, an extrapolation of data from continuous steady-state exercise to intermittent exercise should be made with caution [67]. Information on oxidative stress and antioxidants in soccer is, however, limited. [68].

Thus, the hypothesis of this paper is that psychological stress could induce oxidative damage in the football managers. This hypothesis was tested by examining the activities of ALT and AST, as well as the content of lipid peroxidation (malondialdehyde, MDA level) and antioxidant vitamins A and E, in the serum samples in the volunteers that under the psychological stress.

This result may be a consequence of a compensatory response of the serum samples at the psychological stress. However, we found that an increased level of oxidative stress was induced in managers subjected to psychological stress along the weeks, which was evidenced by significantly increased activities of ALT and AST.

Lipid peroxidation has been considered to be the most common consequence of oxidative stress. MDA, which constitutes the most abundant toxic aldehyde formed from the peroxidation of polyunsaturated fatty acids, can be used as general biomarker for biological oxidative stress [69,70].

We found that the level of MDA in the serum samples (Tables 1,2,3 ) strongly increased in the managers which were psychologically stressed for weeks after psychological stress for this period which considering the hypothesis that increase in a derby. These findings suggest that the managers are likely susceptible to free radical attack under sustained psychological stress. Moreover, our results would further support the 'free radical hypothesis' that the parafunction in the managers exposed to psychological stress may be associated with increased susceptibility to oxidative injury.

For serum ALT, serum AST and MDA there were very clear findings. It could be argued that serum lipids and enzymes are influenced by psychosocial stress. A tentative conclusion could accordingly be that league and derby stress of psychological adverse conditions may explain the findings. There is substantial evidence in the literature for the notion that psychological stress does influence serum lipids [26].

The findings of the study illustrate that the importance of psychological factors in the work situation. In the present study, it is interesting that psychological stress induced oxidative stress in the football managers.

In conclusion, due to the excessive excitement and stress, professional football managers can also be affected during derby matches. This study indicated that stress affects not only the football players but also managers. It is the most important that football manager need to understand individuals and adjust their behavior to suit the individual's personality as well as their emotional state.

## References

1. Bucher, C.A., *Management of Physical Education and Athletic Programs*, St.Louis, Toronto, Santa Clana: Times Mirror Mosby College Publishing. 1978; pp24
2. Tosi, H. L.; John R. Rizzo; Stephen J. Carroll, *Managing Organizational Behavior*. Cambridge: 4.th Edition, Blackwell Publishers Ltd. 1996; pp214
3. Warrick, D.D., *Managing the Stress of Organization Development*. *Training and Development Journal*, 1981, April; 37-41.
4. Hindle, T., 1998. *Reducing Stress*. London: Dorling Kindersley, pp:61
5. Jezova D, Kristova V, Slamova J, Mlynarik M, Pirnik Z, Kiss A, Kriska M., *Stress-Induced Rise Endothelalemia, Von Willebrand Factor and Hypothalamic-Pituitary-Adrenocorticalaxis Activation is Reduced by Pre-treatment With Pentoxifylline*. *J Physiol Pharmacol* 2003; 54(3):329-338
6. Holmes A, Heilig M, Rupniak NM, Steckler T, Griebel G., *Neuropeptide Systems As Novel Therapeutic Targets For Depression And Anxiety Disorders*. *Trends Pharmacol Sci*, 2003; 24(11):580-588
7. Black P.H., *The Inflammatory Response is An Integral Part of The Stress Response: Implications for Atherosclerosis, Insulin Resistance, Type II Diabetes and Metabolic Syndrome X*. *Brain Behav Immun*, 2003; 17(5):350-364

8. Ángela C., Alberto C & M. Encarnación L.F., Rocío R., Concha G. A., Federico N., *Relationship Between Oxidative And Occupational Stress and Aging In Nurses Of An Intensive Care Unit*, 2008; AGE 30:229–236 DOI 10.1007/s11357-008-9052-5
9. Bingöl, D., *National Congress of Management and Organization*, Published No:10, Istanbul University Faculty of Business, Istanbul; 2001. 24-26 May (in Turkish)
10. Jonathan P., *What could an Executive Coach do for an Association Football Manager? Annual Review of High Performance Coaching & Consulting*, 2010; pp 61-64
11. Gyllensyen, K., Palmer, S., *The Relationship Between Coaching and Workplace Stress*, *International Journal of Health Promotion and Education*, 2005;43(3), 97-103.
12. Lisa M. M., *Qualitative Investigation Of Intercollegiate Coaches' Perceptions Of Altruistic Leadership*, Dissertation, The Ohio State University, 2003; pp.44
13. Ashton, J.K., Gerrard, B., & Hudson, R., *Economic Impact of National Sporting Success: Evidence from the London Stock Exchange*. *Applied Economic Letters*, 2003;10, 783–785.
14. Boyle, G., Walter, B., *Reflected Glory And Failure: International Sporting Success And The Stock Market*. *Applied Financial Economics*, 2003; 13, 225–235.
15. Luthans, F. *Organizational Behavior*, Sixth Edition, McGraw Hill Inc., New York; 1992.
16. Barbara J. Braham *Stress Management*. (Translate: Vedat G. Diker, Hayat Publishing, Bag Books Series:4, İstanbul;1994, pp.28 (in Turkish)
17. Şimşek M. Şerif *Management and Organization 7. Edition*, Günay Offset, Konya; 2002 (in Turkish)
18. Çavdar C, Sifil A, Çamsar T. *Particles of Reactive Oxygen and Antioxidant Defense*. *Turkish Nephrology, Dialysis and Transplantation Journal*, 1997; Volume 3-4: 96-101.
19. Burçak G, Andican G. 2004. *Oxidative DNA Damage and Aging*. *Cerrahpaşa J Med* 2004; 35: 159-169.
20. Diplock AT. *Antioxidant Nutrients And Disease Prevention: An Overview*. *Am J Clin Nutr.*; 1991;53(1 Suppl):189.-193.
21. Nordberg J and Arnere .S.J., *Reactive Oxygen Species, Antioxidants, and the Mammalian Thiredoxin System*, *Free Radical Biology and Medicine*,2001; 31: 1287- 1312.
22. Maccarrone M, Catani MV, Iraci S, Melino G, Agro AF. *A Survey of Reactive Oxygen Species and their Role of Dermatology*. *J. Eu. Acad. Derm. Venereol*,1997; 8: 185- 202.
23. Morrow JD., *The Isoprostanes: Their Quantification as an Index of Oxidant Stress Status in vivo*. *Drug Metab. Rev.* 2000; 32:377-85
24. Qujeq, D., Laghaie, B., Gholipour, A., Solimani, N., Hassenzadeh, S., *Effects of sodium fluoride on total serum protein levels and transaminase activity in rats*. *Biomed. Pharmacol.*2002; 56: 169–172.
25. Shanthakumari, D., Srinivasalu, S., Subramanian, S., *Effect of Fluoride Intoxication on Lipidperoxidation And Antioxidant Status In Experimental Rats*. *Toxicology*, 2004; 204: 214–228.
26. Akila, G., Rajakrishnan, V., Viswanathan, P., Rajashekar, K.N., Menon, V.P., *Effects Of Curcumin On Lipid Profile And Lipid Peroxidation Status In Experimental Hepatic Fibrosis*. *Hepatol. Res.* 1998; 11:147–157.
27. Hassoun, E.A., Stohs, S.J., *Comparative Studies on Oxidative Stress As A Mechanism For The Fetotoxic of TCDD, Endrin And Lindane In C57BL/6J And DBA/ 2J Mice*. *Teratology* 1995; 51:186–192.
28. Miller, K.W., Lorr, N.A., Yang, C.S., *Simultaneous Determination Of Plasma Retinol A-Tocopherol, Lycopene, B-Carotene, And B-Carotene By High Performance Liquid Chromatography*. *Analytical Biochemistry*. 1984; 138: 340-345.
29. Cerhata, D., Bauerova, A., Ginter, E., *Determination Of Ascorbic Acid In Blood Serum Using High Performance Liquid Chromatography And Its Correlation With Spectrofotometric (Colorometric) Determination*, *Caska-Slov-Farm*. 1994; 43:166-168.
30. Karatepe, M., *Simultaneous Determination Of Ascorbic Acid And Free Malondialdehyde In Human Serum by HPLC/UV*. *LC-GC North America*. 2004; 22(4); 362-5.
31. Hans S., *The Stress of Life*. New York; 1956, McGraw-Hill
32. Wang L, Wang W, Zhao M, Ma L, Li M., *Psychological Stress Induces Dysregulation Of Iron Metabolism In Rat Brain*. *Neuroscience*, 2008; 155(1):24–30.
33. Van Oudenhove L, Aziz Q., *Recent Insights On Central Processing And Psychological Processes In Functional Gastrointestinal Disorders*. *Dig Liver Dis*, 2009; 41(11): 781–87
34. Robbins MT, DeBerry J, Ness TJ, *Chronic Psychological Stress Enhances Nociceptive Processing In The Urinary Bladder In High-Anxiety Rats*. *Physiol Behav*,2007: 91(5): 544–50.
35. Berdina NA, Kolenko OL, Kotz IM, Kuznetsov AP, Rodionov IM, Savtchenko AP, et al., *Increase in skeletal muscle performance during emotional stress in man*. *Circ Res*,1972;30(6):642–50.

36. Yudkin JS, Kumari M, Humphries SE, Mohamed-Ali V. Inflammation, Obesity, Stress And Coronary Heart Disease: Is Interleukin-6 The Link?, *Atherosclerosis*, 2000;148:209-14.
37. Muller JR, Le KM, Haines WR, Gan Q, Knuepfer MM. Hemodynamic Response Pattern Predicts Susceptibility To Stress-Induced Elevation In Arterial Pressure In The Rat, *Am J Physiol*, 2001; 281:R31-7.
38. Black PH, Garbutt LD, Stress, Inflammation And Cardiovascular Disease. *J Psychosom Med* 2002;52: 1-23
39. Oliveira AC, Suchecki D, Cohen S, D'Almeida V., Acute Stressor-Selective Effect On Total Plasma Homocysteine Concentration In Rats, *Pharmacol Biochem Behav*, 2004; 77:269-73.
40. Setnik B, Souza FG, D'Almeida V, Nobrega JN., Increased Homocysteine Levels Associated With Gender And Stress In The Learned Helplessness Model Of Depression. *Pharmacol Biochem Behav*, 2004; 77:155-61.
41. Blumenthal JA, Jiang W, Waugh RA, Frid DJ, Morris JJ, Coleman RE, et al. Mental Stress-Induced Ischemia In The Laboratory And Ambulatory Ischemia During Daily Life. Association And Hemodynamic Features. *Circulation*, 1995; 92:2102-8
42. Manuck SB, Marsland AL, Kaplan JR, Williams JK., The Pathogenicity Of Behavior And Its Neuroendocrine Mediation: An Example From Coronary Artery Disease. *Psychosom Med*, 1995.;57:275-83
43. Agid O, Kohn Y, Lerer B., Environmental Stress And Psychiatric Illness. *Biomed Pharmacother*, 2000; 54:135-41.
44. Møller P, Wallin H, Knudsen LE. Oxidative Stress Associated With Exercise, Psychological Stress And Life-Style Factors., *Chem Biol Interact*, 1996;102(1):17-36
45. Lucca G, Comim CM, Valvassori SS, Reus GZ, Vuolo F, Petronilho F, et al. Effects Of Chronic Mild Stress On The Oxidative Parameters In The Rat Brain. *Neurochem Int*, 2009; 54:358-62.
46. Berdina NA, Kolenko OL, Kotz IM, Kuznetsov AP, Rodionov IM, Savtchenko AP, et al. Increase in skeletal muscle performance during emotional stress in man. *Circ Res* 1972;30(6):642-50.
47. Finaud J, Lac G, Filaire E. Oxidative Stress: Relationship With Exercise And Training. *Sports Medicine*, 2006;36:327-358.
48. Gutteridge J.M.C. Lipid Proxidation And Antioxidants As Biomarkers Of Tissue Damage, *Clinchem*, 1995; 41(12):1819-1828
49. Markesbery W.R. Oxidative Alterations in Alzheimer's Disease. *Brain Pathol*, 1999; 9: 133-146,
50. Hanton, S., Neil, R., & Mellalieu, S. D., *Recent Developments in Competitive Anxiety Direction and Competition Stress Research. International Review of Sport and Exercise Psychology*, 2008; 1:45-57.
51. Lazarus, R. S., *Emotion and Adaptation*. Oxford University Press. New York; 1991.
52. Lazarus, R. S., & Folkman, S. *Stress, Appraisal, and Coping*. Springer. New York; 1984.
53. Fletcher, D. and Fletcher, J. A., *Meta-Model Of Stress, Emotions And Performance: Conceptual Foundations, Theoretical Framework, And Research Directions. Journal of Sports Sciences* 2005; 23:157-158.
54. Fletcher, D., Hanton, S. and Mellalieu, S. D. Hanton, S. and Mellalieu, S. D. (ed.) *An Organizational Stress Review: Conceptual and Theoretical Issues In Competitive Sport. Literature Reviews In Sport Psychology*. Nova Science, Hauppauge, NY; 2006: 321-373.
55. Stephen D., Neil, Richard, Hanton, Sheldon and Fletcher, David *Competition Stress In Sport Performers: Stressors Experienced In The Competition Environment', Journal of Sports Sciences*, 2009; 27, (7): 729-744.
56. McGrath, J. E. *Stress and behavior in organizations*. Chap. 31 in Dunnette, M. (Ed.), *Handbook of Industrial Organizational Psychology*. Chicago: Rand McNally Co., Inc. 1976; pp.1351-1395
57. Cam, E. *Stress At Work And Female Employees In Public Sector. International Journal of Human Sciences*. 2004; Volume 1 ; 1
58. Ivancevich, J. M., Matteson, M. T., *Organizational behavior and management*, 4th edition, Chicago, Irwin; 1996,
59. Cooper, C. L., Cartwright, S., *Healthy Mind, Healthy Organization: A Proactive Approach to Stress Management*, *Human Relations*, 1994;47(4): 455-71
60. Bumin, B. Şengül, A., *Worthiness and Human Resources A Study on the Role Based Sources of Stress in Organizations*, 8.National Congress of Management and Organization Erciyes University, Nevşehir, 2000; pp. 571-579.
61. Camkurt, M. Z, *Operating System and Impact on Work Accidents of Physical Factors in the Workplace*, *Journal of Business Law and Economics*, 2007; 20,21:6-1: 80-106.
62. Allen, M.P., Panian, S.K. and Lotz, R.E. *Managerial Succession and Organizational Performance: A Recalcitrant Problem Revisited*, *Administrative Science Quarterly*, 1979; 24: 167-180.
63. Cazzola R, Russo-Volpe S, Cervato G, Cestaro B.. *Biochemical Assessments Of Oxidative Stress, Erythrocyte Membrane Fluidity And Antioxidant Status In Professional Soccer Players And Sedentary Controls. Eur J Clin Invest. Oct; 2003; 33(10):924-30*



64. Aguiló A, Tauler P, Fuentespina E, Tur J, Córdoba A, Pons., *Antioxidant Response To Oxidative Stress Induced By Exhaustive Exercise. Physiol Behav.*2005;84: 1–7
65. Cases, A. Sureda, I. Maestre, P. Tauler, A. Aguiló, A. Córdoba, E. Roche, J.A. Tur and A. Pons, *Response Of Antioxidant Defenses To Oxidative Stress Induced By Prolonged Exercise: Antioxidant Enzyme Gene Expression In Lymphocytes. Eur. J. Appl. Physiol.* 2006;**98**:263–269.
66. Tauler P, Aguiló A, Guix P, Jiménez F, Villa G, Tur JA, Córdoba A, Pons., *Pre-Exercise Antioxidant Enzyme Activities Determine The Antioxidant Enzyme Erythrocyte Response To Exercise. J Sports Sci:* 2005; 23: 5–13.
67. Nieman, D., Bishop, N., *Nutritional Strategies To Counter Stress To The Immune System In Athletes, With Special Reference To Football. J Sports Sci.* 2006; 24, 763-772
68. Andersson, H. M. *The physiological impact of soccer on elite female players and the effects of active recovery training Örebro Studies in Sport Sciences, ISSN 1654-7535; 8, Örebro universitet, Hälsoakademin; 201* Draper HH, Hadley M., *Malondialdehyde Determination As Index Of Lipid Peroxidation. Methods Enzymol,*1990; 186:421–31.
69. Kadiiska MB, Gladen BC, Baird DD, Germolec D, Graham LB, Parker CE, et al. *Biomarkers Of Oxidative Stress Study II: Are Oxidation Products Of Lipids, Proteins, And DNA Markers Of Ccl4 Poisoning? Free Radic Biol Med.,*2005;38(6):698–710.

*Corresponding Author*  
*Sebahattin Devecioğlu,*  
*Firat University,*  
*Department of Physical Education and Sports*  
*School,*  
*Elazig,*  
*Turkey,*  
*E-mail: sdevecioglu@firat.edu.tr*

# Effect of Core Stability Training on patients with chronic low back pain

Wang Xueqiang<sup>1,2</sup>, Zheng Jiejiao<sup>2</sup>, Bi Xia<sup>3</sup>, Liu Jing<sup>1</sup>

<sup>1</sup> Department of sport rehabilitation, Shanghai University of Sport, Shanghai, China

<sup>2</sup> Department of rehabilitation medicine, Huadong Hospital affiliated to Fudan University, Shanghai, China

<sup>3</sup> Department of Rehabilitation Medicine, Shanghai Gongli Hospital, Shanghai, China

## Abstract

**Objective:** The aim of this study was to demonstrate that core stability training could produce more beneficial effects than conventional exercise in patients with chronic low back pain.

**Methods:** Sixty patients with low back pain were randomly allocated into core stability training group and control group. Control group received conventional exercise, training group received core stability training. Subjects were asked to exercise 3 times a week (40min/time) for 12 weeks. In the pre- and post-training sessions, all participants performed tests of pain scale, Oswestry Low Back Pain Disability Questionnaire and trunk muscle endurance test.

**Results:** Five of the 60 participants (training group, n=29; control group, n=26) completed the 12 weeks program. Pain index, Oswestry Low Back Pain Disability Questionnaire and trunk muscle endurance in the training group were significantly better than those in the control group after 8 weeks ( $P < 0.05$ ).

**Conclusions:** Our results demonstrate that core stability exercise using unstable, can be more effective decreasing pain, improving trunk muscle endurance and reducing the disability of daily life dysfunction.

**Key words:** Rehabilitation; Core stability; Low back pain; Pain; Exercise therapy

## 1. Introduction

Low back pain (LBP) is a common musculoskeletal disorder affecting 80% of people at some point in their lives<sup>[1,2]</sup>. Although most patients self-treat back pain and only 25 to 30 percent seek medical care, chronic low back pain is one of the most common reasons for visits to family physi-

cians<sup>[3,4,5]</sup>. In the United States, statistics show that total direct and indirect costs for the treatment of LBP are estimated to be greater than \$100 billion annually, with two-thirds of that due to decreased wages and productivity<sup>[6,7]</sup>.

Many research projects<sup>[8,9]</sup> show exercise is commonly used in the management of chronic low back pain. The focus of exercise is varied and may include parameters ranging from strength and endurance training, to specific training of muscle coordination and control. Core stability is the ability to control the position and movement of the central portion of the body. In other words, better core stability can serve to effectively recruit the trunk musculature and then learn to control the position of the lumbar spine during dynamic and static movements<sup>[10]</sup>.

Core stability training has become increasingly popular for treating people with chronic LBP. The primary reason is that it has the ability to enhance performance and reduce pain and disability. Reviews point to beneficial effects of specific training of muscle coordination and control in people with chronic LBP<sup>[11,12]</sup>, but there are a few clear evidences that any specific type of exercise is better than other forms of exercise<sup>[13,14]</sup>. Hence we designed the present study to examine the effects of a 12-week core stability training program versus conventional exercise on pain, low back disability and core muscle strength in subjects with chronic LBP.

It was hypothesized that a conventional exercise program combined with specific trunk muscle stabilization exercise techniques would be more effective than a general exercise program in reducing patient self-reported pain, disability and improving core muscle strength. We hope to find a more effective exercise for reducing patient self-reported pain and improving core muscle strength in patients with chronic LBP.

## 2. Materials and methods

### 2.1. Subjects

Subjects with chronic LBP (n=60) were recruited from an outpatient PT department at Shanghai City of China. Outpatients were recruited from the Department of Rehabilitation Medicine of Shanghai Huadong Hospital, China. All subjects were randomly assigned by using a computer-generated random number sequence to either core stability training (CST) group or control group. The CST group and the control group were both performed three times a week (45 min/session) for 12 weeks. Assessment and exercise in all patients with CLBP were performed at the Physical Therapy Room, Department of Sport Rehabilitation, Shanghai University of Sport, China from March 2010 to March 2011.

Eligible subjects included individuals 18 to 60 years of age who had a primary complaint of non-specific LBP of at least 3 months duration with or without radiating pain to the lower extremity. Non-specific LBP was defined as pain that had no specific identifiable etiology but that could be reproduced by back movements or provocation tests.

Exclusion criteria were: subjects who had had continuous pain with a score above 8 on the Visual Analogue Scale (VAS), those who had already attended the core stability training program, subjects who had undergone previous surgery, who had progressive neurological deficits, structural anomalies, acute infections, ongoing treatment for back pain by other health care providers, severe instabilities, severe osteoporosis, severe cardiovascular or metabolic diseases. The project was approved by the ethics committee of the Shanghai University of Sport, and written informed consent was obtained from all subjects before the study.

### 2.2. Procedure

All participants are first accepted the questionnaire, content for its basic information, past and present job status, medical history, Oswestry Disability Index, and exercise habits (frequency and time/session). This study was a 2-armed randomized, controlled trial with blinding of patients and assessors with respect to the nature of therapy. With the use of opaque closed envelopes and stratified by center, included patients were randomi-

zed to CST group or control group by an independent collaborator within 2 days after admission. At baseline and after the 12-week intervention, all patients characteristics and outcome measures were assessed.

All assessments were done by 3 independent, experienced physical therapists, who were not working in the participating rehabilitation centers, who were blind with regard to treatment allocations and who had no contact with any of the patients during the study. Patients were instructed not to discuss their treatment with these assessors. Each assessor received the same practical instructions. All assessments took place in one rehabilitation center.

### 2.3. Training Program

All patients were treated with either core stability exercise or conventional exercise during 12 weeks of their admission in the rehabilitation center. Both exercise programs were led by registered physical therapists for 40 minutes.

**The conventional exercise intervention:** The exercise protocol emphasized muscle strength exercises, including abdominal muscles and trunk extensor muscles. Each lesson incorporated a similar general plan: (1) 5 minutes warm-up, (2) 15 minutes abdominal muscles strength exercise, such as sit-up performed with foot fixation, the single straight leg raise, and bilateral straight legs raise, (3) 15 minutes trunk extensor muscles strength exercises, such as prone trunk extension, and (4) 5 minutes of cool-down. Exercises gradually increased in difficulty and training load during the 12 weeks. The conventional exercise intervention is shown in Figure 1.

**The core stability training:** The training program was based on coordination and control of the trunk muscles, and strength and endurance of the trunk muscles. Each lesson incorporated a similar general plan: (1) 5 minutes warm-up, (2) neutral alignment and posture exercise, such as sitting alignment, finding neutral—prone (3) core stability exercise, such as bridge with leg lifts, bridge and double knee flex, reverse bridge, and (4) 5 minutes of cool-down. The subject was challenged with increasingly difficult tasks. The core stability training intervention is shown in Figure 2.

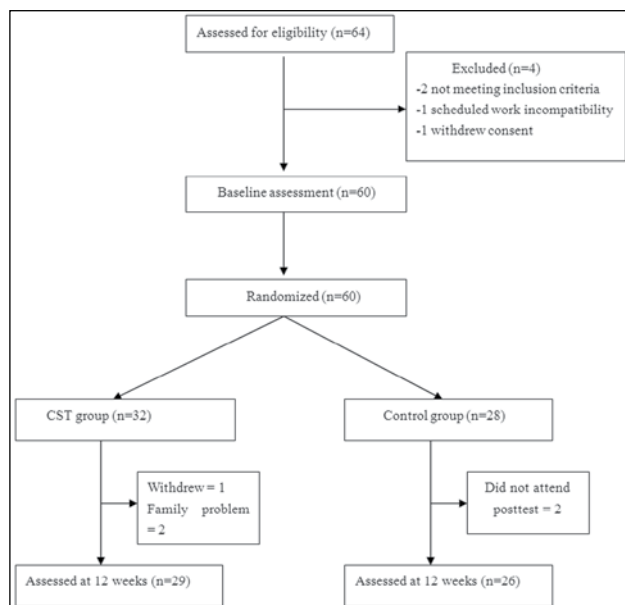


Figure 1. Flow chart of the participants

#### 2.4. Outcome Measures

All outcome measures were applied at baseline and after the intervention period. (1) Average pain intensity over the last week was measured on a visual analogue scale, where 0 represented no pain and 10 represented the worst pain possible<sup>[15]</sup>. (2) Disability was measured using the Oswestry Disability Index which consists of 10 sections related to activities of daily living commonly affected by low back pain<sup>[16]</sup>. Each section scored from 0 to 5 with higher values indicating more severe impact. Participants were asked to check the statements that represented their status on that day. (3) static and dynamic muscle endurance: static muscle endurance of trunk flexors and extensors was assessed using established methods<sup>[17,18]</sup>. The length of time the patient was able to maintain an unsupported upper body in the prone and supine position was recorded in seconds. A method of performing dynamic muscle endurance of trunk flexors and extensors test is to record the maximum number of sit-up and prone trunk extension in a minute<sup>[19]</sup>.

#### 2.5. Statistical Analyses

Statistical analyses were performed with the SPSS 17.0 and Microsoft Excel 2003 software. Data are expressed as mean±SD. Changes in variables between pre-training and post-training and between groups were analyzed.

The independent samples t test and Chi-square test were used to compare both groups at baseline. A 2-way analysis of variance (group×time) was used to assess the effects of treatment depending on group allocation. We performed an intention-to-treat analysis by carrying the last value forward in the case of missing values at the second assessment. Statistical significance was assumed at P less than 0.05.

### 3. Results

The study design is outlined in figure 1. Sixty of the 64 individuals initially recruited, 2 subjects did not meet the inclusion criteria, 1 subject scheduled work incompatibility and 1 subject withdrew consent. After 12-week program, there were 55 subjects. Three participants from CST group, 2 participants from control group were lost to follow-up. Reasons for dropout included withdrew and serious family problems. Additionally, 2 patients did not attend the final evaluation session. Hence, follow-up data were available for 29 of 32 subjects in the CST group, 26 of 28 subjects in the control group. Table 1 lists baseline characteristics of the 2 groups. The groups were well matched at the baseline assessment, with no differences in key outcome variables apparent.

Table 2 shows the values of all outcome measures with their standard deviations. The results showed a significant difference in pain severity score and ODI in the CST group as compared with the control group ( $P = 0.036$ ;  $P = 0.027$ ). And static endurance and dynamic endurance of trunk extensors of subjects in the CST group were significantly better than those in the control group after 12 weeks ( $P = 0.034$ ;  $P = 0.039$ ). There were significant differences in the dynamic endurance of trunk flexors between the 2 groups ( $P = 0.041$ ).

### Discussion

The specific aim of this randomized controlled study was to demonstrate that core stability training could produce more beneficial effects on patients with chronic LBP than conventional exercise. Our results showed that a 12-week exercise program improved trunk muscle endurance, decreased pain and reduced the disability of daily life dysfunction.

Table 1. Baseline Values for the 2 Groups

Variable	CST group (n=32)	Control group (n=28)	P
Men/Femen	17/15	18/14	0.802*
Age (years)	39.03 ± 4.74	38.07 ± 4.11	0.463 <sup>#</sup>
Height (cm)	170.78 ± 6.88	167.18 ± 6.34	0.473 <sup>#</sup>
Body weight (kg)	63.45 ± 6.77	60.18 ± 5.62	0.475 <sup>#</sup>
BMI (kg/m <sup>2</sup> )	21.65 ± 2.16	21.59 ± 2.31	0.297 <sup>#</sup>
Duration of back pain (months)	7.66 ± 2.57	8.14 ± 3.55	0.300 <sup>#</sup>
Pain severity score (0=no pain, 10=worst pain )	5.52 ± 3.46	5.11 ± 2.78	0.485 <sup>#</sup>
ODI (0 ~ 100)	33.11 ± 5.73	30.42 ± 7.44	0.186 <sup>#</sup>
Back performance			
Static endurance (s)			
Flexion	45.04 ± 21.22	48.72 ± 19.53	0.639 <sup>#</sup>
Extension	54.78 ± 16.40	57.18 ± 15.21	0.385 <sup>#</sup>
Dynamic endurance (maximum repetitions)			
Flexion	37.32 ± 14.13	35.71 ± 13.24	0.528 <sup>#</sup>
Extension	18.69 ± 8.84	17.37 ± 7.35	0.367 <sup>#</sup>

NOTE. Data reported as mean ± SD. BMI: Body Mass Index;

ODI: Oswestry Disability Index. \* Chi-square test; <sup>#</sup> independent samples t test.

Table 2. Pain, ODI and back performances after 12 weeks of intervention

Variable	CST group (n = 29)	Control group (n = 26)	P*
Pain severity score (0 = no pain, 10 = worst pain )	2.15 ± 1.58	2.92 ± 2.13	0.036
ODI (0 ~ 100)	15.34 ± 7.65	19.18 ± 10.21	0.027
Back performance			
Static endurance (s)			
Flexion	75.34±31.24	67.25±28.70	0.118
Extension	87.24±32.57	75.31±28.23	0.034
Dynamic endurance (maximum repetitions)			
Flexion	58.56 ± 20.52	51.77 ± 15.03	0.041
Extension	29.85 ± 11.40	20.11 ± 8.57	0.039

NOTE. Data reported as mean ± SD. ODI: Oswestry Disability Index; \*: a 2-way analysis of variance.

In addition, as anticipated, the results supported our hypothesis that core stability exercise using unstable, can be more effective decreasing pain, improving trunk muscle endurance and reducing the disability of daily life dysfunction.

Core stability training protocol used in this study aimed at providing the coactivation of global and local muscles of the core. The CST and control groups showed a significant difference in pain score, trunk muscle endurance and ODI after 12 weeks practice. The results showed a significant difference in pain severity score and ODI in the CST group as compared with the control group (P = 0.036; P = 0.027). And static endurance and dynamic endurance of trunk extensors of subjects in the CST group were

significantly better than those in the control group after 12 weeks (P = 0.034; P = 0.039). There were significant differences in the dynamic endurance of trunk flexors between the 2 groups (P = 0.041). Our results were consistent to previous study<sup>[18]</sup>, which showed core strengthening program was superior to simple strengthening exercises for chronic low back pain. However, some papers<sup>[14,20-23]</sup> indicate that, compared with conventional physiotherapy exercises, core stability exercises do not appear to provide additional benefit to patients with chronic LBP in terms of reducing pain and disability.

There can be several reasons for this result. First, conventional exercise used in this study mainly improves global dynamic muscles strength,

such as erector spinae, rectus abdominus, internal oblique, external oblique. But core stability training protocol needs to strengthen global dynamic and local postural muscles<sup>[24]</sup>. It is essential to be able to properly activate the deep core muscles, such as multifidus, transverses abdominus, diaphragm, pelvic Floor. And core stability training appears a coordinated contraction of all global and local core muscles.

Second, as is known to all, stability of the spine is not only dependent on muscular strength, but also proper sensory input that alerts the central nervous system about interaction between the body and the environment, providing constant feedback and allowing refinement of movement<sup>[11]</sup>. The stabilizing system of the spine consists of passive and active stabilization structures as well as a third, often disregarded subsystem, called the neuromotor system. Core stability training program consists of neural control exercise and spinal muscles exercise. However, conventional exercise does not include neural control exercise.

### Conclusion

Core stability training has a strong theoretical basis in treatment and prevention of LBP, as is evidenced by its widespread clinical use. And our results showed that core stability exercise using unstable, can be more effective decreasing pain, improving trunk muscle endurance and reducing the disability of daily life dysfunction in comparison with control group. But studies are limited, and some show conflicting results. Future studies are needed to elucidate precise core stability training programs and their effects on treatment and prevention of chronic LBP, in comparison with other exercise training programs.

### Author contributions

Wang Xueqiang was responsible for the data acquisition and integration, the data analysis and statistical management, as well as manuscript writing. Zheng Jiejiao was responsible for the study proposal and design, provided technical and information support. Liu Jing, Bi Xia, Hua Yinghui and Huang Qiangmin instructed the study, checked the manuscript, and provided technical and informa-

tion support. Fan Shuai, Shen Liyan, Feng Yan, Zhong Jiugen were responsible for subject recruitment and basic data collection.

### Funding

The National Science Foundation for Distinguished Young Scholars of China (Grant No.81101391); the Science and Technology Foundation Program of Shanghai University of Sport (Grant No. YJSCX201120); the Shanghai Natural Science Foundation of China (Grant No.11ZR1434900).

### Acknowledgments

We thank all patients for their willingness to participate in this study.

Supported by: the National Science Foundation for Distinguished Young Scholars of China (Grant No.81101391); the Science and Technology Foundation Program of Shanghai University of Sport (Grant No. YJSCX201120); the Shanghai Natural Science Foundation of China (Grant No.11ZR1434900)

### References

1. Beith ID, Kemp A, Kenyon J, Prout M, Chestnut TJ. Identifying neuropathic back and leg pain: a cross-sectional study. *Pain* 2011 Jul; 152(7):1511-6.
2. Andersson GB. Epidemiological features of chronic low-back pain. *Lancet* 1999 Aug 14; 354 (9178): 581-5.
3. Wolsko PM, Eisenberg DM, Davis RB, Kessler R, Phillips RS. Patterns and perceptions of care for treatment of back and neck pain: results of a national survey. *Spine (Phila Pa 1976)* 2003 Feb 1; 28(3):292-7; discussion 298.
4. Jones GT, Macfarlane GJ. Epidemiology of low back pain in children and adolescents. *Arch Dis Child* 2005; 90:312-6.
5. Lind BK, Lafferty WE, Tyree PT, Sherman KJ, Deyo RA, Cherkin DC. The role of alternative medical providers for the outpatient treatment of insured patients with back pain. *Spine* 2005; 30:1454-9.
6. Frymoyer JW, Cats-Baril WL. An overview of the incidences and costs of low back pain. *Orthop Clin North Am* 1991; 22(2):263-71.

7. Crow WT, Willis DR. Estimating cost of care for patients with acute low back pain: a retrospective review of patient records. *J Am Osteopath Assoc* 2009; 109(4):229-33.
8. Bell JA, Burnett A. Exercise for the primary, secondary and tertiary prevention of low back pain in the workplace: a systematic review. *J Occup Rehabil* 2009; 19(1):8-24.
9. Oesch P, Kool J, Hagen KB, Bachmann S. Effectiveness of exercise on work disability in patients with non-acute non-specific low back pain: Systematic review and meta-analysis of randomised controlled trials. *J Rehabil Med* 2010; 42(3):193-205.
10. Omkar SN, Vishwas S, Tech B. Yoga techniques as a means of core stability training. *J Bodyw Mov Ther* 2009; 13(1):98-103.
11. Hodges PW. Core stability exercise in chronic low back pain. *Orthop Clin North Am* 2003; 34(2) : 245-54.
12. Lederman E. The myth of core stability. *J Bodyw Mov Ther* 2010; 14(1):84-98.
13. Standaert CJ, Weinstein SM, Rumpeltes J. Evidence-informed management of chronic low back pain with lumbar stabilization exercises. *Spine J* 2008; 8: 114 -120.
14. Koumantakis GA, Watson PJ, Oldham JA. Trunk muscle stabilization training plus general exercise versus general exercise only: randomized controlled trial of patients with recurrent low back pain. *Phys Ther* 2005; 85(3):209-25.
15. Langley GB, Sheppard H. The visual analogue scale: its use in pain measurement. *Rheumatol Int* 1985; 5(4):145-8.
16. Fairbank JC, Couper J, Davies JB, O'Brien JP. The Oswestry low back pain disability questionnaire. *Physiotherapy* 1980; 66(8):271-3.
17. Nicolaisen T, Jørgensen K. Trunk strength, back muscle endurance and low-back trouble. *Scand J Rehabil Med* 1985; 17(3):121-7.
18. Bronfort G, Maiers MJ, Evans RL, Schulz CA, Bracha Y, Svendsen KH, Grimm RH Jr, Owens EF Jr, Garvey TA, Transfeldt EE. Supervised exercise, spinal manipulation, and home exercise for chronic low back pain: a randomized clinical trial. *Spine J* 2011; 11(7):585-98. Epub 2011 May 31.
19. Kofotolis N, Kellis E. Effects of two 4-week proprioceptive neuromuscular facilitation programs on muscle endurance, flexibility, and functional performance in women with chronic low back pain. *Phys Ther* 2006; 86(7):1001-12.
20. Unsgaard-Tøndel M, Fladmark AM, Salvesen Ø, Vasseljen O. Motor control exercises, sling exercises, and general exercises for patients with chronic low back pain: a randomized controlled trial with 1-year follow-up. *Phys Ther* 2010; 90(10):1426-40.
21. Muthukrishnan R, Shenoy SD, Jaspal SS, Nellikunja S, Fernandes S. The differential effects of core stabilization exercise regime and conventional physiotherapy regime on postural control parameters during perturbation in patients with movement and control impairment chronic low back pain. *Sports Med Arthrosc Rehabil Ther Technol*. 2010 May 31;2: 13.
22. Ferreira ML, Ferreira PH, Latimer J, Herbert RD, Hodges PW, Jennings MD, Maher CG, Refshauge KM. Comparison of general exercise, motor control exercise and spinal manipulative therapy for chronic low back pain: A randomized trial. *Pain* 2007; 131(1-2):31-7.
23. Koumantakis GA, Watson PJ, Oldham JA. Supplementation of general endurance exercise with stabilisation training versus general exercise only. Physiological and functional outcomes of a randomised controlled trial of patients with recurrent low back pain. *Clin Biomech (Bristol, Avon)* 2005; 20(5): 474-82.
24. Akuthota V, Ferreiro A, Moore T, Fredericson M. Core stability exercise principles. *Curr Sports Med Rep* 2008; 7(1):39-44.

Corresponding Author

Zheng Jiejiao,

Department of rehabilitation medicine,

Huadong Hospital affiliated to Fudan University,

Shanghai,

China,

E-mail: zjjcss@126.com

# A Study on Etiologic Agents and Drug Resistance Pattern of Entropathogens Isolates from Stool Specimens of Children Less Than Five Years Old Admitted in an Iranian Hospital

Mona Mohammad Zadeh<sup>1</sup>, Mohammad Rahbar<sup>2,3</sup>, Mahnaz Saremi<sup>2</sup>, Mohammad Aghazadeh<sup>4</sup>, Mohammad Reza Montazer Khorasan<sup>5</sup>, Mehrdad Peyrovi<sup>6</sup>, Khatere Saeidi Varnamkhasti<sup>7</sup>, Abdolaziz Rastegar Lari<sup>3</sup>

<sup>1</sup> Department of microbiology, Milad Hospital, Tehran, Iran,

<sup>2</sup> Department of Microbiology, Iranian Reference Health Laboratory, Ministry of Health and Medical Education, Tehran Iran,

<sup>3</sup> Antimicrobial Resistance Research Center, Tehran University of Medical sciences, Tehran, Iran,

<sup>4</sup> Department of Microbiology Faculty of Medicine, Tabriz University of Medical Sciences. Tabriz, Iran,

<sup>5</sup> Centers for Communicable Disease Control, Ministry of Health and Medical Education, Tehran, Iran,

<sup>6</sup> Department of Microbiology, Faculty of Basic Sciences, Azad university of Bonab Bonab, Iran,

<sup>7</sup> Department of Microbiology, Faculty of Sciences, University of Teacher Training, Tehran, Iran.

## Abstract

**Background and Objective:** Acute gastroenteritis is an important health public issue especially in developing countries. The aim of this study was to determine the enteropathogens causing acute diarrheal disease in children less than five years old admitted to Milad Hospital of Tehran during a 24-month period from April 2009 to December, 2010

**Methods:** Stool samples were collected from patients with diarrhea who attended to Milad Hospital. All specimens were cultured on routine microbiological media for isolation of enteropathogens. Biochemical tests were performed to determine of salmonella spp, shigella spp. and enteropathogenic *E.coli* as a common enteropathogens. Susceptibility testing was performed according to CLSI guidelines.

**Results** Of the 2207 stool samples, 153 (6.93%) were culture positive for one of the enteropathogens bacteria.. Enteropathogenic *E.coli* (EPEC), *Shigella* spp and *Salmonell* spp accounted for 82/153 (53.59%), 26/153 (16.99%) and 45/153 (29.41%) of all isolates respectively. *Shigella sonnei* with 22 isolates being the most prevalent serotype among shigella isolates. Nalidixic acid was the most effective antibiotic against *Shigella* spp. Chloramphenicol with the rate of 18.29% resistance was the most effective antibiotic against

EPEC spp. Resistance rate of *Salmonella* spp to ampicillin, nalidixic acid and Co-trimoxazole was 4.44%, 35.55% and 22.225% respectively.

**Conclusion:** During of our two years study in total 153 pathogens were isolated from stool cultures. *Shigella sonnei* was the most prevalent serotype among shigella spp Resistance to commonly used antibiotic was prevalent among all isolates.

**Key words:** Entropathogens, diarrhoea

## Introduction

The World Health Organization (WHO) defines diarrhoea as the passing of three or more loose stools (which take the shape of the container) within a 24 hour period. A new episode of diarrhoea can occur after two full days without diarrhoea. Episodes of diarrhoea lasting for less than 14 days are defined as acute; episodes lasting for more than 14 days are defined as persistent.( 1)

Diarrheal disease is one of the most common causes of mortality and morbidity among infants and children under five years old especially in developing countries (2, 3, 4, 5). Among children aged less than five years in the developing countries, the annual burden of diarrhea is estimated to be 1.5 billion cases, accounting for three million deaths. In addition the WHO has emphasized the need to understand the disease burden and epidemiology of diarrheal infections in developing



countries (6) In our country it has been estimated that nearly 18 million cases of diarrheal disease with one million hospital admission and 516 deaths in children occur annually ( 7 ) The infectious agents of diarrhea are usually transmitted via fecal oral routes such as digestion of contaminated food and water. Diarrhoea is caused by several organisms such as parasites viruses and bacteria. Among bacterial agents some of them such as salmonella spp ,shigella and EPEC are important.( 8 )

In recent years, the ability of microbiology laboratories for identification of enteropathogens has been increased due to the introducing of new molecular methods. However, these methods are not available in many microbiology laboratories especially in developing countries. There are many studies worldwide regarding prevalence and drug resistance pattern of enteropathogens However, there are only a few documented studies regarding the prevalence and susceptibility testing of etiologic agents for diarrheal disease in our country.

The aim of this study was to determine the prevalence of common enteropathogens isolated from stool specimens and performance of susceptibility testing of isolates in children under five years old admitted in an Iranian 1000-bed tertiary care hospital.

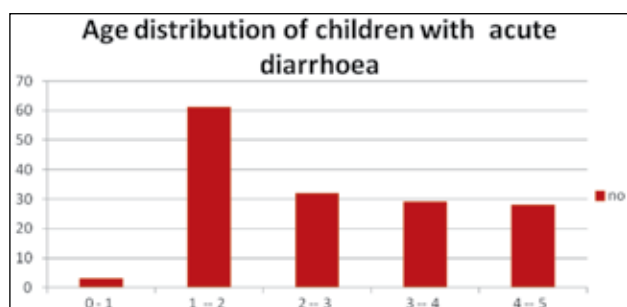
### Materials and Methods

In a study which was carried out between December 2009 and January 2011, in total 8195 stool samples were processed in microbiology laboratory of Milad hospital in Tehran. If the patients could not provide a stool during the visit, a swab specimen from the rectum was obtained. Of 8195 specimens 2207 specimens belonged to children under five years old. In the laboratory, stool specimens were evaluated for visible blood, and for RBCs and WBCs by microscopic examination. All stool specimens were cultured on Blood agar, MacConkey agar, Xylose-Lysine-Desoxycholate agar. All plates were incubated in 35°C for 24 hours. Colonies morphology resembling salmonella, shigella spp and enteropathogenic *E.coli* were further identified based on biochemical reactions. Slide agglutination tests by commercial antisera were performed for serotyping all isolated enteropathogenes.(9) Susceptibility testing of all isolates were performed with ampicillin (10 µg)

and nalidixic acid (30 µg) and sulfamethoxazole / trimethoprim ( 1.25/23.75 µg ) disks, using Mueller Hinton agar with a suspension equivalent to 0.5 McFarland standard of salmonella and shigella spp .We also used above mentioned antibiotics in addition chloramphenicol (30µg), ceftriaxone (30 µg) and cefixim(5 µg) for susceptibility testing of EPEC. All plates were incubated at 35°C for 24h. Zone of inhibition were measured and interpreted as guideline recommended by CLSI. *S.aureus* ATCC 25923, *E.coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were used as a control strains for quality control of susceptibility testing antibiotics disks.(10)

### Results

During our study in total, 8195 stool samples were sent to microbiology laboratory of Milad hospital for culture and susceptibility testing. Of total 8195 specimens, 2207 (26.93%) specimens were obtained from children under five years old. In total 153 (6.93%) enteropathogenes were isolated from stool of children. Of 153 patients who had positive cultures for enteropathogenes, 94 patients (61.43%) were male and 59(38.56%) female. 78(50.98%) patients were hospitalized and 75 (49.1%) patients were outpatients. Nearly one third isolates were from children 1-2year aged. The rate of isolation was: Shigella spp 26 (16.99%) isolates, salmonella spp 45 (29.41%) and enteropathogenic *E.coli* 82 (53.59%). In our study EPEC had the highest isolation rate. Of 26 shigella strains isolated, 22 (84.61%) were *S .sonnei* followed by *Sh.flexneri* 2 (7.69%) *Sh.boydii* and *Sh.dysenteriae* each with one isolates. (3.84%). Of 45 isolates of salmonella, salmonella group D with 17 isolates (37.77%) accounted the highest isolation. Other isolate groups included group C, B A and Salmonella spp . EPEC with 82 isolates accounted the highest enteropathogenes, EPEC group III with 74 (90.24%) isolates accounted nearly 50% of all enteropathogenes isolates. The frequency all enteropathogenic are shown in table 1. Microscopically examination of stool specimens showed Leukocytes and red blood cells in more than 90% of dysenteric specimens.



Picture 1.

Table 1. Prevalence of different enteropathogene isolated from stool specimens of children under 5 years old in an Iranian Hospital

Enteropathogenes	No	%
<b>Salmonella</b>		
Samonella group A	1	2.22
Salmoonella group B	6	13.33
Salmonella group C	9	20.0
Salmonella group D	17	37.77
Salmonella spp	12	26.66
<b>Shigella</b>		
<i>Shigella sonnei</i>	22	84.61
<i>Shigella flexneri</i>	2	7.69
<i>Shigella dysenteria</i>	1	3.84
<i>Shigella boydi</i>	1	3.84
<b>Entropathogenic <i>E.coli</i> (EPEC)</b>		
EPEC group I	7	8.53
EPEC group II	1	1.21
EPEC group III	74	90.24
Total	153	

Nalidixic acid was the most effective antibiotic against shigella spp and only 19.23% isolates of Shigella spp were resistant to nalidixic acid. The majority of isolates of shigella spp were resistant to ampicillin and sulfamethoxazole /trimethopri-me. Chloramphenicol with the rate of 18.29% resistance was the most effective antibiotic aga-against EPEC spp. Resistance rate of EPEC to other tested antibiotics including ampicillin, nalidixic acid, sulfamethoxazole /trimethopri-me, ceftriaxo-

ne and cefexime was 74.39%, 56.09%, 63.41%, 40.24% and 71.95% respectively. Resistance rate of salmonella spp to ampicillin, nalidixic acid and sulfamethoxazole / trimethopri-me was 26.66%, 35.55 and 22.22 respectively. The most prevalent serotype among shigella spp was *Sh. sonnei*. Resi-stance to commonly used antibiotic was prevalent among all isolates. Table 2

### Discussion

Acute diarrhea is a prevalent disease worl-dwide. The annual incidence of diarrhea in Asia, Africa and Latin America is much higher than in other developed countries. (8, 11). *Escherichia coli* is one of the most common cause of diarrhoea agent in children under five years old particularly in developing countries (12). In our study EPEC included more than 50 % of all entropathogenic isolate. Other studies from our country also has been reported a high rate of EPEC isolation. In a study by Aslani and et al in Tehran, they found that EPEC was the 44.9% etiology agent of diarrhea in children under five year old (3). In another study in west of Iran the rate of EPEC was 21.2%. Stud-ies from other countries has been found that EPEC to be a cause of 60-80 gastroenteritis in children.

Shigelosis is an acute gastroenteritis caused by shigella species, including *Shigella dysenteri-ae*, *Shigella flexneri*, *Shigella boydii* and *Shigella sonnei*. It is one of the most common causes of morbidity and mortality in children with diarrhea in developing countries. Worldwide, approxima-tely 165 million cases of shigellosis occur and 1,100,000 deaths are caused by the disease per year, which two-third of the patients are children under 5 years old. (12) .In, our study. Shigella spe-cies accounted 26(16.99%) isolation, and *Shigella sonnei* with 22 episodes had the highest isolation rate among shigella spp *Sh. sonnei* serotype is be-

Table 2. Drug resistance pattern of Enteorpathogens isolated from children with acute diarrhea

	Resistance .n(%)					
	AMP	NA	SXT	CHL	CRO	CFM
Salmonella spp	12 (26.66)	16 (35.55)	10(22.22)	N	N	N
Shigella spp	18 (69.23)	5(19.23)	17(65.38)	N	N	N
EPEC	63 (76.82)	49 (59.75)	52(63.41)	15(18.29)	35(4268)	59(71.95)

AMP= Ampicillin, NA=Nalidix acid, SXT= Sulfamethoxazole /trimethopri-me, CHL= chloramphenicol . CRO= Ceftriaxo-  
ne, CEM = Cefixime N=Not tested

lieved to be predominant and endemic in industrialized countries and known to cause milder self limited disease and to be less resistant to antimicrobial agents. However, recently *Sh.sonnei* has become the prevalent serotype in developing countries. Studies from different regions of our country confirm these findings. (12, 13)

*Salmonella* spp are the common cause of gastroenteritis worldwide. Salmonellosis is caused by several serotypes by the consumption of contaminated food products (1,). In our study it was the second prevalent isolated from diarrhoea disease. The salmonella isolates in our study included group A, B,C,D and salmonella spp. Salmonella group D with 17 isolates had the highest isolation. Group D consists of salmonella Typhi and a wide variety of salmonella spp including salmonella enteridis. Although Salmonella Typhi belongs to salmonella group D, it isolates rarely from diarrhea cases and this organism is not currently our health problem.

Ampicillin, sulfamethoxazole /trimethoprim and nalidixic acid are the most common antibiotics for treatment of bacterial diarrhoea. However following the emergency of resistance to above mentioned antibiotics, other antibiotics such as quinolones and third generation of cephalosporins are currently in use. (1, 14). In our study resistance rate of enteropathogenes including salmonella shigella and EPEC to ampicillin was nearly 70%. Resistance rate of salmonella, shigella and EPEC to sulfamethoxazole /trimethoprim was 22.22%, 65.38 and 63.41% respectively. The most effective antibiotics against salmonella, shigella and EPEC were sulfamethoxazole /trimethoprim, nalidixic acid and chloramphenicol respectively. In another study by Zali et al sulfamethoxazole /trimethoprim resistance rate of salmonella enterica to ampicillin, nalidixic acid and sulfamethoxazole /trimethoprim was 15.5%, 45% and 14.7% respectively, which agrees with our study except for ampicillin. (1). Among shigella spp resistance to nalidixic acid was found to have increased gradually in recent years, however like other studies nalidixic acid is a selective antibiotic for treatment of shigellosis. Other studies in our country confirm these findings.

Drug resistance pattern of EPEC in our study was very high. The resistance rate of EPEC to routinely used antibiotics such as ampicillin, nalidixic acid, sulfamethoxazole /trimethoprim, ceftroxo-

ne and cefixime was 76.82%, 59.75%, 63.41%, 18.29% and 71.95% respectively. Our findings resemble to other studies which has been carried out in our country.(15). In our study the most effective antibiotic against EPEC was chloramphenicol, which is not agrees with other studies such as carried out by Klantar and co-workers in west of Iran (16).

## Conclusion

During of our two years study, in total 153 pathogens were isolated from stool cultures. *Shigella sonnei* was the most prevalent serotype among shigella spp. Resistance to commonly used antibiotic was prevalent among all isolates.

## References

1. Zali MR, Alebouyeh M and Tajbaksh M. Emergence of resistance salmonella spp : new challenges, new trends. *Gastr Hepto from bed to bench*. 2011; 4 :99-101.
2. Jafari F, Hamidian M, Rezadehbashi M, Doyle M, Salmazadeh-Ahrabi S, Derakhshan F, Reza Zali M. Prevalence and antimicrobial resistance of diarrheagenic *Escherichia coli* and *Shigella* species associated with acute diarrhea in Tehran, Iran. *Can J Infect Dis Med Microbiol*. 2009; 20:56-62.
3. Pourakbari B, Mamishi S, Mashoori N, Mahboobi N, Ashtiani MH, Afsharpaiman S, Abedini M. Frequency and antimicrobial susceptibility of *Shigella* species isolated in Children Medical Center Hospital, Tehran, Iran, 2001-2006. *Braz J Infect Dis*. 2010 ;14:153-7.
4. Mamishi S, Mashoori N, Mahboobi N, Pour Akbari B. Increasing resistance to nalidixic acid in *Shigella* subgroups in a comparative study between 2001-2003 and 2004-2006. *Singapore Med J*. 2009 ;50:791-3
5. Ranjbar R, Soltan-Dallal MM, Pourshafie MR, Mammia C. Antibiotic resistance among *Shigella* serogroups isolated in Tehran, Iran (2002-2004). *J Infect Dev Ctries*. 2009 ; 3 :647-8.
6. Tajbaksh M, Nayer BN, Motavaze K, Kharaziha P, Chiani M, Zali MR, Klana JD. Phylogenetic relationship of *Salmonella enterica* strains in Tehran, Iran, using 16S rRNA and *gyrB* gene sequences. *J Infect Dev Ctries*. 2011; 5 :465-72.
7. Hamidian M, Tajbaksh M, Tohidpour A, Rahbar M, Zali MR, Walther-Rasmussen J. Detection of novel *gyrA* mutations in nalidixic acid-resistant isolates of *Salmonella enterica* from patients with diarrhea. *Int J Antimicrob Agents*. 2011 ;37 :360-4.

8. Ashtiani MT, Monajemzadeh M, Kashi L. Trends in antimicrobial resistance of fecal Shigella and Salmonella isolates in Tehran, Iran. *Indian J Pathol Microbiol.* 2009.;52-55
9. Alikhani MY, Mirsalehian A, Fatollahzadeh B, Pourshafie MR, Aslani MM. Prevalence of enteropathogenic and shiga toxin-producing Escherichia coli among children with and without diarrhoea in Iran. *J Health Popul Nutr.* 2007; 25 :88-93.
10. Aslani MM and Alikhani MY. Serotypes of enteropathogenic Escherichia coli isolated from children under 5 Years of age. *Iranian J public health* 2009; 38: 70-77
11. Jafari F, Shokrzadeh L, Hamidian M, Salmanzadeh-Ahrabi S, Zali MR. Acute diarrhea due to enteropathogenic bacteria in patients at hospitals in Tehran *Jpn J Infect Dis.* 2008; 61:269-73.
12. Rahbar M, Deldari M, Hajia M. Changing prevalence and antibiotic susceptibility patterns of different shigella species in Tehran, Iran. *The Internet J Microbiol.* 2007; 3(2) online
13. Ranjbar R, Soltan Dallal MM, Pourshafie MR, Aslani MM, Majidzadeh R, Khramizadeh MR. Serogroup distribution of Shigella in Tehran. *Iranian J Public Health.* 2004; 33:32-35
14. Ashtiani MT, Monajemzadeh M, Kashi L. Trends in antimicrobial resistance of shigella and salmonella isolates in Tehran, Iran. *Indian J Pathol Microbiol.* 2009; 52:52-55
15. Aslani MM, Ahrabi SS, Alikhani YM, Jafari F, Zali RM, Mani M. Molecular detection and antimicrobial resistance of diarrheagenic Escherichia coli strains isolated from diarrheal cases. *Saudi Med J.* 2008; 29 388-92.
16. Kalantar E, Soheili F, Salimi H, Soltan Dalla MM. Frequency, antimicrobial susceptibility and plasmid profiles of Escherichia coli pathotypes obtained from children with acute diarrhea. *JJM.* 2011; 4: 23-2

*Corresponding Author*

Mohammad Rahbar,

Department of Microbiology,

Iranian Reference health Laboratory,

Ministry of Health and Medical Education,

Tehran,

Iran,

E-mail: rahbar\_reflab@yahoo.com

# Determination of physical assessment skills used by nurses in Turkey

Zeliha Koç, Zeynep Sağlam

Ondokuz Mayıs University, Samsun School of Nursing, Turkey,

## Abstract

**Background:** Compared to other professions, physical assessment is a comparatively new concept for the nursing profession. Traditionally, physical assessment has been viewed as part of the doctors' role and has not routinely been taught in nurse training. With the advancement of the role of nursing, it has been argued that physical assessment has become a key nursing skill

**Objective:** The purpose of this study was to identify physical assessment skills used by nurses in Turkey.

**Methods and material:** This defining research was conducted between 01.03.2011 and 30.04.2011. The data in the research were collected by using a questionnaire, which consisted of two major parts: socio-demographic and professional questions and a list of physical assessment skills. Physical examination skills routinely performed by nurses were identified. Data were evaluated using the SPSS 15.0 program.

**Results:** It is determined in this study that 41.5% of the nurses feel they are inadequate in terms of professional skills, The nurses who do not apply physical assessment skills (77.9%) say that this is the case because of a lack of knowledge, they consider physical diagnosis and assessment to be the doctors' duties, too many patients, heavy workload, and a limited number of the nurses.

**Conclusion:** It is determined in this study that the use of the nurses' physical assessment skills is rare. More educational opportunities in physical assessment should be provided, including educational programs based on the nurses' skill levels and needs in the clinical area.

**Key words:** frequency, knowledge, nurse, physical assessment, skill, Turkey.

## Introduction

Compared to other professions, physical assessment is a comparatively new concept for the nursing profession. Traditionally, physical assessment has been viewed as part of the doctors' role and has not routinely been taught in nurse training. With the advancement of the role of nursing, it has been argued that physical assessment has become a key nursing skill [1].

Nurses use physical assessment for the following: to gather baseline data about the client's health; to supplement, confirm, or refute data obtained in the nursing history; to confirm and identify nursing diagnoses; to make clinical judgements about a client's changing health status and management; and to evaluate the physiological outcomes of care [2].

Physical assessment provides a systematic method for collecting all types of data that serve to identify the client's presenting strengths and problems. Also, the ability to obtain a comprehensive health history and perform a complete physical examination is one of the integral components of the advanced practise role [3]. When competently completed and combined with information obtained from the patient's psychosocial and health history, a structured physical assessment and examination can assist in clarifying clinical events or situations [4].

Lillibridge and Wilson (1999) reviewed the literature on nurse health assessment, which included criteria for evaluating assessment knowledge and skill level. They found that nurses perceived physical assessment as a medically focused practise [5]. In contrast, in a study on assessment practises in the United Kingdom, West (2006) found that assessment is viewed as a fundamental aspect of nursing practise [1]. According to Duff and colleagues (2007) the need for nurses to perform accurate physical assessments is becoming more evident as the scope of nursing roles and clinical practise continues to expand. Recent advances in

technology do not decrease the need for assessment skills; in fact, they actually increase the need for these skills [6]. Nurses in the USA, and more recently in Canada and Australia, readily incorporate physical assessment skills into their nursing practise as a component of health assessment [7].

Yamauchi (2001) reported that performing a nursing assessment is a unique nursing activity and is not the same as a medical assessment. Nursing assessment is not merely a practise that nurses are allowed to do, but a skill that is actually required by professional nursing practise standards. A comprehensive understanding of the skills and knowledge needed to complete a thorough physical assessment provides the nurse with a database that increases the nurse's ability to monitor and identify changes in a patient's condition [8].

As noted in the literature, physical assessment skills used to be learned on the job [8]. Nowadays, nursing education must prepare nurses to meet the health-care needs of the patients. Education is an effective way to provide people with precise knowledge and skills and to promote nurses' confidence in using these newly acquired skills.

Knowing more about the how physical assessment skills are actually used in clinical settings is crucial for the development of educational programs that would enable nurses to function more independently. However, little research has been conducted on the skills that are actually used in practise [4]. Practises, expectations, and beliefs about what constitutes a comprehensive physical assessment are just now being examined [9].

An examination of other studies about this subject in the literature reveals that there is a limited number of studies assessing the use of nurses' physical assessment skills [8,10-13]. To date, no study has assessing the use of nurses' physical assessment skills in Turkey. This was the starting point of our study. It is observed that nurses, who work in various health care institutions in Turkey, adopt a work-based approach instead of a patient-based approach. In other words, the applications of the nurses regarding the patient care are limited to occasionally taking vital findings, giving oral and parenteral medicine, entering the doctor's orders, providing medicine and material, and executing care and treatment functions of the individual. In this light, it is found that the use of

the nurses' physical assessments skills is rare. It is important to establish which factors influence the implementation of these skills in practise, including the types of skills most commonly used and their frequency of use.

Consistent with the other research, the framework of this study was a systematic physical assessment model based on a physiological model [8]. The systematic physical assessment practises were intended to gather as much information as possible on the function, size, and appearance of organs and body parts in order to carry out a comprehensive and integrated evaluation of the presence or absence of pathology and of the total body response to pathological processes. The physiological model provides guidelines for detecting signs of change in the client's health status, assessing the client's living activities, and facilitating preventive care and health promotion. The physiological model also provides a common communication tool among health-care professionals. By using a physiological model as a communication tool, nurses who use different nursing models can translate and exchange findings on the physical aspects of their clients [8].

This descriptive study is made to determine the use of the physical assessment skills of the nurses. The findings of this study will be useful in guiding both the education and practise of nurses. The purpose of this study was to answer the following questions:

1. Which physical assessment skills do the nurses apply the most?
2. According to the nurses, which physical assessment skills are more important and necessary for nursing applications?
3. Do the nurses feel adequately prepared to apply physical assessment skills?
4. How often do the nurses apply their physical assessment skills in the clinical environment?

## Method

### *Design, Sample, and Setting*

This descriptive study was conducted in a university hospital between 01.03.2011 and 30.04.2011. A descriptive methodology was chosen because little information regarding the health assessment skills of nurses could be found

in nursing literature. Participants included nurses practicing in a variety of areas, including general medical and surgical nursing units. They were working a minimum of 40 hours per week and were providing direct patient care in both in-patient and outpatient settings. The hospital in which the research was conducted has 1000-in-patient bed availability.

Sampling was not done in this study. The authors aimed to include the entire population (N=512). However, nurses who were nursing supervisors, nurse administrators, managers, educators, and nurse-midwives who did not agree to participate in the study or who did not fill out the form completely were excluded; this left a total of 362 (70.7%) nurses who participated in the study.

### ***Instrument***

The researchers developed a self-administered questionnaire following previous literature [8,9,10,13]. The questionnaire consisted of two major parts: socio-demographic, professional questions and list of physical assessment skills. The demographic and professional data are composed of questions regarding age, gender, level of education, work experience, department, the adequacy of nurses in the professional field, the inadequacy of nurses in certain fields, the use of physical assessment skills in the clinic, the reasons the nurses have for not using physical assessment skills, and the frequency of such use.

The second section of the survey form was composed of a list of physical assessment skills. The participants were asked whether they needed or did not need these assessment skills in their professional applications, whether they used or did not use the physical assessment skills, whether they felt sufficiently or insufficiently prepared while applying physical assessment skills, and how frequently they used physical assessment skills (1 = never, 2 = rarely, 3 = sometimes, 4 = usually, and 5 = always). Furthermore, there was a question at the end of the survey form for the nurses to write down any skills that were not on the list.

### ***Data Collection***

Data were collected from the nurses over a two-month period. Before implementation, five

Turkish nursing educators examined the questionnaire items and the questionnaire was tested with a group of ten nurses. Questions that were difficult to understand or incomplete were identified and corrected. After this pilot study, the final draft of the questionnaire took shape.

### ***Ethical Considerations***

This study was conducted while taking into account the principles of the Helsinki Declaration. The study commenced after ethics approval from the Ondokuz Mayıs University scientific committee. Before starting the data collection, each nurse was verbally informed about the nature of the study and its objectives and was then invited to participate. Participation was voluntary; only individuals who agreed to participate completed the survey. They were also given the opportunity to not be involved in the study. All nurses involved in the study were asked to sign a consent form. The survey contained no personal identifiers and was directly administered and collected by the researchers. Written instructions were given on how to complete the questionnaire. The response time was estimated at 10-12 min.

### ***Data Analysis***

Data were evaluated using SPSS 15.0 program. In the evaluation of data, descriptive statistics and chi-square tests were used. The level of significance was set at  $p < 0.05$ . In this study, the independent variables were the nurses' socio-demographic and professional characteristics (such as age, gender, education level, and clinical experiences), and the frequency of the use of physical assessment skills. The dependent variable was the nurses' use of physical assessment skills. Chi-square analyses were used to examine the differences between the physical assessment skills and nurses' sociodemographic and professional characteristics.

### **Results**

In this study, it is found that 79.0% of the nurses had graduated from a school of nursing, 68.0% had worked for 1-8 years, and 41.5% felt insufficiently prepared in terms of professional skills. The average age of the nurses is  $28.3 \pm 5.5$ , and the average working time is  $7.6 \pm 4.3$  (Table 1).

**Table 1.** The distribution of socio-demographic and professionals characteristics of the nurses (N=362)

Characteristics	n	%
<b>Age group 28.3±5.5</b>		
20-27	193	53.3
28-35	132	36.5
36-43	30	8.3
44-50	7	1.9
<b>Gender</b>		
Female	347	95.9
Male	15	4.1
<b>Education level</b>		
Health vocational school	10	2.8
Medical vocational school	59	16.3
School of Nursing	286	79.0
Master	7	1.9
Doctorate	-	-
<b>Clinical experiences 7.6±4.3</b>		
1-8 years	246	68.0
9-16 years	78	21.5
17-24 years	31	8.6
25-32 years	7	1.9
<b>Department</b>		
Internal units	187	51.7
Surgical units	175	48.3
<b>Finding herself adequate in professional field</b>		
Yes	268	74.0
No	94	26.0
<b>The fields of inadequacy (n=94)</b>		
Professional knowledge	35	37.2
Professional skill	39	41.5
Professional approach and values	20	21.3
<b>Is it important that the nurses have physical assessment skills in diagnose / treatment of the patients?</b>		
Yes	359	99.2
No	3	0.8
<b>The use of physical assessment skill in the clinic</b>		
Yes	80	22.1
No	282	77.9
<b>The frequency of the use of physical assessment skills (n=80)</b>		
Never	-	-
Rare	27	33.7
Sometimes	23	28.8
Usually	18	22.5
Always	12	15.0
<b>* The reasons for not using physical assessment skills (n=282)</b>		
Heavy workload	49	17.4
Too many patients	54	19.1
Not enough nurses	48	17.0
Considering physical assessment skills as the duty of the doctor	58	20.6
Not having enough knowledge on this subject	84	29.8



Table 2. The distribution of application of the nurses concerning physical assessment skills (N=362)

Characteristics	Needing		Not needing		Applying		Not applying		Considering herself adequate		Considering herself inadequate	
	n	%	n	%	n	%	n	%	n	%	n	%
1) The assessment of vital findings	360	99.4	2	0.6	343	94.8	19	5.2	320	88.4	42	11.6
2) The assessment of skin turgor	342	94.5	20	5.5	272	75.1	90	24.9	230	63.5	132	36.5
3) The assessment of skin lesions	346	95.6	16	4.4	250	69.1	112	30.9	186	51.4	176	48.6
4) The assessment of edema level	344	95.0	18	5.0	244	67.4	118	32.6	187	51.7	175	48.3
5) The assessment of hair and nails	338	93.4	24	6.6	235	64.9	127	35.1	196	54.1	166	45.9
6) The assessment of mouth and farynx	340	93.9	22	6.1	217	59.9	145	40.1	147	40.6	215	59.4
7) The assessment of nose and sinuses	315	87.0	47	13.0	124	34.3	238	64.7	90	24.9	272	75.1
8) The assessment of the extraocular movement of the eye	334	92.3	28	7.7	127	35.1	235	64.9	77	21.3	285	78.7
9) The assessment of visual fields	320	88.4	42	11.6	95	26.2	267	73.8	53	14.6	309	85.4
10) The assessment of outer eye structures	331	91.4	31	8.6	161	44.5	201	55.5	98	27.1	264	72.9
11) The assessment of inner eye structures	314	86.7	48	13.3	111	30.7	251	69.3	50	13.8	312	86.2
12) The assessment of the ear and audition	327	90.3	35	9.7	132	36.5	230	63.5	66	18.2	296	81.8
13) The assessment of trachea	318	87.8	44	12.2	99	27.3	263	72.7	46	12.7	316	87.3
14) The assessment of thyroid glands	311	85.9	51	14.1	82	22.7	280	77.3	54	14.9	308	85.1
15) The palpation of the neck lymph nodes	317	87.6	45	12.4	110	30.4	252	69.6	66	18.2	296	81.8
16) The palpation of the axillar nodes	322	89.0	40	11.0	88	24.3	274	75.7	62	17.1	300	82.9
17) The assessment of breath sounds	342	94.5	20	5.5	205	56.6	157	43.4	115	31.8	247	68.2
18) The assessment of chest and thorax	327	90.3	35	9.7	154	42.5	208	57.5	88	24.3	274	75.7
19) The assessment of breast and axilla	331	91.4	31	8.6	136	37.6	226	62.4	87	24.0	275	76.0
20) The assessment of auscultation. murmur of the heart	317	87.6	45	12.4	117	32.3	235	67.7	49	13.5	313	86.5
21) The assessment of peripheral veins	326	90.1	36	9.9	186	51.4	176	48.6	85	23.5	277	76.5
22) The assessment of jugular vein	323	89.2	39	10.8	143	39.5	219	60.5	75	20.7	287	79.3
23) The assessment of peripheral pulse	337	93.1	25	6.9	245	67.7	117	32.3	139	38.4	223	61.6
24) The assessment of carotid artery	325	89.8	37	10.2	160	44.2	202	55.8	99	27.3	263	72.7
25) The assessment of peripheral blood flow	327	90.3	35	9.7	157	43.4	205	56.6	90	24.9	272	75.1
26) The abdominal palpation	328	90.6	34	9.4	157	43.4	205	56.6	89	24.6	273	75.4
27) The abdominal percussion	313	86.5	49	13.5	103	28.5	259	71.5	62	17.1	300	82.9
28) The assessment of periton sensibility	328	90.6	34	9.4	133	36.7	229	63.3	67	18.5	295	81.5
29) The assessment of bowel sounds	328	90.6	34	9.4	169	46.7	193	53.3	102	28.2	260	71.8
30) The assessment of conscious	340	93.9	22	6.1	251	69.3	111	30.7	143	39.5	219	60.5
31) The assessment of speak functions	333	92.0	29	8.0	224	61.9	138	38.1	138	38.1	224	61.9
32) The assessment of the cranial nerves	310	85.6	52	14.4	93	25.7	269	74.3	48	13.3	314	86.7
33) The assessment of motor function and movement	333	92.0	29	8.0	198	54.7	164	45.3	109	30.1	253	69.9
34) The assessment of deep tendon reflex	322	89.0	40	11.0	138	38.1	224	61.9	80	22.1	282	77.9
35) The assessment of the senses	339	93.6	23	6.4	207	57.2	155	42.8	116	32.0	246	68.0
36) The assessment of pupil reaction	340	93.9	22	6.1	215	59.4	147	40.6	103	28.5	259	71.5
37) The assessment of sensual state	337	93.1	25	6.9	202	55.8	160	44.2	117	32.3	245	67.7
38) The assessment of the muscles	329	90.9	33	9.1	159	43.9	203	56.1	86	23.8	276	76.2
39) The assessment of the joints	328	90.6	34	9.4	158	43.6	204	56.4	101	27.9	261	72.1
40) The assessment of walking and coordination	336	92.8	26	7.2	172	47.5	190	52.5	106	29.3	256	70.7

Table 3. The distribution the application frequency of the physical assessment skills by the nurses (N= 362)

Characteristics	Never		Rarely		Sometimes		Usually		Always	
	n	%	n	%	n	%	n	%	n	%
1) The assessment of vital findings	1	0.3	4	1.1	5	1.4	40	11.0	312	86.2
2) The assessment of skin turgor	26	7.2	52	14.4	98	27.1	100	27.6	86	23.8
3) The assessment of skin lesions	23	6.4	36	9.9	101	27.9	111	30.7	91	25.1
4) The assessment of edema level	24	6.6	30	8.3	131	36.2	100	27.6	77	21.3
5) The assessment of hair and nails	33	9.1	38	10.5	91	25.1	113	31.2	87	24.0
6) The assessment of mouth and farynx	40	11.0	56	15.5	72	19.9	121	33.4	73	20.2
7) The assessment of nose and sinuses	137	37.8	65	18.0	87	24.0	39	10.8	34	9.4
8) The assessment of the extraocular movement of the eye	147	40.6	76	21.0	83	22.9	34	9.4	22	6.1
9) The assessment of visual fields	172	47.5	70	19.3	74	20.4	28	7.7	18	5.0
10) The assessment of outer eye structures	106	29.3	86	23.8	81	22.4	44	12.2	45	12.4
11) The assessment of inner eye structures	180	49.7	82	22.7	67	18.5	20	5.5	13	3.6
12) The assessment of the ear and audition	119	32.9	82	22.7	74	20.4	43	11.9	44	12.2
13) The assessment of trachea	217	59.9	51	14.1	67	18.5	8	2.2	19	5.2
14) The assessment of thyroid glands	242	66.9	63	17.4	44	12.2	7	1.9	6	1.7
15) The palpation of the neck lymph nodes	214	59.1	70	19.3	53	14.6	14	3.9	11	3.0
16) The palpation of the axillar nodes	230	63.5	55	15.2	48	13.3	14	3.9	15	4.1
17) The assessment of breath sounds	58	16.0	48	13.3	63	17.4	81	22.4	112	30.9
18) The assessment of chest and thorax	115	31.8	63	17.4	71	19.6	58	16.0	55	15.2
19) The assessment of breast and axilla	177	48.9	74	20.4	55	15.2	32	8.8	24	6.6
20) The assessment of auscultation. murmur of the heart	187	51.7	50	13.8	45	12.4	40	11.0	40	11.0
21) The assessment of peripheral veins	87	24.0	57	15.7	64	17.7	90	24.9	64	17.7
22) The assessment of jugular vein	149	41.2	71	19.6	77	21.3	36	9.9	29	8.0
23) The assessment of peripheral pulse	54	14.9	34	9.4	47	13.0	68	18.8	159	43.9
24) The assessment of carotid artery	145	40.1	59	16.3	79	21.8	49	13.5	30	8.3
25) The assessment of peripheral blood flow	117	32.3	59	16.3	55	15.2	77	21.3	54	14.9
26) The abdominal palpation	125	34.5	86	23.8	79	21.8	41	11.3	31	8.6
27) The abdominal percussion	181	50.0	65	18.0	62	17.1	30	8.3	24	6.6
28) The assessment of periton sensibility	155	42.8	81	22.4	62	17.1	37	10.2	27	7.5
29) The assessment of bowel sounds	104	28.7	82	22.7	79	21.8	55	15.2	42	11.6
30) The assessment of conscious	26	7.2	19	5.2	38	10.5	104	28.7	175	48.3
31) The assessment of speak functions	50	13.8	39	10.8	68	18.8	86	23.8	119	32.9
32) The assessment of the cranial nerves	225	62.2	46	12.7	47	13.0	19	5.2	25	6.9
33) The assessment of motor function and movement	74	20.4	56	15.5	66	18.2	74	20.4	92	25.4
34) The assessment of deep tendon reflex	153	42.3	76	21.0	62	17.1	32	8.8	39	10.8
35) The assessment of the senses	55	15.2	56	15.5	64	17.7	93	25.7	94	26.0
36) The assessment of pupil reaction	50	13.8	78	21.5	76	21.0	81	22.4	77	21.3
37) The assessment of sensual state	54	14.9	69	19.1	74	20.4	85	23.5	80	22.1
38) The assessment of the muscles	92	25.4	67	18.5	65	18.0	79	21.8	59	16.3
39) The assessment of the joints	80	22.1	92	25.4	64	17.7	67	18.5	59	16.3
40) The assessment of walking and coordination	73	20.2	70	19.3	55	15.2	87	24.0	77	21.3

### ***Physical Assessment Skills***

In this study, 99.2% of the nurses state that having physical assessment skills is important for the diagnosis and treatment of the patients, but only 33.7% use such skills only “rarely.” The reasons that 77.9% of the nurses did not use physical assessment skills were as follows: not having enough knowledge about this subject (29.8%), considering physical diagnostics and assessments as the doctor’s duty (20.6%), too many patients (19.1%), a heavy workload (17.4%), and a limited number of nurses (17.0%) (Table 1).

### ***Use of Physical Assessment Skills***

In this study, it is determined that the physical assessment skills the nurses used the least are the assessment of thyroid glands, the palpation of axillary nodes, the assessment of cranial nerves, the assessment of vision fields, the assessment of trachea, abdominal percussion, the palpation of neck lymph nodes, the assessment of inner-eye structure, the assessment of the auscultation and murmur of the heart, the assessment of the nose and sinuses, the assessment of extraocular movement of the eye, the assessment of the ear and audition, the assessment of periton sensibility, the assessment of breast and axilla, the assessment of deep tendon reflexes, and the assessment of jugular vein (the non-application rates are, respectively, 77.3%, 75.7%, 74.3%, 73.8%, 72.7%, 71.5%, 69.6%, 69.3%, 67.7%, 65.7%, 64.9%, 63.5%, 63.3%, 62.4%, 61.9%, 60.5%) (Table 2).

### ***Frequency of Physical Assessment Skills***

In this research, when the nurses analyzed the frequency with which they used physical assessment skills, it was found that in general, they always use the assessment of vital findings (86.2%), the assessment of consciousness level (48.3%), the assessment of peripheral pulse (43.9%), the assessment of speech functions (32.9%), and the assessment of breathing sounds (30.9%). In contrast, they never use the assessment of thyroid glands (66.9%), the assessment of cranial nerves (62.2%), abdominal percussion (50.0%), the periton sensibility (42.8%), or the assessment of deep tendon reflexes (42.3%) (Table 3).

The relationship between the use of physical assessment skills by the nurses and some socio-

demographic and professional characteristics is found to be statistically significant ( $p < 0.05$ ). In this study, the use of physical diagnostic skills is determined to be higher in nurses who are in the 20-27 age group ( $\chi^2: 15.012, p < 0.000$ ), those who graduated from a school of nursing ( $\chi^2: 12.369, p < 0.002$ ), those who have worked for 1-8 years ( $\chi^2: 9.641, p < 0.02$ ), those who feel sufficiently prepared in the professional field ( $\chi^2: 7.548, p < 0.01$ ), and those who work in surgery ( $\chi^2: 11.888, p < 0.003$ ).

### **Discussion**

Assessment is unquestionably a fundamental skill performed by all nurses in clinical practice. Assessment data provide the foundation on which nurses base their decisions, interventions, and evaluations. In this study, it is determined that 1/5 of the nurses use physical assessment skills in the clinics, and nearly half of them feel insufficiently prepared in terms of professional skills. In accordance with the findings of another study on this subject [8], it is considered that the reason the of physical assessment skills are used so rarely by nurses is that they feel insufficient in terms of their professional skills and they do not know how to use them.

In this study, it is determined that 4/5 of the nurses do not use physical assessment skills, and the most important reasons for not using physical assessment skills are as follows: not having enough knowledge, considering physical assessment skills the doctor’s duty, too many patients, a heavy workload, and a limited number of nurses. In line with Yamauchi (2001) it is determined that the most important factors affecting the use of physical assessment skills are “lack of knowledge” [8], and “considering physical assessment skills as the duty of the doctor” [14]. As previous literature has noted [1], despite the fact that they consider physical assessment skills to be one of the doctor’s duties, with the development of the role of nurses, these skills are becoming the key to physical diagnosis and assessment of the patients.

In this study, it is found that, out of the skills on the list of physical assessment skills, most of the nurses always use the assessment of vital findings, consciousness level, peripheral pulse, and

speech functions; and they never use the assessment of thyroid glands, the assessment of cranial nerves, abdominal percussion, the determination of periton sensibility, or the assessment of deep tendon reflexes. These findings suggest that this sample of nurses incorporates a relatively small set of physical examination skills into practise on a regular basis. Also it is determined that the least used physical assessment skills by the nurses have to do with the physical examination applications requiring palpation, percussion, and auscultation skills; the physical examination applications, which are physical assessment skills always used by the nurses, are limited to inspection.

In a similar study, Giddens (2007) stated that the physical assessment skills used routinely by nurses mostly involve inspection and general observation [9]; Shin et al. (2009) concurred with these findings [13]. In this light, it is considered that the nurses do not rely on themselves for palpation, percussion, and auscultation techniques, which require a high level of experience and diagnostic and assessment skills, as well as theoretical knowledge. They simply find themselves insufficiently prepared to use these skills.

Although the frequency of the use of the physical assessment skills by the nurses varies according to the country where the research was carried out, in a study conducted in Japan (Yamauchi, 2001), it was determined that four skills—the assessment of vital signs, the assessment of pulse deficit, pulse deficit consciousness level, and examining pitting—were used by more than half of the participants every day [8]. In a study conducted in Korea, it was found that 46 skills of a 126-item skill list were rarely used by the participants [13]. In a study conducted in Canada, it was determined that 90.4% of the participants frequently used abdominal palpation, one of the physical assessment skills [14].

Secrest et al. (2005) found that practicing nurses never used 37% of the skills they had learnt and use 29% daily or weekly [10]. Giddens (2007) reported findings from a study evaluating the physical assessment skills performed by nurses in clinical practise. Of 124 assessment skills, only 30 were reported to be routinely performed by nurses across practise settings; the remaining skills were performed occasionally or not at all [2007]

In this study, it is determined that the physical assessment skills least needed by the nurses are the assessment of cranial nerves, the assessment of thyroid glands, and abdominal percussion. It is possible that this situation might arise from the fact that the applications of the nurses practicing patient care at some health care institutions in Turkey are limited to occasionally taking vital findings, giving oral and parenteral medicine, entering the doctor's orders, executing care and treatment functions for the individual; it also may be due to the fact that there are too many patients whose care and treatment they are responsible for and that they do not consider physical assessment skills to be a part of the applications of nurses.

In light of the findings of this study, it is seen that there are many reasons the nurses in Turkey cannot use physical assessment skills effectively when compared to nurses in developed countries such as USA, Canada, and Australia. These reasons include: the lack of knowledge and experience among the nurses regarding the use of these skills; the idea that physical assessment skills are the duty of other health-care professionals, especially the doctors; the feeling that the use of physical assessment skills increases the workload of the nurses; the opinion that physical assessment skills are not necessary for the work of nurses; and unsatisfactory training in physical assessment skills at nursing education programs. In this perspective, it is rather important to determine the roles of the nurses for the use of physical assessment skills in clinical environments in order to organise educational programs for nurses who feel insufficiently prepared for the use of these skills and, at the same time, to build up confidence. All nursing action is dependent on the adequacy of the data collected through a history and physical examination. In order to fulfill society's expectations, nurses must be prepared in health assessment skills [15]. Continuing education in conducting physical assessment can help the nurses feel more confident in their nursing practise; interpret individual patient findings better; understand physicians' progress notes and examinations better; improve their interactions with patients; feel more comfortable in reporting their findings and in initiating specific nursing actions; and provide direct referrals to appropriate resource persons [8],

## Limitations

The limitations of the current study are:

The research was carried out only in a hospital.

The number of the nurses in the scope of the study is low.

No generalisation can be made due to the lack of similar studies in Turkey.

## Conclusions

This study has provided valuable information for both educators and practitioners on the use of physical examination skills. In this study, it is found that 41.5% of the nurses feel insufficient in terms of their professional skills. It is rather important that the nurses be able to use physical assessment skills in order to provide efficient and qualified care to the patients under their care and treatment. Scientific studies to further examine the use of physical assessment skills by nurses should be done, awareness about this subject should be increased, and post-graduate education programs should be organised.

## Acknowledgements

We would like to thank the hospital manager and staff.

## References

1. West SL. *Physical assessment: whose role is it anyway?* *Nurs Crit Care*. 2006; 11(4): 161-167.
2. Heath HBM. *Foundations in Nursing Theory and Practice. Physical Assessment*. London: Mosby Company, 1985.
3. Kelley FJ, Kopac CA. *Advanced health assessment in nurse practitioner programs*. *J Prof Nurs*. 2001; 17(5): 218-225.
4. Fennessey A, Wittman-Price RA. *Physical Assessment: A Continuing Need for Clarification*. *Nurs Forum* 2011; 46(1):45-50.
5. Lillibridge J, Wilson M. *Registered nurses' descriptions of their health assessment practices*. *Int J Nurs Pract*. 1999; 5: 29-37.
6. Duff B, Gardiner G, Barnes M. *The impact of surgical ward nurses practising respiratory assessment on positive patient outcomes*. *Aust J Adv Nurs*. 2007; 24(4): 52-56.
7. Lesa R, Dixon A. *Physical assessment: implications for nurse educators and nursing practice*. *Int Nurs Rev*. 2007; 54: 166-172.
8. Yamauchi T. *Correlation between work experiences and physical assessment in Japan*. *Nursing and Health Sciences* 2001; 3: 213-224.
9. Giddens JF. *A Survey of physical assessment techniques performed by RNs: lessons for nursing education*. *Research Briefs* 2007; 46(2):83-87.
10. Secests JA, Norwood BR, Dumont PM. *Physical assessment skills: a descriptive study of what is taught and what is practiced*. *J Prof Nurs*. 2005; 21(2): 114-118.
11. Giddens JF. *Comparing the frequency of physical examination techniques performed by associate and baccalaureate degree prepared nurses in clinical practice: Does education make a difference?* *J Nurs Educ*. 2006; 45(3):136-139.
12. Giddens JF, Eddy L. *A survey of physical examination skills taught in undergraduate nursing programs: Are we teaching too much?* *J Nurs Educ*. 2009; 48(1):24-29.
13. Shin H, Kim B, Kang HS. *Use of Physical Assessment Skills and Education Needs of Advanced Practice Nurses and Nurse Specialists*. *J Korean Acad Nurs*. 2009; 39(5): 709-719.
14. Sony SD. *Baccalaureate nurse graduates' perception of barriers to the use of physical assessment skills in the clinical setting*. *J Contin Educ Nurs*. 1992; 23: 83-87.
15. Wales MA, Skillen DL. *Using scenarios as a testing method in teaching health assessment*. *J Nurs Educ*. 1997; 36(6): 256-262.

Corresponding Author

Zeliha Koç,  
Ondokuz Mayıs University Campus,  
Kurupelit,  
Samsun,  
Turkey,  
E-mail: zelihaceren@hotmail.com

# Premenstrual syndrome prevalence, and correlation with carbohydrate intake in young women

Rania A Hussein, Hafiz M, Bin-Afif S, Al-Omari E, Al-Helou M

King Abdulaziz University, Al Jamea district, Faculty of Applied Medical Sciences, Department of Clinical Nutrition, Kingdom of Saudi Arabia.

## Abstract

**Purpose:** A carbohydrate intake may be interpreted in terms of glycemic index, and glycemic load; carbohydrates may increase brain serotonin, and in turn, act to alleviate premenstrual symptoms.

**Methods:** a descriptive observational cross-sectional study was conducted at Faculty of Applied Medical Sciences.

We carried out the study in January, February 2011. Sample included 166 female students, 18–22 y of age. We assessed dietary carbohydrate intake using a self-administered, comprehensive food frequency questionnaire. Menstrual cycle symptoms were assessed using the retrospective version of the Moos.

**Results:** Refined sugars constituted 80% of total carbohydrate intake among the sample. There was a significant positive association between dietary glycemic load, and some of Moos distress questionnaire subscale scores (impaired concentration, behavioral change, autonomic reactions, and water retention) in the premenstrual phase. Caffeine intake correlated positively with autonomic reactions in the premenstrual phase.

**Conclusion:** A high carbohydrate intake may worsen premenstrual symptoms, if mainly composed of refined sugars. The extent to which carbohydrate quality correlates with premenstrual syndrome, may help confirm whether such nutritional treatment can be a reliable alternative to pharmacotherapy for women with mild to moderate premenstrual syndrome.

**Key words:** Dietary glycemic load; glycemic index; Refined sugars; Premenstrual symptoms; Moos Menstrual Distress Questionnaire.

## Introduction

Premenstrual syndrome, a common cyclic disorder of young and middle-aged women, is characterized by emotional and physical symptoms that consistently occur during the luteal phase of the menstrual cycle. <sup>(1)</sup>

The exact etiology of premenstrual syndrome (PMS) is probably a result of an interaction between sex steroids and central neurotransmitters. <sup>(2)</sup> The role of ovarian hormones is unclear, but symptoms often improve when ovulation is suppressed <sup>(3)</sup>. In addition, changes in hormone levels may influence centrally acting neurotransmitters such as serotonin. <sup>(4)</sup>

Mood improvement following carbohydrate ingestion is thought to occur via a tryptophan-mediated increase in serotonin, <sup>(5)</sup> potentially alleviating a functional deficiency in brain serotonin, and thus serving as self-medication. <sup>(6)</sup> However, compared to symptom-free women, PMS patients consume more sugar. <sup>(7)</sup>

So, we conducted our study to investigate the effect of dietary glycemic load (DGL) on manifestations of PMS.

## Participants and Methods

A Cross sectional study was conducted in January, February 2011.

Our target population was girls aged 18- 22 years, students in 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> years, at faculty of Applied Medical Sciences, Jeddah, Saudi Arabia. An official approval was obtained from Ethics committee review board of the faculty of Applied Medical Sciences.

Among a sample of 200 female students, we excluded married women, those with diagnosed endometabolic diseases such as diabetes and thyroid

diseases, those currently taking oral contraceptives or steroid hormones, those who had few or no menstruations during the preceding year, those currently receiving dietary counseling from a doctor or a dietitian, those taking vitamins (A, E, and B6), calcium, magnesium, multivitamin/ mineral supplements, or evening primrose oil, those taking nonprescription products that might contain diuretics, analgesics, prostaglandin inhibitors, and antihistamines.

In addition, some girls did not complete the survey questionnaires, or anthropometric measurements. The final sample comprised 166 girls.

The questionnaire comprised the following data:

#### 1. PMS assessment:

Menstrual cycle symptoms during the preceding month were assessed using the retrospective version of the Moos Menstrual Distress Questionnaire (MDQ). The MDQ consists of a total of 47 symptom items, which are grouped into eight subscales: pain, impaired concentration, behavioral change, autonomic reaction, fluid retention, negative affect, exciting, and non-specific adverse symptoms designed to detect those experiencing symptoms (control).<sup>(8)</sup>

Each symptom item was rated by each subject on a 5-point scale from 1 (no experience of the symptom) to 5 (disabling or incapacitating experience of the symptom), separately for the past menstrual cycle phase (menstrual, during menstrual flow; premenstrual, the week before the beginning of menstrual flow; and intermenstrual, remainder of cycle). The MDQ scores were calculated for each subscale and the total score for each cycle phase. The total and subscale MDQ scores in the premenstrual phase were expressed as percentages relative to those in the intermenstrual phase. A particular subscale symptoms were considered as present if the score exceeded 100%.

#### 2. Assessment of anthropometric variables

Body height was measured to the nearest 0.1 cm with the subject standing without shoes. Body weight in light indoor clothes was measured to the nearest 0.1 kg. Body mass index was calculated as body weight (kilograms) divided by the square of body height (meters).

#### 3. Dietary assessment

Dietary habits during the preceding month were assessed using a 3-page semi qualitative self-administered food frequency questionnaire (FFQ),

consisting of the following sections: consumption frequency and number of portion sizes of 23 of carbohydrate rich selected food and non alcoholic beverage items; consumption frequency and number of portion sizes of 14 protein rich foods and beverages, consumption frequency and number of portion sizes of 5 added fats, consumption and frequency of caffeinated beverages.

The food and beverage items were selected as foods commonly consumed in Saudi Arabia, Dietary glycemic index (DGI) was obtained from: "*The Glucose Revolution*".<sup>(9)</sup>

Glycemic load of each food was calculated by multiplying its GI by total daily carbohydrate intake per serving, then divided by 100. Glucose was used as the reference (GI for glucose= 100).

It has often been presumed that fiber will substantially reduce the glycemic response, although this supposition was not supported consistently by the experimental data.<sup>(10)</sup> We did not consider fiber content of the food in estimating GL. One study showed very little difference in the FFQ GL values for those estimated using available carbohydrate versus total carbohydrate, even for foods with modest fiber content such as whole-wheat breads and select fruits. One possible reason for this unexpected lack of influence of fiber is that in general, soluble fibers have greater effects on the glycemic response than do insoluble fibers, by reducing the rate of gastric emptying and intestinal absorption, resulting in a lower GI. However, the predominant sources of fiber in the FFQ-listed foods are insoluble.<sup>(11)</sup>

### Statistical analysis

Statistical analysis was performed using the Statistical Package of Social Sciences version 16.<sup>(12)</sup>

#### 1. Descriptive statistics:

At the end of the study, data obtained were coded, tabulated, and presented by arithmetic range, mean and standard deviation.

#### 2. Analytical statistics:

Data were analysed using the followings:

- a) Pearson's correlation
- b) Multiple Linear regression

## Results

**Table 1.** shows a description of anthropometric, menstrual, and dietary pattern of the whole sample.

**In table 2.,** subjects were categorized into quintiles according to MDQ total score. Means (SD) of

premenstrual symptoms subscale scores were categorized into quintiles according to MDQ total score.

The stepwise selection procedure in multiple regression analysis was used to select variables predictive of MDQ subscale scores.

*Table 1. Anthropometric, menstrual, and dietary pattern of the sample:*

Variable	Range	Mean (SD)
Height in (m)	1.4-1.7 m	1.5 (6.1) m
Weight in (Kg)	40-100 kg	54.1 (10.7) kg
Body Mass Index in (Kg/m <sup>2</sup> )	15.6-39.1	21.7 (3.8)
Age at menarche (years)	10-17	13.3 (1.3) years
cycle length (days)	14-90	27 (7.3) days
number of bleeding days	4-15	6.7 (1.5) days
Pain score	58.3-350	154 (57.1)
Impaired Concentration score	66.6-400	126.8 (47.6)
Behavioral changes score	21.7-500	153.3 (74.3)
autonomic reaction score	30.7-400	123 (59.4)
Water retention score	61.5-400	148.2 (55.5)
Negative affect score	45.8-500	161.2 (68.5)
Exciting score	36.8-500	118.4 (49.3)
Undefined symptoms score	47-280	109.2 (26.4)
MDQ total score	52.8-365.2	134.6 (38.1)
Caffeine Intake in (mg)	0-342	67.8 (65.3) mg
Dietary glycemic load	36.4-346.3	90.5 (47.01)
Dietary glycemic index	44.2-85.9	59.9 ( 5.7)
Refined carbohydrate (g)	41-479.3	129.9 (72.3) g
Non refined carbohydrate (g)	0- 210	31.6 (34.1) g
Number of protein servings	0.1-14.8	3.3 ( 2.3)

*Table 2. Regression of MDQ score with different subscale scores quintiles*

	Quintiles of MDQ total score in the premenstrual phase					(Beta)
	1 (n= 33)	2 (n= 33)	3 (n= 33)	4 (n= 34)	5 (n= 33)	
MDQ percentile total score	96.8 (12.4)	111.5(4.2)	126.8( 4.2)	144.2 ( 7.4)	193 (38.8)	
Pain	111.2( 35.7)	134.6 (32.4)	151 .1 (36.3)	172.4 (54.7)	202 (70.2)	0.2***
Impaired Concentration	100.1 (12.4)	100.8 (11.6)	119 (23.4)	129.9 (28.8)	169.5 (67.1)	0.2***
Behavioral changes	101.2 (28.4)	117.1 (22.1)	134.4 (32.5)	154.9 (34.5)	242.2 (102.8)	0.1***
autonomic reaction	93 (22.7)	104.4 (23)	110.9 (28.4)	115.3 (27.9)	184.1 (91.5)	
Water retention	101.5 (20.4)	135 (36.3)	149.4 (41)	160 ( 41.2)	214.8 (70.8)	0.1**
Negative affect	100.8 (16.2)	133 (34.6)	145.2 (33.4)	183.4 (40.6)	248.4 (89.5)	0.3***
Exciting	96.5 (27.3)	95.3 (19.6)	110.1 (25.5)	123.9 (37.3)	166.2 (80.2)	
Undefined symptoms	96.1 (18.5)	100.6 (7.4)	106.2 (17.6)	117.5 (26.3)	130 (43)	

MDQ: menstrual distress questionnaire. MDQ total and subscale scores in the premenstrual phase were expressed as percentages relative to those in intermenstrual phase

All reported P values are 2-tailed

\*: correlation is significant at the 0.05 level ( 2- tailed )

\*\*: correlation is significant at the 0.01 level ( 2- tailed )

\*\*\*: correlation is significant at the 0.001 level ( 2- tailed )

Values are Means (SD)

A multiple linear regression analysis was used (stepwise selection procedure).



Variables selected as predictive for MDQ total score were negative affect, impaired concentration, pain, behavioral change, and fluid retention. The R<sup>2</sup> indicates that 71.4 % of the variation in MDQ total score is explained by these 5 variable .

As regards the correlation between dietary, anthropometric, and PMS variables, there was a weak positive (still significant) correlation between DGL and three of premenstrual manifestations, namely impaired Concentration, behavioral changes, and autonomic reaction (r= 0.2, 0.2, and 0.3 respectively), and a negligible positive correlation with fluid retention (r= 0.1). By far, DGI did not correlate significantly with any other variables (except with DGL).

In addition, a negligible significant positive correlation (still significant) was observed between caffeine intake, and both BMI and autonomic reaction (r= 0.1 in both). (table 3.)

Figure 1 shows that 89% of our sample experienced at least one symptom of PMS.

**Discussion**

In our study, age of girls ranged between 19 and 22 years, 89% of them experienced at least one symptom. This is nearly consistent with Pray W S, Pray J J study, who found that approximately 40% to 90% of females report symptoms of PMS. (13)Several series have also reported that premen-

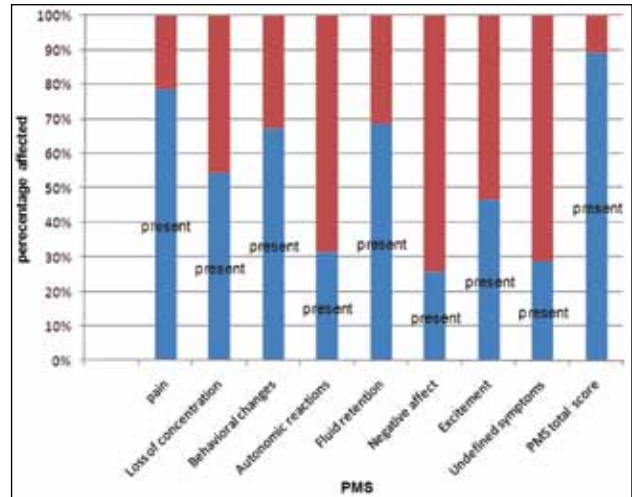


Figure 1. Prevalence of different PMS total and subscale symptoms among the whole sample

strual syndrome is more common among young, urban literate women, especially among those involved in professional studies, than older, rural and illiterate women. This may be related to an increased level of perception and reporting of these symptoms in this group. (14)

In our study, five subscales were highly significant predictors of MDQ total score: namely negative affect, impaired concentration, pain, behavioral change, and fluid retention . They could explain 71.4% of MDQ total score variation (table II).

On the contrary, excitement scored very low (mean (SD)= 118.4(49.3). This is consistent with

Table 3. Correlation between dietary, anthropometric, and PMS variables

Variables	Caffeine	DGL	DGI	Protein servings	Fat servings
BMI (Kg/m <sup>2</sup> )	0.1*	-0.0	-0.0	0.0	-0.0
Pain	0.0	-0.0	0.0	-0.1	0.0
Impaired Concentration	0.0	<b>0.2**</b>	0.0	0.1	0.0
Behavioral changes	-0.0	<b>0.2*</b>	0.0	0.0	-0.0
autonomic reaction	0.1*	<b>0.3**</b>	-0.0	0.0	-0.0
Water retention	0.0	<b>0.1*</b>	-0.0	0.0	0.0
Negative affect	0.0	-0.0	0.0	-0.0	-0.0
Exciting	0.1	<b>0.0</b>	-0.0	0.0	-0.0
Undefined symptoms	0.0	<b>0.1</b>	-0.1	0.1	-0.1
<b>MDQ total score</b>	0.0	<b>0.1</b>	0.0	-0.0	-0.0

MDQ: menstrual distress questionnaire

MDQ total and subscale scores in the premenstrual phase were expressed as percentages relative to those in intermenstrual phase

Values are Pearson's r correlation coefficients

All reported P values are 2 -tailed

\*: correlation is significant at the 0.05 level ( 2- tailed )

\*\* : correlation is significant at the 0.01 level ( 2- tailed )

a previous observation showing that women who are satisfied with their lives are more likely to consider the perimenstrual symptoms as affirming, whereas those who are unhappy interpret the same symptoms negatively.<sup>(15)</sup> Accordingly, the reports of reduced excitement during the perimenstrual phase for girls in the present study are not surprising, since most of them were in good physical condition, and, given the nature of their participation in the study, were concerned with their health.

Refined sugars and carbohydrates constituted about 80% of total carbohydrate intake of our sample. Compared to symptom-free women, PMS patients consume more refined sugar, refined carbohydrates, sodium, and dairy products and less B vitamins, iron, zinc, and manganese.<sup>(7)</sup>

Refined sugars provide calories, but lack vitamins, minerals, and fiber. Such simple sugars are often called "empty calories" and can lead to weight gain.<sup>(16)</sup> It has been found that, over time, the consumption of refined sugar may deplete the body of its reserves of chromium, manganese, zinc, magnesium, and most of the B vitamins because these nutrients are required for the metabolism of glucose.<sup>(7)</sup> Sugar also increases the tendency to hypoglycemia, particularly premenstrually, giving rise to sugar cravings, irritability, and headaches.<sup>(7)</sup> Moreover, refined sugar triggers insulin release, suppressing ketoacid formation and thereby causing decreased kidney clearance of excess sodium and water.<sup>(7)</sup>

Researchers have long suggested that gonadal steroids are also involved in the pathophysiology. Symptoms are absent during non-ovulatory cycles, abolished by ovariectomy, and reinstated by administration of exogenous hormones.<sup>(17)</sup>

Refined sugars lack fiber, and several mechanisms have been proposed for the effect of dietary fiber on estrogen metabolism. These include alteration in enterohepatic circulation of estrogen, which leads to increased fecal estrogen excretion by binding of deconjugated estrogen,<sup>(18)</sup> and suppression of gonadotrophin production<sup>(19)</sup> by direct action on the hypothalamic pituitary gonadal system.<sup>(20)</sup> It was hence logic to find in our study a positive correlation between DGL (with 80% as refined sugars) and impaired Concentration, behavioral changes, autonomic reactions, and water retention.

Indeed, there are a substantial number of unresolved questions related both to the ability to measure GI from the diet and to the clinical interpretation of GI as it relates to PMS risk. For example, person-specific variables such as individual variation in postprandial glucose response, as well as food-specific variables including the influence of food processing and preparation, and the lack of data on GI of mixed meals raise important questions about the validity of GI and its public health relevance.<sup>(10)</sup>

Almost no data exist on whether there is heterogeneity of glycemic response among persons who are obese versus lean. In addition, measuring the glycemic index is not always practical or realistic because there is no universally recognized objective measure of carbohydrate quality (e.g., GI).<sup>(11)</sup> Interestingly, the views of some investigators supporting the reduced consumption of high-GI foods as an effective prevention strategy for lowering the risk of diseases,<sup>(21)</sup> are supported by data from human experimental studies of single test foods.<sup>(22)</sup>

### *Caffeine Intake and PMS*

Caffeine intake in this study showed a significant positive association with autonomic reactions (table III). Instability of the autonomic nervous system, therefore, could induce broadly ranged psychophysiological phenomena, such as premenstrual symptomatology.<sup>(23)</sup> Kondo et al. measured the coefficient of variation of R-R interval during the menstrual cycle, and demonstrated that the parasympathetic nerve activity was lower in the late luteal phase than in the follicular phase in women with PMS.<sup>(24)</sup>

Caffeine activates noradrenaline neurons and seems to affect the local release of dopamine.<sup>(25)</sup> Moreover, it increases energy metabolism throughout the brain but decreases at the same time cerebral blood flow, inducing a relative brain hypoperfusion.<sup>(25)</sup> Hence caffeine may be responsible for induction of more imbalance in the Sympathetic and parasympathetic divisions of the autonomic nervous system,<sup>(25)</sup> and therefore be positively associated with autonomic reactions of PMS.

In our study, caffeine effect was equivocal on impaired concentration, behavioral changes, negative affect, and excitement (table III). The explanation is that caffeine kinetics are nonlinear: the

plasma concentration versus response relationship revealed concentration-dependent increases in anxiety and improvements in cognitive and motor performance at low to intermediate concentrations; whereas the unfavorable effects, were associated with high doses of caffeine.<sup>(26)</sup>

Surprisingly a significantly positive correlation was found between caffeine intake and BMI. Caffeine has been well known as an Appetite suppressant.<sup>(27)</sup> So, it might be possible that overweight and obese girls were consuming more coffee in an attempt to lose weight.

### **Age at Menarche**

According to the present study, age at menarche ranged between 10 and 17 years, with a mean of 13.3 (1.3) years. This is consistent with a study done in Saudi Arabia in 2004, showing that the mean age at menarche of Saudi girls was 13.1 years.<sup>(28)</sup>

Age at menarche in this study showed a non significant negative association with PMS total score, as well as with pain, fluid retention, and negative affect (table 3).

Girls who menstruate younger take on responsibilities at a younger age, both during pregnancy (inside and outside of marriage) and in the work market, assuming adult roles.<sup>(29)</sup>

### **References**

1. Dickerson LM, Mazyck PJ, Hunter MH (2003). Premenstrual syndrome. *Am Fam Physician*; 67, 8:1743-52.
2. Braverman P K (2007). Premenstrual syndrome and premenstrual dysphoric disorder. *J Pediatr Adol Gynec*; 20:3-12.
3. Freeman EW, Sondheimer SJ, Rickels K (1997). Gonadotropin-releasing hormone agonist in the treatment of premenstrual symptoms with and without ongoing dysphoria: a controlled study. *Psychopharmacol Bull*;33:303-9.
4. Kendler KS, Karkowski LM, Corey LA, Neale MC (1998). Longitudinal population-based twin study of retrospectively reported premenstrual symptoms and lifetime major depression. *Am J Psychiat*; 155:1234-40
5. Gendall KA, Joyce PR (2000). Meal-induced changes in tryptophan: LNAA ratio: effects on craving and binge eating. *Eat behav*;1:53-62.
6. Pijl H, Koppeschaar HP, Cohen AF, Iestra JA, Schoemaker HC, Frolich M (1993). Evidence for brain serotonin-mediated control of carbohydrate consumption in normal weight and obese humans. *Int J Obesity*;17:513-20.
7. Mayo J L (1999). Premenstrual Syndrome: A natural approach to management Applied nutritional science reports. CNI 5 (6) Available at [http://www.healing-points.com/Premenstrual\\_Syndrome.PDF](http://www.healing-points.com/Premenstrual_Syndrome.PDF). Accessed 20/4/2011.
8. Moos RH (1968). The development of a menstrual distress questionnaire. *Psychosom Med*;30, 6:853-67.
9. Brand-Miller J, Wolever T.M.S, Colagiuri S, Foster-Powell K(1999). Glycemic index, carbohydrate and fat. *The glucose revolution: the authoritative guide to the glycemic index : the groundbreaking medical discovery.* Marlowe and company 1<sup>st</sup> edition.
10. Pi-Sunyer FX (2002). Glycemic index and disease. *Am J Clin Nutr*;76: 290S-8S.
11. Neuhaus M L, Tinker LF, Thomson C, Caan B, Horn L V, Snetselaar L (2006). Development of a glycemic index database for food frequency questionnaires used in epidemiologic studies. *J Nutr*; 136, 6:1604-9
12. Fiddler L, Hecht L, Nelson EE, Nelson EN, Ross J. SPSS for Windows 16.0: A Basic Tutorial. Social Science Research and Instruction Center. California State University. Accessed 25/8/2011. Available at <http://www.ssrc.org/trd/spss16>.
13. Pray WS, Pray JJ. Menstrual cycle-related discomforts. *Medscape2005*.available at <http://www.medscape.com/viewarticle/513070> accessed 5/5/2011.
14. Marvan ML, Diaz-Erosa M, Montesinos A (1998). Premenstrual symptoms in Mexican women with different educational levels. *J Psychol*; 132:517-26.
15. Cleckner-Smith CS, Doughty AS, Grossman JA (1998).Premenstrual symptoms: prevalence and severity in an adolescent sample. *J Adolescent health*;22:403-8.
16. Farrell JJ (2010). Digestion and absorption of nutrients and vitamins. In: Feldman M, Friedman LS, Brandt LJ (eds). *Sleisenger and Fordtran's gastrointestinal and liver disease. 9th ed.* Philadelphia Saunders Elsevier:chap 100.
17. Schmidt PJ, Nieman LK, Danaceau MA, Adams LF, Rubinow DR (1998). Differential behavioral effects of gonadal steroids in women with and in those without premenstrual syndrome. *New Engl J Med*;338: 209-16.

18. Arts CJM, Govers CARL, Van den Berg H, Wolters MGE, Van Leeuwen P, Thijssen JHH (1991). *In vitro* binding of estrogens by dietary fiber and the *in vivo* apparent digestibility tested in pigs. *J Steroid Biochem*; 38: 621–8.
19. De Ridder CM, Thijssen JHH, Van't Veer, Duurn RV, Bruning PF, Zonderland ML (1991). Dietary habits, sexual maturation, and plasma hormones in pubertal girls: a longitudinal study. *Am J Clin Nutr*; 54: 805–13.
20. Koo M, Rohan T, Jain M, McLaughlin J, Corey P (2001). A cohort study of dietary fiber intake and menarche. *Public Health Nutr*: 353-60.
21. Ludwig DS (2002). The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *JAMA*; 287: 2414–23.
22. Brand-Miller JC, Thomas M, Swan V, Ahmad Z, Petocz P, Colagiuri S (2003). Physiological validation of the concept of glycemic load in lean adults. *J Nutr*; 133: 2728–32.
23. Matsumoto T, Ushiroyama T, Kimura T, Hayashi T, Moritani T (2007). Altered autonomic nervous system activity as a potential etiological factor of premenstrual syndrome and premenstrual dysphoric disorder. *Biopsychosocial Medicine* 1:24
24. Kondo M, Hirano T, Okamura Y (1989). Changes in autonomic nerve function during the normal menstrual cycle measured by the coefficient of variation of R-R intervals. *Acta Obstet Gyn Jpn*; 41:513-8.
25. Nehlig A, Daval JL, Debry G (1992). Caffeine and the central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects. *Brain Res Rev*; 17, 2:139-70.
26. Kaplan GB, Greenblatt DJ, Ehrenberg BL, Goddard JE, Cotreau MM, Harmatz JS (1997). Dose-dependent pharmacokinetics and psychomotor effects of caffeine in humans. *J Clin Pharmacol*; 37, 8: 693-703.
27. National Institute of Health. Caffeine in the diet . Medlineplus2011. Available at <http://www.nlm.nih.gov/medlineplus/ency/article/002445.htm>. Accessed 5/7/2011
28. Babay ZA, Addar M H, Shahid K, Meriki N (2004). Age at menarche and the reproductive performance of Saudi women. *Ann Saudi Med*: 354- 6.
29. Silva CM, Gigante DP, Minten GC (2008). Premenstrual symptoms and syndrome according to age at menarche in a 1982 birth cohort in southern Brazil. *Cad Saude Publica* ; 24, 4: 835-44

Corresponding Author  
 Rania Abd El Hamid Hussein,  
 'King Abdulaziz University,  
 Al Jamea district,  
 Faculty of Applied Medical Sciences,  
 Department of Clinical Nutrition,  
 Jeddah,  
 Kingdom of Saudi Arabia,  
 E-mail: rahussein2002@yahoo.com

# A snapshot of primary care physicians educational needs regarding COPD in Crete, Greece: an exploratory case study

Nikolaos I. Kakoliris<sup>1\*</sup>, Emmanouil K. Symvoulakis<sup>1</sup>, Katerina M. Antoniou<sup>2</sup>, Ilias Grammatikopoulos<sup>1</sup>, Nikolaos Tzanakis<sup>2</sup>, Nikolaos M. Siafakas<sup>2</sup>, Christos Lionis<sup>1</sup>

<sup>1</sup> Clinic of Social and Family Medicine, Faculty of Medicine, University of Crete, Greece,

<sup>2</sup> Department of Thoracic Medicine of the University General Hospital of Heraklion, Greece.

## Abstract

**Aim:** Misdiagnosis of Chronic Obstructive Pulmonary Disease (COPD) in primary health care appears to be common. The objective of this exploratory case study was to describe the self-reported level of knowledge regarding COPD among primary healthcare physicians, before and after a two day intensive educational course.

**Method:** Nine primary health care physicians, eight serving different rural areas of the island of Crete and one in the wider area of Athens (Greece), were invited to a two day educational course on COPD. Questionnaires were used to stratify the level of physicians' knowledge before and after the course. Utility and suitability of this educational experience was also assessed at the end of the course.

**Results:** Topics such as the ability to perform spirometry and the management of smokers in primary care achieved the greater median score variation before and after course [from 2.0 to 5.0 ( $P=0.010$ ) and from 3.0 to 6.0 ( $P=0.011$ ), respectively]. There was a statistical significant difference between the median scores in pre- and post-course responses indicating an immediate positive impact due to the course.

**Conclusion:** These preliminary results showed that a brief and intensive educational course among primary health care physicians, could have a benefit in improving their level of knowledge regarding COPD.

**Key words:** education, primary care, COPD, exploration

## Introduction

The mortality rate due to Chronic Obstructive Pulmonary Disease (COPD) has continued to in-

crease and currently stands as the fourth leading cause of death in the United States [1]. In recent years, new treatments and evidence-based algorithms [2, 3] have been introduced to help manage COPD. It has been estimated that 24 million adults in the United States alone have COPD, but more than 50% of them are either misdiagnosed or undiagnosed [3].

Many studies have been accomplished that highlight the large amount of undiagnosed COPD in general practice settings [4-7]. According to the literature, to raise awareness of the disease among primary care physicians and patients is considered as an urgent need [8]. This requires education and empowerment. A recent medical audit, from rural Crete, reported that the majority of the diagnosed patients with COPD had received inadequate advice on quitting smoking and the disease itself [9]. Considering the above study findings, the advantages of even a short term educational initiative for primary health care professionals, may prove to be of considerable benefit [10-13].

In regards to COPD, a two day intensive educational course and training session was developed at the University of Crete. This course was designed by using information retrieved with rapid appraisal techniques so as to focus on concrete primary health care educational needs. As Murray *et al.* suggested, an expanded primary care team can use these techniques in order to meet the local health or social needs and to translate them into policy making actions [14]. The aim of this exploratory case study was to report on the pre- and post-course knowledge perception among the participating primary care physicians in regards to COPD. The emerging findings can create a case discussion between primary and secondary care for future multidisciplinary research and clinical collaboration.

## Materials and Methods

### *Study participants*

To fulfill the requirements of this educational intervention, qualified general practitioners serving rural or semi-rural areas were among the participants. Taking into account that the working conditions within the different practices of the public network were similar in terms of infrastructure and functional process, a convenience sample of primary care physicians was formed. A single group pre-test/post-test design was used for this exploratory study [15].

Nine primary health care physicians (PHCPs) were recruited to attend an educational course on COPD. Eight of these participants came from five primary health care centres of Crete and one from a primary health care centre of the greater area of Athens (Greece). Female and male participants were five and four respectively. The mean age was 40.3 years (SD: 5.7 years) and their mean work experience as GPs was 8.1 years (SD: 3.2 years). Ethical approval was received from the Ethics Committee of the University General Hospital of Heraklion. (No Protocol 81/20.07.2005).

### *The educational course*

All of the participating physicians attended an intensive two day educational course on COPD, focusing on prevention, diagnosis and disease management.

The contents of this course, in terms of relevance to general practice, were chosen by using qualitative approaches, literature sources and expert opinions, through triangulation, prior to course implementation [16]. A conceptual framework was shaped by integrating thorough literature information and seeking specialists opinion [17,18].

During the course, lectures were given by chest physicians, from the Department of Thoracic Medicine of University of Crete and by a PHCP with special interest in respiratory diseases.

On the first day, the course was focused on the following topics:

- a. Definition and pathogenesis of COPD
- b. Measures of assessment, monitoring of COPD patients, and goals of therapy
- c. Initial assessment, diagnosis, differential diagnosis versus asthma and periodic follow-up of patients

- d. Preventive issues
- e. Pharmacological therapy
- f. Stages of severity of COPD according to GOLD guidelines (3) and stepwise approach
- g. Patient education

On the second day, there were educational initiatives on performing spirometry and then the participants were given the opportunity to practice the technique.

### *Questionnaires*

Two questionnaires were used and completed anonymously (Table 1). Questionnaire A included seven clinical topics derived from the GPs' reported needs and selected in terms of appropriateness and relevance to the study purpose. Questionnaire A appraised the level of knowledge immediately before and after the educational course. The questionnaire included seven questions using a Likkert scale (grade from 1 to 7): one being the lowest and seven the maximum grade of positive response. The purpose of questionnaire B was to evaluate the utility and the suitability of the course itself (evaluation form). This was achieved by asking for the opinion of the participants on each scientific area covered in this seminar. Questionnaire B also included items evaluating technical features such as mode, duration, and organization of the program as shown in Table 1. Due to the fact that our goal was process evaluation, the above responses were collected after the completion of the course.

*Table 1. Questionnaire forms used*

#### **A: Level of knowledge before and after the 2-day educational course (Likkert scale-seven grade)**

1. Theoretical knowledge for the COPD management
2. Differential diagnosis between COPD and asthma
3. The ability of performing spirometry
4. Assessment of the spirometry results
5. The management of smokers in Primary Health Care
6. Instructions for smoking cessation
7. Counseling and treating smokers

### B: Utility and suitability after the 2-day educational course (Likkert scale-seven grade)

1. Theoretical knowledge for the COPD management
2. Differential diagnosis between COPD and asthma
3. The ability of performing spirometry
4. Assessment of the spirometry results
5. The management of smokers in Primary Health Care
6. Instructions for smoking cessation
7. Counseling and treating smokers
8. The educational mode
9. The duration of educational program
10. The organization of educational program

#### Statistical analysis

For each item of questionnaire A, differences between median scores (pre- and post-course) were assessed using the Wilcoxon test (non parametric test for matched pairs). A *p* value of less than 0.05 was considered statistically significant.

#### Results

The median scores within the domains of the questionnaire A, before and after the course, are shown in Table 2. The ability of performing spirometry (item 3) achieved the lower median score before the educational course while the differential diagnosis between COPD and asthma (item 2) achieved the higher pre-course median score.

The differences between the median scores for each of the domains in pre- and post-course phases were statistically significant ( $P < 0.05$ ) and are shown in Table 2.

In regards to questionnaire B, the median scores for all topics explored were high (Table 3). The organization (item 10) and duration of the educational program (item 9) achieved the lower median scores. The item focusing on the management of smokers in primary health care (item 5) achieved the higher median score in terms of utility, while the assessment (interpretation) of the spirometry results (item 4) achieved the higher median score in terms of suitability.

Table 3. Questionnaire B-Utility and suitability after the 2-day educational course

Question labels	Utility	Suitability
	Median	Median
Theoretical knowledge for COPD management	6.0	6.0
Differential diagnosis between COPD and asthma	6.0	6.0
Ability of performing spirometry	6.0	6.0
Assessment of spirometry results	7.0	7.0
Management of smokers in primary health care	6.0	7.0
Instructions for smoking cessation	6.0	6.0
Counseling and treating smokers	6.0	6.0
The educational mode	6.0	6.0
The duration of educational program	6.0	5.0
The organization of educational program	5.0	6.0

Table 2. Questionnaire A-Level of knowledge before and after the 2-day educational course

Question labels	Participants	Pre –course rated level	Post-course rated level	<i>P</i>
	N	Median	Median	
Theoretical knowledge for COPD management	9	4.0	6.0	0.011
Differential diagnosis between COPD and asthma	9	5.0	6.0	0.023
Ability of performing spirometry	9	2.0	5.0	0.010
Assessment of spirometry results	9	4.0	6.0	0.006
Management of smokers in primary health care	9	3.0	6.0	0.011
Instructions for smoking cessation	9	4.0	6.0	0.017
Counseling and treating smokers	9	4.0	6.0	0.011

## Discussion

Primary care physicians should be on the frontlines in both, the prevention and early diagnosis of this deadly chronic disease and should take the lead in implementing spirometry and core recommendations of the latest management guidelines. However, these crude results re-enforce previously reported findings that certain areas of knowledge within primary care physicians in rural Crete (Greece) need improvement [9,11]. For instance, the widest gap between pre- and post-course responses was registered in relation to the ability to perform spirometry and to manage smoking cessation in primary care. This study can not assess how much impact the lack of knowledge or the patient-physician relationship hold in these findings. Misdiagnosis of COPD is a missed opportunity to intervene early and alter the disease course. Therefore further knowledge can only bring positive results. The findings of this exploratory study should be treated with great attention since a convenience sample of participants inevitably leads to some concerns and weaknesses when issues of generalisation are discussed. It is also truth that one would expect an increase in self-reported knowledge from pre-test to immediate post-test given the fact that the recall period was too short. This may represent a major study limitation.

One of the weaknesses of asking for the clinician's perception of their knowledge, is their reported perception does not differentiate the clinician who is very knowledgeable, but modestly reports an underestimation of their true knowledge from those who are over-confident but less knowledgeable. The latter expression of perception of knowledge is quite concerning. It appears what this study demonstrated was that the attendees confirmed the topics of the course were beneficial (utility & suitability), but whether behaviour changed, is not known with the methods used. However, in a recent phone interview (and three years after the educational course), all participants declared that carry out spirometry in their settings and only one that still has difficulty in reading and interpreting spirometry. They also reported that they manage patients with COPD without performing unnecessary referrals. Even such responses can not provide a gauge of sustained knowledge

recall, may indirectly suggest the long term usefulness of the undertaken educational course.

Greece has got one of the highest levels of tobacco smoking in Europe [19]. The first population-based study on the epidemiology of COPD that was carried out in Greece, showed that the average prevalence of COPD among people older than 35 years, with a smoking history of > 100 cigarettes per lifetime, was 8.4% [20]. The findings of this study can be used to actively promote actions towards prevention and management of COPD at a national level. Very close attention should be given to the rural and remote primary health care settings in Greece. Considering that this country is made up of hundreds of islands this endeavour becomes even more challenging.

As mentioned above, participants were recruited from rural primary care settings. Limited national data suggest that rural areas show a different COPD occurrence pattern in comparison with urban settings [20]. In particular, COPD among men in urban areas was 7.1% as opposed to 15.1% in men from rural areas, whereas among women the highest rate (9%) was observed in urban settings and the lowest (1.7%) in rural areas [20]. This observation could be partially explained by the different patterns in smoking habits, and by risk factors other than active smoking contributing differently within each geographic area [20,21]. However, more studies are required to investigate geographic or (micro)environmental factors in order to provide new insights into the epidemiology and pathogenesis of COPD in Greece. The primary care role should be shaped to effectively meet these clinical and research challenges. Furthermore, diagnosis of COPD could reduce the disease burden on the patient's future life. This could be achieved by implementing symptomatic pharmacotherapy, prevention of exacerbations and pulmonary rehabilitation [22]. Recent findings showed that over 60% of undiagnosed COPD patients had already moderate to severe disease [7, 23,24].

Smoking cessation and the use of spirometry in primary care could greatly influence the natural history of COPD [25]. Spirometry remains the "gold standard" for diagnosing COPD and for monitoring the progression of the disease [3]. The ability to perform spirometry has been significantly improved in our group after the course. In addition, the ability to assess spirometry results (item 4) achieved the higher median score in terms of suitability within



the questionnaire B. Although spirometry is fundamental for the diagnosis and management of COPD it is used far less than it could [26]. Neglecting to use routine spirometry, in the evaluation of smokers and ex-smokers, leads to underdiagnosis of early COPD. Accessibility of hand-held office spirometers to general practitioners and their staff is an important instrument in the early diagnosis of asymptomatic patients with COPD [27]. With adequate training, and correct utilisation of spirometry, patients with obstructive airway disease can also be detected much earlier [28]. Moreover, evidence of the positive effects of the usage of spirometry has also been reported [29]. Utility of spirometry in confirming or excluding obstructive airway disease under 'primary care conditions', in rural areas, is a fundamental tool in the diagnosis and treatment of chronic respiratory disorders [30].

Smoking cessation in patients with COPD is of paramount importance. It is more likely for smokers to quit after diagnoses of airway disease through spirometry [31]. Despite the continuation of airway inflammation in COPD among ex smokers [32], the annual decline in FEV<sub>1</sub> approaches that in healthy non smokers [33]. There is also a remarkable reduction of deaths caused by diseases such as lung cancer, myocardial infarction, and stroke in sustained non smokers compared with those in current smokers [34,35]. Using spirometry to detect airway obstruction in smokers, as well as advising them on the benefits of quitting, potentially reduces the burden of COPD.

Item 2 in questionnaire A (diagnosis between COPD and asthma) has achieved the highest pre-course score. It is a paradox because this differential diagnosis is based on the ability to perform spirometry. The cardinal symptoms of COPD, including dyspnea, cough, and sputum production, overlap with many other respiratory diseases such as asthma [36]. In order to explain this paradox we need to clarify the rate of misdiagnosed and over diagnosed patients for each illness in primary health care. In addition, broad introduction in the primary care setting still needs further justification in the form of a proper cost effectiveness analysis as favourable long-term effects on exercise tolerance and quality of life have been recently demonstrated [37].

The predominant message is that this educational course had a positive immediate impact on

the level of knowledge among the participants regarding COPD. This exploratory study can guide the design and testing of joint educational programs in Greece. This can be done by promoting multidisciplinary collaboration and enabling primary care physicians to better focus on the management of chronic diseases such as COPD.

### Acknowledgments

We thank Dr Alegakis A. for his advice in statistical analysis. We also thank Dr Tsiligianni I. and Mrs Moraitaki D. for their contribution in the educational course. This study was supported by a grant from ASTRA-ZENECA.

### References

1. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance—United States, 1971- 2000. *Respir Care*. 2002; 47:1148-1149.
2. Celli BR, MacNee W, for the ATS/ERS Task Force. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*. 2004;23: 932-946.
3. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. [<http://www.goldcopd.com/>].
4. Renwick DS, Connolly MJ. Prevalence and treatment of chronic airways obstruction in adults over the age of 45. *Thorax*. 1996;51(2):164-8.
5. Dickinson JA, Meaker M, Searle M, Ratcliffe G. Screening older patients for obstructive airways disease in a semi-rural practice. *Thorax*. 1999;54(6):501-5.
6. Van Schayck CP, Loozen JM, Wagena E, Akkermans RP, Wesseling GJ. Detecting patients at a high risk of developing chronic obstructive pulmonary disease in general practice: cross sectional case finding study. *BMJ*. 2002;324(7350):1370.
7. Tinkelman DG, Price D, Nordyke RJ, Halbert RJ. COPD screening efforts in primary care: what is the yield? *Prim Care Respir J*. 2007;16(1):41-8.
8. Voelkel NF. Raising awareness of COPD in primary care. *Chest*. 2000; 117 (5 Suppl 2): 372S-5S.
9. Kotsoni C, Antonakis N, Markaki A, Lionis C. Do patients with chronic obstructive pulmonary disease receive smoking cessation advice and interventions in rural Crete? Report from a medical audit study. *Aust J Rural Health*. 2008; 16 (6): 385-6.
10. Yawn BP, Wollan PC. Knowledge and attitudes of family physicians coming to COPD continuing medical education. *Int J Chron Obstruct Pulmon Dis*. 2008;3(2):311-7.

11. Rovithis E, Lionis C, Schiza SE, Bouros D, Karokis A, Vlachonikolis I, Siafakas NM. Assessing the knowledge of bronchial asthma among primary health care physicians in Crete: a pre- and post-test following an educational course. *BMC Med Educ.* 2001;1:2.
12. Ruiz Espiricueta JE, González Diaz SN, Rodríguez GG, Cruz AA, Canseco Villarreal C, Valdez Ramirez MA. Assessment of an educational course on asthma for primary care physicians. *Rev Alerg Mex.* 2005;52(2):83-9.
13. Haque AS, Zubairi AB, Shiraz A, Zuberi F, Karim SI, Pervez R, Awan S. Asthma knowledge and approach among Pakistani family physicians and the impact of an educational programme. *Int J Tuberc Lung Dis.* 2007;11(11):1260-5.
14. Murray SA, Tapson J, Turnbull L, McCallum J, Little A. Listening to local voices: adapting rapid appraisal to assess health and social needs in general practice. *BMJ.* 1994;308(6930):698-700.
15. Crites GE, Schuster RJ. A preliminary report of an educational intervention in practice management. *BMC Med Educ.* 2004; 4:15
16. Murray SA. Experiences with "rapid appraisal" in primary care: involving the public in assessing health needs, orientating staff, and educating medical students. *BMJ.* 1999;318(7181):440-4.
17. Parsian Nasrin, Dunning T. Developing and validating a questionnaire to measure spirituality: a psychometric process. *Global Journal of Health Science.* 2009;1(1): 2-11.
18. Kakoliris N, Grammatikopoulos I, Alegakis T, Tzanakis N, Lionis C. Designing an educational program for GPs regarding issues of COPD management in Greece [Abstract in Greek]. 19<sup>o</sup> Hellenic Congress of General Practice 2007, Abstract Book: 157.
19. WHO report on the global tobacco epidemic, 2008. [[http://www.who.int/tobacco/mpower/mpower\\_report\\_prevalence\\_data\\_2008.pdf](http://www.who.int/tobacco/mpower/mpower_report_prevalence_data_2008.pdf)].
20. Tzanakis N, Anagnostopoulou U, Filaditaki V, Christaki P, Siafakas N; COPD group of the Hellenic Thoracic Society. Prevalence of COPD in Greece. *Chest.* 2004;125(3):892-900.
21. Tzonou A, Maragoudakis G, Trichopoulos D, Zavitsanos X, Dimopoulou I, Toupadaki N, Kremastinou J. Urban living, tobacco smoking, and chronic obstructive pulmonary disease: a study in Athens. *Epidemiology.* 1992;3(1):57-60.
22. Rennard SI. Treatment of stable chronic obstructive pulmonary disease. *Lancet.* 2004;364(9436):791-802.
23. Takahashi T, Ichinose M, Inoue H, Shirato K, Hattori T, Takishima T. Underdiagnosis and undertreatment of COPD in primary care settings. *Respirology.* 2003;8(4):504-8.
24. Buffels J, Degryse J, Heyrman J, Decramer M; DIDASCO Study. Office spirometry significantly improves early detection of COPD in general practice: the DIDASCO Study. *Chest.* 2004;125(4):1394-9.
25. Radin A, Cote C. Primary care of the patient with chronic obstructive pulmonary disease-part I: front-line prevention and early diagnosis. *Am J Med.* 2008;121(7 Suppl):S3-12.
26. Damarla M, Celli BR, Mullerova H, Pinto-Plata V. Discrepancy in the use of confirmatory tests in patients hospitalized with the diagnosis of chronic obstructive pulmonary disease. *Respir Care.* 2006;51:1120-1124.
27. Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. *Chest.* 2000;117:1146-1161.
28. O'Dowd LC, Fife D, Tenhave T, Panettieri RA Jr. Attitudes of physicians toward objective measures of airway function in asthma. *Am J Med.* 2003;114:391-396.
29. Bellia V, Pistelli R, Catalano F, Antonelli-Incalzi R, Grassi V, Melillo G, Olivieri D, Rengo F. Quality control of spirometry in the elderly. The SA.R.A. study. *SAIute Respiration nell'Anziano = Respiratory Health in the Elderly. Am J Respir Crit Care Med.* 2000;161:1094-1100.
30. Derom E, van Weel C, Liistro G, Buffels J, Schermer T, Lammers E, Wouters E, Decramer M. Primary care spirometry. *Eur Respir J.* 2008;31(1):197-203.
31. Bednarek M, Gorecka D, Wielgomas J, et al. Smokers with airway obstruction are more likely to quit smoking. *Thorax.* 2006; 61:869-873.
32. Rutgers SR, Postma DS, ten Hacken NH, Kauffman HF, van Der Mark TW, Koëter GH, Timens W. Ongoing airway inflammation in patients with COPD who do not currently smoke. *Thorax.* 2000; 55(1):12-8.
33. Anthonisen N R, Connett J E, Murray R P. Smoking and lung function of Lung Health Study participants after 11 years. *Am J Respir Crit Care Med.* 2002; 166 (5):675-679.
34. Pelkonen M, Tukiainen H, Tervahauta M, Notkola IL, Kivelä SL, Salorinne Y, Nissinen A. Pulmonary function, smoking cessation and 30 year mortality in middle aged Finnish men. *Thorax.* 2000; 55(9):746-50.
35. Anthonisen N R. Smoking, lung function, and mortality. *Thorax.* 2000; 55(9):729-30.
36. Tinkelman DG, Price DB, Nordyke RJ, Halbert RJ. Misdiagnosis of COPD and asthma in primary care patients 40 years of age and over. *J Asthma.* 2006; 43:75-80.
37. Kruis AL, Chavannes NH. Potential benefits of integrated COPD management in primary care. *Monaldi Arch Chest Dis.* 2010;73:130-4.

Corresponding Author

Nikolaos Kakoliris,  
Clinic of Social and Family Medicine,  
Faculty of Medicine,  
University of Crete,  
Greece,  
E-mail: kakolirinick@yahoo.com

# Discourse and bipolar disorder: Narrative therapy on northeast Brazil

*Modesto Leite Rolim Neto<sup>1</sup>, Alberto Olavo Advincula Reis<sup>1</sup>, Luiz Carlos de Abreu<sup>1</sup>, Saulo Araujo Teixeira<sup>2</sup>, Cicero Hedilberto Pereira Filgueiras Macedo<sup>2</sup>, Nádia Nara Rolim Lina<sup>3</sup>, Jesus de Souza Cartaxo<sup>3</sup>, Elizabeth Alves Silva<sup>3</sup>*

<sup>1</sup> Departamento de Saúde Materno-Infantil, Faculdade de Saúde Pública, Universidade de São Paulo, São Paulo, Brasil,

<sup>2</sup> Faculdade de Medicina do Cariri, Universidade Federal do Ceará, Barbalha, Brasil,

<sup>3</sup> Coordenação de Pós-Graduação, Universidade do Vale do Acaraú, Juazeiro do Norte, Brasil.

## Abstract

**Background:** The expression ‘bipolar disorder’ refers to any of several psychological disorders of mood that alternate episodes of depression and mania. Also called manic depression or manic-depressive illness, it is a relatively common but unknown pathology that brings some stigmas for patients and provokes deleterious effects for their lives. This research aimed to comprehend actions, behaviors and emotions involved with bipolar disorder, through narratives of patient’s personal and familiar histories.

**Methods:** We surveyed 30 patients from a psychiatric service located in Aparecida, Paraíba, Brazil. Selected patients had bipolar disorder according to DSM-IV. For data collection, we used non-structured interview, approaching specific aspects related to bipolar disorder. Quantitative and qualitative analysis were done and Hamilton Rating Scale for Depression (HAM-D) was used.

**Results:** Most of patients presented depressive actions associated with moderate euphoria. 11 of them related familiar history of psychopathology. Mania and hypomania were prevalent on male gender, while psychotic symptoms overlay ate female.

**Conclusion:** Patients lack a translation of behavioral and temperamental processes to minimize harm caused to their lives.

**Key words:** bipolar disorder; narratives; depression; mania.

## Background

Even though there are many studies about developing diagnosing and treating depression, is necessary to consider and differentiate the ou-

lines of bipolar disorder. Unipolar and bipolar depression can be confused and must be clearly differentiated<sup>[1]</sup>. Identifying patients of the wide group of bipolar people is very important for clinical practice<sup>[2]</sup>. There is an efficient pharmacologic treatment, but bipolar disorder keeps on being misdiagnosed and mistreated<sup>[3]</sup>, taking an average time of more than 10 years for patient to receive correct diagnosis<sup>[4,5]</sup>.

According to reality articulated by individual and collective trajectories, despite of clinical symptoms manifested as pain and psychic illness involved in this disorder, several researches try to disclose some dynamics under behavioral and temperamental aspects of bipolar mechanisms and their complications since diagnosis<sup>[6]</sup>. According to proper patients, the most important failure on diagnosis comes from the patients’ complaints about depressive symptoms and the non-questioning of doctors about maniac symptoms<sup>[2]</sup>.

We recognize up-to-date studies about depression and bipolarity, but there are insignificant researches in focusing on changes and autonomy of mood in needful populations that come from rural areas. This research aimed to understand and comprehend behavioral and temperamental actions involved on bipolar disorder, through personal and familiar histories of patients originated from rural areas in a public basic healthcare unit located at countryside Paraíba, considering diagnosis of bipolar disorder.

## Methods

We did a qualitative approach with a sample of 100 patients from both genders and ages between 12 to 67 year-old on the Auta Alves Ferreira public

healthcare unit, located in Aparecida, countryside of Paraíba, northeast Brazil. Our purposeful sampling was composed by 30 patients. 22 of them were women and 8 were men. Patients came from a healthcare unit of Programa Saúde da Família (PSF), Brazilian national basic public health program. They had clinical suspicion for bipolar disorder according to DSM-IV criteria. Patients were accompanied along 2004.

For data collection we used narrative deep non-structured interviews<sup>[7]</sup> with specific characteristics related to bipolar disorder. We also tried to compare different perspectives<sup>[9]</sup> on translating psychic illness, through detailed transcription of patients' spoken narratives<sup>[7]</sup>. We developed a category system in which all narratives were de-crypted by social cartography<sup>[10]</sup>. Hamilton Rating Scale for Depression (HAMD) based the evaluation of patients. Obtained results were the paradigm for psychic conduct and reflexivity process between researchers.

Interpreting the interviews through themes analysis<sup>[11,12]</sup> constituted final product. We joined important structures of both informants and interviewers. This process made possible to us to proceed a quantitative and quantitative classical analysis<sup>[7]</sup>.

Six steps was used for comprehending the interviews: 1) detailed transcription of patients verbal expressions; 2) material classification between indexed and non-indexed. Indexed propositions had concrete references of "who" did "what", "when" and "why". Non-indexed propositions contained values, events, judgments and popular knowledge; 3) use of indexed speeches to analyze sequence of events for each patient; 5) comprehension of grouping and comparison between individual histories; 6) establishing similarities. This process allowed us to identify collective narratives.

A logbook recorded all the information given by patients' relatives about behavior and mood characteristics they perceived along the development of disorder. These data formed repertoires of possible interpretations for patients' narrative elements. Starting from the narratives, researcher aims to establish an episode's structure, organize the sequence of events, design explanations through events interpretation, identifying dramas or conflicts and meanings that gives reason to experience<sup>[13]</sup>.

All these procedures were approved by official council for ethics in research from Universidade Federal do Rio Grande do Norte, Brazil.

## Results and discussion

21 of 30 interviewed patients had achieved the confirmation of bipolar disorder diagnosis. Depressive actions in association with euphoria were the most prevalent bipolar spectrum. Eleven of them confirmed some indications of familiar history of the disease.

Twelve patients presented some difficult in remembering the data of disorder origin. They use several terms referring to their pathology, disclosing an imprecise diagnosis on first medical attending. Another important aspect of patients was affective instability (79,8%), especially in ages from 12 to 22. In elder ages, over the third decade, hypomanic cycles, mania and depression were more frequent. Mania and hypomania episodes prevail on male gender, while psychotic symptoms triumph on female patients. It is important to highlight that mixed mania was most prevalent in five patients (a man and four women).

Agriculture work was the main occupation for 64% of prospecting patients. Scholarship levels differed between patients from zero to eight years of formal education. It seems that low annual familiar income has some kind of association with bipolarity. Eleven of bipolar patients were married, two of them were widowed and eight were not married. Espoused patients presented greater rates of depressive symptoms than bachelors.

The most recent studies about this theme were accredited by our survey. We identified the following temperamental traces: 18% were hyperthymic, 61% were depressive, 12% were cyclothymic and 9% had dysthymia. Association of depression and bipolarity configures an important factor for clinical identification, notably on establishing the differential diagnosis, but also for treatment and prognostic<sup>[2]</sup>.

More than 42% of patients used antipsychotic drugs and 54,2% of total have used some kind of pharmacologic treatment for depressive symptoms. Average scores of HAMD were 22,02 on starting, with a SD of 7,24%. Suicide ideation was manifested by 48,9% of patients.

The incidence of bipolar disorder in patients sent for evaluation reached high levels, even more expressive on that group with positive familiar history for this pathology. Identifying risk factors is fundamental for achieving success on treatment, because an efficient translation of behavioral and temperamental actions depends on a well-done strategy for obtaining information about intervening situations of bipolarity.

The analysis of these data highlight the urgent necessity of think and rethink the diagnosis, treatment and prognostic of bipolar disorder, through new possibilities of disclose the real need for patient treatment. It also makes us to think about the human dimension on articulating individual and collective trajectories, facing the constitution of pain and psychic illness, interlaced with mood changing.

These concepts make connections between knowledge and situations faced by disease and patients, as good as comprehending variables and predictors outlined on a schedule or a plan, based on patients needs. Patient with bipolar disorder adds to its behavior several and strong confronts and oscillations, giving reflexive aspects to life histories and considering suffering, illness dimension and relationships surrounded by a necessity of connecting to new interpretation about clinic characteristics and personal traces that configure bipolarity.

Although they are marked by various symptoms, patients with bipolar disorder think about determinate procedures on focusing their illness and recovering therapeutic situations that bring extended affective stability, but need some interpreters for constructing behavioral and temperamental situations<sup>[14]</sup>.

## Conclusions

We consider narratives as a fundamental medium for rescue the patient's control and gather information that runs slowly while patient speak some happenings and conflicts<sup>[15]</sup>. Through their enunciations of pain and psychic illnesses, patients achieve good results on translating behavioral manifestation and defining some aspects of their care.

Therefore, health professional need to establish a relationship that gives to patient some logics, adopting procedures, measures and actions connected to the feelings that fill the spaces of pain and

illnesses. This is the route for stability. Although this relationship is influenced by the nearness of healthcare professional, it gives a wide new field of possibilities and opportunities to control bipolarity, surrounded by patients' own cultural and social characteristics<sup>[16]</sup>.

To humanize treatment for bipolar disorder is giving patients prevention for consequences that comes from this pathology. Most of the times, these consequences are manifested by suicide ideation. Because of this reason, the assistance should be installed on finding the language expressed by patient that carries disturb. Comprehending patients' speech is a way to find what upsets them or make them change mood profile<sup>[17]</sup>.

We choose patients with bipolar disorder from rural areas to confirm actual relationship between public health and society, especially in what regards to knowledge mobility, considering the links formed between both sides of dialogue. This kind of human insertion and its clinical and social aspects is the established rule for the act of care and caring.

Spaces outlined by patients with diagnosed bipolar disorder need and wish a human resources management capable of purposing new strategies on recovering their histories beyond the disease. It can give them the freedom on expressing their feelings, like pain and illness, to who owns it. It doesn't purposes absolute truth, but dividing it between multiple enchantment zones of healthcare professional and the human discourses. Claiming on a Chinese proverb<sup>[18]</sup>, we believe that before you can defeat a monster, you need first to make it beautiful to your eyes.

## References

1. Lara D. *Temperamento forte e bipolaridade: dominando os altos e baixos do humor*. Rio Grande do Sul: Diogo Lara; 2004.
2. Moreno DH, Dias RS. *Epidemiologia*. In: Moreno RA, Moreno DH. *Transtorno Bipolar do Humor*. São Paulo: Lemos Editorial; 2002. p. 97- 109.
3. Ghaemi SN, Boiman EE, Goodwin FK. *Diagnosing bipolar disorder and the effect of antidepressants: a naturalistic study*. *J Clin Psychiatry* 2000; 61:804-808.
4. Suppes T, Leverich GS, Keck PE, Nolen WA. *The Stanley Foundation bipolar treatment outcome network II. Demographics and illness characteristics of the first 261 patients*. *J Affect Disord* 2001;67:45-59.

5. *Ellicott A, Hammen C, Gitlin M. Life events and the course of bipolar disorder. Am J Psychiatry 1990;147:1194-1198.*
6. *Bauer MW. Análise de conteúdo clássica: uma revisão. In: Bauer MW, Gaskell G. Pesquisa qualitativa com texto, imagem e som: um manual prático. Rio de Janeiro: Vozes; 2002. P. 189-127.*
7. *Joychelovitch S, Bauer MW. Entrevista narrativa. In: Bauer MW, Gaskell G. Pesquisa qualitativa com texto, imagem e som: um manual prático. Petrópolis. RJ: Vozes; 2002. P.91.*
8. *Farr RM. Interviewing: the social psychology of the interview. In: Fransella F, editor. Psychology for occupational therapists. London: Macmillan; 1982. P. 151-70.*
9. *Santos BS. Uma cartografia simbólica das representações sociais. Ver Crít Ciênc Soc 1988;24:139-172.*
10. *Mayring PH. Qualitative inhaltsanalyse: Grundlagen und Techiken. Basel: Beltz; 1983.*
11. *Minayo MCS. O desafio do conhecimento: pesquisa qualitativa em saúde. São Paulo/Rio de Janeiro: Hucitec/ ABRAPSO; 1994.*
12. *Silva DGV, Mercedes T. Narrativas como técnica de pesquisa em enfermagem. Ver: Latino- Am. Enfermagem 2002 maio-jun; 423-432.*
13. *Solomon A. Demônio do meio-dia: uma anatomia da depressão. Rio de Janeiro: Objetiva; 2002.*
14. *Landdon EJM. A negociação do oculto: xamanismo, família e medicina entre o Siona no contexto pluri-étnico. Florianópolis: UFSC; 1994.*
15. *Helman CG. Cultura, saúde e doença. 4ª Ed. Porto Alegre: Artmed; 2003.*
16. *Nogueira-Martins MCF. Humanização das relações assistenciais: a formação do profissional de saúde. São Paulo: Casa do Psicólogo; 2001.*
17. *Jamison KR. Uma mente inquieta: memórias de loucura e instabilidade de humor. São Paulo: Martins Fontes; 1996.*

*Corresponding Author*

*Modesto Leite Rolim Neto,  
Departamento de Saúde Materno-Infantil,  
Faculdade de Saúde Pública,  
Universidade de São Paulo,  
São Paulo,  
Brasil,  
E-mail: modestorolim@yahoo.com.br*

# Performance assessment indicators: How DEA and Pabon Lasso describe Iranian hospitals' performance

Ahmad Barati Marnani<sup>1</sup>, Jamil Sadeghifar<sup>2</sup>, Kimia Pourmohammadi<sup>3</sup>, Davood Mostafaie<sup>2</sup>, Masood Abolhalaj<sup>4</sup>, Peivand Bastani<sup>5</sup>

<sup>1</sup> School of Management and Information Sciences, Tehran University of Medical Sciences, Tehran, Iran,

<sup>2</sup> School of Management and Information Sciences, Tehran University of Medical Sciences

<sup>3</sup> Msc in health service administration

<sup>4</sup> Faculty member of Ministry of Health and Medical Education

<sup>5</sup> Department of health services management, School of health management and information sciences, Tehran University of Medical Sciences, Tehran, Iran.

## Abstract

**Back ground:** Assessing the hospitals' performance is considered as a focal point because of their vital role in healthcare systems. This study was conducted to assess the performance of hospitals affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran comparing the results of Pabon Lasso model and DEA.

**Methods:** This was a cross-sectional study on 23 Iranian hospitals in 2010. Related data was collected through two special checklists one for indicators of Pabon Lasso and the other for assessing efficiency applying with DEA. The former data was analyzed using Excel and SPSS version 17 and the latter interpreted applying with Wind-eap software version 2.1.

**Results:** Pabon Lasso graph indicates that there were four hospitals in the first zone that represents for inefficiency and underuse of resources, in contrast, another four hospitals were located in the third part of the graph which stands for efficiency and optimal level of productivity. Results of Deap2 also mentioned that the mean efficiency of these hospitals in 2010 was 0.914 and only 21.7% of them could reach the complete scale efficiency score ( $SE=1$ ). Furthermore there was no complete accordance between those hospitals occurred in the third zone with those DEA recognized as fully efficient on the other hand, the hospitals considered in the first zone did not fully match to those situated under efficient frontier.

**Conclusion:** As it is not rational to judge the hospitals performance only by attention to their

separate indexes, applying multi factorial models is inevitable. At the same time, attention to the results gained from different methods of performance assessment for a more realistic status picture is considered necessary.

**Key words:** performance indicator, Pabon Lasso Model, DEA, Hospital

## Background

As hospitals have a major and central role in achieving the threefold goals introduced in the World Health Report 2000 for a health care system (1-2), assessing their performance is considered as a focal point. Furthermore, since hospitals account for about 80 percent of the all healthcare system costs in developing countries (3), and they are considered as one of the most important economic units in health industry as well, the hospitals are encountered with lots of problems in these countries for competing peers and managing the growing pressure of government and social security institutions for decreasing prices and improving quality of services, So in adding up, applying a proper technique to evaluate the performance of hospitals is inevitable (4).

Catching this aim, some techniques have been proposed for hospital performance assessment (5) including different indexes of efficiency specially technical efficiency that stand for how a hospital be successful in producing maximal output for a given set of inputs or how they generate the constant amount of output using minimal resources (6).

Data Envelopment Analysis (DEA) is a non-parametric linear programming method that has been presented since 1978 in order to estimate technical efficiency in the agencies with multiple inputs and outputs in one unit the same as hospitals (7-9). Considering that the basic concept of DEA is underlain on Pareto optimality, thus each unit is supposed relatively efficient whether there is no other unit(s) to generate at least the same amount of all products with less resources (10).

After DEA has been suggested as a superior method and an appropriate tool in the World Health Organization (WHO) report in 2003 for efficiency assessment in health systems (11), it is increasingly becoming a popular and practical management instrument for demonstrating hospital performance (10).

Despite mathematical devices like DEA, Pabon lasso is a graphical model for demonstrating hospital performance applying with three indicators: bed occupancy rate (BOR), bed turnover (BTO) and average length of stay (ALS) (12). This graph compartmentalizes the hospitals into four divisions: The first part stands for those hospitals with low BTO and BOR implying a surplus in hospital beds against the existing demand, however the second sector shows the hospitals with high BTO and low BOR which characterized by unnecessary hospitalizations, an oversupply of beds, or applying the hospital beds for simply observing patients. The third segment indicates those hospitals with high BTO and BOR that simply means an appropriate level of efficiency, with relatively few vacant beds at any time and finally the last category presents the low BTO and high BOR that may emerge because of admitting chronic patients or unnecessarily long ALS (13).

This graphical illustration of the hospitals can be used for rapid investigation and identification of those with poor performance and is helpful to offer the ideas for reducing inefficiency (14). However it is significant to consider that these three indicators constructing Pabon Lasso model can be influenced by some inevitable and non measurable factors (15), so this limitation reminds and emphasizes on applying this model together with the other assessment techniques to achieve a real and more complete image of the hospital performance.

This study was conducted to assess the performance of hospitals affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran comparing the results of Pabon Lasso model and DEA to offer a scientific document to policy makers for their future decisions and strategies about resource allocation in Iranian health sector.

## Method

This was a cross-sectional study that was conducted on 23 hospitals affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran in 2010. This university offers health care services along with Tehran University of Medical Sciences to clients from Tehran province and even the whole country as referral centers.

Data was collected through two special checklists one for indicators of Pabon Lasso and the other for assessing efficiency applying with DEA both were designed according to the research purposes.

The first checklist includes the number of active beds, number of active bed-days, number of occupied bed-days, number of discharges and performance data consisting BOR, BTO, and ALS. The items of this checklists were firstly filled for each month of year 2010 by all the hospitals as our statistical populations and then were rechecked in the statistical center of Shahid Beheshti University of Medical Sciences for assuring accuracy and reliability.

Data achieved in the first phase, was analyzed using Excel and SPSS version 17 according to Pabon lasso model for presenting the related graphs.

In the second phase, another checklist was designed for obtaining necessary data in order to form an input-oriented DEA model. This data was collected from the statistical center of Shahid Beheshti University of Medical Sciences for a total of 23 hospitals in 2010. Windeap software was applied for later analysis.

From the mathematical point of view, the CRS input-oriented DEA model is formulated with the following non-linear fractional programming which determines the Relative efficiency  $\theta_{pp}^*$  of DMU  $p$  :



$$\theta_{pp}^* = \max \frac{\sum_{j=1}^s u_{jp} \cdot y_{jp}}{\sum_{i=1}^m v_{ip} \cdot x_{ip}}, \quad p \in \{1, 2, \dots, n\}'$$

Subject to the following conditions:

$$\theta_{rp} = \frac{\sum_{j=1}^s u_{jp} \cdot y_{jr}}{\sum_{i=1}^m v_{ip} \cdot x_{ir}} \leq 1, \forall r = 1, 2, \dots, n$$

$$u_{jp} \geq \varepsilon > 0, v_{ip} \geq \varepsilon \forall i, j, p$$

In the above notation it is supposed that there are  $n$  DMUs that each one  $p$  ( $p=1, 2, \dots, n$ ) is consuming varying quantities of  $m$  inputs ( $x_{1p}, x_{2p}, \dots, x_{mp}$ ) to produce different quantities of outputs ( $y_{1p}, y_{2p}, \dots, y_{sp}$ ). The multipliers  $u_{jp}$  and  $v_{ip}$  are the weights given by DMU  $p$  to  $j$ th outputs ( $y_{jp}$ ) and to  $i$ th inputs ( $x_{ip}$ ) of itself and every other DMU  $r$  ( $r=1, 2, \dots, p, \dots, n$ ). ( $\varepsilon$ ) stands for a small positive number defined to be smaller than any positive real number. The corresponding VRS input-oriented DEA model is formulated with following fractional programming problem:

$$\theta_{pp}^* = \max \frac{\sum_{j=1}^s u_{jp} \cdot y_{jp} - u_{0p}}{\sum_{i=1}^m v_{ip} \cdot x_{ip}}, p \in \{1, 2, \dots, n\}$$

Subject to the following conditions:

$$\theta_{rp} = \frac{\sum_{j=1}^s u_{jp} \cdot y_{jr} - u_{0p}}{\sum_{i=1}^m v_{ip} \cdot x_{ir}} \leq 1, \forall r = 1, 2, \dots, n$$

$$u_{jp} \geq \varepsilon > 0, v_{ip} \geq \varepsilon > 0, \quad \forall i, j, p$$

$$u_{0p} \in R$$

Therefore the VRS formulation ensures that each benchmark unit is comparable in size to the DMU being evaluated.

According to the model, those variables have the greatest effect on the hospitals efficiency were selected as output consisting the number of inpatient admissions, the number of outpatient visits, the number of surgical operations, and bed occupancy rate regarding to the previous studies and also using expert view versus the number of fixed hospital beds was considered as the only input variable because it was the most accessible data for all the studied units.

### Results

There was about 3890 active beds in all the studied hospitals in the spectrum from 25 to 502 beds in the smallest and largest units respectively. Three performance indicators were estimated in the studied hospitals such that the average length of stay (ALS) was 4.9 days, bed occupancy rate (BOR) was 74.50% and bed turnover (BTO) was 56 times throughout the year.

Pabon Lasso graph indicated that there were four hospitals in the first zone that represents for inefficiency and underuse of resources in these four units. In contrast, another four hospitals were located in the third part of the graph which stands for efficiency and optimal level of productivity of them. Finally two hospitals were situated in the second sector and five were in the fourth zone that may be respectively because of unnecessary hospitalizations, an oversupply of beds, applying the hospital beds for simply observing patients (second zone) or admitting chronic patients with unnecessarily long ALS (fourth zone) (Figure 1).

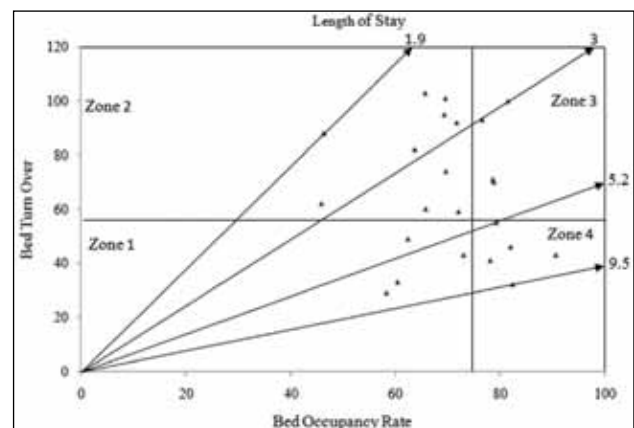


Figure 1. Pabon Lasso graph indicating the performance status of Shahid Beheshti University of Medical Sciences` hospitals, Tehran Iran, 2010

Table one presents the range of efficiency in the studied hospitals applying DEAP 2, This range within the efficient hospitals was from 0.878 to 0.993 considering 0.8 as an efficient cut of point. The related results also mentioned that the mean efficiency of these hospitals in 2010 was 0.914 such a way that except 5 hospitals (21.7%) that were fully efficient in technical efficiency, the others (87.3%) could not gain complete scale efficiency scores (SE=1).

*Table 1. The range of technical efficiency of Shahid Beheshti University of Medical Sciences` hospitals, Tehran Iran, 2010*

The range of efficiency by DEA	The average of technical efficiency (Percent of hospitals)
0.8-1	82.6
0.6-0.8	13.1
Less than 0.6	4.3

*Table 2. Comparison between Number of present beds in Shahid Beheshti University of Medical Sciences` hospitals with the target beds*

Hospital Number	Number of present beds	Number of target beds
1	394	191
2	117	42
3	502	500
4	90	89
5	329	152
6	264	82
7	223	128
8	361	362
9	249	76
10	116	82
11	87	53
12	25	25
13	50	37
14	108	121
15	47	70
16	31	76
17	44	81
18	220	44
19	117	85
20	203	47
21	81	31
22	132	132
23	100	90

Moreover the findings of the study revealed that only 21.63% of the hospitals were function-

ing in the optimum scale (constant return to scale) though 27.83% of them had a decreasing return to scale (DRS ) and most of the hospitals (30.44%) had an increasing return to scale (IRS).

As the number of active beds were considered as the only input variable in the present study, results did not indicate any input slack in the above hospitals.

Calculating the target inputs in these hospitals has shown that 69.6% of the studied hospitals can reach the efficiency applying with less active beds that they possess now, in contrast 21.7% of them need more beds as an optimum input and there was only 8.7% of these hospitals that had the same number of available and target beds (Table 2).

## Discussion

Although one of the health policy makers and health care managers` concerns is to be aware of the hospitals` performance and efficiency, application of a unique scientific technique in order to evaluate hospital performance, estimate efficiency and determine the effective factors has not been achieved yet. In another word, all these methods have their own limitations for instance despite DEA`s advantages to mention relative and not absolute efficiency and incorporate multiple inputs and outputs and also determining optimum level of practice and performance targets (16), there are some noticeable restrictions attributed to this method such as illuminating significant variables and the effect of outliers and missing data (10) that all may lead to wrong estimations of efficiency (17).

Moreover in spite of instant picture of hospital performance that can be presented by Pabon Lasso, its constructing indexes may be influenced by many factors that can not be calculated applying this simple model (15).

Considering all stated above, this study tries to compare and approach one of the economical techniques of performance and efficiency assessment with a graphical ones although the authors could not find any related studies that consider the results of Pabon Lasso and DEA simultaneously in a comprehensive review process .

The present findings indicate that in spite of Pabon Lasso results that determine forth of the hospitals in the third zone (Hospitals number

8,13,17,22) having the best and the most satisfactory efficiency and productivity, DEA recognized five hospitals (Number 4,12,17,20,22) with the fully efficient in technical efficiency and at the same time constant return to scale that stand for the best efficiency.

As this comparison shows, there is not a complete accordance between the results of this graphical model with those of DEA in another word only in two hospitals (No. 17, 22 ) a similar conclusion can be considered so this emphasized on applying these models alongside to achieve a valid picture of the hospitals` performance.

Similarly our finding show that there is not a fully coordination between the results of DEA for estimating those hospitals which located under efficient frontier (hospitals number 1,2,3,8) with those are situated in the first zone of Pabon Lasso that is recognized as the least desirable and efficient zone(No. 2,5,6,12).

Although most of the studies focused on not applying a single performance indicator and ratio to gain a better and more real image of the hospitals` status (12-13), some studies have shown the significant correlation between the increase in DEA technical efficiency scores and rising in hospitals` BOR(18). Interpreting by the graphical model it occurs in the third and fourth zones that the latter zone is not assumed efficient in Pabon Lasso model.

Results of the present study implied that increasing return to scale was the most prevalent reason for technical inefficiency of these selected Iranian hospitals so it is recommended to merge some of these hospitals that are located in near proximity.

Furthermore there are some evidences of the positive relationship between the number of hospital beds and their efficiency level (19-20) even though there is no agreement on the exact amount of increase in the bed numbers, for instant when some suggested the maximum number of 190 beds for developing countries(21) the others recommended 120 hospital beds for achieving the optimum level of efficiency and the shortest ALS (22).

As this study stated that most of the selected hospitals can reach the optimum efficiency applying with less active beds that they possess now it is important to think about a manageable size of hospital considering Iranian circumstances.

In conclusion, as it is not rational to judge the hospitals performance only by attention to their separate indexes we need to use those models that can apply multiple factors in their interpretation but as it was stated, Pabon Lasso may mislead the managers in their decisions because of its great simplification and at the same time DEA is more deterministic rather than statistical, in another word, DEA just assesses efficiency relative to the best practice within the specified sample. Therefore, it is meaningless to have a comparison between the scores achieved from two different conditions in different studies(23).

So it is highly recommended to use different methods of performance evaluations together to reach a complete view of the real status of the hospitals.

## References

1. *The World Health Report 2000. Health Systems: Improving Performance.* Geneva: World Health Organization, 2000.
2. Mc Kee M, Healy J, eds. *Investigating in hospitals (chap. 7).* In *Hospitals in a Changing Europe.* Buckingham: Open University, 2002; 119.
3. Aversion A. *Comparative study of evaluation and supervision mechanism of services delivery in public and private hospitals of Tehran.* Tehran: Islamic Azad University, Science and Research Branch; 2002.
4. Moslehi,S., *Estimating Efficiency in Public-general Hospitals in Iran: Data Envelopment Analysis,* MS thesis, Shiraz University of Medical Sciences, school of management, 2005; 15-9.
5. Mehrotra A, Lee S, Dudley RA. *Hospital performance evaluation: what date do we want, how do we get it, and how should we use it?* National Business Coalitions on Health, Washington D.C,2006
6. Gannon, B., *Technical efficiency of hospital in Ireland, Economic and Social Research Institute, working paper, 2004.*
7. Giokas D., *The use of goal programming ,regression analysis and data envelopment analysis for estimating efficient marginal cost of hospital services.* Multi -criteria decision analysis, 2002;11:261-268.
8. Nyhan,R., and Cruise, P., *Comparitive performance assessment in managed care: Data Envelopment Analysis for health care managers.* *Managed Care Q.*2000;8(1):18-27.
9. Thanassoulis,E., *Introduction to theory and application of Data Envelopment Analysis. A Foundation Text With Integrated Software.* Kluwer academic publisher, Boston,2001.

10. Kengil BC, Cokmen N, Tozan H. Efficiency measures in the health services with DEA- An overview. *Journal of Naval Science and Engineering*, 2010, 6(1):1-14
11. Mehregan, M.R., *Quantitative Modeling for Evaluating System Performance –DEA.*, School of Management, Tehran University. 2008; 5-60.
12. Bahadori MK, Sadeghifar J, Hamouzadeh P, Hakimzadeh SM, Nejati M. Combining multiple indicators to assess hospital performance in Iran using the Pabon Lasso Model, *Australasian Medical Journal AMJ*, 2011; 4( 4): 175-179
13. Goshtasebi A, Vahdaninia M, Gorgipour R, Samanpour A, Maftoon F, Farzadi F, et al. Assessing Hospital Performance by the Pabon Lasso Model, *Iranian J Publ Health*,2009;38(2):119-24
14. Jakab M, Harding A, Preker A, Hawkins L ,*Organizational reform and management of public providers: focus on hospitals: appendix 3: critical skills: monitoring and evaluating hospital performance*, Washington D.C, World Bank, 2000
15. Thomas S, Normand C, Smith S. *Social health insurance:further options for Ireland. Report prepared by TCD and published by the Adelaide Hospital Society*; 2008 : 1-48.
16. Kontodimopoulos N, Niakas D, *Efficiency measurement of hemodialysis units in Greece with data envelopment analysis*, *Health Policy*,2005;71 : 195–204.
17. Donthu N, Hershberger E. K, Osmonbekov T. *Benchmarking marketing productivity using data envelopment analysis* , *Journal of Business Research* , 2005; 58:1474-82
18. *The technical efficiency of district hospitals in Namibia*, Ministry of health and social services, 2008:32
19. Ghoadarzi G.H, Ghaderi H, Askari Baghbani R.A. *Determining technical efficiency of Iran University of Medical Sciences` hospitals applying SFA*, Abstract presented in the sixth national conference of health service administration students, Tehran`s student research committee ;2008:76[In Persian]
20. Ahmad Kia Daliri A.A, *Technical Efficiency of Iran University of Medical Sciences*, Thesis for Master degree of health service management, Iran University of Medical Sciences, 2004 [In Persian]
21. New Brander W, Kutzin j, Barnum H. *Hospital economic and financing in developing countries*. World health organization.1999:78-80
22. Pangilinan M. *Production cost inefficiency and flexible cost functions. The cost of New York State hospitals*. State University of New York at Albany. Degree PhD DAIA 53/04, 1999:235
23. Giuffrida A, Gravelle H. *Measuring performance in primary care: econometric analysis and DEA*, *Applied Economics*,2001;33:163-75

Corresponding Author

Peivand Bastani,

Department of health services management,

School of health management and information sciences,

Tehran University of Medical Sciences,

Tehran,

Iran,

E-mail: p-bastani@razi.tums.ac.ir

# Radioisotope Synovectomy and the role of nurses in Hemophilia care

Selmin Senol<sup>1, 2, 3</sup>

<sup>1</sup> Ege University Izmir Ataturk School of Health, Department of Nursing, Izmir, Turkey,

<sup>2</sup> Chairman of Nursing Working Sub-Committee of The Federation of Hemophilia, Turkey,

<sup>3</sup> Nurse member in Ege Hemophilia Center, Ege University, Izmir, Turkey.

## Abstract

Hemophilia is the most common hereditary X-linked recessive bleeding disorder. In patients with severe hemophilia (Hemophilia A-deficiency of factor VIII), although bleeding may occur spontaneously or as a result of trauma at any site of the body, clinical experiences have revealed that it most commonly occur within the joints. If factor replacement therapy is started in patients with knee, elbow and ankle hemophilia (primary prophylaxis) during early childhood (before the joint damage develops), joints are not damaged. However, today, more than half of the patients with hemophilia cannot fully benefit from this effective treatment; since the factor replacement therapy which is started during the early stage of the disease, is expensive and often requires intravenous intervention.

If this kind of bleeding is not treated in time and appropriately, target joint development results in hemophilic synovitis and hemophilic arthropathy. This undesirable condition occurs in severe hemophilic patients whose factor level is less than 1%. If these patients are diagnosed to have clinical signs of chronic hemophilic synovitis and their bleeding cannot be taken under control with the use of factor, there exists Radioisotope Synovectomy (RS) indication in them.

In the last decade, RS has been widely employed in the treatment of hemophilic synovitis. RS is a simple, effective, economical, and reliable treatment application even in children; therefore, it is a preferred method.

RS treatment is performed by an experienced multidisciplinary team. The team consists of a hematologist, an orthopedic surgeon, a nuclear medicine specialist, a physical therapist and a nurse. The nurse plays the role of a coordinator who establishes communication between patients with hemophilia and the team members. The nurse also

plays a role before, during and after the implementation of radioisotope synovectomy treatment.

In this paper, the extremely important role of the nurse in ensuring the safety of patients during the pre-implementation, implementation and post implementation phases of RS will be presented within the framework of the protocol of the Ege Hemophilia Center.

**Key words:** Hemophilia, radioisotope synovectomy, nurse's role

## Introduction

**Hemophilia** disease is an X-linked inherited bleeding disorder and is caused by the congenital deficiency of coagulation factor proteins. Different types of hemophilia are named according to the type of coagulation factor proteins missing in the blood. The most common types of hemophilia are hemophilia A (due to deficiency of factor VIII) and hemophilia B (due to deficiency of factor IX). Whereas hemophilia A affects one in 5,000 males, hemophilia B is 4-5 times less prevalent. The clinical course of the disease is defined according to the factor level. If the factor level is less than 1%, it is classified as severe, between 1 and 5% moderate and between 5 and 25% mild [1-3].

Patients with hemophilia A or hemophilia B are at the risk of facing spontaneous bleedings or bleedings as a result of trauma due to lack or absence of blood clotting factors. Especially in childhood, although bleedings which occur due to traumas during the child's growth may seem innocent, head traumas occurring when the child falls down can be life threatening. However, bleedings which patients with hemophilia suffer most during childhood and adulthood and which decrease their quality of life are intra-articular bleedings. Knee, elbow and wrist joints are the most com-

monly affected bleeding points. If not treated in time and appropriately, these bleedings can lead to permanent disabilities and serious complications. The second most frequent bleeding is muscle and other soft-tissue bleedings [4-7].

What leads to intra-articular bleedings in hemophilia is synovial membrane, the tissue which contains most blood vessels within a joint. Repeated intra-articular bleedings in large amounts will force synovial membrane to multiply and grow more and more in order to reabsorb the bleeding. As a result, a persistent and non-regressive swelling develops in the joint, which is called synovitis. Blood vessels present in the growing and swollen synovial membrane proliferate further, which causes the lining of the joint to bleed more easily.

Thus, there arises a vicious circle, in which the membrane becomes more swollen as it bleeds and it bleeds more as it gets swollen. This course of the disease restricts the movement of the joint in a hemophilic child or adult (loss of extension and flexion starts) and if it is not treated, the ability to move is entirely lost. Sequelae in joints (loss of ability to move) which begin during childhood and become permanent during adolescence and adulthood affect an individual's quality of life adversely. In order to maintain quality of life of a hemophilic individual with chronic synovitis from his childhood, implementation of RS is indicated regardless of his age. This is a great gain for patients with hemophilia [2,5,8].

Synovectomy in hemophilic synovitis can be performed as open synovectomy, arthroscopic synovectomy, chemical synovectomy, and radioisotope synovectomy [9,10]. Today, RS is the first-line intervention in patients with chronic synovitis not responding to adequate factor replacement therapy. It is employed in both developed and developing countries. However, it is performed much more frequently and effectively in developing countries because prophylaxis is not performed in developing countries as easily and effectively as it is performed in developed countries. Since primary prophylaxis is costly and can only be performed intravenously, it brings restrictions on patients [1,4,11]. Therefore, in the last decade, there has been an increase in the number of studies indicating that RS is an appropriate option for the prevention of the joint sequelae in patients with hemophilia in developing countries.

## Radioisotope Synovectomy (RS)

The terms Radioisotope Synovectomy, Radioisotope Synoviorthesis, Radioactive Synovectomy and Radionuclide synovectomy are used interchangeably. The basic logic of the process is to provide the desired effect in the treatment through the fibrosis of fragile and hypertrophic synovial tissue that causes frequent bleedings after injecting radioactive isotopes into intra-articular synovial space [12-14].

In the last decade, RS has gained importance in the treatment of hemophilia and it is implemented for intra-articular hemorrhages which do not respond drug treatment sufficiently enough. Through this implementation, joint injuries possibly to occur can be prevented. RS induces the fibrosis of subsynovial connective tissue of joint capsule and of the synovial joint and obstructs the vascular structures in this region. For the application, minimally active hemophilic synovitis is suitable. RS is current treatment performed by injecting the radioisotope substance into the target joints and the joints of hemophilic patients developing chronic synovitis. Today, the most preferred isotopes are Yttrium-90 (Y-90), Erbium-169 (Er-90), Rhenium-186 (Re-186), and Phosphorus-32 (P-32). The process is performed through radio-scopic control and sedation or local anesthesia under sterile conditions [15,16].

RS has been performed in patients with rheumatoid arthritis to clear up swelling and pains in their joints since 1952. The first applications began with Au-198, and since 1971, H-90, P-32, Re-186, Er-169 colloidal radioisotopes have been used. The most commonly used radioisotopes in the studies which have been presented in the scientific literature since 1981 are Y-90 colloid (radioactive half-life of 2.7 days), Er-169 (radioactive half-life of 9.4 days) and Re-186 colloid (radioactive half-life of 3.2 days) (Table 1) [1,11].

As everywhere else in the world, in RS applications in Ege University Hemophilia Center, Y-90 (on the large joints and often on the knee) and Re-186 colloid (on small joints and often on the elbow, hand-foot wrist) are preferred [13].

Radioactive half-life: Radioactive half-life which varies from one radiation-emitting atom to another is the term used to express the amount of time dur-

ing which the number of the radioactive nuclei of an atom falls to half of its original reading [8,13].

Half-life of Y-90 radioactive material used for the treatment of patients with hemophilia is 2.7 days, in other words, 64.5 hours. After 7 half-lives elapse, practically, a radioactive substance will disappear. In other words, there will be no remaining radiation in a patient's joints 19 days after he has undergone radiosynovectomy and the bleeding in his synovial tissue will have been eliminated and the condition likely to cause permanent injury will have been treated by then. The size of a Y-90 colloid particle is about 10 nm. The importance of such a small size is that the smaller the size of a particle is, the more homogeneous the activity's dispersion in the joint is. Y-90 colloid is held by the surface cells of synovia after its intra-articular injection, and the beta rays emitted by this radionuclide destroy these cells. This damage causes an inflammatory reaction, necrosis and demarcation line in synovia in the given order. Thus, synovia which causes frequent bleeding can be easily destroyed by beta-ray-emitting radioisotopes. This

method is an alternative treatment approach to surgery. It is extremely easy to apply, repeatable and inexpensive [5,14].

In patients with hemophilia, Y-90 colloid is injected into the joint by an experienced orthopedic surgeon. During injection, extra caution is taken in order to prevent it from leaking into bloodstream. The distance Y-90 can penetrate in the joint varies between 5 and 11 mm. Therefore, while the synovia is treated, it is unlikely for the patient and the environment to be exposed to any harmful effects. After Y-90 colloid is injected into the joint, the colloid, due to its colloidal structure, does not interfere with other tissues, and because of its 10-mm range, it only destroys synovia and thus contributes to the treatment [16,17].

If a fully successful treatment is to be achieved with radioisotope application, it should be implemented in the early stages of synovitis (stages II and III on Table 2). At this point, monitoring the patient is not only the physician's responsibility but also the nurse's responsibility [18,19]. The nurse should keep the records of how often and at which

Table 1. Features of Radioisotopes used in RS

Type of Isotope	Type of the radiation emitted	Half-Life	Application site	Penetration
YTTRIUM (H 90)	beta	2.7 days	ideal for knee	3.6-11 mm
PHOSPHORUS (P 32)	beta	14 days	knee or elbow	2.6-7.9 mm
RHENIUM (Re 186)	beta and gamma	3.7 days	elbow and wrist	1.2-3.6 mm
ERBIUM (Er 169)	beta	9.4 days	hands, feet, fingers	0.3-1 mm
GOLD (Au 198)	beta and gamma	2.7 days	all joints	1.2-3.6 mm

Table 2. Stages of synovitis radioisotope reaction and the timing of radioisotope application [12,13]

<b>Grade I. Transient Synovitis</b>
Medical treatment is sufficient. However, it is recommended that patients who do not respond to 3-6 months of secondary prophylaxis (factor infusion 2 or 3 times a week) should be administered isotopes in order to prevent the disorder from worsening.
<b>Grade II. Permanent Synovitis</b>
It is the synovitis lasting more than six months. The muscle atrophy has not started yet, but the process of permanent damage has started. An increase in the size of the joint, synovial thickening and limited range of movements are observed. RS should be started immediately.
<b>Grade III. Chronic Active Synovitis</b>
There exists chronic arthropathy with axial deformities and muscle atrophy (the patient constantly walks with swollen joints. Muscle atrophy gradually sets in). The disorder is permanent. At this stage, the chances of success are slim after radioisotope application.
<b>Grade IV. Terminal Arthropathy / Ankylosis</b>
Joint destruction has occurred and ankylosis has developed. After this stage, radioisotopes application is contraindicated and it will not be of any benefit.

intervals the hemophilic child or adult patients visit the clinic, and should invite the patients who have not presented to the clinic for a long time [19]. In addition, during the patients' clinical visits, physical examination of the joints should especially be performed. The nurse should not be contented with the patient's complaints of pain or not being able to walk thus, he should palpate and inspect the joints. These observations must be recorded before the patient is referred to the physician [18-20]. This monitoring prevents the rapidly progressing synovitis in the joint from being overlooked.

### Advantages of RS

- It is very valuable for developing countries. The chances for widespread practice are high.
- 2 days of factor implementation is sufficient for the process. It is cost-effective.
- The cost of the nuclear material is cheaper than the cost of clotting factor concentrates.
- It is performed by an experienced orthopedic surgeon. It is simpler than open surgical operation.
- General anesthesia is not used. Local anesthesia is sufficient.
- It is a pain-free practice. It provides comfort for the patient.
- Compared to open synovectomy operation, it is not an invasive application.
- Hospital admission is not required. It is performed at outpatient clinics [5,9,11,21].

**Complications after application of RS;** Early and late complications after application of radioisotope synovectomy to be defined.

Early complications; Bleeding, inflammatory reaction (radiation synovitis), leakage of radioisotope substance from the joint, local complications (ulceration of the skin, necrosis in the periarticular tissue) and systemic spread (through the lymphoreticular system) [15,22].

Late-term complications; Although chromosomal defects and malignancy are theoretically defined in the literature, there have been no reports presented in the studies conducted so far. In addition, the results of the studies performed in recent years have revealed that chromosomal aberrations

induced by radiosynovectomy conducted with the Y-90 and Re-186 are not statistically significant, that genotoxic effects are not permanent since radio-nuclei tends to disappear over time and cannot be related with carcinogenesis [22, 25].

### RS and Nursing Initiatives

Radioactive Synovectomy the role of nurse in **nursing initiatives**; application before, during and after the application, including a three step process.

#### I. Pre-application

##### *a) Informing the child and the family:*

Severe hemophilic patients with chronic synovitis (stage II and III) are evaluated by the hemophilia council made up of a pediatric hematologist, an orthopedist, an adult hematologist, a nurse and a physical therapist. Then, the patients chosen are given an appointment for the application. If patients with stage-I synovitis do not have the chance for medical treatment or do not respond to continuous secondary prophylaxis treatment for 6 months, then isotope application can be considered. The nurse prepares the necessary documents, the replacement factor and the appropriate clothing by the day of RS, and informs and guides the patient so that he can become psychologically ready for the application [13,18-20].

■ In the patients chosen, before the application, MRI should be carried out and joint anatomy should be evaluated. This way, information on synovial fluid and synovial range is obtained prior to application and complication risk is reduced.

■ If the patient to undergo RS has no social security, the nurse must report it. The nurse refers the patient to the Ege Hemophilia Association, which provides medication and social support for hemophilia patients who have no social security, in order that he can get the factors and the isotopes needed for the implementation of the RS. If the patient has a job and social security, RS expenses are met by their own security institutions.

■ Taking into account the patient' age, and educational and cultural background, the nurse clearly and simply explains to him/her how to get prepared and what to do in the morning when he is to undergo the RS. In addition, the nurse gives a written form to the patient or the family including



what he has told before, and recommends them to read it again at home and call him/her on the phone number he/she has provided for them in case they have questions.

■ The hemophilia patient and the family are informed by the physician in charge about the procedure and are asked to give their written informed consent before the RS application.

*b) Preparation of the place in which RS will be applied*

The application is performed approximately at Fluoroscopy Unit of Radiology Department at Ege University School of Medicine every three months. In every application, approximately 15-20 different joints of at least 10-15 patients are exposed to the application so that radionuclide substance can be used cost-effectively and that the application team can save time and effort.

■ Materials (2-5-10 and 20 cc injectors, citanest, sterile sponge, bandage, baticon, sterile pack, apron, mask and gloves and protective lead vest, medical supplies, medical waste box -yellow box- and special radioactive waste box to be used during the application are prepared by taking into account the number of the patients and the number and characteristics of the joints to be aspirated (child-adult, large and small joints, the degree of joint swelling, fluid to be discharged). The nurse carefully prepares the place where RS will be applied for the patient and the orthopedic surgeon who will conduct the application.

*c) Preparation of the patient*

On the morning of RS application, before the synovectomy operation is performed, the prescribed dose of factor is intravenously (IV) administered from either the left or right arm of the haemophilia patient whose blood factor level was previously determined. The factor level should be 50%. The time the factor is administered is recorded and 15 minutes later, another blood sample is taken from the other arm. After the blood tube is labeled as 15 min., the sample is sent to the laboratory in order that APTT (Activated Partial Thromboplastin Time), Prothrombin time and factor level should be determined.

■ The nurse should make sure that he draws blood from one arm of the patient with hemophilia at 0 min. and from the other arm at 15 min. If both

blood samples are drawn from the same arm, lab results can be high. If the laboratory tests reveal less than 50% factor level, additional factor determined by the hematologist should be administered. Therefore, nurses should carefully check the results of the laboratory tests, and inform the physician in time. During the operation if needed (i.e. very small or extremely restless children), a branula is inserted for vascular access (the branula should not be inserted into the arm on the side of the joint to undergo RS, because a splint will be installed over the joint which will undergo RS application). Following this process, all the patients to have RS application are moved to the operation unit.

■ In the process, general anesthesia is not applied. Half an hour prior to the application, 0.5-1 mg/kg of Midozalam (Dormicum ampoule) is mixed with fruit juice and taken perorally before medication is administered. In small children, Midozalam IV can be used.

## II. During the application

The patient is tied regarding the joint to undergo the surgery. The patient is laid in supine position. Especially in young children who cannot do what is said or do just the opposite, it is important that the nurse should tie (fastened) the limbs except the one with the joint to undergo application. During the process, having a talk with the child and informing him of the process will encourage the child.

■ The nurse assists the orthopedist to perform the operation in a sterile environment (such as providing lead vest, sterile gown, sterile gloves, sterile sponge, cleaning the joint to be operated with an antiseptic solution and covering it with a sterile green cloth). The nurse should be extremely careful to prevent the sterile environment from becoming contaminated.

The orthopedist cleans the joint to be treated with an antiseptic solution and sterile sponge, determines the operating field under the green cloth and inserts the sterile syringe needle (20 or 22 gauge) into the joint (intra-articular) space. After making sure that the needle is in the joint (intra-articular) space, the synovial fluid is aspirated. While the aspirated fluid is assessed by the surgeon in terms of its color, consistency and quantity, the nurse records this assessment onto RS applica-

tion form (Table 3). Once any fluid was extracted, the syringe is withdrawn, but the needle is left in place. Then, the radioisotope material (previously loaded into syringes at different doses by the orthopedist) is injected into the intra-articular space.

■After the application, in order to provide long-term local anesthesia, at least 1 cc of prilocaine (Citanest) is injected into the intra-articular space. Another important aspect of this application is that it prevents the radioisotope material from leaking to the skin after the application. While the needle is being removed from the intra-articular space after the isotope application of the isotope, a local anesthetic agent is administered.

■After the orthopedist completes the radioisotope application, the radioactive material, the injector and the needle is placed into the sponge and thrown into the special radioactive waste box in order not to contaminate the environment. Citanest injector is thrown into the medical waste box –yellow box-. The nurse should be extremely careful about this procedure. The nurse takes the necessary measures in order to prevent the application area from being contaminated.

■Right after the application, a sterile sponge is placed on the operating field.

■After the application, the joint is passively moved several times so that the isotope substance can be homogeneously distributed into the joint.

### III After the application

After the application, the orthopedist fastens (immobilizes) the joint by encasing it in plaster.

#### *a) Period in clinic*

After the application, the nurse keeps track of pain. While doing this, the nurse should consider not only the patient's verbal expressions, but also his facial expressions. Pain is an important finding in case of bleeding. Therefore, the patient's complaints of pain should be taken into consideration carefully and evaluated appropriately by the nurses. In case pain occurs, analgesics not containing salicylate are preferred, and medicine likely to increase bleeding (especially aspirin and its derivatives) are not administered. The patient and the family should certainly be provided with the information on this issue.

■While the patient whose limb is encased in plaster is transported, the nurse should ensure that he is not moved.

■This operation does not require admission to hospital. The patient is followed approximately 4-6 hours after the operation and then is sent back home.

#### *b) Period at home*

In the evening after the application, a second dose of factor is applied. On the next two days after the application, factor support continues every 12 hours; on the third it is stopped. In hemophilia B patients, administering a single maintenance dose a day can be enough. Secondary prophylaxis implementation is not routinely applied before and after the application.

■In patients with inhibitors, Recombinant Factor VIIa (Novo Seven) or FEIBA is used. For Novo Seven, one hour before the application, 90 mcg/kg IV bolus is administered, and following the prothrombin time control 3 more doses are administered at intervals of 2 hours. Tranexamic acid (transaminases capsules, 200 mg) is initiated 24 hours prior to the application, and 25 mg/kg /dose is given perorally three times a day for at least seven days. If FEIBA is to be used, 50-75 IU/kg dose is infused within 30 min. three hours before the implementation. Then, two more doses are given at intervals of 12 hours. Transaminase is not used with FEIBA.

■ Immobilization is provided at home for three days. The nurse informs the patient and family about why immobilization is necessary. The immobilization process of pediatric patients may especially be troublesome because the child would want to act or to play; therefore, in order to keep him immobile, it would be appropriate to keep him busy with the things consistent with his age. For example, his favorite books, puzzles or films will help him spend this period less stressfully. The child's school friends can be allowed to visit him; thus, he can share his feelings with them. If the child has hobbies such as making model airplanes, cars, etc., he is encouraged to engage in his hobbies. However, the nurses should remind both the patient and the family the risks of being active for a long time.

■ On the third day, the plaster is removed and an elastic bandage is applied. At the end of the first week, the bandage is removed and the person continues his normal school or work activities.

■After the application, long-term follow-up of bleeding is of importance. If the results are unsatisfactory, application can be repeated up to 3 times at intervals of 4-6 months.

■After the application, eligible patients can have physical therapy. Physical therapy is not a routine practice.

■After the application, the patient's joint bleedings, episodes of synovitis and joint functions are evaluated through physical examination at 1<sup>st</sup> Week, 1<sup>st</sup> Month, 3<sup>rd</sup> month, 6<sup>th</sup> month and at the end of the first year. Although MRI control after the procedure is not routine, if the physician responsible considers it necessary, it is taken. Controls are performed at 3-month intervals after the first year (13,25).

■The nurse should carefully follow the patient in terms of early complications [bleeding, inflammatory reaction (radiation synovitis), leakage of radioisotope substance from the joint, a local (skin ulceration, necrosis in the periarticular tissue) and systemic spread (via the lymphoreticular system)]. The nurse should also be aware of the long-term follow-up of the patient in terms of late complications.

RS implementation steps to facilitate its tracking and prevent errors in medical practice/ prepared by the center in order to minimize RSA (Radioisotope Synovectomy Application) used a checklist (Table 3)

## Conclusion

In general, the RS is expected to treat 75% - 95% of intra-articular bleeding and painful synovitis. The method is more successful if it is applied in the early stages when frequent bleedings due to hemophilic synovitis occur before permanent cartilage damage develops. Therefore, application of RS in small children gains importance. RS is a common practice which improves the quality of life of patients with hemophilia. However, for children less than 10 years of age, the first option should be medical treatment (secondary prophylaxis).

Nurses play a preventive, curative and rehabilitative role in all the stages of hemophilia care. The basic principle of RS in the treatment of hemophilia is the patient and family-centered approach. RS application is highly effective and beneficial for patients, but the team implementing it should be extremely experienced and careful. Administration of

radioactive material requires all the members of the RS application team to be extremely well equipped.

Therefore, the nurse assumes an important role in the fulfillment of the requirements before, during and after the RS application. The nurse's using the checklist formed by recording all the steps of RS application prevents application errors from occurring. RS application and fulfilled nursing role provide support for the quality of life of patients with hemophilia not only in the physical area but also in the emotional and social areas.

## References

1. Raffini L, Mano C. *Modern management of hemophilic arthropathy, British Journal of Haematology* 2007;136:777-787
2. Kavaklı K. *School of hemophilic patients 2003 (ed. Kaan Kavaklı), Meta-printing, İzmir 2003; 3-17.*
3. Kupesiz A. *Hedef Eklem ve kronik sinovitli çocuğa yaklaşım. 8.Ulusal Hemofili Kongresi, Kongre Kitabı (ed.Kaan Kavaklı), 5-8Mayıs 2011 Antalya, 2011:71-73*
4. Rodriguez-Merchan EC. *Musculoskeletal complications of hemophilia, HSSJ* 2010;6:37-42.
5. Ghosh K, Ghosh K. *Management of chronic synovitis in patients with hemophilia.with special reference to developing countries. Indian J.Hematol.Blood Transfus* 2008;24(4):151-54.
6. Grmek M, Milcinski M, Fettich J, Benedik-Dolnicar M, Brecej J. *Radiosynoviorthesis for treatment of hemophilic hemarthrosis-Slovenian experience. Cancer Biother Radiopharm* 2008; 20: 338-343
7. Jansen NW, Roosendaal G, Lafeber FP. *Understanding hemophilic arthropathy: an exploration of current open issues. Br J Haematol.* 2008;143(5):632-40.
8. Turkmen C. *Radiosynovectomy. Sağlıkli Duruş, 7. Ulusal Hemofili Kongresi Özet Kitabı, 15-17 Nisan 2010: 65-67.*
9. Cho YJ, Kim KI, Chun YS, Rhyu KH, Kwon BK, Kim DY, Yoo MC. *Radioisotope synoviorthesis with Holmium-166-chitosan complex in haemophilic arthropaty. Haemophilia* 2010;16:640-46.
10. Aydoğdu S. *Hemofili Hastalarında Ortopedik Yaklaşımlar, Türkiye Klinikleri, Dahili Tıp Bilimleri, Hematoloji* 2006;2:2:20-28.
11. Silva M, Luck JV Jr. *Hemophilic Synovitis: The Role of Radiosynovectomy, Treatment of Hemophilia, World Federation of Hemophilia April 2004:3*
12. Rodriguez-Merchan EC, Wiedel JD. *General principles and indications of synoviorthesis (medical synovectomy) in hemophilia. Hemophila* 2001; 7 Suppl.2): 6-10
13. Kavaklı K. *The place of Radioisotope synovectomy in the treatment of hemophilia. Clinics of Turkey J Pediatr Sci* 2005;1(3):69-73

Table 3. The Checklist of The Steps Taken During Radioactive Synovectomy Application (RSA) at Ege Hemophilia Center

<b>The patient's name and family name:</b>		<b>Protocol number: Date:</b>	
<b>Age:</b>		<b>Parents' name:</b>	
<b>Obtaining the written consent before the procedure</b> • (necessary explanation about RSA is given and the patient or the parents' written consent is obtained) • (they are also told that blood samples will be taken from the patient on the morning of surgery and that children under 10 years of age will undergo intravenous anesthesia)		Patient <input type="checkbox"/>	Family <input type="checkbox"/>
Blood sample is taken <b>at 0 min.</b> before synovectomy operation (since you will administer the factor after taking the blood sample, do not remove the injector from the vein)		Right Arm 0 min. <input type="checkbox"/>	Left arm 0 min. <input type="checkbox"/>
With the <b>50% target level</b> of factor in mind, the factor is intravenously administered at RPT doses by doctor		Right Arm <input type="checkbox"/>	Left arm <input type="checkbox"/>
The blood sample tube is labeled as <b>0 min.</b>		Hour ⌚	
Another blood sample is taken from <b>the other arm</b> 20 min. later.		Right Arm 20 min. <input type="checkbox"/>	Left arm 20 min. <input type="checkbox"/>
The blood sample tube is labeled as <b>20 min.</b>		Hour ⌚	
Patients to have synovectomy are moved to the operation unit.		Moved <input type="checkbox"/>	Not moved <input type="checkbox"/>
<b>The number of the target joints : Location</b> of the Joint: 1. .... 2. .... 3. ....			
<b>Preparation before Radioactive Synovectomy</b>		<b>P</b> performed	<b>NP</b> not performed
⌚ Preparation of the materials to be used during the application; Protective lead vest			
Injectors • injector 2 cc • injector 5 cc • injector 10 cc • injector 20 cc • The needle (no )	The number of the materials (considering the number of joints)		
Sterile pack • sterile gown • sterile mask • sterile gloves • sterile sponge			
Baticon			
Citanest			
Bandage			
⌚ Preparing a sterile environment for the application			
• Laying the sterile green cloth over the operating field			
• Cleaning the joint to be treated with an antiseptic solution (baticon)			
• Aspiration of synovial fluid			
• Recording the amount of the fluid aspirated		... cc	
⌚ Preparing the Radioisotope substance			
YTTRIUM 90		... cc	
RHENIUM 186		... cc	

Intra-articular administration of radioisotope material <b>Knee Elbow Wrist Other</b> Right <input type="checkbox"/> Right <input type="checkbox"/> Right <input type="checkbox"/> Right <input type="checkbox"/> Left <input type="checkbox"/> Left <input type="checkbox"/> Left <input type="checkbox"/> Left <input type="checkbox"/>	.... cc		
🕒 Post-application			
• The joint is passively moved 10-15 times before the plaster splint is placed / After the application, the joint is encased in the plaster splint			
• Transporting the patient whose limb is encased in plaster without moving him			
• The patient is followed approximately 4-6 hours after the operation (This operation does not require admission to hospital).			
During the observation, vital signs are determined and recorded. [Fever (F), Pulse (P), Blood Pressure (BP)]	F: P: BP:		
Bleeding control yes <input type="checkbox"/> no <input type="checkbox"/>			
Pain control yes <input type="checkbox"/> no <input type="checkbox"/>			
Analgesic requirements yes <input type="checkbox"/> no <input type="checkbox"/>			
Analgesic to be used when needed: IMPORTANT: never use aspirin and its derivatives!			
Immobilization is provided at home for three days. After the operation, especially in patients with hemophilia-A, a factor product is administered twice a day for two days in the morning and evening.			
Three days later, the plaster splint is removed and an elastic bandage is applied (not too tight).			

14. Ozkılıc H. Hemofilide izotop uygulamaları. 6.Ulusal Hemofili Kongresi, Kongre Kitabı (ed.Kaan Kavakli), 7-10 Mayıs 2009 Antalya, 2009:146-149
15. Corte-Rodriguez H, Rodriguez-Merchan CE, Jimenez-Yuste V. Radiosynovectomy in patients with chronic haemophilic synovitis: when is more than one injection necessary? *European Journal of Haematology* 2011;86:430-435.
16. Aydogdu S, Hemophilia, and Orthopedics. School of hemophilic patients 2003 (ed.Kaan Kavakli), Meta-printing, 2003;68-78.
17. Duman H, Taner S.M. Applications of nuclear medicine in hemophilia disease, school of hemophilic patients 2003 (ed.Kaan Kavakli), Meta-printing, 2003;195-97.
18. Rodriguez-Merchan EC. Orthopaedic surgery of haemophilia in the 21st. Century: an overview. *Haemophilia* 2002;8:360-68.
19. Şenol S. Hemofili Hastalarında Kapsamlı Bakım Ve Hemşirelik Rolü. *Türkiye Klinikleri J Int Med Sci* 2006;2:59-64.
20. Christie A.B. Nurses' Guide to Bleeding Disorders, National Hemophilia Foundation 2002;7-14.
21. Doria AS. State-of-the-art imaging techniques for the evaluation of haemophilic arthropathy: present and future. *Haemophilia* 2010;16 (Suppl.5):107-14.
22. Turkmen C. Radiosinovektomide kullanılan İzotopların Güvenirliği, 6. Ulusal Hemofili Kongresi, Kongre Kitabı (ed.Kaan Kavakli), 7-10 Mayıs 2009 Antalya, 2009:101-4.
23. Turkmen C, Ozturk S, unal SN, Zulfikar B, Taser O, Sanli Y, Cefle K, Kilicoglu O, Palanduz S. The genotoxic effects in lymphocyte cultures of children treated with radiosynovectomy by using yttrium 90 citrate colloid. *Cancer Bioter Radiopharm.* 2007;22(3):393-9.
24. Kavakli K, Cogulu O, Aydogdu S, Ozkılıc H, et al. Long-term evaluation of chromosomal breakages after radioisotope synovectomy for treatment of target joints in patients with haemophilia. *Haemophilia* 2010;16:474-78.
25. Kavakli K, Aydogdu S, Taner M, Balkan C. Radioisotope synovectomy with yttrium 90 and rhenium 186 for hemophilic synovitis: 7 years, 181 patients, 209 joints, 221 applications: Izmir experience. *Haemophilia* 2008;14 (Suppl 2):1-12

Corresponding Author

Selmin Senol,

Ege University Izmir Ataturk School of Health

Bornova,

Izmir,

Turkey,

E-mail: senonselmin@yahoo.com

# An approach for early and appropriate prediction of dengue fever using white blood cells and platelets

Wen-Pin Lai<sup>1,2</sup>, Tsair-Wei Chien<sup>2,3</sup>, Ming-Ting Chow<sup>4</sup>

<sup>1</sup> Department of Emergency Medicine, Chi-Mei Medical Center, Taiwan,

<sup>2</sup> Department of Hospital and Health Care Administration, Chia-Nan University of Pharmacy and Science, Tainan, Taiwan,

<sup>3</sup> Department of Administration, Chi-Mei Medical Center, Taiwan,

<sup>4</sup> Department of Cardiology, Chi Mei Medical Center, Tainan, Taiwan.

## Abstract

**Introduction:** Dengue fever (DF) is common in Asia. Dengue hemorrhagic fever (DHF) occurs predominantly in children less than 16 years old. In practice, the results of diagnostic tests, whenever available, are rarely received in time to be useful for immediate treatment in endemic regions. Our goal is to identify simple laboratory features to discriminate DF from non-dengue fever (NDF).

**Methods:** There are two parts used to investigate the simple way discriminating DF. First, multivariate discrimination analyses were applied to those three statistical techniques of rotate axis, logistic regression and principle component analysis in detecting their effects. Second, three scaling schemes of dichotomy with coding 2 and 1, 1 and 0 as well as of polytomy coding 2, 1 and 0 on WBC and PLT by adding category scores were applied to verify the best model to predict Dengue fever. In this model, lower values tend to be DF.

**Results:** WBC and PLT are the discriminatory variables that enable distinction between DF and NDF. Using the area under the ROC curve (AUC) to verify the efficacies of the three statistical prediction methods and coding schemes, we recommend that polytomy with a cut-point  $\leq 2$  by the coding scheme from 2 to 0 can be applied to clinical practice because it is easier and faster than other available prediction methods.

**Conclusions:** We suggest using a polytomous coding scheme with a cut-point  $\leq 2$  as a technique for rapidly detecting DF. Further studies should be performed in different countries and areas in the future.

**Key words:** Dengue fever, white blood cells, platelets, ROC curve, discrimination analysis

## Introduction

Dengue fever (DF) is one of the most common worldwide arthropod-borne viral diseases [1]. It often presents as acute febrile illness of unclear aetiology. Infection with dengue virus causes a spectrum of illness ranging from no symptoms to mild fever to severe or even to fatal haemorrhage and shock [2, 3]. DF is an important epidemic illness in Southern East Asia, Africa, the Western Pacific and the Americas [4, 5]. Globally, it is estimated that 2.5 billion people in more than 100 countries are at risk for dengue viral infection [5]. Among them, approximately 50 to 100 million new infections occur annually. About 250,000-500,000 cases of potential life-threatening dengue hemorrhagic fever (DHF)/ dengue shock syndrome (DSS) are reported annually [6].

Some studies have reported that it is so imprecise in diagnosis of DF that the signs or symptoms are fairly implicative for use in detecting DF [7,8]. That means that DF initially has no outward symptoms. Symptoms may not appear until severe complications have occurred.

However, thrombocytopenia and leukopenia have been reported to be highly associated with dengue fever [9-11]. Two of these studies [9, 11] used dichotomous categorization on white blood cells (WBC) and platelets (PLT) to detect DF. We are interested in studying whether polytomous categorization on WBC and platelet counts could detect DF more accurately than dichotomy. In this study, we attempt to investigate the sensitivity of different coding schemes and three multivariate approaches, i.e., rotated axis, logistic regression and principle component analysis (PCA) to evaluate their effectiveness in detecting DF.

## Methods

### *Subjects and studied elements*

Retrospective study data were collected from patients' medical records from January to December 2007. Of these patients, a total of 177 were children ( $\leq 16$  years of age) with a suspected dengue virus infection who visited a medical centre emergency department for treatment in southern Taiwan. The patients experienced clinically suspicious febrile illnesses and underwent routine blood testing, including white blood counts and platelet values. Serological confirmation of DF was performed using Dengue Duo IgM Rapid Strips (Pan Bio, Australia) [12, 13] to ensure that dengue viral infection occurred. Patients were hence grouped into two strata: DF when the strip test was positive and NDF when the test was negative (Table 1).

This study is verification that these two factors with white blood cells and platelets lead to successful identification of DF. There are two parts introduced in the next section to select an alternative rapid screening method to detect dengue fever.

#### *A. Statistics for Distinguishing DF*

##### *Distinguishing DF by both WBC and PLT using discriminant analysis*

Traditionally, a *t*-test for two independent groups is done on a continuous variable using a univariate approach. Recently, multivariate tests are done for two simultaneous continuous variables that jointly describe a common characteristic. One of them is called rotated *Z* from which a newly derived axis makes a rotated angle, for example  $70^\circ$ , with both variable axes that shows a new composite score on rotated *Z*. It will be given by:

$$Z_p = w_1 \times \text{variable}_1 + w_2 \times \text{variable}_2, \dots \dots (1)$$

The above equation clearly represents a linear combination of the two variables (i.e., WBC and PLT in this study) for patient *p*. That rotated *Z* axis becomes a new variable representing a linear combination of the original two variables [14] when DF and NDF are known. The ratio of the between-group to within-group sum of squares for each angle implies that the composite score derived from equation (1) on the new axis provides

the maximum separation between the two groups. The cut-point can be determined by the number of observations, and the average distinguishing score for groups is as follows: [14].

$$\text{cutoff} = \frac{n_1 \bar{Z}_1 + n_2 \bar{Z}_2}{n_1 + n_2}, \dots \dots \dots (2)$$

##### *Distinguishing DF by both WBC and PLT using logistic regression*

When the two independent variables of WBC and PLT are used to predict DF, the logistic regression can be applied without assuming the distribution of the independent variables. For example, WBC and PLT are not usually normally distributed. Logistical regression is normally recommended when the independent variables do not satisfy the multivariate normality assumption [14, 15]. We hereby illustrate the logistic regression by using those two independent variables of WBC and PLT to predict DF.

##### *Distinguishing DF by both WBC and PLT using PCA*

When DF and NDF are not known before analysis, we could use principle component analysis (PCA), which is also formed a new variable derived from WBC and PLT. The linear combination of the original variables, such as WBC and PLT, could be used to develop a regression model when there is multicollinearity in the data [14]. It is well known that in the presence of multicollinearity, the standard errors of the parameter estimates could be quite high, resulting in unstable estimates from the regression model [15]. In this study, we attempted to form a new variable, different from the rotation axis mentioned above, for prospective use when DF status is unknown.

#### *B. Coding schemes for Distinguishing DF*

##### *Polytomous and dichotomous coding scheme on WBC and PLT for detecting DF*

For practice, we attempted to categorize the two continued variables of WBC and PLT to be (1) polytomy coding from 2 to 0 (WBC count(1/ $\mu$ l)  $>5000$ , 3000-5000 and  $\leq 3000$ ; PLT(1/ $\mu$ l)  $>150K$ , 100K-150K and  $\leq 100K$ , the lower num-

ber increases the probability that the patient has DF); (2) dichotomy coding from 2 to 1 (namely D-U: WBC( $1/\mu\text{l}$ )  $>5000$  and  $\leq 5000$ ; PLT( $1/\mu\text{l}$ )  $>150\text{K}$  and  $\leq 150\text{K}$ , lower sum indicates a higher tendency toward DF); (3) dichotomy coding from 1-0 (namely D-L: WBC( $1/\mu\text{l}$ )  $>3000$  and  $\leq 3000$ ; PLT( $1/\mu\text{l}$ )  $>100\text{K}$  and  $\leq 100\text{K}$  lower sum indicates a higher tendency toward DF).

### Statistical analysis

Statistical analyses were performed using MedCalc for Windows, version 9.5.0.0 (MedCalc Software, Mariakerke, Belgium), and SPSS for Windows (Version 15). The cut-off value results from the recommendation from MedCalc plots of the receiver operating characteristic (ROC) curve [16] when the cut-off value from equation 2 does not perform well.

### Ethics Review Board Approval

The protocol of this study was approved by the Research and Ethics Review Board of Chi-Mei Medical Center. All authors certify that there are no known conflicts of interest with any third party.

## Results

### Clinical symptoms and laboratory characteristics

Sixty-nine patients with DF presented at a mean of 4.53 days (ranged in 1–10 days) after the onset of fever. The median patient age was 10 years (range 0–16 years), and 40 subjects (58.0%) were male. The 108 NDF patients were recruited as a reference group. They presented with a mean of 2.97 days (ranged in 1–9 days) after the onset of fever. The median age for this group was 5 years (range in 0–16 years), and 61 subjects (56.5%) were male (Table 1). Patients with NDF were consecutive, and we found no evidence of dengue viral infection.

The proportions of patients are shown in Table 2 according to abnormal laboratory results. A significant higher proportion in DF than in NDF displayed with abnormal values of reduced platelet and WBC counts. In contrast, a significant higher proportion in NDF than in DF showed relatively normal values of WBC and platelet counts.

Table 1. Gender and age data for the study

	NDF	DF	Total
Count	108	69	177
	61.02%	38.98%	100.00%
Gender			
Female	47	29	76
	26.55%	16.38%	42.94%
Male	61	40	101
	34.46%	22.60%	57.06%
Age			
0-4	48	11	59
	44.4%	16.2%	33.5%
5-9	24	20	44
	22.2%	29.4%	25%
9-16	36	37	73
	33.3%	54.4%	41.5%

DF: patients with Dengue Duo IgM Rapid Strips test(+)

NDF: patients with Dengue Duo IgM Rapid Strips test(-)

### A. statistics for Distinguishing DF

#### Discriminant analysis identifying a New Axis

Identifying a set of variables that best differentiates between the two groups of DF and NDF is the first objective of discriminant analysis. From Table 2 we can see that WBC and PLT are the discriminator variables for discrimination of DF and NDF. The Chi-square test in Table 2 suggests that the two groups are statistically different in both WBC and PLT ( $p < .05$ ).

From Figure 1, it can be seen that a new rotated axis in the two-dimensional space makes an angle of  $84^\circ$  with the WBC and PLT axes, on which the projection of any point of a patient  $p$  on the rotated axis will be given. It clearly represents a linear combination of WBC and PLT for patient  $p$ . Table 3 shows each ratio,  $\lambda$ , of the between-group to the within-group sum of squares for each angle ( $\theta$ ), implying that the greatest  $\lambda$  on the new axis provides the maximum separation between the two groups. We choose an angle of  $84^\circ$  as the optimal solution as well as a cut-point of 1.88 that refers to the score of rotated new axis resulting from a formula of  $0.1045 \times \text{WBC}(1,000/\mu\text{l}) + 0.9945 \times \text{PLT}(100,000/\mu\text{l})$ . This gave an overall accuracy of 81.17%, as shown in Table 4.



Table 2. Laboratory findings for the studied patients at hospital visits

Variables	Scoring		N	Mean(SD)	N	Mean(SD)	N	Mean(SD)	p <sup>a</sup>
WBC count (1/μl)			104	7.4(3.1)	66	3.6(2.4)	170	5.9(3.8)	<.001
Platelet count (1/μl)			104	235.5(92.3)	66	128.8(60.8)	170	194.1(96.6)	<.001
	Coding	Thresholds	N	%	N	%	N	%	
<b>Polytomy</b>									
WBC count (1/μl)	2	>5000	74	71.2	10	15.2	84	49.4	< .001
	1	3000-5000	17	16.3	17	25.8	34	20	
	0	<=3000	13	12.5	39	59.1	52	30.6	
Platelet count (1/μl)	2	>150K	82	78.8	15	22.7	97	57.1	< .001
	1	100K-150K	18	17.3	27	40.9	45	26.5	
	0	<=100K	4	3.8	24	36.4	28	16.5	
<b>U_dichotomy (U-D)</b>									
WBC count (1/μl)	2	>5000	74	71.2	10	15.2	84	49.4	< .001
	1	<=500	30	28.8	56	84.9	86	20.6	
Platelet count (1/μl)	2	>150K	82	78.8	15	22.7	97	57.1	< .001
	1	<=150K	22	21.1	51	77.3	73	33	
<b>L_dichotomy (L-D)</b>									
WBC count (1/μl)	1	>3000	91	86.5	27	38	118	69.4	< .001
	0	<=3000	13	12.5	39	59.1	52	30.6	
Platelet count (1/μl)	1	>100K	100	96.1	42	63.6	142	83.6	< .001
	0	<=100K	4	3.8	24	36.4	28	16.5	

a: Chi-square test

Note. Seven patients with Dengue Duo IgM Strip test had no laboratory data available at their hospital visit.

Table 3. Summary statistics for various linear combinations

Angle	Weights	Sum of Squares	λ					
θ	w1(Cosθ)	w2(Sinθ)	SSt	SSw	SSb	(SSb/SSw)	F-value	
0	1	0	598368	396380	201988	0.51	43.824	
10	1	0	598368	396380	201988	0.51	43.824	
20	0.94	0.342	540383	357360	183023	0.512	44.045	
30	0.866	0.5	465045	307248	157797	0.514	44.168	
40	0.766	0.643	369759	244022	125736	0.515	44.313	
50	0.643	0.766	266016	175310	90706	0.517	44.497	
60	0.5	0.866	166331	109399	56932	0.52	44.755	
70	0.342	0.94	82727	54239	28488	0.525	45.171	
80	0.174	0.985	25288	16482	8805	0.534	45.944	
84	0.105	0.995	11318	7358	3960	0.538	46.286	
90	0	1	8500	7365	1135	0.154	13.251	

Table 4. Comparison among alternatives for AUC

Alternatives	Accuracy %	AUC	SE	95% CI	cut-off	sensi-tivity	speci-ficity	LR+	LR-	scale	Opt.
1 Logistic Reg.	81.18%	0.873	0.0302	0.81- 0.92	<=0.28	0.78	0.86	5.47	0.25	Cont.	*
2 Rotated	81.17%	0.87	0.0267	0.81- 0.92	<=13.62	0.78	0.83	4.47	0.22	Cont.	*
3 PCA	81.18%	0.873	0.0263	0.81- 0.92	<=-0.31	0.88	0.77	3.81	0.16	Cont.	*
4 Polytomy	80.00%	0.856	0.028	0.79-0.91	<=2	0.85	0.77	3.67	0.2	0,1,2	*
5 U_dichotomy(U-D)	80.00%	0.829	0.0306	0.76- 0.88	<=2	0.74	0.84	4.55	0.31	1,2	
6 L_dichotomy(L-D)	80.00%	0.797	0.0333	0.73- 0.80	<=1	0.73	0.85	4.72	0.32	0,1	

Note. The likelihood ratio for a positive result (LR+) tells us how much the odds of the DF increase when a test is positive. The likelihood ratio for a negative result (LR-) tells us how much the odds of the DF decrease when a test is negative.

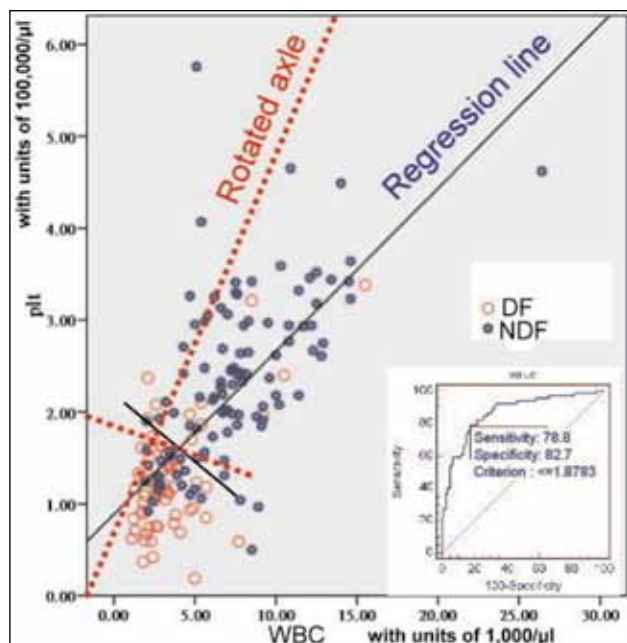


Figure 1. Rotated axis with a cut-point of 1.88 with sensitivity of 78.8 and specificity of 82.7

**PCA and Logistic regression**

We obtained a PCA score from SPSS statistical software to verify an overall accuracy of 81.18%, as shown in Table 4. The areas under the ROC curve (AUC) were also obtained, as shown in Table 4 and Figure 2 with plausible and acceptable responses similar to those derived by the rotation axis of discriminant analysis and logistic regression with a formula of  $DF = 3.2572 - 0.2852 \times WBC(1,000/\mu l) - 1.3204 \times PLT(100,000/\mu l)$ . Beyond that, in Table 4 we see that PCA had the highest sensitivity compared to the other five.

**B. Coding schemes for Distinguishing DF**

**Polytomy and dichotomy when recoding WBC and PLT**

The L dichotomy (L-D) in Table 4 had the lower AUC. In contrast, polytomy had an acceptable higher sensitivity (0.85) than other two dichotomous coding schemes (0.74, 0.73). For clinical practice, the higher sensitivity indicates a better screen for patients with DF. We are therefore concerned with the top four with an asterisk in the extreme right column of Table 4.

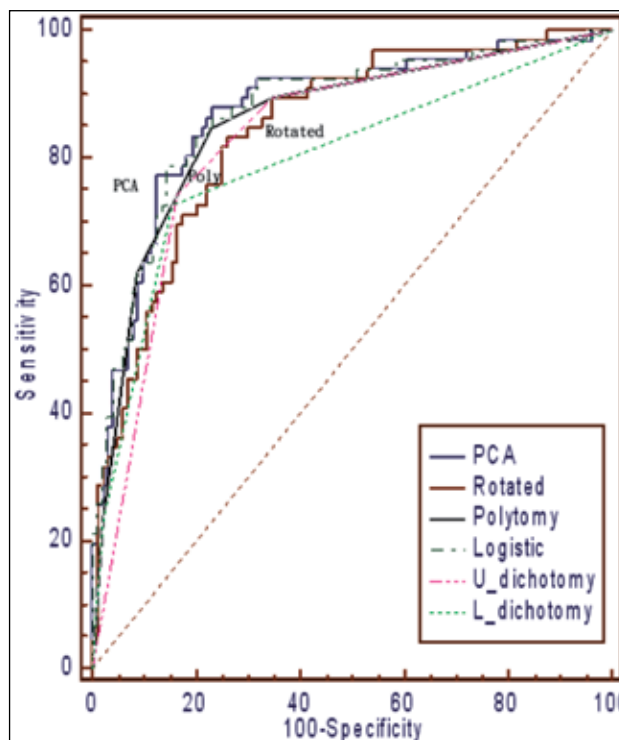


Figure 2. Comparison among alternatives for AUC

**Discussions**

In some countries, both DF and DHF is primarily a clinical diagnosis without awaiting laboratory confirmation, [17]. However, the presumptive diagnosis is rather imprecise [7, 8]. Some proposals suggest that methodologies should be applied earlier to improve the diagnostic accuracy and precision; these methodologies include RT-PCR [17, 18], IgM capture ELISA [17, 18, 19] and rapid bed-site tests [12, 13, 20]. Nevertheless, these tests are neither available outside urban areas and nor routinely applied in the clinical setting [21]. As a result, there is a considerable need for a rapid, inexpensive screening test that is both sensitive and specific.

**Features and findings**

We found that thrombocytopenia and leukopenia are highly associated with dengue fever, findings similar to those previously published by other groups [9-11,22]. WBC and PLT are often performed in primary clinical settings; therefore, a combination of these laboratory variables (low platelet or leukocyte count) for early detection of dengue infection could be clinically useful.

The PCA could not provide a formula easily used by practitioners as the other three candidates marked with an asterisk in the extreme right column of Table 4. For instance, there are the rotated one with a formula of  $0.1045 \times \text{WBC}(1,000/\mu\text{l}) + 0.9945 \times \text{PLT}(100,000/\mu\text{l})$ , the polytomous one with a coding from 2 to 0 for WBC and PLT, and the logistic regression with a formula of  $\text{DF}=3.2572 - 0.2852 \times \text{WBC}(1,000/\mu\text{l}) - 1.3204 \times \text{PLT}(100,000/\mu\text{l})$ . All of these alternatives are easier in computation than the PCA. Considering the remaining three alternatives, the rotated axis and logistic regression can yield a higher AUC and overall percentage of accuracy as well as higher positive and negative likelihood ratios than polytomy. However, polytomy has a higher sensitivity (0.85) than the other two, which have a joint sensitivity of 0.78. From public health points of view, the polytomy coding method from 2 to 0 can be recommended for clinical detection of DF.

### Limitation and further studies

There are several limitations of this study. First, it lacks serotype identification and hospital-based design. Laboratory investigations for patients were obtained and recorded only at their first hospital visits before performing therapy. Further studies on the natural history of dengue and non-dengue disease can be carried out with a more appropriate hospital-based design. Second, the sample size was small, though a highly accurate discriminatory screening feature appeared in this study. It should be further confirmed by prospective studies in other areas or countries affected by dengue.

### Conclusion

We recommend the polytomy method with a cut-point  $\leq 2$  by that coding scheme from 2 to 0 as a simple use of laboratory data to differentiate DF from NDF through computer calculation to screen the possible DF. This recommendation is of importance for medical practitioners, particularly those who practice in primary clinics, to detect DF using polytomy as early as possible when dengue IgM/IgG antibody, PCR or virus isolation are not available in their clinical settings, especially in the remote rural area. For further studies, we recom-

mend that researchers focus their efforts on the studied six alternatives shown in Table 4, to repeat and apply them as they wish while jointly comparing results from other diseases.

### List of abbreviations

DF: dengue fever; NDF: non-dengue fever; DHF: dengue hemorrhagic fever; WBC : white blood cells; PLT: platelets; AUC: area under ROC curve; PCA: principle component analysis; DSS: dengue shock syndrome. MNSQ: mean square errors; CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; RT-PCR: reverse transcriptase polymerase chain reaction; ROC: receiver operating characteristic.

### Authors' contributions

WP collected all data and built up the database, designed and performed the statistical analysis and wrote the manuscript. TW contributed to the development of the study design and advised on the performance of the statistical analysis. The analysis and results were discussed by all authors who jointly interpreted the results and helped to draft the manuscript. All authors read and approved the final manuscript.

### Acknowledgments

This study was supported by Grant CM-FHR9820 from the Chi Mei Medical Center, Taiwan.

### Reference

1. WHO. World Health Organization. Geneva: World Health Organization 2002; Fact sheet No 117.
2. Henchal EA, Putnak JB. The dengue viruses. *Clin Microbiol Rev* 1990; 3: 376–396.
3. Gubler DJ. Dengue and dengue hemorrhagic fever. *Clin Microbiol Rev* 1998; 11: 480–496.
4. Calisher CH. Persistent emergence of dengue. *Emerg Infect Dis* 2005; 11: 738–9.
5. Guzman MG, Kouri G. Dengue: an update. *Lancet Infect Dis* 2002; 2: 33–42.
6. Gibbons RV, Vaughn DW. Dengue: an escalating problem. *BMJ* 2002; 324: 1563-6.

7. *Phuong HL, de Vries PJ, Nga TTT, Giao PT, Hung LQ, Binh TQ, Nam NV et al.. Dengue as a cause of acute undifferentiated fever in Vietnam. BMC Infectious Diseases 2006; 6:123.*
8. *Nunes-Araújo FR, Ferreira MS, Nishioka SD. Dengue fever in Brazilian adults and children: assessment of clinical findings and their validity for diagnosis. Ann Trop Med Parasitol. 2003; 97(4):415-419*
9. *Annelies WS, Earnest A, Nicholas IP. Use of Simple Laboratory Features to Distinguish the Early Stage of Severe Acute Respiratory Syndrome from Dengue Fever. Clinical Infectious Diseases 2004; 39:1818–23*
10. *Liu HW, Ho TL, Hwang CS, Liao YH. Clinical Observations of Virologically Confirmed Dengue Fever in the 1987 Outbreak in Southern Taiwan. Kaohsiung J Med Sci 1989; 5: 42-49*
11. *George W, Krisada J, Charoen C, Paris R. Differentiating Dengue Virus Infection from Scrub Typhus in Thai Adults with Fever. Am J. Med. Hyg. 2003; 536-538*
12. *Kittigul L, Suankeow K. Use of a rapid immunochromatographic test for early diagnosis of dengue virus infection. Eur J Clin Microbiol Infect Dis 2002; 21: 224–6.*
13. *Vaughn DW, Nisalak A, Kalayanaroj S, Solomon T, Dung NM, Cuzzubbo A, et al. Evaluation of a rapid immunochromatographic test for diagnosis of dengue virus infection. J Clin Microbiol 1998;36:234–8.*
14. *Vaughn DW, Nisalak A, Kalayanaroj S, Solomon T, Dung NM, Cuzzubbo A, et al.. Evaluation of a rapid immunochromatographic test for diagnosis of dengue virus infection. J Clin Microbiol 1998, 36: 234–8.*
15. *Sharma S. Applied multivariate techniques. John Wiley & sons, Inc.: Canada, 1996.*
16. *Eack, S.M., Singer, J.B., Greeno, C.G.(2008).Screening for anxiety and depression in community mental health: the beck anxiety and depression inventories. Community Ment Health J., 44(6): 465-74.*
17. *Kamaljit S, Ajit L, Eng EO, Chiu LL, Vincent TK, Chow PT, Evelyn SC,. A prospective clinical study on the use of reverse transcription-polymerase chain reaction for the early diagnosis of dengue fever. Journal of Molecular Diagnostics 2006; 8(5): 613-616*
18. *Yamada KM, Nawa T, Takasaki SY, Kurane I. Laboratory diagnosis of dengue virus infection by reverse transcriptase polymerase chain reaction (RT-PCR) and IgM-capture enzyme-linked immunosorbent assay (ELISA). Jpn. J. Infect. Dis. 1999; 52:150–155.*
19. *Nawa MT, Takasaki K, Yamada TA, Kurane I. Development of dengue IgM-capture enzyme-linked immunosorbent assay with higher sensitivity using monoclonal detection antibody. J. Virol. Methods 2001; 92: 65–70.*
20. *Blacksell SD, Newton PN, Bell D, Kelley J, Mammen MP Jr, Vaughn DW, et al.: The comparative accuracy of 8 commercial rapid immunochromatographic assays for the diagnosis of acute dengue virus infection. Clin Infect Dis 2006; 42:1127-1134.*
21. *Annelies WS, Eli S. Dengue in Travelers. N Engl J Med 2005; 353:924-32.*
22. *Lai WP,Chien TW,Lin HJ,Lin CH,Chuang YC, Su SB:Rasch scaling of clinical criteria for early detection of dengue fever in Children. HeathMed 2011,5(5):*

Corresponding Author  
Ming-Ting Chou,  
Department of Cardiology,  
Chi Mei Medical Center,  
Tainan,  
Taiwan,  
E-mail: smile@mail.chimei.org.tw

# Histopathological types of colonic adenomas incidence of dysplastic changes in Riyadh, Saudi Arabia

*Al-Dahmash B.<sup>1</sup>, Saad Alkahtani I<sup>2</sup>, AL-Farraj S. A.<sup>2</sup>, Saud A. Alarifi<sup>3</sup>, AL-Eissa Mohammed Saad<sup>4</sup>, Hamad Al-Yahya<sup>2</sup>, Marie M. A<sup>5</sup>*

<sup>1</sup> Department of Medical Laboratory, College of Health Sciences, King Saud University, Riyadh, Saudi Arabia

<sup>2</sup> Department of Biology, Teachers College, King Saud University, Riyadh, Saudi Arabia.

<sup>3</sup> Department of Zoology, Science College, King Saud University, Riyadh, Saudi Arabia.

<sup>4</sup> Department of Biology, Science College, Hail University, Hail, Saudi Arabia.

<sup>5</sup> Department of Clinical Laboratory Sciences, College of Applied medical Sciences, King Saud University, Riyadh, Saudi Arabia

## Abstract

One hundred thirty seven adenomas of the colon from 112 patients were identified by histological examination of surgically or colonoscopically removed adenomas. All lesions had a radial diameter of 1.0 cm or less. Fifty six of 137 adenomas (41%) contained high-grade epithelial dysplasia, twenty five patients had multiple adenomas. Colonoscopically and grossly, the lesions were described as sessile, tubular, villous or tubulovillous growth. These lesions may be precursors of small, flat, ulcerated colonic carcinomas. Our study encompasses the histology and differential diagnosis of screen detected polyps, focusing on features which discriminate lesions at highest risk of malignant transformation.

**Key words:** Dysplasia, colon, lesions, carcinoma

## Introduction

The majority of published clinical, histologic, and genetic data on colonic neoplasia indicate that colonic adenomas are precursors to most or all of colonic carcinomas, and that the risk of development of carcinoma within an adenoma increases with the size and histologic grade of the lesion (1-5). Since the majority of colonic adenomas have an exophytic, polypoid configuration which are a circumscribed lesions projecting in the bowel lumen, colonoscopic identification and removal of polyps has been widely used as an effective prophylactic against the development of colonic carcinoma (6-7). Nevertheless, many advanced carcinomas and

a small percentage of early carcinomas fail to contain a residual precursor adenoma (8-13). While it is very probable that large advanced carcinomas progressively destroy adjacent non-carcinomatous dysplastic epithelium (9-12), the identification of small, superficially invasive carcinomas without an identifiable contiguous polypoid adenoma has led to the reemergence of the concept of "de novo" development of colonic carcinoma (14-15). An alternate explanation for the existence of small, invasive carcinomas without a precursor polypoid adenoma is that these lesions may arise from very small, highly dysplastic adenomas which are rapidly re-placed by the expanding malignancy. The sporadic identification of similar lesions at our institution has prompted us to undertake a systematic analysis of colonoscopically and surgically excised adenomas in order to determine the relative frequency and clinicopathologic changes of adenomas.

## Materials and methods

The surgical pathology files from different hospitals in Riyadh, Saudi Arabia were searched for all cases coded during previous 2 years period (2009-2010) as containing colonic adenoma. One hundred thirty seven adenomas were obtained from colonoscopically and surgically excised specimens from 112 patients, following exclusion of specimens from patients with familial polyposis or long-standing ulcerative colitis. Multiple level hematoxylin-eosin-(H&E) stained sections from lesions were independently examined by

two observers. Patient demographic data lesion location (ascending, transverse, descending or rectosigmoid colon) lesion size (< 1cm, 1-2cm, or > 2cm). Histologic picture as (tubular, tubulovillous, villous, or flat), and grade of epithelial dysplasia (low or high grade) were determined for all lesions. Adenomas were classified as flat when they lacked the exophytic configuration. The dysplastic mucosa was never greater than two times the thickness of the adjacent non dysplastic mucosal segment. The histologic grade of the epithelial dysplasia in each adenoma was determined by the following criteria: high-grade lesions showed stratification of nuclei and numerous mitotic figures through the full thickness of crypt epithelium, with loss of nuclear polarity, marked nuclear atypia, and complete absence of cytoplasmic mucinous differentiation. These cytologic features had to involve at least three tubules or crypts. The presence of marked crypt architectural complexity or nuclear karyorrhexis was not used as an independent criterion for determination of dysplasia grade. Clinical records, including colonoscopy reports, were reviewed for all patients in whom adenomas were identified.

### Data analysis

Fisher's exact test was used for analysis of data. A *P* value of < 0.05 was accepted as statistically significant.

### Results

Of the 137 adenomas. These were found in patients. The demographic, gross, and histologic features are presented in Table (1). The mean age of the patients was 43 years (range, 14 - 78) and 83% were Male. However, a non-polyposis cancer family syndrome had not been documented in any of these patients. Multiple adenomas were identified in 25 patients of the 137 patients ( 18% of total adenomas). Tubular adenomas were classified as tubular, tubulovillous or villous adenoma. They are also classified as low grade and high grade according to the degree of dysplasia. High grade dysplasia considered to be more sensitive marker of malignant potential. Low grade dysplasia includes mild to moderate loss of normal epithelial

maturation, nuclear stratification and mucin depletion accompanied by variable degrees of simple glandular crowding. Tubular adenomas were 10 cases (7.3 %), tubulovillous 17 (12.4 %) and purely villous 6 (4.4 %). One hundred thirty of the adenomas were excised colonoscopically by snare and electrocautery or, in two lesions, by pincer biopsy. Seven adenomas were removed as part of a segmental colectomy for a separate invasive carcinoma. In these specimens, the adenomas were identified incidentally during the gross pathologic examination and sectioning. Both of these carcinomas had a grossly sessile, ulcerated appearance without exophytic polypoid component. As sessile flat, plaque-like, or an "abnormal mucosal fold ". Ten flat adenomas were located in the ascending colon, four in the transverse colon, five in the descending colon, and 10 in the rectosigmoid colon.

Analysis of histologic sections of the flat adenomas supported the colonoscopic impression that all (104) had a purely tubular morphology. The low-magnification configuration was of a slightly raised plaque, regardless of whether the lesion was located within flat mucosa or on the tip of a mucosal fold (Figure 1).

The characteristic architecture of a crowded collection of dysplastic crypts located at the superficial luminal surface of the mucosa, with underlying, well-spaced, nondysplastic crypts, was identified in serial sections in all cases (Figure 2). In some lesions, focal full thickness mucosal dysplasia was present, often with mucosal invagination and thinning, and always in the center of an adenoma which showed only superficial mucosal dysplasia at the periphery of the lesion (Figure 3).

High-grade dysplasia, based upon the identification of full thickness crypt epithelial nuclear stratification and loss of cytoplasmic mucinous differentiation, was found in (97) of (137) adenomas in total (Figure 4). Concomitant crypt budding and excessive nuclear debris were present in (9) lesions, respectively (Figure 5).

In at least (42) cases, the degree of nuclear complexity was such that a diagnosis of intramucosal carcinoma was considered

In comparison, histologic grading was also performed upon the polypoid tubular adenomas. The rectosigmoid colon, 67 cases were specified. Histologic grading revealed (3) of the (10) polyp-

oid tubular adenomas (30 %) to be high grade. A tubular had a ten-fold greater frequency of containing high-grade dysplasia than an analogous polypoid adenoma with an equivalent spherical diameter ( $p < 0.05$ ).

Both of the colonic surgical resection specimens in which flat adenomas were identified contained simultaneous, non contiguous, flat and ulcerated carcinomas without a residual polypoid adenoma at the periphery of the lesion. These cancers were located in the ascending and rectosigmoid colon Cularis propria, and the larger lesion extended into pericolic adipose tissue. The edge of both lesions showed an abrupt transition from benign colonic mucosa to ulcercinoma (Fig6), with focal extension of highly dysplastic crypts along the surface of rolled benign mucosa in one of these lesions. A single regional lymph node metastasis was found in one of these patients, Villous structures form at least 80% of villous adenomas and more than 20% of tubulovillous adenomas. Villi may be long slender, finger like palmate villi, leaf like, broad branched processes or foreshortened villi , isolated slender overgrowths. The presence of at least one identifiable villous in polyp biopsies or fragments deserves to report as predominantly tubular histology.

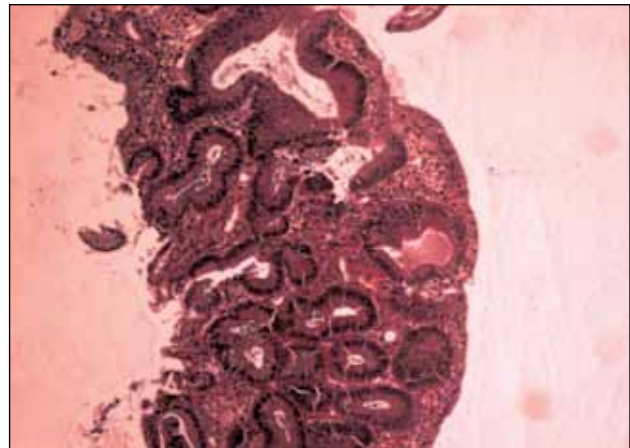


Figure 1. Flat colonic adenomas from involving (top) flat and (bottom)folded mucosa .(H&E stain: magnification x 15).

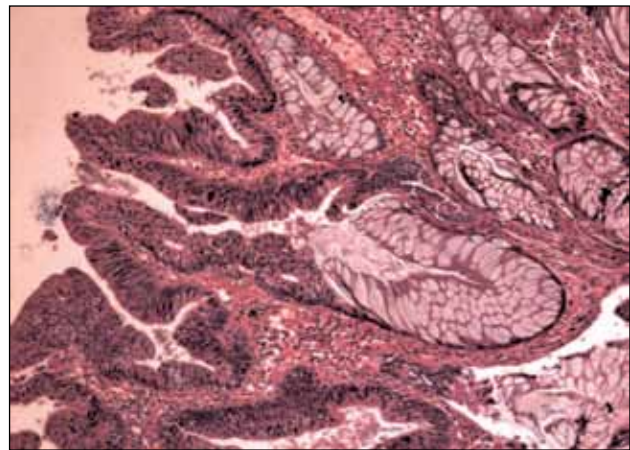


Figure 2. Colonic adenoma from patient dysplastic crypts clustered at the superficial lumens surface of the mucosa with underlying non- dysplastic crypt epithelium.(H&E stain: magnification x 48)

Table 1. Shows the age of the patients

Years	10-19	20-29	30-39	40-49	50-59	60-69	70-80	Total
Male	4	12	14	20	32	4	5	91
Female	3	3	3	2	5	2	1	19

Table 2. Shows the Percentage of Dysplastic changes

	Flat	Tubular	Tubular villous	Villous	Total
High grade	73	3	15	6	97
Low grade	31	7	2	0	40

Table 3. Shows the Histological types according to the site affected

Site	Total	Flat	Tubular	Tubular villous	Villous
Rectosigmoid	67	50	6	8	3
Transverse	32	29	1	2	0
Descending	26	18	2	5	1
Ascending	12	7	1	2	2
	137	104	10	17	6

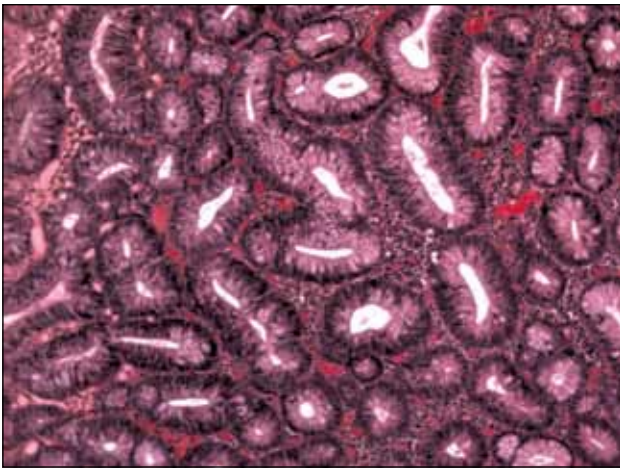


Figure 3. Colonic adenoma ,showing full thickness mucosal dysplasia in the central ,invaginated portion of the lesion. (H&E stain; magnification x 25 ).

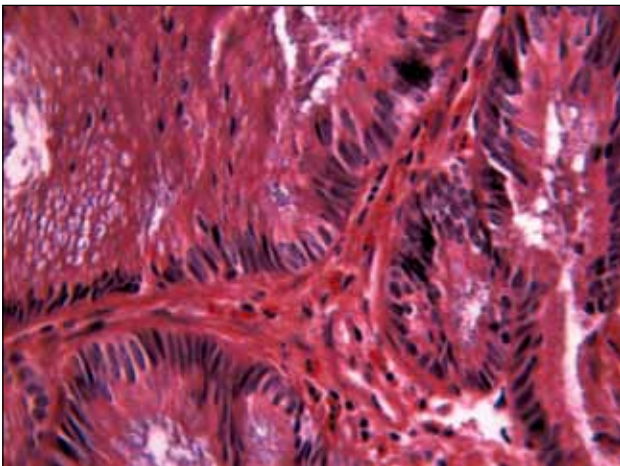


Figure 4. High grade flat colonic adenomas from full thickness epithelial nuclear stratification, loss of cytoplasmic mucin production, and marked nuclear atypia. (H&E stain; magnification x 120)

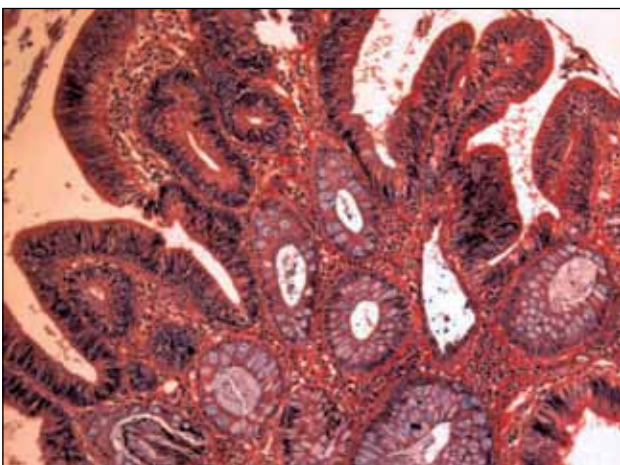


Figure 5. Excessive nuclear debris and crypts complexity in flat colonic adenoma (H&E; stain; magnification x 240).

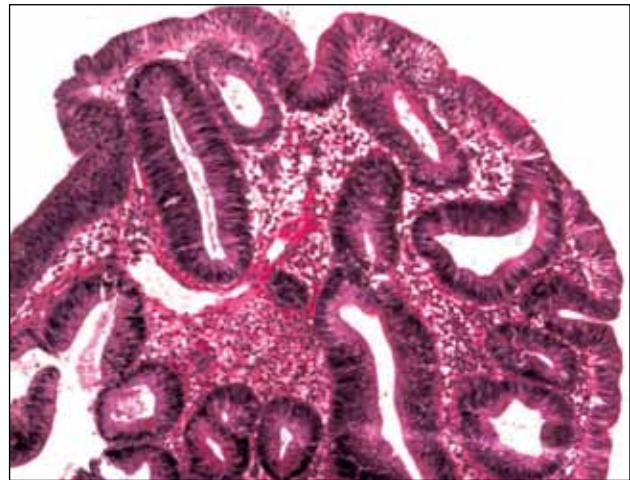


Figure 6. Flat, ulcerating carcinoma, showing abrupt transition from benign to carcinomatous epithelium. (H&E stain: magnification x15.)

### Discussion

The most widely accepted morphologic classification of dysplastic colonic polyps includes tubular, tubulovillous, and villous adenomas (1-2), Adenoma type, size, and grade of epithelial dysplasia have been emphasized as factors associated with those lesions containing carcinoma. The gross configuration of exophytic colonic polyps (pedunculated and sessile) has also been shown to correlate with these parameters (16). Sessile adenomas tend to be larger and more often have a prominent villous histologic component. Polyp configuration also dictates, in large part, the mechanical feasibility of complete colonoscopic removal.

Characteristically, they consisted of slightly elevated, erythematous mucosal plaques, often with a central invagination or depression. These authors focused on the histologic architecture of the lesions, consisting of dysplastic tubules clustered at the luminal surface of the mucosa, with sparing of the deeper crypt compartment . Apart from these reports, the clinical and pathologic features of adenomas have remained largely unrecognized, and a systematic analysis of colonic adenomas in order to determine the relative frequency of these lesions has not been performed. The results of the present study indicate that colonic adenomas are not exceedingly uncommon lesions. Of the patients who underwent surgical or colonoscopic excision of adenomas at our institution during the period included in the study. However, this may



be an underestimate of the relative frequency of these lesions due to their inconspicuous endoscopic configuration, particularly in a poorly cleansed bowel. Histologic recognition of flat adenomas is not difficult, especially if the appropriate colonoscopic description is available. Most striking is the dominant radial growth phase of dysplastic crypt epithelium at the mucosal surface with absent, or only focal, central vertical extension of dysplastic epithelium to the base of the mucosa, a feature which allows the recognition of flat adenomas even in folded or distorted mucosal specimens.

Flat colonic adenomas appear to be a striking exception to the observation, applicable to polypoid adenomas, that small lesions less than 1 cm in diameter are very unlikely to exhibit high-grade dysplasia and, by implication, represent a low cancer risk. The frequency of high – grade dysplasia observed in flat adenomas in the present study (75 %) and previous studies (12) indicates that colonoscopic recognition and removal of these lesions is likely to be of importance to any colon cancer surveillance program. Recognition of these lesions by the histologist and communication of their potential significance to the clinician may also be of importance, since 25 patients of the 112 patients in this study had multiple adenomas. Identification of one of these adenomas, particularly if it exhibits high – grade dysplasia, may warrant heightened colonoscopic surveillance with particular attention to small, lesions.

Although invasive carcinoma was not observed to arise within any of the flat adenomas described in this study, an increased risk for the development of carcinoma within these lesions is implied by the high frequency of high grade dysplasia found within them (73). Furthermore, at least (32) of the lesions in this study showed a high degree of architectural complexity and nuclear atypia and may have classified as "intramucosal carcinoma" by some observers (10).

It is also interesting to note that adenomas were found in two surgical resection specimens in this study, both of which contained flat, ulcerating invasive carcinomas without a residual polypoid adenoma at the cancer margin. Carcinomas of this type, particularly small lesions, have been described in several.

Case reports and larger series (3-9) and have been stated to represent "denovo" colon carcino-

ma, has spontaneous concept, particularly in light of recent data obtained form DNA hybridization analysis indicating a progressive accumulation of genetic allelic deletions and point mutations in advancing stages of colonic neoplasms (4).

A more likely possibility is that small, ulcerating carcinomas arise from small adenomas , which are rapidly destroyed by the expanding carcinomatous epithelium The small, flat, highly dysplastic adenomas described in this study are likely candidates for these precursor lesions .

### Conclusion

The results of this study indicate that small, flat adenomas represent a limited, but significant, percentage of sporadic colonic adenomas encountered at our institution, and are much more likely to exhibit high –grade epithelial dysplasia than similarly sized polypoid tubular adenomas. They may occur simultaneously at multiple sites within an individual colon. Therefore colonoscopic and histologic recognition of these lesions may play an important role in prophylactic colon cancer surveillance programs. Histologically, these lesions consist of a plaque-like proliferation of dysplastic tubules, particularly along the superficial luminal mucosal surface, often with architectural complexity and prominent intracellular nuclear debris. Non dysplastic flat polyps were considered to have no malignant potential. There is increasing evidence that all lesions in the flat adenomas spectrum represent potential precursors in an alternative pathway to adeno carcinoma .Colonic adenomas may be precursors to small, ulcerating carcinomas which lack an associated residual polypoid adenoma. Prospective analyses of patients in whom flat adenomas have been identified will be required in order to precisely define the natural history and carcinoma risk associated with these lesions. Our study has highlighted that the management of patients with colorectal polyps is highly dependent on the quality of pathological evaluation.

### Acknowledgment

"The authors extend their appreciation to the Deanship of Scientific Research at King Saud University for funding the work through the research group project No RGP-VPP-018"

## References

1. Snover DC. Serrated polyps of the large intestine. *Semin Diagn pathol* 2005; 22: 301- 8
2. Hornick JL, Odze RD: Polyps of the large intestine. Philadelphia: saunders 2009: 481 -533
3. Sieber OM, Lipton L, Crbtree M et al. Multiple colorectal adenomas, classic adenomatous polyposis and germ – line mutations in MYH .*N Engl. J med* 2003;348:791-799.
4. Stankovic V, Mitrovic S, Jancic S, Knezevic M, Azanjac G, Tanaskovic I. Correlation of p53 expression levels with the degree of histological differentiation histological stages of colorectal carcinomas, *HealthMed* 2011; 5: 151-164
5. Redston M, epithelial neoplasms of the large intestine. *Surgical pathology of the GI tract , liver, biliary tract, and pancreas.* Philadelphia: Saunders, 2009: 597-637.
6. Jass JR classification of colorectal cancer based on correlation of clinical, morphological and molecular features. *Histopathology* 2007; 50: 113-30.
7. Wynter CV, Walsh MD ,Higushi T et al, Methylation patterns define two types of hyperplastic polyp associated with colorectal cancer. *Gut* 2004 53;573-580
8. Glazer E, Golla V, Forman R , et al. Serrated adenoma is a risk factor for subsequent adenomatous polyp .*Dig dis Sci* 2008: 53: 2204-2207 .
9. Morita T ,Tamura S, Miyazaki J eta al .Evaluation of endoscopic and histopathological features of serrated adenoma of the colon . *Endoscopy* 2001; 33 ; 761 -765.
10. Brown LJ, Smeeton NC, Dixon MF, Assessment of dysplasia in colo-rectal adenomas; an observer variation and morphometric study. *J Clin Pathol* 1985; 38 174 -9
11. Silcocks PB, measuring repeatability and validity of histological diagnosis – a brief review with some practical examples *J Clin Path* 1983 36 : 1269 -75
12. Denis B, Peters C, Chpelain, et al . Diagnostic accuracy of community pathologists in the intepretation of colorectal polyps. *Eur J Gastroent hepatol* 2009; 21: 1153 -60
13. Strut, H, Karive R, Leshro M, et al. Prevalence rate and anatomic location of colorectal adenoma and cancer detected by colonoscopy in average risk individuals aged 40-80 years. *Am J gastroentrol* 2006; 101:255-62.
14. Konishi F, Morson MC: Pathology of colorectal adenomas Colonoscopic survey *J Clin Path* 1982; 35: 830-41
15. Hetzal JT, Hung CS, Coukos JA et al. variation in the detection of serrated polyps in average risk colorectal screening cohort . *Am J gastroenterol* 2010; 105: 2656-64.
16. Rex DK, Hewett DG, Snover DC, Detection targets for colonoscopy from variable detection to validation *Am. J. Gastroenterol*, 2010: 105, 2665 -9
17. Yoon H, martin A, Benamouzig R, et al. Inter-observer agreement on histological diagnosis of colorectal polyps: *Gastroenterol Clin Biol* 2002; 26: 220-4

Corresponding author  
Al-Dahmash B.,  
Department of Medical Laboratory,  
College of Health Sciences,  
King Saud University,  
Riyadh,  
Saudi Arabia,  
E-mail: baldhmash@ksu.edu.sa

# Pregnancy resulting from sexual abuse: Reasons alleged by Brazilian women for carrying out the abortion - Pregnancy and violence

*Jefferson Drezett<sup>1,3</sup>, Daniela Pedroso<sup>2,3</sup>, Maria Auxiliadora Vertamatti<sup>3</sup>, Hugo Macedo Junior<sup>3</sup>, Marcia de Toledo Blake<sup>3</sup>, Luiz Henrique Gebrim<sup>4</sup>, Vitor E. Valenti<sup>3</sup>, Luiz Carlos de Abreu<sup>3</sup>*

<sup>1</sup> Coordinator of the Núcleo de Violência Sexual e Aborto Previsto em Lei do Centro de Referência da Saúde da Mulher, Brasil,

<sup>2</sup> Master Degree in Maternal and Child Health. Psychologist at the Núcleo de Violência Sexual e Aborto Previsto em Lei do Centro de Referência da Saúde da Mulher, Brasil,

<sup>3</sup> Scientific Writing Laboratory. Faculdade de Medicina do ABC, Brasil,

<sup>4</sup> Director of the Centro de Referência da Saúde da Mulher. Professor of the Department of Gynecology at Universidade Federal de São Paulo, Brasil.

## Abstract

**Objective:** to know the reasons for women to perform the abortion when in pregnancy resulting from sexual violence.

**Method:** A descriptive study of 43 women aged 19-44 years who carried out legally permitted abortion between January 2000 and June 2007. It was applied a structured questionnaire with open questions to unstimulated multiple responses. It was analyzed the typification of the perpetrators of sexual violence, kind of intimidation, women's activity at the moment of the approach; information about the right to abortion; person consulted about the decision, post-abortion feelings and reasons for the choice.

**Results:** sexual violence committed by strangers predominated (65.1%), through threat (46.5%) and during daily activities (83.7%). The Police were the main source of information on abortion (44.2%). The decision to interrupt the pregnancy was made alone by 41.9% of the women. Among the reasons for abortion, the rejection of the pregnancy was found in 88.4% of respondents; connection with violence in 86.0%; violation of the right to decide about motherhood in 76.7%, fear of social and family negative effect for the future child in 44.2%, and fear of psychological damage in 18.6%. Relief after the abortion was reported by 74.4% and no case of repentance.

**Conclusions:** the decision-making on abortion had close ties with the sexual violence and the expectation of social or psychological harm to the unborn child.

**Key words:** sexual violence, legal abortion, mental health.

## Introduction

Many factors are involved in women quality of life [1-5]. The International Conference on Population and Development (ICPD) held in Cairo in 1994, declared abortion as a serious public health problem and stated that in cases which are not against the law, you must ensure the woman has access to a safe and humanized interruption of pregnancy [6]. Brazilian legislation is restrictive on abortion, typified as crime with a penalty for the woman and the doctor who practice it. However, Article 128 of the Penal Code allows abortion to be carried out to prevent the mother's death or when pregnancy results from sexual violence [7]. In these exceptions, abortion is a right of the Brazilian woman and protection of their sexual and reproductive health is guaranteed by the Constitution and international treaties.

During the UN General Assembly in 1999, Brazil signed the ICPD +5 assuming commitment to training and equipping health care providers to ensure safe abortion to women in cases prescribed by law [6]. The rising number of Brazilian health services in the last two decades to adopt this practice, though encouraging, is still insufficient to ensure opportunity for all women. Of the 1,600 legal abortions performed between 1989 and 2005, most occurred in more developed regions of the country, while poor women from disadvantaged

regions face great difficulty to carry out a legally interrupted pregnancy [8].

Regardless of where it occurs or which population it reaches, pregnancy resulting from violence represents a serious violation of women's human rights and a strong deterrent for sexual and reproductive autonomy [9, 10]. Sexual violence is considered a universal phenomenon of high prevalence [9]. In Brazil, governmental records indicate incidence of 15.9 cases per 100 000 inhabitants, which poorly express the magnitude of the problem. It is estimated that 10% of Brazilian women in reproductive age have been forced, at least once in life, to perform humiliating sexual acts, to have sex even not wanting it, or have been afraid to deny having a sexual relationship [6].

The woman who seeks deliberate abortion may consider different reasons such as economic difficulties, health problems, neglect or lack of a partner, interference on the project life, conflict with society's rules, or social vulnerability. In all cases, the common element is unwanted pregnancy, which makes the decision of abortion complex and multifactorial [10].

Many women who have undergone voluntary induced abortion state that they were contrary to the procedure until they were in such a situation, in which abortion was considered necessary [11]. Other women keep negative opinion on abortion, even adopting and justifying its recent practice [12]. Different cultural, religious and social values contribute to ambivalent feelings and positions on abortion, making the decision process difficult and troublesome for women [13].

It is assumed that the woman who gets pregnant from sexual violence has a legitimate motivation for resorting to abortion and it is reasonable to infer that their choice is based on the rejection of the forced and unwanted pregnancy [10]. However, little is known about these women's motivations in our midst. Furthermore, there is insufficient evidence to say that abortion in cases of violence have the same motivations of other situations that lead to unwanted pregnancy, which is associated with ambivalent feelings, or incurs regret. The objective of this study is to describe the alleged reasons for Brazilian women to perform the abortion in cases of pregnancy resulting from sexual violence and the processes involved in the decision.

## Method

A descriptive study with 43 women registered at the Centro de Referência da Saúde da Mulher (CRSM) aged between 19 and 44 years, who performed abortion for pregnancies resulting from sexual abuse between January 2000 and June 2007. The inclusion criteria were: abortion that had been carried out for at least one year before, characterization of sexual violence according to the Brazilian penal legislation, and age  $\geq 19$  years at the time of interview. We excluded adolescents, women with mental disabilities of any etiology; legally carried out abortions at the risk of death or fetal anomalies, pregnant or postpartum women at the time of interview.

Variables of study were considered: 1) the author of violence's typification; 2) forms of intimidation; 3) the woman's activity at the moment of approach; 4) source of information about the abortion right; 5) the person who the woman consulted to decide to interrupt the pregnancy; 6) immediate feelings after abortion; 7) regret or not the decision; and 8) reasons for choosing abortion.

Regarding the choice of abortion, one or more unstimulated responses were considered, classified into the following categories: rejection of the pregnancy; bond of pregnancy to sexual violence, violation of the right to choose motherhood; perspective of social and family negative effects for the future child; perspective of negative psychological effects for the future child; economic reasons; interference on the life project; lack of partner or his refusal to continue the pregnancy up to the end; lack of social or family support to keep the pregnancy; or any other reason. The classification of the spontaneous responses in these categories was preceded by the woman's agreement after the interviewer's presentation.

Pre-tested questionnaire structured with open questions was used for the collection of information. The interviews were administered by a psychologist at CRSM qualified to deal with the instruments, including participation in pre-test. The psychologist was responsible for phone contact with potential participants, application of inclusion and exclusion criteria, and the formal invitation to the study.

The inclusion of the interviewee was preceded by signing of Free and Clarified Consent Term af-

ter presentation of the study purposes, the ethical aspects and clarifying doubts. The ethical and legal principles of confidentiality and secrecy of the data source were followed. The individual interviews were conducted at CRSM or in a place defined by the woman. There was no communication among the participants. The woman had the right to discontinue participation at any time and to refuse to answer one or more questions. Participation was voluntary and did not involve payment, benefit or advantage.

It was offered for each interviewee psychological care after the interview, if necessary, as a result of participation in the study. All abortions were based on Decree-Law 2848, section II of Article 128 of the Brazilian Penal Code and followed procedures established by law and technical rules of the Ministry of Health.

## Results

Of the 53 women identified in the inclusion criteria, six (3.2%) lived in areas far from CRSM and six (3.2%) refused to participate. With 43 women included, the loss recorded was 18.9%. The time elapsed between abortion and the interview ranged from one to five years, an average of 23.7 months. There was no waiver of participation or refusal to answer questions. No psychological care was asked after the interview.

The age ranged from 19 to 44 years ( $28.9 \pm 5.4$  years). The catholic religion was declared by 20 women (46.5%), evangelical by 11 (25.6%) and spiritualism in four cases (9.4%). Other religions were reported in six cases (13.9%) and two women (4.6%) said they had no religion. About marital status, 28 respondents (65.1%) were single, 13 married (30.2%) and two legally separate (4.7%).

The white color/race was declared in 25 cases (58.2%), black in 12 cases (27.9%) and mixed in six cases (13.9%). Schooling was compatible with high school education in 23 cases (53.3%) completed higher in 12 cases (27.9%) elementary school in four cases (9.4%) and incomplete elementary school in four cases (9.4%).

In 28 cases (65.1%) the perpetrator of sexual violence was a stranger. In four cases (9.3%) two or more unknown practiced sexual violence. Among 15 identified authors, former intimate partner was

observed in nine cases (60%), a resident of the community in three cases (20%), paternal uncle in one case (6.6%), co-worker in one case (6.6%) and brother-in-law in one case (6.6%).

The woman intimidation with serious threat occurred in 20 cases (46.5%), with physical violence in nine cases (20.9%) and a combination of both in 12 cases (27.9%). Two respondents (4.6%) claimed that the rape occurred in vulnerable condition because they could not resist.

The most often approach occurred during the woman's route to work, reported in 15 cases (34.9%). The woman said that was in leisure activity in 14 cases (32.5%), at home in five cases (11.6%), in the route from school in one case (2.3%), and at the offender's home in one case (2.3%). Other daily activities have been identified in seven cases (16.3%).

The police stations were the source of information about abortion rights for 19 respondents (44.2%). Public health guidance provided information in ten cases (23.3%), relatives and friends in seven cases (16.3%) and medical-legal department in five cases (11.6%). Two women (4.6%) did not remember the source of information. Three respondents (7.0%) reported difficulty in obtaining information about abortion and referral to CRSM. There was no multiple response for this variable.

In 18 cases (41.9%) the abortion decision was taken without the woman consulting a trusted person. Of the 25 women who shared their situation, 14 of them (56.0%) sought guidance from parents, seven (28.0%) with a brother or sister, three (12.0%) with a friend, and one (4.0%) with the religious leader of her church. There was no multiple response for this variable.

Table 1 summarizes the reasons given by women to resort to abortion, predominantly the rejection of the pregnancy (88.4%), linking the pregnancy with sexual violence (86.0%), and violation of the right to choose motherhood (76, 7%). There were no responses based on economic reasons, interference on the life project, difficulty related to partner or lack of family or social support to maintain the pregnancy.

Among the feelings experienced by women after abortion, the sense of relief was the most frequently, for 32 respondents (74.4%). Other feelings were reported by a short time, restricted to the first days after the abortion, such as depression (16.3%)

and feeling of guilt (9.3%). None of the 43 interviewed stated regret for having an abortion.

*Table 1. Reasons alleged by the respondent to decide for the legal interruption of pregnancy resulting from sexual violence*

reason for abortion*	n	%
rejection of the pregnancy	38	88,4
linking the pregnancy with sexual violence	37	86,0
violation of the right to choose motherhood	33	76,7
negative social and family effects for the future child	19	44,2
negative psychological effects for the future child	8	18,6
other	4	9,3

\* one or more reasons considered for each interviewee

## Discussion

The unwanted pregnancy certainly has important repercussions on women's health. It is estimated that 75 million unintended pregnancies ending in 46 million induced abortions occur each year, many carried insecurely and with high rates of morbidity and mortality [14]. While not questioning the impact of contraception to avoid unwanted pregnancy, social, cultural and economic factors influence the availability and quality of reproductive planning [10]. Even among populations with high prevalence of effective contraceptive, it is estimated that the failure inherent in each method is responsible for thousands of unplanned pregnancies [15]. In addition, some studies indicate that almost half of the women who perform deliberate abortion used some method of contraception [12, 16].

The contraceptive issues are not the only determinants of unwanted pregnancy. The Fourth World Conference on Women (FWCW) held in Beijing in 1995, recognizes women's right to decide freely about their fertility and sexuality, free of coercion, discrimination or violence [6]. However, the restriction of these rights can still be observed in almost all societies, especially those in which the woman holds position of greater submission in relation to man.

In many cases, women do not have enough autonomy to decide the timing and condition of sexual intercourse, nor feature for avoiding pregnancy [17].

Evidence shows that many men, teenagers or adults, still assign women the sole responsibility of avoiding pregnancy [18]. A study conducted in India found that nearly 30% of requests for legal abortion the cause of unwanted pregnancy was the refusal or irregular use of condoms by the partner [19]. Cultural factors lead to almost 30% of Brazilian women believe they have the obligation to have sex when partners seek them, even if they do not want [20].

Sexual violence represents the extreme of all these forms of restrictions on women's reproductive autonomy. It is estimated that sexual violence reaches 12 million people each year in the world [21]. In the U.S., rape is considered the violent crime that advances the incidence faster [22]. The highest prevalence of sexual violence are logged in countries involved into armed conflict, as the war in Bosnia-Herzegovina or in the civil conflict in Liberia. It is estimated that in the former Yugoslavia 50 000 women were raped in order to force pregnancy and promote the ethnic elimination [23].

Brazilian criminal law classified sexual violence as crime against sexual dignity, considered heinous crime and treated harshly. In addition to the deprivation of liberty, fully met in a closed regime, the aggressor has no right to pardon, provisional liberty or other benefit [7]. However, the same legislation that strongly condemns violence against women, still considers abortion a crime, what makes the practice illegal and unsafe. The most recent evidence estimated that up to 1.2 million induced abortions occur in Brazil each year, resulting in 240,000 hospitalizations for treatment of complications [24].

Although there is a decrease of these numbers in the last decade, abortion rates in our midst are much larger than observed in the countries of Western Europe, where abortion is permitted, safe and accessible [6, 24]. In contrast, there is a small number of legal abortions for pregnancies resulting from sexual violence, an average of 100 cases per year [8].

The undercount and the understandable tendency of women to conceal the event, make it difficult to identify cases of pregnancy related to violence [9]. In countries where deliberate abortion is allowed, there are indicators that half the women resorted to abortion and a third decides to accept pregnancy [25]. In Brazil, there is no study on the outcome of these pregnancies. Still, it is believed

that pregnancy that results from violence involves emotional and social impact sufficient to justify abortion-seeking [10].

Although the study had limited the sample age to avoid possible particularities of adolescence, the average of 28.9 years found did not differ from research that indicate the reproductive age young women as the main victims of sexual violence [9, 10, 25, 26]. Most respondents were white (58.2%) and single (65.1%), features seen in other publications in our country [9].

Although it has not been the purpose to establishing the relationship between religion and abortion, the majority of respondents (81.5%) declared to belong to religions with uncompromising position of condemnation of abortion, even when the pregnancy results from violence or endangers the woman's life. For the interviewees, religion was not impediment to carry out the abortion.

The perpetrator of violence is known to the victim in between 50% and 70% of sex crimes. In these cases, there is greater resistance to make the complaint and more difficult to take legal action, regardless of the woman's social, educational or economic background [9, 26, 27]. This aspect can explain the high frequency of unknown assailants found (65.1%). However, the distribution of identified authors showed no deviation from the literature, with the participation of former intimate partner and member of the community in 80% of cases [9, 10, 24]. Almost 10% of women were raped by multiple assailants, which significantly increases the risk of sexually transmitted diseases, HIV infection and severe emotional damage [9].

The threat of death, associated or not with physical force, was the main form of intimidation applied by the aggressor (74.4%), similar to that found by other researchers [28, 29]. The vulnerable condition was characterized in the lower portion of the cases (4.6%), based on alleged involuntary use of substance or drug that could prevent resistance. The frequent approach in public spaces (83.7%) suggests agreement with the violence author's profile, in most cases unknown (65.1%). Approaches in private spaces were less frequently found, at the victim's home (11.6%) or at the perpetrator's (2.3%), compatible with the authors pointed as former intimate partners (20.9%), similar to the studies conducted in our midst [9, 10, 24].

Most women said they found no difficulty in receiving information about abortion rights and reference for CRSM. The participation of police stations (44.2%) and health care providers (23.3%) suggests the importance of a network of quality care for these women, often without knowledge of their rights [8]. The role of police is noteworthy considering that Brazilian law does not require the crime reporting to the police to perform the legal abortion [7, 24]. Although positive, the data found is regional and can not be extrapolated to other regions of the country where most women still face discrimination and barriers to reach health services that perform legal abortion.

In addition to information about abortion rights, it is assumed that a woman who becomes pregnant by violence seeks support and advice to decision-making. In this sense, the majority of respondents (68.1%) sought guidance from a trusted person, especially parents, siblings and friends. Results indicate conflict with the existing literature, which states that most women who suffer sexual violence do not seek help and hide what happened, even from the family [9, 10, 24, 25, 27]. It is reasonable to assume that the offense of rape-induced pregnancy and the abortion dilemma have been facilitators to reveal the facts.

Most of the grounds for choosing abortion had sexual violence as the focal point. This reason was directly attributed by 86.0% of women and emphasized, indirectly, the rejection of the pregnancy (88.4%) and violation of the right to choose motherhood (76.6%). The highly frequent association of these responses indicates link between the choice of abortion and sexual violence, which does not occur in other circumstances of unwanted pregnancy.

The data suggests that for these women, pregnancy and violence can not be treated as isolated events. So, keep the pregnancy may mean the continuation of violence, making it difficult to overcome [10]. This hypothesis may also explain the high frequency of suicidal ideation among women who experience a rape-induced pregnancy, which reduces significantly after the abortion [9].

Almost half of the respondents joined other reasons for choosing abortion rife with rationality, considering possible social and family grievances to the unborn child, if maintained the pregnancy. The same was true about the fear of psychological

damage, although less frequently (18.6%). These data are similar to those found in other studies, suggesting that abortion is not based on women's selfishness or disrespect for motherhood. Some authors maintain that there is accountability in decision-making to avoid the birth in a condition or environment that does not allow healthy and appropriate development [10].

In fact, more than half of the interviewees expressed concern about the fetus' future, even rejecting the pregnancy, which removes the possibility of indifference for him as element of decision for abortion. Moreover, the concern is well founded, considering the possibility of adverse psychological consequences for children born from unwanted pregnancies who have abortions denied [30].

There were no reports of spontaneous responses related to economic reasons, interference on the project life, difficulty associated with the partner, or lack of support to keep the pregnancy, often cited by women undergoing deliberate abortion in other conditions. However, the results do not even make it possible to rule out these factors as supporting decision-making, which could have occurred in an interview with encouraged questions.

Although abortion is considered a difficult experience for women, most of them reported relief at the end of the procedure, situation found in this study [10]. Manifestation of guilt deserves comment, reported as transient and restricted to the first days after abortion. It is possible that the religious condemnation interferes in decision-making, consciously or not, and is associated with this kind of feeling.

Actually, most of the interviewees declared to belong to religions that strongly disapprove abortion, even in cases of sexual violence or risk of death for women. Almost half of the interviewees declared themselves catholic, religion that takes excommunication as a response to abortion while, paradoxically, does not punish the aggressor the same way. It is possible that social condemnation exerts a synergistic effect in these circumstances. In addition, the fault is often found among women who do not report serious sexual violence, committed by strangers, without having any responsibility for what happened to them [9].

There is no evidence indicating the existence of so-called "abortion trauma syndrome" as sug-

gested by some authors, which cause severe psychological damage to women [31]. Rather, studies have found satisfactory and appropriate emotional responses to legally induced abortion. Negative effects are exceptional, usually less severe than those arising from pregnancy maintained until the end against woman's desire [32-34]. In this study, the respondents' answers did not suggest emotional harm related to abortion. The negative feelings identified, transient and of short duration, can be part of the normal and proper emotional response to the crisis [35].

## References

1. Arslan C, Savucu Y, Ceviz D. Evaluation of the body composition, blood lipids and health life-style in employment and unemployment women. *HealthMED J* 2011;5:699-710.
2. Caylan A, Aydemir I, Dagdeviren N, Akturk Z, Set T, Oztora S, FE Ca. Evaluation of health related quality of life among perimenopausal Turkish women. *HealthMED J* 2011;5:741-752.
3. Erenel AS, Efe SY, Vura G. Determining the nurse's health problems and work stress level in Turkey. *HealthMED J* 2011;5:759-765.
4. Kılıç D, Kılıç M, Reis N, Özka H. The effect of Caesarean delivery care on postpartum problems and satisfaction. *HealthMED J* 2011;5:794-801.
5. Kılıç M, Eryılma G. The determination of women's fatigue levels in the third trimester of pregnancy and in the postpartum period. *HealthMED J* 2011;5:826-830.
6. Souza CM, Adesse L. *Sexual violence in Brazil: perspectives and challenges*. Brasília: Secretaria Especial de Políticas para Mulheres; 2005.
7. Delmanto C, Delmanto R, Delmanto-Jr R, Delmanto FMA, editors. *Código penal comentado*. São Paulo: Saraiva; 2010.
8. Talib RA, Citeli MT. *Dossiê: serviços de aborto legal em hospitais públicos brasileiros (1989-2004)*. São Paulo: Católicas pelo Direito de Decidir; 2005.
9. Drezett J, Junqueira L, Antonio IP, Campos F, Leal MCP, Iannetta R. *Contribution to the study of the sexual violence against the adolescent: a perspective of sexual and reproductive health and violation of human rights*. *Adolescência & Saúde* 2004; 1:31-9.
10. Faúndes A, Barzelatto J, editors. *The drama of abortion: in search of a consensus*. Campinas: Komedi; 2004.



11. Bengtsson AM, Wahlberg V. Interruption of pregnancy: motives, attitudes and contraceptive use. Interviews before abortion, at a family planning clinic, Rome. *Gynecol Obstet Invest* 1991; 32:139-43.
12. Alvarez L, Garcia CT, Catusus S, Benitez ME, Martinez MT. Abortion practice in a municipality of Havana, Cuba. In: Mundigo AI, Indriso C, editors. *Abortion in the developing world*. New Deli: Vistar Publications; 1999.
13. Osis MJD, Hardy E, Faúndes A, Alves G, Balarezo G. Women's opinions on circumstances under which hospitals should perform abortions. *Cad Saude Publica* 1994; 10:320-30.
14. Alan Guttmacher Institute. *Sharing responsibility: women, society & abortion worldwide*. New York and Washington DC: The Alan Guttmacher Institute; 1999.
15. World Health Organization. *Safe abortion: technical and policy guidance for health systems*. Geneva: World Health Organization; 2003.
16. Sparrow MJ. Condom failures in women presenting for abortion. *N Z Med J* 1999; 112:319-21.
17. Golding JM, Wilsnack SC, Learman LE. Prevalence of sexual assault history among women with common gynecologic symptoms. *Am J Obstet Gynecol* 1998; 179:1013-9.
18. Pachauri S. Male involvement in reproductive health care. *J Indian Med Assoc* 2001; 99:138-41.
19. Banerjee N, Sinha A, Kriplani A, Roy KK, Takkar D. Factors determining the occurrence of unwanted pregnancies. *Natl Med J India* 2001; 14:211-4.
20. Faúndes A, Hardy E, Osis MJ, Duarte G. Risk of gynecologic complaints and sexual dysfunctions according to history of sexual violence. *Rev Bras Ginecol Obstet* 2000; 22:153-7.
21. Beebe DK. Sexual assault: the physician's role in prevention and treatment. *J Miss State Assoc* 1998; 39:366-9.
22. Petter LM, Whitehill DL. Management of female sexual assault. *Am Fam Physician* 1998; 58:920-6.
23. Kozaric-Kovacic D, Folnegovic-Smalc V, Skrinjaric J, Szajnberg NM, Marusic A. Rape, torture, and traumatization of Bosnian and Croatian women: psychological sequelae. *Am J Orthopsychiatry* 1995; 65:428-33.
24. Brasil. Ministério da Saúde. *Prevention and treatment of damages resulting from sexual violence against women and adolescents: technical standard*. 3ª ed. Brasília: Ministério da Saúde; 2010.
25. Holmes MM, Resnick HS, Kilpatrick DG, Best CL. Rape-related pregnancy: estimates and descriptive characteristics from a national sample of women. *Am J Obstet Gynecol* 1996; 175:320-4.
26. Daneri RA, Urueña Tincani EM, Góngora AM, Boscarino GL. Sexual abuse in children. *Med Infant* 2008; 15:312-9.
27. Muram D, Hostetler BR, Jones CE, Speck PM. Adolescent victims of sexual assault. *J Adolesc Health* 1995; 17:372-5.
28. Aguilar A, Salcedo M. Characteristics of sexual violence in adolescents from 10 to 19 years of age, Cali 2001-2003. *Colomb Med* 2008; 39:356-63.
29. Biggs M, Stermac LE, Divinsky M. Genital injuries following sexual assault of women with and without prior sexual intercourse experience. *CMAJ* 1998; 159:33-7.
30. Dagg PK. The psychological sequelae of therapeutic abortion-denied and completed. *Am J Psychiatric* 1991; 148:578-85.
31. Stotland NL. The myth of the abortion trauma syndrome. *JAMA* 1992; 268:2078-9.
32. Adler NE, David HP, Major BN, Roth SH, Russo NF, Wyatt GE. Psychological responses after abortion. *Science* 1990; 248, 41-4.
33. Kero A, Hogberg U, Lalos A. Wellbeing and mental growth: long-term effects of legal abortion. *Soc Sci Med* 2004; 58: 559-69.
34. Rogers JL, Stoms GB, Phifer JL. Psychological impact of abortion: methodological and outcomes summary of empirical research between 1966 and 1988. *Health Care Women Int* 1989; 10:347-76.
35. Romans- Clarkson SE. Psychological sequelae of induced abortion. *Aust N Z J Psychiatry* 1989; 23:555-65.

## Corresponding Author

Jefferson Drezett,

Coordinator of the Núcleo de Violência Sexual e Aborto Previsto em Lei do Centro de Referência da Saúde da Mulher,

Brasil,

E-mail: cdh.fsp@gmail.com

# Development of Emergency Medical Services (EMS) in Iran: Component of Transportation

Mohammadkarim Bahadori<sup>1</sup>, Ramin Ravangard<sup>2</sup>, Mostafa Nejati<sup>3</sup>

<sup>1</sup> Health Management Research Centre, Baqiyatallah University of Medical Sciences, Tehran, Iran,

<sup>2</sup> School of Management and Medical Information Sciences, Shiraz University of Medical Sciences (SUMS), Shiraz, Iran,

<sup>3</sup> School of Management, Universiti Sains Malaysia (USM), Malaysia.

## Abstract

**Introduction:** One of the major barriers for providing emergency medical services (EMS) is the inappropriate and poor transportation. The aim of this study was to prioritize the EMS transportation components in Iran.

**Methods:** This study is a kind of descriptive and cross-sectional study that conducted in the first half of 2010 using DEMATEL method. The transportation components of emergency medical services in different systems were collected and a questionnaire was developed. The respondents consisted of 30 Iranian experts in pre-hospital emergency who were asked to evaluate the list of suggested transportation components and revise them using their scientific, practical and visionary experience. The components were identified using Delphi method. The priority of components was then depicted using MATLAB and Edraw Max 5 softwares.

**Results:** The components of the ambulance type B, ambulance type C, helicopter, large jet aircraft, motorcycle ambulance and support ambulance were determined as transportation components. Also, the components of ambulance type B and large jet aircraft were determined as the most affecting and affected care model components, respectively, with the coordinates (1.33 and 1.33) and (1.53 and -1.53) on the pre-hospital emergency transportation components graph.

**Conclusion:** Given the scarce resources and unlimited needs, and in order to develop EMS transportation, resource allocation should be based on a set of priorities. According to current study findings, using the Ambulances type B, support and motorcycle ambulances have great importance to develop EMS in Iran.

**Key words:** EMS, Transportation, Component

## Introduction

Development of emergency medical services is one of the essential indicators of every health system. Population growth, increasing urbanization, aging populations, increased traffic accidents, increased cardiovascular diseases, increased industrial disasters, increased air pollution, and stress-related diseases, as well as the increased rates of social disorders have raised the need for emergency medical services (EMS). Therefore, emergency care reforms should be prioritized in the system (1).

Over the past few years, due to the aforementioned problems, the health systems of most countries have made efforts to develop the EMS. Iran has not been an exception; the country has invested on the EMS sector by developing an EMS universal coverage plan, development of emergency medicine, training emergency medical technicians, reconstruction of transportation systems, increasing the number of EMS bases, etc (2-3). Such efforts were deemed quite necessary given the high rate of mortality due to heart diseases and unintentional injuries, particularly traffic injuries in the country.. However, of the scarcity of resources and existence of extensive needs forces healthcare policy-makers to prioritize healthcare services. In fact, resource scarcity is considered as a major barrier to access to health care, especially EMS (4).

The purpose of emergency medical services in Iran is "improvement and development of these services to treat victims of accidents and sudden diseases, as well as, to address other medical emergencies." For the timely treatment of patients, emergency medical services system is composed of several components. Such a system requires both emergency ambulances and emergency facilities (emergency departments). There are four timeline components from the time an accident

happens until the victims reach health care centers; namely: response time, the care at the scene, retrieval, and transfer to health care centers which all are associated with ambulances (5). On the other hand, 75% of emergency deaths happen before reaching a hospital. Thus utilizing a suitable emergency transportation system plays a crucial role in reducing emergency death rates (6).

One of the components of the EMS which has been largely criticized is the timely and quick transportation. The transportation of the injured from the accident scene to hospital is the key element of pre-hospital EMS (7-8). Van Rooyen et al. have introduced 15 components for evaluating EMS one of which is the current methods of patient transportation (9).

One of the major barriers for providing EMS is the inappropriate and poor transportation which could be due to various reasons, including unsuitable ambulances, inappropriate roads, heavy traffics and the inability to pay. The findings of Razzak et al. study show that the transportation methods used in advanced American and European countries are not practical in the low-income countries because of being too costly and expensive for such poor countries. Therefore, these countries should make optimal use of their limited resources (10).

Based on the findings of a study conducted in Guinea-Bissau - a poor country in the West Africa - 16% of children who required emergency care lost their lives during transporting to a hospital or waiting to receive needed services (11). The findings of Geefhuysen's and his colleagues' study show that the efficient transportation systems have a very important role in reducing pregnant women mortalities (12). In Mexico, increasing the ambulance bases has been one of the factors of reducing the trauma patients' mortality rate (13). Some countries, including Canada, have special plans to provide emergency transportation services for patients such as burned children (14). Based on another research by Gil et al. who studies a large number of patients, they preferred to use ambulances for transportation, though they could use other vehicles which has had an important role in prioritizing patients and improving the emergency departments performances (15). Other research findings also indicate that a small number of patients had been given first aid before the ambulance arrived (16). In England, in-

roducing some strategies and developing national standards have led to a significant improvement in ambulance services (17).

Ambulance services include assessment at the scene, referral and consultation. However, in some organizations, changes are made without conducting any evidence-based research. Statistic shows that there is no need for referral to hospital in more than 30% of contacts with emergency bases, as well as, ambulance attendance at the accident scene in England. This figure ranges between 23%-33% in America (18).

Ambulance standards for providing EMS include the following: Ambulance type A (as a simple carrier), Ambulance type B (for Basic Life Support (BLS)) and Ambulance type C (for Advance Life Support (ALS)). The ambulance type A should consist of specialized equipment for providing first aid and nursing care. The ambulance type B consists of four-fold equipment including oxygen cylinder, stretcher, resuscitation bag and suction. However, the ambulance type C, besides the ambulance type B equipment, has also a DC shock (19).

The demand for ambulance services has currently increased throughout the world and providing efficient and effective services requires more resources. However, considering the resource limitation, the priorities should be set for improving the medical emergency services (19). To that end, the current study was conducted to prioritize EMS transportation components in Iran.

## Materials and Methods

The present study is a descriptive and cross-sectional study that was conducted in the first half of 2010 using DEMATEL method, which is a group decision-making technique. The transportation components of emergency medical services in different systems were collected and a questionnaire was developed. Afterwards, a sample of 30 Iranian experts in pre-hospital emergency were selected using available sampling method and were asked to evaluate the proposed list of components and revise them using their scientific, practical and visionary experience. The main criteria for selecting these experts were their former academic backgrounds as well as prior experience or administrative responsibilities in emergency

medical services. The components were identified using Delphi method. Then, the components were determined using SPSS 17.0 software (One-Sample T-Test) and the experts were asked to indicate the priority of components and, finally, the related graph was depicted using MATLAB and Edraw Max 5 softwares.

The DEMATEL technique was developed by Battelle Memorial Institute Research Program during 1972-1976 to study and solve the complex issues. The reason behind the development of DEMATEL technique was that the proper use of scientific research methods could improve the complicated structure of issues and help to recognize and choose the practical solutions with hierarchical structures. The DEMATEL technique is based on oriented graphs (also known as diagraphs) which can divide effective components into the two groups, cause and effect. These diagraphs depict the dependency relationship between the components of a system. Causal diagraphs are obtained through regular pairs  $(D_k+R_k, D_k-R_k)$  in which the horizontal (D+R) and vertical (D-R) axes are called the “prominence” (that can be made by adding  $D_k$  to  $R_k$ ), and the “relation” (that can be made by subtracting  $R_k$  from  $D_k$ ), respectively. If the quantity of  $(D_k-R_k)$  is positive, that criterion will relate to the cause group and if it is negative, the criterion will relate to the effect group. There-

fore, the causal diagraphs can convert complex causal relationships among components into a visible structural model and provide an accurate insight for resolving the considered issues. Furthermore, the right decisions can be made using causal diagraphs and recognizing the differences between cause and effect criteria (20-21).

### Results

According to the initial findings of this research, ambulance type A, ambulance type B, ambulance type C, helicopter, piston aircraft with one or two engines, turboprop aircraft, large jet aircraft, motorcycle ambulance and support ambulance, were suggested. However, Iranian pre-hospital emergency experts agreed with ambulance type B, ambulance type C, helicopter, large jet aircraft, motorcycle ambulance and support ambulance ( $P=0.001$ ) (Table1).

Also, the results of this study showed that the components of the ambulance type B (P1), motorcycle ambulance (P2) and support ambulance (P3) certainly penetrating the system, which were placed in the cause group as first to third priorities; whereas the components of ambulance type C (P4), Helicopter (P5) and large jet aircraft (P6) were partially influenced and were in the effect group as forth to fifth priorities (Table 2 and Figure 1).

Table 1. The results of the expert opinions about pre-hospital emergency transportation in Iran

Components	Expert Responses					Mean	SD	P-Value
	Completely agreed	agreed	Without any Responses	Opponent	Completely Opponent			
Ambulance type A (Simple transportation)	1	2	8	13	6	2.30	0.98	0.0001
Ambulance type B (BLS)	26	4	0	0	0	4.86	0.34	
Ambulance type C (ALS)	9	20	0	0	1	4.23	0.23	
Helicopter (Minor roads and impassable areas)	20	10	0	0	0	4.66	0.47	
Piston aircraft with one or two engines (Short distance and large disasters)	2	3	10	10	5	2.56	1.20	
Turboprop aircraft (Ability to bad weather withstand with high speed)	3	3	9	10	5	2.40	0.99	
Large jet aircraft (Secondary response and high number of injuries, the high cost of flight)	15	9	3	3	0	4.76	0.44	
Motorcycle ambulance (Traffic areas)	23	7	0	0	0	4.76	0.43	
Support ambulance	19	11	0	0	0	4.63	0.49	

The components of ambulance type B and large jet aircraft were determined as the most affecting and affected care model components, respectively, with the coordinates of (1.33 and 1.33) and (1.53 and -1.53) on the pre-hospital emergency transportation components graph.

Table 2. The hierarchy of affecting and affected pre-hospital emergency transportation components in Iran

Components	D	R	D+R	D-R
Ambulance type B	1.33	0	1.33	1.33
Motorcycle ambulance	1.03	0.18	1.21	0.85
Support ambulance	0.72	0.3	1.02	0.42
Ambulance type C	0.46	0.62	1.08	- 0.16
Helicopter	0.09	1	1.09	- 0.91
Large jet aircraft	0	1.53	1.53	-1.53

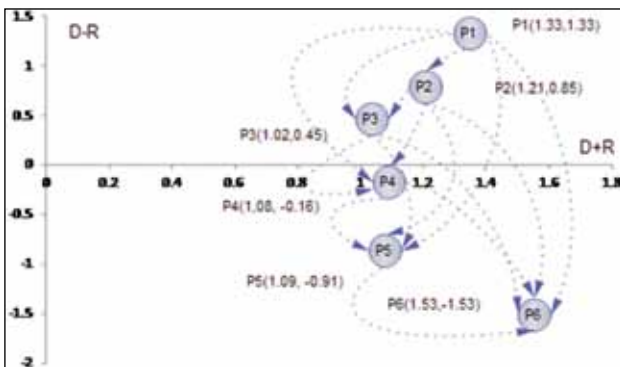


Figure 1. The prioritization of pre-hospital emergency transportation components in Iran

**Discussion**

This study aimed to identify the components of pre-hospital emergency transportation in Iran and prioritize them using one of the common methods of operations research. Given the important role of ambulances in human survival, they have widely been considered and studies in operations research field (22). The findings of prior research show that EMS system has three basic stages: the care at the scene, the care during transferring to a hospital and the care in the hospital. The first two stages are related to proper transportation system which confirms its importance (23). It should be remembered that the proper transportation of patients reduces the required time for diagnosing and treating their diseases (24).

Based on current study findings, the ambulances type B, the motorcycle ambulances, the support ambulances, the ambulances type C, the heli-

copter ambulance and the large jet aircrafts were identified as pre-hospital emergency transportation components in Iran. Besides, ambulances type B had priority compared to other components of transportation. This reflects the importance of this component and its cost-effectiveness for the development of EMS in Iran.

Another point to consider is the evolution of land ambulances into air ambulances in order to provide quick transportation services. Increased demand for emergency medical services has led to increasing the ambulance development costs and, hence making it difficult to carry out analyses of their cost-benefit, though the interpretation of their findings for evaluating and decision-making is usually very difficult (25).

In Portugal, the ambulances are equipped with two responders with great skills in BLS for transferring patients to the nearest hospital, which are the ambulances type B (26). In United State, BLS and ALS ambulances are usually used for transferring patients (27). In Greece, two types of ambulances are used: Basic Ambulance as the ambulance type B and Special Ambulances as the ambulances for providing intensive care or the ambulances type C (28). Also, based on the Law of universal coverage of pre-hospital emergency medicine services in Iran, the ambulances used in the urban and road bases should meet the ambulances type B specifications and, also, every three bases should have one support ambulance (29). All the above indicates the importance of ambulances type B, as a principal component of proper emergency medical services transportation.

One of the high priority components in developing EMS transportation in Iran is the utilization of the motorcycle ambulances, especially in areas of heavy traffic. EMS response time is a crucial factor in rescuing patients' lives. Therefore, all required alternative measures should be taken to reduce the response time. There are many documents that show the motorcycle ambulances have an important role in reducing response time at the peak of city traffic (30). One of the vital needs to reach the hospital is the availability and accessibility to a proper and economical transportation system. Based on Hofman et al. findings, the use of motorcycle ambulances is a suitable and economical method for providing emergency medical services (31).

Also, Kiefe and Soares-Oliveira in their study concluded that the use of motorcycle ambulances as a quick and safe vehicle has a very important role in providing EMS (32). In some countries, especially in their major cities, motorcycle ambulances equipped with paramedics are used to improve rapid provision of emergency medical services (28).

One of the significant components of EMS transportation is the use of the Support ambulance and based on available standards there should be one support ambulance for every three bases (29). In some countries such as Austria, ambulances equipped with the ALS services, or the ambulances type C, are used for direct transporting, as well as, advanced supervision over patients. Also, the cars equipped with the ALS services and limited supervision, which provide emergency care for patients until reaching a hospital and lead to decrease in the response time, are used (33).

The experience of developed countries in the use of helicopter ambulances is very useful for developing and underdeveloped countries. In some cases, using helicopter ambulances has been discontinued in developed countries due to lack of cost-effectiveness (34). Although the air ambulances are very expensive, they can be effective for large geographic areas (35). The findings of a study conducted in Norway showed that reaching the scene using the helicopters took about an hour while a significant number of this transportation could be done by the ambulances without losing health benefits (23). Nicholl and et al, in a study compared the performance of helicopter and land ambulances and concluded that the helicopters performance had never been better than that of land ambulances. In fact, the activation time, response time and on-scene time in helicopters were on average longer than those in land ambulances. However, transferring to a hospital by helicopters has sometimes been faster (36).

Compared with helicopters, using ambulance services in areas of higher population density, standard roads and shorter paths is cost-effective (37). Based on Roudsari et al. study findings, Austria, Germany and Australia have the highest use of the air ambulances (38). Langhelle et al, in their study conclude that Finland, Iceland, Norway and Sweden have bases for helicopter ambulances, review and rescue (SAR) helicopters and the fixed wing aircrafts (39). However, the helicopters and

the large jet aircrafts have got the lowest priorities because they are expensive and uneconomical.

## Conclusion

Given the scarce resources and unlimited needs, as well as, in order to develop EMS transportation, resource allocation should be based on the set priorities. According to current study findings, using the Ambulances type B, support and motorcycle ambulances have great importance to develop EMS in Iran.

## References

1. Robertson-Steel I. "Reforming Emergency Care": the ambulance impact. A personal view. *Emerg Med J*. 2004 Mar;21(2):207-11.
2. Bahadori M. Prioritization of determinants influencing preparedness of Iranian Pre-hospital Emergency Services. *Iranian Journal of Critical Care Nursing*. 2011;4(2):73-8.
3. Bahadori M, Nasiripur A, Tofighi S, Gohari M. Emergency medical services in Iran. *Australasian Medical Journal-AMJ*. 2010;3(6):335-9.
4. Goins RT, Williams KA, Carter MW, Spencer SM, Solovieva T. Perceived barriers to health care access among rural older adults: a qualitative study. *The Journal of Rural Health*. 2005;21(3):206-13.
5. Siler KF. Evaluation of emergency ambulance characteristics under several criteria. *Health Serv Res*. 1979 Summer;14(2):160-76.
6. Howard CR. Emergency care and medical transportation in the eastern quarter of the United States of America, 1963. *J Coll Gen Pract*. 1965 Jan;9:48-54.
7. Lungu K, Kamfose V, Chilwa B, Hussein J. Are bicycle ambulances and community transport plans effective in strengthening obstetric referral systems in Southern Malawi? *International Journal of Gynecology & Obstetrics*. 2000;70:B86-B.
8. Samai O, Sengeh P, PMM Team) TB. Facilitating emergency obstetric care through transportation and communication, Bo, Sierra Leone. *International Journal of Gynecology and Obstetrics*. 1997; 59:157-64.
9. VanRooyen MJ, Thomas TL, Clem KJ. International emergency medical services: assessment of developing prehospital systems abroad. *The Journal of emergency medicine*. [doi: 10.1016/S0736-4679(99)00065-7]. 17(4):691-6.
10. Razzak JA, Kellermann AL. Emergency medical care in developing countries: is it worthwhile? *Bulletin of the World Health Organization*. 2002;80(11):900-5.
11. Sodemann M, Jakobsen M, Mølbak K, Alvarenga Jr I, Aaby P. High mortality despite good care-seeking behaviour: a community study of childhood deaths in Guinea-Bissau. *Bulletin of the World Health Organization*. 1997;75(3):205.

12. Geefhuysen CJ, Isa AR, Hashim M, Barnes A. Malaysian antenatal risk coding and the outcome of pregnancy. *Journal of Obstetrics and Gynaecology Research*. 1998;24(1):13-20.
13. Arreola-Risa C, Mock CN, Lojero-Wheatly L, de la Cruz O, Garcia C, Canavati-Ayub F, et al. Low-cost improvements in prehospital trauma care in a Latin American city. *The Journal of trauma*. 2000; 48(1):119.
14. Fuller T, Herold M. Community-based Responses to Rural Transportation Issues in Ontario: a review of the Ontario Community Transportation Action Program (CTAP) 1998-2000. 2002; Available from: [http://www.rural.gc.ca/researchreprots/transport/no1\\_e.pdf](http://www.rural.gc.ca/researchreprots/transport/no1_e.pdf).
15. Gil Aparicio R, Trenchs Sainz de la Maza V, Munoz-Santanach D, Cayuela Guerrero C, Luaces Cubells C. [Study on the suitability of ambulance transportation to a paediatric medical emergency department]. *An Pediatr (Barc)*. 2010 Jul; 73(1):19-24.
16. West IM, Gettinger CE, Jr., Meyer D, Rosenthal M, Snow R, Weiner FR, et al. Emergency medical transportation. A survey of California ambulance operations. *Calif Med*. 1972 Feb; 116(2):35-43.
17. Stoykova B, Dowie R, Bastow P, Rowsell KV, Gregory RP. Ambulance emergency services for patients with coronary heart disease in Lancashire: achieving standards and improving performance. *Emerg Med J*. 2004 Jan; 21(1):99-104.
18. Snooks HA, Dale J, Hartley-Sharpe C, Halter M. On-scene alternatives for emergency ambulance crews attending patients who do not need to travel to the accident and emergency department: a review of the literature. *Emerg Med J*. 2004 Mar; 21(2):212-5.
19. Judge TP. "Reforming emergency care" and ambulance services. *Emerg Med J*. 2004 Jan; 21(1):4.
20. Tzeng GH, Chiang CH, Li CW. Evaluating intertwined effects in e-learning programs: A novel hybrid MCDM model based on factor analysis and DEMATEL. *Expert Systems with Applications*. 2007; 32(4):1028-44.
21. Wu WW, Lee YT. Developing global managers' competencies using the fuzzy DEMATEL method. *Expert Systems with Applications*. 2007; 32(2):499-507.
22. Goldberg JB. Operations research models for the deployment of emergency services vehicles. *EMS Management Journal*. 2004; 1(1):20-39.
23. Ulvik A, Rannestad BS, Carlsen AW, Nielsen EW. [Rescue helicopter service in Bodo--advanced emergency service or alternative transportation?]. *Tidsskr Nor Laegeforen*. 2002 Jan 10; 122(1):25-9.
24. Swor R, Anderson W, Jackson R, Wilson A. Effects of EMS transportation on time to diagnosis and treatment of acute myocardial infarction in the emergency department. *Prehosp Disaster Med*. 1994 Jul-Sep; 9(3):160-4.
25. Brismar B, Dahlgren B-E, Larsson J. Ambulance utilization in Sweden: Analysis of emergency ambulance missions in urban and rural areas. *Annals of Emergency Medicine*. [doi: 10.1016/S0196-0644(84)80065-7]. 1984; 13(11):1037-9.
26. Gomes E, Araujo R, Soares-Oliveira M, Pereira N. International EMS systems: Portugal. *Resuscitation*. [doi: 10.1016/j.resuscitation.2004.04.013]. 2004; 62(3): 257-60.
27. Pozner CN, Zane R, Nelson SJ, Levine M. International EMS Systems: The United States: past, present, and future. *Resuscitation*. [doi: 10.1016/j.resuscitation.2003.11.004]. 2004; 60(3):239-44.
28. Papaspyrou E, Setzis D, Grosomanidis V, Manikis D, Boutlis D, Ressos C. International EMS systems: Greece. *Resuscitation*. 2004; 63(3):255-9.
29. Law of universal coverage of pre-hospital emergency medicine services [database on the Internet]. Health Ministry of Iran. 2007 [cited Nov,16]. Available from: <http://www.spac.ir/hoghoghi/index-2-3.htm>.
30. Soares-Oliveira M, Egipto P, Costa I, Cunha-Ribeiro LM. Emergency motorcycle: has it a place in a medical emergency system? *Am J Emerg Med*. 2007 Jul; 25(6):620-2.
31. Hofman JJ, Dzimadzi C, Lungu K, Ratsma EY, Hussein J. Motorcycle ambulances for referral of obstetric emergencies in rural Malawi: Do they reduce delay and what do they cost? *International Journal of Gynecology & Obstetrics*. [doi: 10.1016/j.ijgo.2008.04.001]. 2008; 102(2):191-7.
32. Kiefe CC, Soares-Oliveira M. Medical emergency motorcycles: are they safe? *Eur J Emerg Med*. 2008 Feb; 15(1):40-2.
33. Weninger P, Hertz H, Mauritz W. International EMS: Austria. *Resuscitation*. 2005; 65(3):249.
34. Hutton K. The End of an Era: The Demise of Life Flight San Diego. *Air Medical Journal*. 1995; 10:11-3.
35. Sellwood N. An ambulance helicopter for emergency calls. *Arch Emerg Med*. 1992 Sep; 9(3):280-9.
36. Nicholl JP, Beeby NR, Brazier JE. A comparison of the costs and performance of an emergency helicopter and land ambulances in a rural area. *Injury*. [doi: 10.1016/0020-1383(94)90151-1]. 1994; 25(3) : 145-53.
37. Kobusingye OC, Hyder AA, Bishai D, Joshipura M, Hicks ER, Mock C. Emergency medical services. *Health Systems*. 2006:87.
38. Roudsari BS, Nathens AB, Arreola-Risa C, Cameron P, Civil I, Grigoriou G, et al. Emergency Medical Service (EMS) systems in developed and developing countries. *Injury*. 2007; 38(9):1001-13.
39. Langhelle A, Lossius HM, Silfvast T, Björnsson HM, Lippert FK, Ersson A, et al. International EMS Systems: the Nordic countries. *Resuscitation*. [doi: 10.1016/j.resuscitation.2003.12.008]. 2004; 61(1): 9-21.

Corresponding Author  
 Mohammadkarim Bahadori,  
 Health Management Research Centre,  
 Baqiyatallah University of Medical Sciences,  
 Tehran,  
 Iran,  
 E-mail: bahadorihealth@gmail.com

# Knowledge levels of intensive care nurses regarding usage of Pulse Oximetry in a university hospital in Turkey

*Dilek Yıldız, Emine İyigün, Berna Eren Fidancı*

Gulhane Military Medical Academy (GATA) School of Nursing, Etlik/Ankara, Turkey

## Abstract

**Aim:** Pulse oximetry has become one of the most commonly used tools in the clinical environment for assessing patients' oxygenation status. To determine the knowledge levels of intensive care nurses in relation to usage and fundamental principles of pulse oximetry.

**Materials and methods:** The research was conducted as a descriptive study in intensive care units of a university hospital in Ankara. The data were collected using a questionnaire. The study was completed with 72 intensive care nurses. The percentage, mean and chi-square tests were used for the analysis of data.

**Results:** %59.7 of nurses had gained their initial knowledge regarding the usage of pulse oximetry informally at the clinic. %48.6 of nurses did not have adequate training regarding oximetry. Most of the nurses stated that the best place for the application of the pulse oximetry was the index finger of the hand. The nurses' answers regarding the clinical scenario demonstrated that most nurses did not have adequate knowledge regarding first aid to be applied to the hypoxic patient.

**Conclusions:** The results stated the importance of topics regarding usage and fundamental principles of pulse oximetry during basic nursing education and continuing education programs. The results of the study connected with pulse oximetry must distribute to all nurses.

**Key words:** Oximetry, intensive care, nurse, knowledge

## Introduction

The pulse oximetry is a diagnostic appliance that is used in a noninvasive manner to monitor the oxygen saturation (SpO<sub>2</sub>) in the capillary ar-

terial blood of patients at risk of hypoxia and it is also frequently used in patients in the anaesthesia, pediatric and intensive care units and during perioperative periods. It can be administered by trained individuals in various environments such as a hospital or outpatient department and at home. Although pulse oximetry gives a good estimation of adequate oxygenation, it doesn't provide information on ventilation (1-6).

The pulse oximeter was invented in the early 1970s by Takua Aoyagi, a Japanese biomedical engineer. Pulse oximetry technology became widely used in the USA in the early 1980s. It was initially used in perioperative care, but was later frequently employed in the neonatal, pediatric and adult intensive care units. The risk of hypoxaemia and the need for pulse oximetry monitoring of haemoglobin saturation in both the operating room and the postanaesthesia care unit are well recognized and have been formalized in treatment standards adopted by the American Society of Anesthesiologists (ASA) in 1990 (7).

Providing adequate SpO<sub>2</sub> is one of the main components of critical patient care. Pulse oximetry therefore constitutes an important part of patient care. It is defined as one of the most important technological innovations used in monitoring the well-being and safety of the patient (8-10). The need for arterial blood gas analysis was found to have decreased when the respiratory status of patients in clinics where a pulse oximetry was used was evaluated (10). Arterial blood gas is a direct measurement and considered the golden standard for the measurement of blood oxygen saturation (SaO<sub>2</sub>). However, arterial blood gas samples can create undesired results, such as minimal blood loss, physical-psychological trauma due to the constant collection of blood with injectors, infection risk in the arterial blood vessel line, delay in



obtaining the results, and the cost of the sample analysis. On the other hand, pulse oximetry is a painless, cost-effective, portable, easy, noninvasive, continuous and direct application providing immediate results (7,11,12). Pulse oximetry monitoring is indicated whenever a patient is at risk for developing hypoxemia. However, because of the inherent limitations of noninvasive technology, it is very important to know how to use the pulse oximetry, its principles and limitations in order to understand the potential errors, interpret the results correctly and obtain the maximum clinical benefit. Conventional vital findings include body temperature, pulse, respiration rate, and blood pressure. It has lately been suggested that these four parameters might be supported by pulse oximetry as the “fifth vital finding”, especially in pediatric emergency clinics (3,6,11,13-17).

The pulse oximeter measures the light absorbance of human tissue beds at only two wavelengths, one in the red (660 nm) and the other in the near infrared (940 nm) ranges (14,18-20).

The oxygen saturation as calculated by pulse oximetry has a 95% confidence rate of  $\pm 4\%$ , so oximetry is considered to be reliable at readings that range between 70% and 100% SpO<sub>2</sub>. This means that, although pulse oximetry is not a replacement for blood gas testing, it can be used as a screening tool when poor oxygen saturation is suspected (8,13,20).

In a published study stated that “it can be difficult for nurses to critically evaluate information given by the pulse oximetry if they do not have sufficient knowledge of the physiology associated with oxygen transport and delivery in the body”. The risks associated with knowledge deficits are not limited to the nursing profession as pulse oximetry is also a routine component of patient assessment for medical and many allied health clinicians. Whilst the measurement of patients’ oxygen saturation seems quite simple, in reality the correct interpretation of the results is much more complicated. Failure by any clinician to appreciate the broader clinical picture or identify factors that can result in false high or low readings could lead to a significant risk for compromised patient safety, management and outcomes (6,21).

## Subjects and Methods

### *Research Design and Sample*

This study was performed in a descriptive in order to determine the knowledge levels of the nurses working in the surgery, cardiovascular intensive care, neonatal intensive care, internal disease intensive care and anesthesia units of Gulhane Military Medical Academy a university hospital regarding the usage and fundamental principles of pulse oximetry.

The study universe consisted of the 102 nurses working at university hospital intensive care unit. All ICU nurses were invited to participate in this study. But the study sample was constituted of 72 intensive care nurses who agreed to participate (rate of participation 70.6%). The data collection instrument developed by the researchers as a result of a literature survey was used to collect data in the study. The data collection instrument was a 30-item. Of the 30 questions,

- Four items related to the descriptive characteristics of the nurses
- Five items was related to experience with oximeters and perceived adequacy of knowledge on pulse oximetry
- 15 items was related to factors affecting readings
- 1 item was related to its use in hypothetical a hypoxic clinical situation. Clinical situation: immediate interventions to be performed in case of a sudden decrease in the patient’s saturation.
- Five items was designed to assess knowledge level of the nurses concerning the use of the pulse oximeter

Content validity was established by two critical care nurses educators review the questionnaire. The questionnaire was pilot tested by five critical care nurses and additional revisions were made to improve clarity. Various studies use published literature to develop the questions in the survey form (10,12).

The study was approved by the Institutional Board at the Training Hospital. The intensive care nurses were informed about the purpose and content of the research. Informed consent was obtained from all nurses orally. Data were collected 4-week period in March 2007. Instrument was

distributed to 72 intensive care nurses who were working the daytime shift (08-24) on weekdays during March 2007 and who agreed to participate.

The questionnaire was given by the researchers to the intensive care unit nurses in the various intensive care units. The nurses were asked to complete the questionnaire during work hours. After the questionnaires were completed they were collected by the researchers from the nurses.

The SPSS 11.0 statistics program percentage mean, and chi-square tests were used in the analysis of the data. A p value <0.05 was accepted as statistically significant.

### Results

We see from the descriptive characteristics of the participants that 59.7% of the nurses graduated from vocational high school of health. Most of nurses (36.1%) work in the cardiovascular intensive care unit, and 86.1% have four or more years of professional experience (mean of 51 months).

Information on the use of pulse oximetry had been obtained during clinical use by 59.7% of the participants in Table 1. The mean age of the nurses was 29 years. 48.6% of nurses indicated that they did not receive adequate formal education about usage of the pulse oximetry.

Oxygen saturation measured by pulse oximetry (SPO2) closely correlates with arterial blood gas levels (SaO2) if the patient doesn't have peripheral vascular disease and her oxygen saturation is greater than 70%. In our study, the question of "What does pulse oximetry measure?" was asked to nurses. 69.4% of the nurses stated that the pulse oximetry measures the oxygenated haemoglobin percentage. The most frequently given incorrect answer at a rate of 34.7% was that the pulse oximetry measures the partial oxygen pressure (paO2) (Table 1).

The nurse's knowledge of usage and principles of pulse oximetry was evaluated based on their answers to 26 relevant questions. 15.3 % of the nurses were able to give to correct answers to maximum thirteen of the 26 knowledge questions and the mean

Table 1. Answers to the question "What does pulse oximetry measure?"

	n	%
Oxygenated haemoglobin percentage	50	69.4
Percentage of the body surface area which is sufficiently oxygenated	10	13.9
Partial oxygen pressure (PaO2)	25	34.7
Transcutaneous partial oxygen pressure (TCO2)	18	25.0

\*Percentage row

\*n is multiple, more than one answer was given

Table 2. Distribution of the correct answers given for the questions

Number of correct answers	Nurses who answered correctly		
	n	%	Mean
7	1	1.4	14.52
8	1	1.4	
9	3	4.2	
10	6	8.3	
11	3	4.2	
12	7	9.7	
13	11	15.3	
14	7	9.7	
15	6	8.3	
16	9	12.5	
17	3	4.2	
18	2	2.8	
19	5	6.9	
20	1	1.4	
21	4	5.6	
22	3	4.2	

number of correct answers was 14.52. The participants with the best score answered twenty-two questions correctly; the participant with the worst score answered seven questions correctly (Table 2).

Table 3 shows the distribution of the correct answers about factors affecting the correct reading of the saturation and about pulse oximetry application regions of the nurses who use pulse oximetry frequently and those who don't; the first group (the nurses who use pulse oximetry frequently) had a higher number of correct answers. In our study, 70 (97.2%) participants stated that nail polish, 69 (95.8%) parti-

cipants stated that a cold extremity and 57 (79.1%) participants stated that anemia are among the factors affecting the reading of saturation.

Most of the nurses (86.1%) expressed that the place for applying the pulse oximetry is the index finger in Table 4.

The answer "Administer oxygen" was provided to the question "What is your immediate intervention in case of a sudden decrease in the patient's saturation?" by 41.7% of the nurses, as seen in Table 5.

Table 3. Distribution of the correct answers of the nurses according to whether they frequently use pulse oximetry or not (n=72)

Factors affecting the correct reading of the saturation	Use pulse oximetry frequently		Did not use pulse oximetry frequently		p
	Correct	Incorrect	Correct	Incorrect	
	n* (%)**	n* (%)**	n* (%)**	n* (%)**	
Nail polish	60 (83.3)	2 (2.8)	10 (13.9)	-	0.565
Cold extremity	60 (83.3)	2 (2.8)	9 (12.5)	1 (1.4)	0.320
Peripheral vasoconstriction	56 (77.8)	6 (8.3)	10 (13.9)	-	0.304
Presence of edema in the extremity	51 (70.8)	11 (15.3)	9 (12.5)	1 (1.4)	0.542
Severe anaemia	50 (69.4)	12 (16.7)	7 (9.7)	3 (4.2)	0.442
Shock	49 (68.1)	13 (18.0)	9 (12.5)	1 (1.4)	0.416
Moving the extremity	51 (70.8)	11 (15.3)	5 (6.9)	5 (6.9)	0.023
Carbon monoxide poisoning	44 (61.1)	18 (25.0)	7 (9.7)	3 (4.2)	0.950
Cardiac arrhythmias	37 (51.4)	25 (34.7)	4 (5.6)	6 (8.3)	0.244
Presence of a dressing in the extremity	32 (44.4)	30 (41.7)	6 (8.3)	4 (5.6)	0.622
Hyperbilirubinaemia	28 (38.9)	34 (47.2)	1 (1.4)	9 (12.5)	0.035
Hypertension	21 (29.2)	41 (56.9)	2 (2.8)	8 (11.1)	0.383
Presence of an I.V. catheter in the extremity	21 (29.2)	41 (56.9)	1 (1.4)	9 (12.5)	0.128
Excessive brightness of the room lamp	16 (22.2)	46 (63.9)	-	10 (13.9)	0.069
High serum lipid levels	14 (19.4)	48 (66.7)	-	10 (13.9)	0.094

\* More than one answer was given

\*\* Percentage was calculated according to n

Table 4. Distribution of pulse oximetry application regions (n=72)

	Use pulse oximetry frequently		Did not use pulse oximetry frequently		p
	Correct	Incorrect	Correct	Incorrect	
	n* (%)**	n* (%)**	n* (%)**	n* (%)**	
Index finger	62 (86.1)	0	7 (9.7)	3 (4.2)	0.000
Thumb	11 (15.3)	51 (70.8)	2 (2.8)	8 (11.1)	0.863
Toe	53 (73.6)	9 (12.5)	8 (11.1)	2 (2.8)	0.655
Earlobe	45 (62.5)	17 (23.6)	4 (5.6)	6 (8.3)	0.040
Nasal bridge	12 (16.7)	50 (69.4)	2 (2.8)	8 (11.1)	0.962

\*More than one answer was given

\*\*Percentage was calculated according to n

*Table 5. Clinical scenario: distribution of immediate interventions to be performed in case of a sudden decrease in the patient's saturation*

	n=72	%
Check the airway, respiration, and circulation of the patient	8	11.1
Administer oxygen	30	41.7
Check if the oximetry functions properly	10	13.9
Analyze blood gases	2	2.8
Inform the physician	15	20.8
No answer	7	9.7
<b>Total</b>	<b>72</b>	<b>100</b>

## Discussion

Measuring the arterial oxygen saturation with a pulse oximetry is a simple, non-invasive observation technique, and it is a standard of care in the anesthetic intensive care and pediatric intensive care units for the monitoring of patients who are intubated and connected to the ventilator, carry a risk of hypoxia, are sedated, or have serious cardio-respiratory problems.

Studies carried out regarding pulse oximetry have shown that many health care workers have insufficient knowledge and are confused about the way in which pulse oximetry works, what it measures, its principles, and the factors affecting its readings (9,10,20,21,23). Incorrect oxygen saturation measurements may cause faulty treatments if the pulse oximetry is not used properly or its limitations and usage principles are not known (9,20-23,24). We detected that 59.7% of the nurses had gained their initial knowledge regarding the usage of the pulse oximetry informally at the clinic during their practices, and 48.6% of nurses indicated that they did not receive adequate formal education about usage of the pulse oximetry. These results show similarities with other studies. In Harper's study that 39% of the participants stated that they gained their initial knowledge about pulse oximetry from their colleagues, 22% stated that they gained it during in-service training, and 6% stated that they gained their knowledge from books or articles (9). In Rodriguez's study, 97% of the participants had the chance of experiencing the use of pulse oximetry but 43% of them expressed that they did not have adequate training concerning its usage (12). In another study, 87% of the nurses stated that they used the pulse oximetry regularly in the evaluation of their patients, but

only 37% of the nurses stated that they had received adequate training and knowledge about pulse oximetry (24). In another study Teoh et al, 64% of the recently graduated physicians and 74% of the experienced physicians stated that they had not received adequate training on the use of pulse oximetry (22). In Stoneham's study, only one of the participants stated that he/she had received adequate training while 10% of the physicians stated that they had gained their knowledge from an article in the British Medical Journal, and the other participants stated that they had not received special training and learned the use of the pulse oximetry informally from their colleagues (10). In contrast to previous research finding the critical care nurses in Giuliano et al study seemed to have more basic SpO<sub>2</sub> knowledge (17).

The oxygen saturation, which is closely related to the blood gas levels, is measured with pulse oximetry if a patient does not have a peripheral vascular disease and the oxygen saturation is higher than 70%. Pulse oximetry is an indicator of oxygenation: the haemoglobin amount saturated with oxygen. It does not directly measure ventilation (9). In our study, 69.4% of the nurses stated that the pulse oximetry measures the oxygenated haemoglobin percentage. The most frequently given incorrect answer at a rate of 34.7% was that the pulse oximetry measures the partial oxygen pressure (paO<sub>2</sub>) (Table 2). These results show similarities with other studies. In a study carried out by Kruger and Longden to determine pulse oximetry knowledge levels, only 68.5% of the participants correctly stated what pulse oximetry were measuring (23). In Stoneham's study, 80% of the nurses correctly answered the question "What does pulse oximetry measure?" (10). In Rodriguez's study, 43% of the participants expressed that they did not

know what pulse oximetry measures, and the most common incorrect answer given to this question at a rate of 34% was that pulse oximetry measures the transcutaneous partial oxygen pressure (12). Using a knowledge test, Howell found that accurate knowledge of what a pulse oximeter measured ranged from 50% to 60% among 30 trained (those who had received formal Spo2 training as part of their orientation) and 12 untrained (those who had not received formal Spo2 training as part of their orientation) nursing staff (25).

In our study, the nurse's knowledge of usage and principles of pulse oximetry was evaluated based on their answers to 26 relevant questions. 15.3 % of the nurses were able to give to correct answers to maximum thirteen of the 26 knowledge questions and the mean number of correct answers was 14.52. The participants with the best score (4.2%) answered twenty-two questions correctly; the participant with the lowest score (1.4%) answered seven questions correctly (Table 2). This result indicates that nurses have a need for information about the usage of pulse oximetry. Specific training for pulse oximetry appears to be scarce. Stoneham et al<sup>10</sup> reported that most hospital staff learned about pulse oximetry informally from their colleagues on the unit, rather than from formal training programs, and most respondents recognized their knowledge deficit and identified a need for more training. Inadequate knowledge was also detected in other studies evaluating the knowledge of health personnel regarding pulse oximetry (6,9,22).

There are a number of potential error sources which should be taken into consideration in the evaluation and proper usage of pulse oximetry. Examples are placement of the probe, signal quality, weak peripheral perfusion, hypotension, hypothermia, hypoxia, dried blood at sensor site, nail polish, pigmentation of the skin, the amount of light in the environment, movement of joint and heavy smoking. These can affect the sensitivity, applicability, and accuracy of the device and reliable readings by the clinician (6,11-14,24,26,27). In the study of Rodriguez et al. 21% of the participants expressed that they did not know that nail polish and moving the extremity affect the correct reading of the pulse oximetry (12). In the study performed by Stoneham et al. ninety-five percent

of the physicians and nurses did not understand the way in which pulse oximetry works and did not know the factors affecting its reading exactly (10). The literature recommend that especially black, brown, green, purple and dark blue nail polish can block light transmission, resulting in an inaccurate reading. Therefore, to decrease the error of measurement, fingernail polish is routinely remove or use another application site (1,2,6,22,26). But in the study of Rodden et al. fingernail polish does not cause a clinically significant change in pulse oximetry readings in healthy people (18). Most of these results show similarities with our study. In our study, 70 (97.2%) participants stated that nail polish, 69 (95.8%) participants stated that a cold extremity and 57 (79.1%) participants stated that anemia are among the factors affecting the reading of saturation (Table 3).

Nurses should select a vascular bed with sufficient pulse beat for correct pulse oximetry application. Although toes, earlobes, the forehead, or nasal bridge with adequate perfusion are used for this purpose, the index finger provides the best readings (3,7,27-30). Most of the nurses (86.1%) expressed that the place for applying the pulse oximetry was the index finger in our study. Application regions such as the nasal bridge, earlobes, and toes were provided at a lower rate compared to the index finger (Table 4). In Harper's study, 63% of the participants stated that placing the probe on the finger might produce better results compared to the other regions (9). In literature previous studies have demonstrated this lack of knowledge among medical staff concerning the principles, practical applications, application regions and associated limitations of pulse oximetry (12,14).

A patient whose saturation is lower than 90% may be seriously hypoxic. Airway obstruction which causes hypoxia is a life-threatening situation requiring immediate intervention. When the saturation level of a patient suddenly decreases in an unacceptable way, the primary procedures to be performed are the fundamental first aid interventions, such as checking the airway, respiration, and circulation. Later, interventions such as giving oxygen, checking whether the oximetry is functioning properly and finally analysis of the blood gas must be performed. Pulse oximetry reading interpretations do not require using oxygen directly.

Although pulse oximetry can determine severe hypoxia, it does not provide information about the arterial partial carbondioxide pressure (9,10,22). In a study, most of the participants stated giving oxygen as the immediate intervention, and none of them mentioned checking the airway, respiration, and circulation. In other study, 53% of the participants stated taking blood gases as the immediate action among the interventions to be performed when the pulse oximetry reading suddenly decreases or shows a decreasing trend (9,10). The answers given by the nurses in our study resemble similarities to the other studies. In case of a sudden decrease in the patient's saturation, administering oxygen was stated as the immediate action by 41.7% of the nurses who participated in our study; however, 11.1% of the participants suggested checking the airway, respiration, and circulation of the patient (Table 5).

Remember that Spo2 is only one patient-assessment tool and should be interpreted along with other patient data including vital signs, cardiac rhythm and breath sounds.

### Conclusion

Pulse oximetry is a standard in health care units as it provides very early notice regarding the development of desaturation and helps determine episodes of arterial hypoxia which are hard to figure out clinically. Therefore there is a need for theoretical and practical training of the nurses on this subject and creating a guide in health care units concerning the usage principles of the pulse oximetry in order to provide clinically effective use of the device.

Our results indicate that competency of nurses should evaluate during orientation and the nurses must increase awareness of the need for the usage principles of the pulse oximetry knowledge. The results of the study connected with pulse oximetry must publish in the hospitals' publication and must distribute to all nurses. We suggest that in undergraduate and postgraduate level, comprehensive training of nurses in the use of pulse oximetry is essential.

### Acknowledgement

No financial or material support was received for his study. The authors wish to thank the staff of our ICU.

### References

1. Paragas J. *Keeping the beat with pulse oximetry. Nursing2008. 2008; November: 56hn1-56hn2.*
2. *By the editors of Nursing2008. Monitoring your adult patient with bedside: pulse oximetry. Nursing2008. 2008;September: 42-44.*
3. Masters KJ. *Pulse oximetry use during physical and mechanical restraints. The Journal of Emergency Medicine. 2007; 33: 289-291.*
4. Trivedi NS, Ghouri AF, Shah NK, et.al. *Effects of motion, ambient light, and hypoperfusion on pulse oximeter function. Journal of Clinical Anesthesia. 1997;9: 179-183.*
5. Davidson JAH, Hoise HE. *Limitations of pulse oximetry: respiratory insufficiency-a failure of detection. BMJ. 1993;307:372-373.*
6. Lowe CV, Ghareeb SA, Artinian NC. *Pulse oximetry in adults. AJN. 2009;109(6):52-59.*
7. Pedersen T. *Does perioperative pulse oximetry improve outcome? Seeking the best available evidence to answer the clinical question. Best Practice & Research Clinical Anaesthesiology. 2005;19:111-123.*
8. Attin M, Cardin S, Dee V, et.al. *An educational project to improve knowledge related to pulse oximetry. American Journal of Critical Care. 2002;11:529-534.*
9. Harper JP. *Post-anesthesia care unit nurses' knowledge of pulse oximetry. Journal for Nurses in Staff Development. 2004; 20(4):177-180.*
10. Stoneham MD, Savilla M, Wilson H. *Knowledge about pulse oximetry medical and nursing staff. The Lancet. 1994;344:1339-1342.*
11. Gibson LY. *Pulse oximeter in the neonatal ICU: A correlational analysis. Pediatric Nursing. 1996; 22: 511-515.*
12. Rodriguez LR, Kotin N, Lowenthal D, Kattan M. *A study of pediatric house staff's knowledge of pulse oximetry. Pediatrics. 1994; 93:810-813.*
13. Demeulenaere S. *Pulse oximetry: uses and limitations. The Journal for Nurse Practitioners. 2007; May:312-317.*
14. Salyer JW. *Neonatal and pediatric pulse oximetry. Respiratory Care. 2003;48:386-398.*

15. Simon SB, Clark RA. (Mis) Using pulse oximetry: a review of pulse oximetry use in acute care medical wards. *Clinical Effectiveness in Nursing*. 2002; 6:106-110.
16. Eichhorn JH. Pulse oximetry monitoring and late postoperative hypoxemia on the general care floor. *Journal of Clinical Monitoring and Computing*. 1998;14:49-55.
17. Giuliano KK, Liu LM. Knowledge of pulse oximetry among critical care nurses. *Dimensions of Critical Care Nursing*. 2006; 25:44-49.
18. Rodden AM, Spicer L, Diaz VA, Steyer TE. Does fingernail polish affect pulse oximeter readings? *Intensive and Critical Care Nursing*. 2007;23:51-55.
19. Wong AW, Chan M, MA K, Law L, Zwieten R, Lam C, et al. Normal pulse oximeter reading in a cyanotic infant. *J. Paediatr. Child Health*. 2001;37:94-95.
20. Sinex JE. Pulse oximetry: principles and limitations. *American Journal of Emergency Medicine*. 1999; 17:59-66.
21. Elliott M, Tate R, Page K. Do clinicians know how to use pulse oximetry? A literature review and clinical implications. *Australian Critical Care*. 2006;19:139-144.
22. Teoh L, Epstein A, Williamson B, Morton J, Papadopoulos D, Teng A. Medical staff's knowledge of pulse oximetry: A prospective survey conducted in a tertiary children's hospital. *J. Paediatr. Child Health*. 2003;39:618-622.
23. Kruger PS, Longden PJ. A study of a hospital staff's knowledge of pulse oximetry. *Niger J Med* 2002; 11:13-15.
24. Fluck RR, Schroeder C, Frani G, Kropf B, Engbretson B. Does ambient light affect the accuracy of pulse oximetry?. *Respiratory Care*. 2003;48:677-680.
25. Howell M. Pulse oximetry: an audit of nursing and medical staff understanding. *British Journal of Nursing*. 2002;11:191-196.
26. Hinkelbein J, Genzwuerker HV, Sogl R, Fiedler F. Effect of nail polish on oxygen saturation determined by pulse oximetry in critically ill patients. *Resuscitation*. 2007; 72:82-91.
27. Ingram G, Munro N. The use (or otherwise) of pulse oximetry in general practice. *British Journal of General Practice*. 2005; July:501-502.
28. Bodin DA. Telemetry beyond the ICU. *Nursing Management*. 2003; 34:46-50.
29. Pullen RL. Caring for a patient on pulse oximetry. *Nursing2003*. 2003; 33:30.
30. McConnell EA. Performing pulse oximetry. *Nursing99*. 1999; November:17.

## Corresponding Author

Dilek Yıldız,  
 Gulhane Military Medical Academy,  
 School of Nursing,  
 Pediatric Department,  
 Etlik,  
 Ankara,  
 Turkey,  
 E-mail: dyz1@yahoo.com

# Cognitive Dual-Task training improves balance function in patients with stroke

Zheng Jiejiao<sup>1</sup>, Wang Xueqiang<sup>2</sup>, Xu Yueying<sup>1</sup>, Yang Ying<sup>1</sup>, Shen Liyan<sup>1</sup>, Liang Zhenwen<sup>1</sup>

<sup>1</sup> Department of rehabilitation medicine, Huadong Hospital affiliated to Fudan University, Shanghai, China,

<sup>2</sup> Department of sport rehabilitation, Shanghai University of Sport, Shanghai, China.

## Abstract

**Objective:** To evaluate the effectiveness of cognitive dual-task training on balance function in patients with stroke.

**Methods:** One hundred patients with stroke were randomly allocated into training group and control group. Control group received conventional balance program, training group received cognitive dual-task training (conventional balance program + cognitive training). Subjects were asked to exercise 3 times a week (40min/time) for 8 weeks. In the pre- and post-training sessions, all participants performed tests of static postural control. Static postural control was assessed via measurement of center of pressure sway under eyes open (EO) and eyes closed (EC) conditions.

**Results:** Ninety-two of the 100 participants (training group, n=47; control group, n=45) completed the 8 weeks program. Control group had significantly greater maximum displacement in the medial-lateral direction with eyes open and closed condition, compared with training group ( $P < 0.05$ ). And anteroposterior balance indices of subjects in the dual task group were significantly better than those in the control group with eyes open after 8 weeks ( $P = 0.000$ ).

**Conclusions:** Our results demonstrate that an integration of a cognitive training and balance program (cognitive dual task) could produce more beneficial effects on balance function than balance exercise alone (single task) in patients with chronic stroke.

**Key word:** stroke, balance, dual-task training, rehabilitation

## Introduction

Falls remain a common complication immediately after a stroke as well as during the post-stroke

life of the patient. Stroke survivors are at high risk for falls in all poststroke stages (1.3–6.5 falls/person/year) [1]. A research [2] show that the rate of falls for individuals with stroke was 1.77 times the rate for the normal population. This may be in part due to weakness, sensory loss, visual disturbances and changes in cognitive function. And older adults with cognitive impairment suffer from a highly increased fall risk rate that is two to three times as high as that of the age- and sex-matched general population.

If the patients have fallen or have a fear of falling, patients tend to do less for themselves and do not want to go out. This may increase their social isolation in addition to predisposing them to medical comorbidities related to immobility; leading to increase hospitalizations, decrease quality of life and ultimately increase mortality. There is also an increase burden placed on the caregiver with stroke patients that have fallen. In daily life people often do several other things while they are standing or walking. Many falls occur during the performance of such dual tasks [3].

Using dual-task paradigms, many studies [4–7] have demonstrated that cognitive resources, in particular attention, are necessary for the proper maintenance of balance and gait and that subjects with an increased risk of falls display a heightened adverse response to dual tasking. In fact, studies [8–10] have suggested that dual task training is effective in improving gait speed and balance function under dual-task conditions in elderly participants.

However, it is not yet known whether cognitive dual-task training has a specific effect on balance function compared with conventional balance exercise in subjects with chronic stroke. Hence we designed the present study to examine the effects of a 8-week cognitive dual-task training versus conventional balance exercise on balance function in subjects after stroke.



## Methods

### Subjects

Subjects (n=100) with stroke, confirmed by computed tomography or magnetic resonance imaging scan, were recruited from several general communities at Shanghai City of China. All subjects were randomly assigned by using a computer-generated random number sequence to either a dual task group (n=52; mean age $\pm$  SD, 64.5 $\pm$  2.1y), or control group (n=48; mean age $\pm$  SD, 68.3 $\pm$  1.7y). The dual task group and the control group were both performed five times a week (40min/session) for 8 weeks.

The eligibility criteria: (1) hemiparetic from a single stroke occurring at least a year earlier, (2) not presently receiving any rehabilitation services, (3) an ability to understand instructions and follow commands, (4) ability to stand with or without assistance and to take at least one or more steps with or without assistance, and (5) stable medical condition to allow participation in the testing protocol and intervention.

The exclusion criteria: (1) non-stroke-related sensory or motor impairments, (2) use of medication that could interfere with balance function, and (3) any uncontrolled health condition for which exercise is contraindicated. After receiving verbal and written information, all subjects gave their written informed consent to participate in the study. The regional medical-ethical committee approved the study.

### Procedure

All participants are first accepted the questionnaire, content for its basic information, past and present job status, medical history, Activity of Daily Living test, and exercise habits(frequency and time/session). This study was a 2-armed randomized, controlled trial with blinding of patients and assessors with respect to the nature of therapy. With the use of opaque closed envelopes and stratified by center, included patients were randomized to either dual task group or control group by an independent collaborator within 2 days after admission. At baseline and after the 8-week intervention, patient characteristics and outcome measures were assessed.

All assessments were done by 3 independent, experienced physical therapists, who were not

working in the stroke unit of the participating rehabilitation centers, who were blind with regard to treatment allocations and who had no contact with any of the patients during the study. Patients were instructed not to discuss their treatment with these assessors. Each assessor received the same practical instructions. All assessments took place in one rehabilitation center (Huadong hospital).

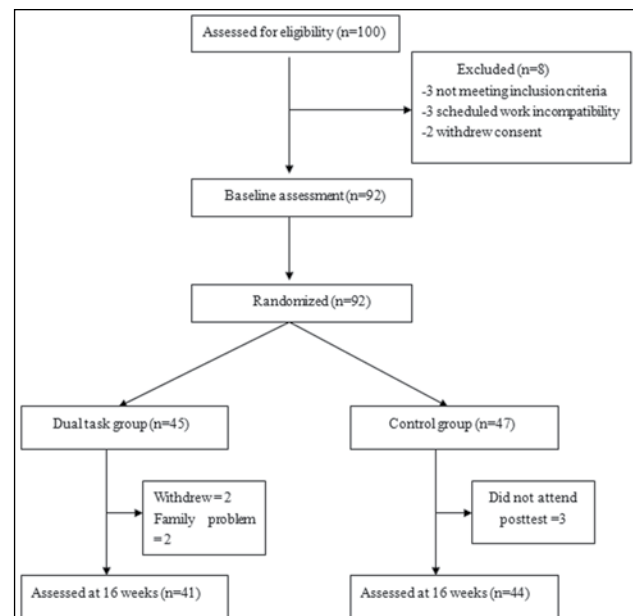


Figure 1. Flow chart of the participants

### Training Program

All patients were treated with either dual task exercise or balance exercise on each working day during 8 weeks of their admission in the rehabilitation center. Both exercise programs were led by registered physical therapists for 40 minutes.

**The balance exercise intervention:** The exercise protocol [11] emphasized static and dynamic balance exercises, including transitions between differing sensory conditions and functional everyday movements. Each lesson incorporated a similar general plan: (1) 5 minutes warm-up, (2) 15 minutes static balance exercises, such as Squats(two-leg stance), One leg stance, (3) dynamic balance exercises, such as Jogging end to end, Sideways walking or running with crossovers, Forward walking or running in a zigzag line, Backward walking or running in a zigzag line, and (4) 5 minutes of cool-down. Exercises gradually increased in difficulty and training load during the 8 weeks.

**The cognitive dual-task training:** The training program was based on a dual-task concept [12].

Each lesson incorporated a similar general plan: (1) 5 minutes warm-up, (2) subjects were asked to give a response to continuous simple addition/subtraction questions (such as  $3 + 2 = 5$ ,  $100 - 7 = 93$ ) while performing static balance exercises for 15 minutes, (3) 15 minutes dynamic balance exercises while performing cognitive tasks simultaneously, such as Sideways walking or running with crossovers while performing addition/subtraction questions, and (4) 5 minutes of cool-down. The subject was challenged with increasingly difficult tasks.

### Outcome Measures

Static balance test evaluating postural control by means of a device (Biodex Balance System; New York, USA) [13]. The level of difficulty while standing on this platform can be manipulated by altering the resistance of the platform to deviations. Each participant stands barefoot on the platform and performs balance test (level 8 = easiest level). The foot position was standardized using a pre-formed triangle (heels together with feet forming an angle of 20 degrees). Patients were instructed to keep their hands at their sides. For safety purposes they were permitted to touch

handrails, but only to re-establish balance during extreme postural deviations. The participants were then instructed to find a position at which they could maintain platform stability. Each recording lasted for 60 s with a 60 s rest between each trial.

### Statistical Analyses

Statistical analyses were performed with the SPSS 17.0 and Microsoft Excel 2003 software. Data are expressed as mean $\pm$ SD. Changes in variables between pre-training and post-training and between groups were analyzed.

The independent samples t test and Chi-square test were used to compare both groups at baseline. A 2-way analysis of variance (group $\times$ time) was used to assess the effects of treatment depending on group allocation. We performed an intention-to-treat analysis by carrying the last value forward in the case of missing values at the second assessment. Statistical significance was assumed at P less than 0.05.

### Result

The study design is outlined in figure 1. Ninety two of the 100 individuals initially recruited, 3

Table 1. Baseline Values for the 2 Groups

Variable	Dual Task group (n=45)	Control group (n=47)	P
Men/Femen	24/21	23/24	0.683*
Age(years)	69.11 $\pm$ 5.01	68.61 $\pm$ 4.62	0.562 <sup>#</sup>
Type of stroke			
Ischemic	20	23	0.682*
Hemorrhagic	25	24	
Location of stroke			
Left hemisphere	25	20	0.297*
Right hemisphere	20	27	
Time post stroke (month)	33.11 $\pm$ 5.73	30.42 $\pm$ 7.44	0.186 <sup>#</sup>
MMSE (score)	23.04 $\pm$ 2.48	22.63 $\pm$ 2.14	0.403 <sup>#</sup>
Eye open			
ML sway distance (mm)	138.78 $\pm$ 12.44	141.14 $\pm$ 11.21	0.339 <sup>#</sup>
AP sway distance (mm)	139.67 $\pm$ 11.13	144.21 $\pm$ 18.28	0.155 <sup>#</sup>
COP area (mm <sup>2</sup> )	192.41 $\pm$ 17.13	196.70 $\pm$ 13.03	0.178 <sup>#</sup>
Eye close			
ML sway distance (mm)	151.02 $\pm$ 12.71	149.44 $\pm$ 14.41	0.580 <sup>#</sup>
AP sway distance (mm)	153.47 $\pm$ 11.98	157.79 $\pm$ 12.59	0.082 <sup>#</sup>
COP area (mm <sup>2</sup> )	244.62 $\pm$ 39.57	257.68 $\pm$ 27.97	0.072 <sup>#</sup>

NOTE. Data reported as mean  $\pm$  SD. MMSE: Mini Mental Status Examination; ML: mediolateral; AP: anteroposterior; COP: center of pressure. NS: indicates not significant.

\* Chi-square test; <sup>#</sup> independent samples t test.

Table 2. Balance function for the 2 Groups

Variable	Dual Task group (n=41)	Control group (n=44)	P*
Eye open			
ML* sway distance (mm)	102.55 ± 18.48	122.19 ± 16.95	0.004
AP* sway distance (mm)	114.36 ± 16.9	136.59 ± 14.68	0.000
COP* area (mm <sup>2</sup> )	184.48 ± 22.17	190.25 ± 21.33	0.818
Eye close			
ML* sway distance (mm)	129.15 ± 12.38	136.36 ± 15.98	0.010
AP* sway distance (mm)	131.72 ± 14.93	142.72 ± 23.12	0.086
COP* area (mm <sup>2</sup> )	209.91 ± 23.31	237.49 ± 30.17	0.164

NOTE. Data reported as mean ± SD. MMSE: Mini Mental Status Examination; ML: mediolateral; AP: anteroposterior; COP: center of pressure; \*: a 2-way analysis of variance.

subjects did not meet the inclusion criteria, 3 subjects scheduled work incompatibility and 2 subjects withdrew consent. After 8-week program, there were 85 subjects. Four participants from dual task group, 3 participants from control group were lost to follow-up. Reasons for dropout included withdrew and serious family problems. Additionally, 3 patients did not attend the final evaluation session. Hence, follow-up data were available for 41 of 44 subjects in the dual task group, 44 of 47 subjects in the control group. Table 1 lists baseline characteristics of the 2 groups. The groups were well matched at the baseline assessment, with no differences in key outcome variables apparent.

Table 2 shows the values of all outcome measures with their standard deviations. The results showed a significant difference in mediolateral sway distance values in the dual task group as compared with the control group with eyes open and closed condition ( $P < 0.05$ ). And anteroposterior balance indices of subjects in the dual task group were significantly better than those in the control group with eyes open after 8 weeks ( $P=0.000$ ).

## Discussion

The specific aim of this randomized controlled study was to demonstrate that an integration of a cognitive training and balance program (cognitive dual task) could produce more beneficial effects on balance function than balance exercise alone (single task). Our results showed that a 8-week exercise program improved balance function under single- and dual-task conditions in patients with stroke. In addition, as anticipated, our results showed that

static balance performance significantly improved in the dual task group in comparison with the control group. And the study demonstrate that an integration of a cognitive exercise and balance program could produce more beneficial effects on balance function than balance exercise alone.

Previous studies have also shown dual task programs could improve walking ability and balance function in elderly people. Silsupadol et al [9] showed older adults may be able to improve their balance under dual-task conditions for 3 months. Karen et al [14] found that the dual task group showed significant improvements in body sway during single-support balance and center of gravity alignment during double-support dynamic balance. So far, but there was only a published randomized controlled clinical trial study to examine the effectiveness of dual-task-based exercise training on walking ability in subjects with chronic stroke [15]. But their study compared a group of chronic stroke who participated in a 4-week dual task program with another group of subjects who did not receive any rehabilitation training. In contrast, the aim of our study was to examine the effects of cognitive dual task training on balance function in chronic stroke patients compared with the effects of single task.

Our results showed a significant difference in mediolateral sway distance values in the dual task group as compared with the control group with eyes open ( $P=0.004$ ) and closed condition ( $P=0.01$ ). And anteroposterior balance indices of subjects in the dual task group were significantly better than those in the control group ( $p=0.000$ ) with eyes open after 8 weeks exercise. The results were similar to

those reported previously in some studies [8,14,16]. These studies show dual task exercise could significantly improve balance function.

There can be several reasons for this result. First, it is well known that cognitive impairments are common after stroke, and many papers [5,17,18] show cognitive status is important for balance. Dual task group of our study requires individuals to balance in standing while simultaneously performing cognitive task (addition/subtraction questions, such as  $3 + 2 = 5$ ,  $100 - 7 = 93$ ). However, control group only receive balance exercise.

Second, cognitive dual task training (the balance and cognitive tasks were performed concurrently) is more difficult than single task exercise (balance exercise). Resch and his colleagues [19] also suggest participants' center of pressure sway length were longer under dual-task conditions than under single-task conditions. As is known to all, as our balance improves, begin adding variations to increase the difficulty of the exercise. In a sense, more difficult balance exercise is, more effective the result is.

The last, patients with stroke can improve their balance function under dual-task conditions only following specific types of training, and that training balance under single-task conditions may not generalize to balance control during dual-task contexts. According to the Task Integration Hypothesis, practicing 2 tasks together (not a single-task practice) allows participants to develop task-coordination skills [9]. Dual-task conditions are highly relevant in clinical practice. In the natural environment, patients often combine tasks necessary for daily life and may need to prioritize one task over another based on changing task or environmental demands [20].

## Conclusion

To our knowledge, this is the first randomized, controlled trial that examine the effects of cognitive dual task training on balance function in patients with stroke compared with the effects of single task. Although our results showed that static balance performance significantly improved in the dual task group in comparison with control group. Further study with long-term follow-up is needed to substantiate the mechanism of cognitive dual task exercise in patients with stroke.

## Acknowledgments

We thank all patients for their willingness to participate in this study.

## Source of Funding

Supported by Shanghai Natural Science Foundation, China(Grant No. 06JC14027).

## References

1. Weerdesteyn V, de Niet M, van Duijnhoven HJ, et al. Falls in individuals with stroke. *J Rehabil Res Dev* 2008; 45(8):1195-213.
2. Simpson LA, Miller WC, Eng JJ. Effect of Stroke on Fall Rate, Location and Predictors: A Prospective Comparison of Older Adults with and without Stroke. *PLoS One* 2011; 6(4):e19431.
3. de Hoon EW, Allum JH, Carpenter MG, et al. Quantitative assessment of the stops walking while talking test in the elderly. *Arch Phys Med Rehabil* 2003; 84(6):838-842.
4. Hausdorff JM, Yogev G. Cognitive function may be important for fall injury prevention trials. *J Am Geriatr Soc* 2006; 54(5):865-6.
5. Shin BM, Han SJ, Jung JH, et al. Effect of mild cognitive impairment on balance. *J Neurol Sci* 2011; 305(1-2):121-125.
6. Armand S, Allet L, Landis T, et al. Interest of dual-task-related gait changes in idiopathic normal pressure hydrocephalus. *Eur J Neurol* 2011; 18(8):1081-1084.
7. Foley JA, Kaschel R, Logie RH, et al. Dual-task performance in Alzheimer's disease, mild cognitive impairment, and normal ageing. *Arch Clin Neuropsychol* 2011; 26(4):340-348.
8. Hiyamizu M, Morioka S, Shomoto K, et al. Effects of dual task balance training on dual task performance ability in elderly people: a randomized controlled trial. *Clin Rehabil* 2011; Mar 18. [Epub ahead of print]
9. Silsupadol P, Shumway-Cook A, Lugade V, et al. Effects of single-task versus dual-task training on balance performance in older adults: a double-blind, randomized controlled trial. *Arch Phys Med Rehabil* 2009; 90(3):381-387.
10. Silsupadol P, Siu KC, Shumway-Cook A, et al. Training of balance under single- and dual-task conditions in older adults with balance impairment. *Phys Ther* 2006; 86(2):269-281.

11. Li KZ, Roudaia E, Lussier M, et al. Benefits of cognitive dual-task training on balance performance in healthy older adults. *J Gerontol A Biol Sci Med Sci* 2010; 65(12):1344-1352.
12. Yang YR, Wang RY, Chen YC, et al. Dual-task exercise improves walking ability in chronic stroke: a randomized controlled trial. *Arch Phys Med Rehabil* 2007; 88(10):1236-1240.
13. Holmes JD, Jenkins ME, Johnson AM, et al. Dual-task interference: the effects of verbal cognitive tasks on upright postural stability in Parkinson's disease. *Parkinsons Dis* 2010; 696492.
14. P Hlman U, Guti Rrez-P Rez C, S Vborg M, et al. Cognitive function and improvement of balance after stroke in elderly people: the Gothenburg Cognitive Stroke Study in the Elderly. *Disabil Rehabil* 2011; 33(21-22):1952-62.
15. Hernandez SS, Coelho FG, Gobbi S, et al. Effects of physical activity on cognitive functions, balance and risk of falls in elderly patients with Alzheimer's dementia. *Rev Bras Fisioter* 2010; 14(1):68-74.
16. Resch JE, May B, Tomporowski PD, et al. Balance performance with a cognitive task: a continuation of the dual-task testing paradigm. *J Athl Train* 2011; 46(2):170-175.
17. McCulloch K. Attention and dual-task conditions: physical therapy implications for individuals with acquired brain injury. *J Neurol Phys Ther* 2007; 31(3):104-118.
18. Westlake KP, Wu Y, Culham EG. Sensory-specific balance training in older adults: effect on position, movement, and velocity sense at the ankle. *Phys Ther* 2007; 87(5):560-568.
19. Broglio SP, Tomporowski PD, Ferrara MS. Balance performance with a cognitive task: a dual-task testing paradigm. *Med Sci Sports Exerc* 2005; 37(4):689-695.
20. Allet L, Armand S, de Bie RA, et al. The gait and balance of patients with diabetes can be improved: a randomised controlled trial. *Diabetologia* 2010; 53(3):458-466.

*Corresponding Author*

Zheng Jiejiao,

Department of rehabilitation medicine,

Huadong Hospital affiliated to Fudan University,

Shanghai,

China,

E-mail: zjjcss@126.com

# Sleep disorders in climacteric women

Sandra Dircinha Teixeira de Araújo Moraes<sup>1,2</sup>, Angela Maggio da Fonseca<sup>1,2</sup>, Eli Mendes de Moraes<sup>1,2</sup>, Vicente Renato Bagnoli<sup>1</sup>, Caio Fábio Schlechta Portella<sup>2</sup>, Luiz Carlos Abreu<sup>1</sup>, Edmundo Chada Baracat<sup>1</sup>

<sup>1</sup> University of São Paulo - Medicine College - Department of Gynecology - General Hospital, Brazil.

<sup>2</sup> Study Nucleus on Violence and Humanization of Health Attention, Brazil.

## Abstract

**Introduction:** This paper examines the various factors that contribute to the occurrence of sleep alterations during peri and post climacteric and thus produce significant imperil to women's quality of life.

Among the probable causes of insomnia or sleep disorders associated to climacteric stand out the occurrence of vasomotor symptoms, depressive state and respiratory distress during sleep, such as sleep apnea, along with chronic pain, although psychosocial factors related to the climacteric bear major influence on such clinical status.

**Method:** The bibliographic analysis was carried out using several electronic data base namely: Cochrane, Medline, Embase, Bni Plus, Biological Abstracts, Psycinfo, Web Of Science, Sigle, Dissertation Abstracts and ZETOC published in English, Spanish and Portuguese. The key terms used were: sleep, REM sleep, slow wave sleep polysomnography; electroencephalogram; sleep disturbances; disturbances of sleep onset and maintenance; excessive somnolence disturbances; climacteric; menopause; depression; neurobiology; biologic models; circadian rhythm; mental health and epidemiology. Case studies and letters to the editor were excluded. The summaries of the identified studies found in the data base were analyzed and assessed, and the data analyzed separately according to the subjective or objective criteria for data collection.

**Results:** The climacteric transition constitutes a period of major risk for the development of depressive, vasomotor and insomnia symptoms although not caused solely by hypoestrogenism. The diagnostic methods used in the study of sleep disorders range from subjective assessment by means of response to specific questionnaires to the objective analysis of actigraphic or polissonographic daytime and nocturnal reports. Polissonographic studies of the whole night, performed at the laboratory, are the golden method of choice for diagnostic of sleep disorders. Studies point to

the high prevalence of sleep disorders in the climacteric, especially insomnia, apnea and periodic movement of legs and also to the fact that this phase of life presents decrease in the quality of sleep. Women in peri and post climacteric show higher sleep latency and difficulty in its maintenance and refer being less satisfied with its quality even when compared to those who are not climacteric.

Exception made to the vasomotor symptomatology, the other climacteric complaints such as mood disturbances, libido alterations, cognitive deficit, articular pain and sleep disorders are markedly associated to psychosocial factors, lifestyle and especially to women's perception of what the climacteric means to their lives.

**Conclusion:** The analysis of the available studies revealed a proneness to deterioration of quality of life of climacteric women markedly in the sleep disturbances, depressed mood and anxiety domains and should not to be basically attributed to the climacteric. It is necessary that the professionals consider the need of assessment of such pathologies as complex phenomena and the literature lacks studies contemplating such dimensions.

**Key words:** Sleep disorders, climacteric, menopause

## Introduction

This article examines the diverse factors that contribute to the occurrence of sleep disorders during peri and post-menopausal phases that impair women's life quality. Sleep disorders are most frequently observed among women than among men, during adulthood and the menopausal transition phase is the period of higher risk for the development of these disorders whether or not associated to vasomotor symptoms.

Menopausal transition is characterized by changes of the menstrual cycle of women, in the presence of heat flashes and high levels of FSH. Most women show vasomotor, psychological, urogenital,

sexual and physical symptoms associated to hypoe-strogenism, impairing sleep and cognition.<sup>1,2</sup>

Based in some Brazilian<sup>3,4</sup> and international<sup>5,6</sup> studies, the domains which are most impaired during climacteric are somatic symptoms, depressive mood, anxiety, sleep disorders and vasomotor symptoms. It is estimated that 50% to 70% of climacteric women show somatic symptoms and emotional difficulties<sup>3,6</sup> and these factors directly interfere in the cognitive capacity and the sleep cycle.

Studies show that women during perimenopause and post menopause present higher sleep latency, difficulty to maintain levels and are more dissatisfied with the quality of their sleep even when compared to those who are not in menopause. Sleep complaints are more prevalent as age rises, being<sup>1,5</sup> times more frequent among persons aged 65 and older.<sup>7</sup>

Lack of sleep affects central nervous system functions and is often associated to malfunction of mental processes and may even cause abnormal behavioral activities<sup>8</sup>. Besides that, it may generate irritation or even psychotic tendencies after prolonged forced vigil. Sleep, therefore, has the function to restore normal levels of brain activity as well as the normal "balance" between the different parts of the central nervous system<sup>8</sup>. These alterations in sleep architecture, particularly those related to the reduction of delta sleep, are generally followed by an impairment of the daily alert and memory functions<sup>9</sup>, reduction of work activities performance, worsening of chronic pain situations as well as a series of neuroendocrine alterations such as increase of glucose intolerance, alterations in the levels of production and secretion of prolactin, of the human growth hormone and cortisol<sup>10,11</sup>.

The study of Young<sup>12</sup>, called "Wisconsin Sleep Cohort Study", conducts evaluation in objective and subjective ways, on the measurement of sleep quality in women during climacteric, concluding that, in objective views, menopause is not associated to reduction of the quality of sleep, using data collected by polysomnography, constituted by EEG, EMG and EOG. In the subjective views, however, women during menopause, when compared to women who are not in this phase of life, were twice as dissatisfied with their sleep.

Studies of Olofsson & Collins<sup>13</sup> and Silva Filho<sup>14</sup> show that, except for the vasomotor symptoms, all

other climacteric complaints, such as mood disturbances, libido alterations, cognitive deficit, pain in the joints, including sleep disorders, are strongly associated to psychosocial factors, lifestyle and especially to the perception of the woman regarding what menopause means in her life.

Some studies have related sleep disorders during menopause to decrease of serotonin levels, which promotes reduction of sleep continuity, increase of the rapid eye movements periods (REM) and a slowing of brain waves during sleep<sup>14, 15</sup>. These factors are related to the increase of the nocturnal concentration of melatonin<sup>16, 17</sup>.

This shows the importance of the consideration of these pathologies as complex phenomena, demanding studies that contemplates these diverse dimensions<sup>18</sup>.

Therefore, this chapter examines the diverse factors that contribute to the occurrence of sleep disorders such as insomnia, sleep apnea and post menopause impairing women's quality of life<sup>4, 19</sup>.

## Method

This study reviews the diverse factors related to sleep disturbances during climacteric and menopause.

### *Research strategy*

Bibliographic compliance was performed with the diverse electronic databanks, including Cochrane, MEDLINE, EMBASE, BNI plus, BIOLOGICAL ABSTRACTS, PSYCINFO, WEB OF SCIENCE, SIGLE, Dissertation Abstracts, ZETOC, published in English, Spanish and Portuguese, resorting to the following key words in Health Sciences: sleep; REM sleep; slow wave sleep; polysomnography; electroencephalogram; sleep disturbances; disturbances of sleep onset and maintenance; excessive somnolence disturbances; climacteric; menopause; depression; neurobiology; biologic models; circadian rhythm; mental health; epidemiology. We excluded case reports and letters to the editor.

### *Recompilation and data analysis*

Abstracts of the studies identified through electronic search in databanks were read and evaluated to determinate if they met the inclusion cri-

teria. Data were separately analyzed according to subjective or objective obtention of results.

### **Critic literary research**

#### ***Sleep – Architecture and sleep cycles***

Normal sleep is a dynamic process, basically integrated by two phases that alternate during the period in which a person sleeps: the phase of Rapid Eye Movements or REM sleep, characterized by the non-synchronization of potentials (low wideness and high frequency of brain waves), episodes of rapid eye movements (REM) and muscular atony, and non REM sleep, or quiet sleep, or slow wave sleep, which is divided in four stages according to the increase of its depth, producing synchronized waves of high wideness and low voltage, the slow waves, phase that ensues physical restoration<sup>4</sup>.

REM sleep is characterized by the low wideness of brain activity, accompanied by the loss of muscle tone, fluctuations in pulse and blood pressure<sup>20</sup>; this is the phase in which dreams occur, and when functions of high importance for data storage and learning, creativity and, possibly, emotional balance take place<sup>20</sup>. Non REM sleep has four different phases or stages: 1 – transition from the state of alert to sleep; stage 2 – first sleep period; stages 3 and 4 – deep sleep, delta sleep of slow wave sleep. Among persons who have normal sleep architecture, slow wave sleep represents circa 80% of the total of a sleep period and seems essential to the physiological homeostasis process and restoration of normal body functions<sup>20</sup>.

Daily sleep needs vary according to person and age; most of the adults sleeps between six to nine hours<sup>21</sup>. For climacteric women, it is known that there is a natural reduction of the length of sleep due to the age; studies show that older people need less sleep than younger persons<sup>22, 7</sup>.

#### ***Sleep disorders diagnosis***

Diagnostic methods employed in the investigation of sleep disorders include subjective evaluation, with the use of specific questionnaires, and objective evaluation consisting of actigraphic registers of daytime or nocturnal polissonographic data.<sup>23</sup>

#### ***Questionnaires***

Different questionnaires may be used in the clinic routine for diagnostic purposes, in monitoring

the response to prescribed treatments, in epidemiologic studies and in clinic research. These are, in their majority international and few are validated for Portuguese; whenever validated for the population in question, they may preview and estimate the severity of sleep disorders and act as screening for objective diagnostic tests<sup>23</sup>.

Among the many different questionnaires, the Sleep Disorders Questionnaire<sup>24</sup>, with questions of quantitative and qualitative evaluation; the Pittsburg Sleep Quality Index<sup>25</sup>, that refers to sleep quality during the previous month, offering an index of seriousness and nature of the disorder; the Mini-sleep Questionnaire (MSQ)<sup>26</sup> that evaluates the frequency of complaints; the Basic Nordic Sleep Questionnaire (BNSQ)<sup>27</sup>, that analyzes the most common complaints in terms of frequency and intensity during the previous three months, with quantitative specification and the Sleep Self-Assessment Questionnaire used in psychopharmacological research.

#### ***Polissonography***

Polissonographic studies of the whole night, performed at the laboratory, are the golden method of choice for diagnostic of sleep disorders<sup>10</sup>. The study consists in the complete monitoring of different vital signs, including the electroencephalogram (EEG) to assess the stages of sleep. To perform this exam, the patient has to stay overnight in a hospital environment, an unknown sleeping environment, which can therefore cause artifacts in the study<sup>10</sup>.

#### ***Actigraphy***

It is a technique of evaluation of the sleep-vigil cycles, allowing the registration of motor activity through movements of the limbs during 24 hours. This is a device placed in the wrist (like a wristwatch) detecting movements in digital registers that may be transferred to the computer. With this technique we may obtain information such as total sleep time, total awake time, number of awakenings and sleep latency. Compared to polissonography, presents and reliability of 0, 8 to 0, 9, and is a cheaper method, when there is the need to carry out register on many days. It is a method that is particularly useful for women who do not tolerate sleeping in a lab, such as insomniac and older women<sup>23</sup>.



### ***Insomnia and sleep disorders during climacteric***

Insomnia, a common symptom during climacteric<sup>28</sup>, may be defined as the difficulty to start/maintain the sleep; the presence of non-restorative sleep, meaning it is insufficient to maintain a good alert quality as well as physical and mental wellbeing during the day, with the consequent impairment of performance in daily activities<sup>29</sup>. Insomnia complaints among women during climacteric are quite frequent, and may be related to the occurrence of vasomotor symptoms such as heat flashes and transpiration<sup>15</sup>, that generally occur at the same time, and higher irritability. Women during menopause present higher sleep latency<sup>30</sup> as well as greater difficulty to maintain sleep<sup>4</sup>.

Insomnia, as well as heat flashes, was related to women who presented sexual symptoms such as a decrease of sexual desire, dry vaginas and pain during intercourse during menopausal transition<sup>32</sup>.

Research shows discordances between the perception of climacteric women regarding their sleep quality and results of polissonographic exams<sup>33</sup>. This discordance would be justified by higher prevalence of somatic and psychological symptoms during climacteric, aspect that could distort women's perception regarding their sleep.<sup>4, 14, 33</sup>

It is also known that there is a close relationship among sleep and cognition and that insomnia may easily be an important factor for cognitive disturbances<sup>9</sup>.

In this fashion, studies also show that more than 60% of the climacteric women complain of sleep disorders<sup>4, 14, 34</sup> and that the number of complaints is much higher than the confirmation of such disorders by polissonography<sup>4</sup>. These authors show the prevalence of subjective insomnia was 61% and, in polissonography was 83%. Apnea complaints were registered in 23% and in 27% in polissonography.

Some studies have related sleep disorders to menopause to the decrease of serotonin levels, what would promote reduction of sleep continuity, increase of REM periods and slowing of brain waves during sleep<sup>14, 15</sup>.

Studies performed in France<sup>35</sup> with more than 1000 middle aged women showed that sleep disorders were associated to the state of menopause, beyond chronologic age. In this study, vasomotor

symptoms were responsible for the low sleep efficiency, even though it is acknowledged that the higher incidence of heat flashes occurs before the usual onset of sleep. Freeman studies<sup>32</sup>, though, show that difficulty to fall asleep is not associated to stages of menopausal transition and post menopause, even after the control of possible confusion factors through multivariate analysis. Another aspect which is relevant in the literature<sup>18</sup> that contributed to sleep disturbance in perimenopause as nocturia, excessive urination during the night. Many women mention that the need to get out of bed at night in order to urinate alters sleep during menopause, sometimes more than vasomotor symptoms<sup>18</sup>.

Existing studies do not make clear if sleep disorders derive from an altered hormonal state during this period or other bio-psycho-social factors associated to menopause or the ageing of women. Young<sup>12</sup> showed, in a prospective Australian study, performed with 172 women, in which only a small increase in the difficulty to fall asleep in the menopausal transition, and concluded that sleep disorders are not a direct effect of the hormonal changes during menopause. Shaver<sup>37</sup>, in his studies, showed that the occurrence of insomnia in women over 30 years of age varies from 26% to 45%, but insomnia incidence increase 28% to 63% after menopause.

One of the causes of insomnia is the so called "restless legs syndrome" (SPL), a clinical manifestation in which patients report an irresistible movement of lower limbs accompanied by a feeling of dragging of the legs. It occurs in persons aged 30 to 50 years (5%), aged 51 to 54 years (29%) and 44% occurs in people over 65 years of age.

### ***Sleep Apnea***

Pathophysiology of obstructive sleep apnea is multifactorial. Sex, obesity, genetic, anatomic and hormonal factors and ventilation control interact in the pathophysiology and the clinical expression of the disease<sup>38</sup>. Obesity is the major risk factor, and increase in the body mass index, increase in visceral fat and neck circumference are strong predictors of the occurrence of this disorder. Progesterone, due to the increase in the muscles that dilate superior air ways generated by this hormone, has a protective role for women before menopause, justifying the higher prevalence of the di-

sease during post menopause, in males and in the polycystic ovarian syndrome<sup>20</sup>.

Evidence point to the fact that age increase promotes a decrease in muscle tonus, with the reduction of the caliber of the superior air ways. There is evidence that hormonal status may influence in the activity of the muscles that dilate superior air ways of the genioglossus muscle, when compared to post-menopausal women and men of the same age.

It is believed that progesterone may have a protective role for apnea before menopause<sup>38, 39</sup>. Higher levels of progesterone occur during the luteous phase of the menstrual cycle, and during this period women undergo an increase in the ventilator command, showing one of the functions of this hormone. Exogenous progesterone has been associated to a small but definite improvement of ventilation during sleep of men and women with apnea. Another hormone that is also important is estrogen, whose administration is associated to plasmatic reduction of interleukin 6, that registers high levels in patients with apnea<sup>39</sup>.

Therefore, women during post menopause undergoing hormone replacement therapy (progesterone and estrogen) have lower prevalence in the obstructive sleep apnea and hipopnea, since they have two protective mechanisms<sup>20, 39</sup>. The exogenous progesterone for its increase of the dilating muscles of upper airways has been associated to a slight but definitive bettering of ventilation of apneic women. The estrogen and its administration is associated to the plasmatic decrease of interleukin 6, which is elevated in apneic patients.<sup>20,39</sup>

The main treatment of sleep apnea is the use of continuous positive airway pressure (CPAP), made with a mask and a flow generator, used at night to prevent apnea, hypoxia, and sleep disturbance.

### ***Narcolepsy***

This is a neurologic condition characterized by recurrent short termed sleep episodes. Narcoleptic syndrome is constituted, beyond sleep crises, by episodes of muscle tone loss (cataplexy), sleep paralysis and hipnagogic hallucinations. Manifestations of this syndrome include alterations that involve the start of REM sleep, nocturnal as well as during the day<sup>20, 39</sup>. This is a rare syndrome (one person in every two thousand people), but difficult to diagnose. Cataplexy<sup>41</sup> is the only specific symp-

tom for narcolepsy, but, in general, it only appears after the occurrence of excessive daily sleep.

This syndrome is associated to genetic factors particularly to the presence of HLA-DQB1\*602 allele and self-immune processes. It is known that in the condition carriers there is a dysfunction on the release of neurotransmitters that regulate sleep, such as hypocretins. This is a disease of genetic character, but genetic transmission of narcolepsy among human do not comply with Mendelian rules. This is, therefore, a complex inheritance, in which probably many diverse genes and environmental factors are involved, most of the cases are sporadic and not familiar, and the risk of a first degree relative of a narcoleptic to develop the disorder is 40 times higher than among the population in general<sup>41</sup>.

From the neuropharmacologic point of view, lack of the hypocretin or orexin neuropeptide in the brain of people with narcolepsy causes a dysfunction in the aminergic and cholinergic neurotransmission<sup>41</sup>.

### ***Diagnosis***

- Clinical: Based on the presence of excessive daily sleepiness and/or sudden starts of sleeping episodes, also during the day, for at least six months and in the presence of cleat cataplexy history<sup>41</sup>.

- Laboratorial: the first test in the dosing of orexin or hypocretin and 85% to 90% of the cases present deficient or undetectable levels in the cefaloraquidian liquid. Therefore, circa 10% of the patients present normal levels of these substances.

- Polissonography and Sleep Multi Latency tests: Sleep Multi latency test is considered the golden method of choice. Polissonography must be performed in the night previous to the Sleep multi latency test. This test is an exam that objectively documents sleepiness and the occurrence of REM sleep during the daylight period, allowing to diagnose with precision narcolepsy and contributing to differential diagnosis of other conditions that curse with hypersony, like, for instance, obstructive apnea syndrome. This procedure constitutes of the obtention of four to five EEG registers lasting 20 to 35 minutes every two hours. In polissonography it is possible to observe a higher fragmentation of the sleep, alterations in the architecture, intrusions of REM phases in any of

the stages; precocious occurrence of REM sleep during the start of the sleep to the first 15 minutes is a significant finding to the diagnosis<sup>42</sup>.

- Genetic diagnosis: in addition to the tests mentioned above, analysis of the presence of the allele HLA-DQB1\*602, but with low specificity

## Treatment

During a long time, the use of hormonal therapies was considered the golden method of choice for diverse symptoms of peri and post menopause, including vasomotor symptoms and sleep disturbances<sup>20, 33, 37</sup>. Other studies also showed positive results with the use of estrogen and/or progestogen therapies with the management of depressive phases for the improvement of breathing disorders during sleep and the quality of life of women during menopause<sup>45, 46</sup>.

However, ever since publishing of the major results of WHI, professionals have become more rigid in the use of long term estrogen therapies for women, particularly those in higher risk for cardiovascular disorders or breast cancer<sup>46, 47, 48</sup>. That was when the use of non-hormonal therapies for the management of these symptoms, such as antidepressants or behavioral therapies<sup>49, 50, 51</sup>. Therefore, most of the studies with hormonal therapies did not present positive impact on objectives sleep parameters in women with insomnia during climacteric.

Studies with positive results are limited to subjective sleep parameters and, even then, with small samples<sup>46, 52</sup>.

Regarding the treatment of respiratory sleep disorders during menopause, there are few studies in the literature, whose results are inconclusive.

Non hormonal therapies on the treatment of insomnia during menopause

Cognitive and behavioral techniques (TCC) produce objective and subjective changes in sleep patterns and in the quality of sleep of adults with insomnia<sup>20</sup>.

Beyond general instructions on sleep hygiene, TCC include the control of sleep stimulus and restriction of sleep among their modalities of proven efficacy in the management of insomnia.

Sleep Stimulus Control Management Therapy is widely used and quite efficacious. Basically, this therapy improves the starting insomnia (or sleep la-

teny) and reduces the time of vigil after the starting of sleep (wake onset after sleep onset or WASO) through the new learning of the association between time of permanence in bed and efficient sleep.

Patients are instructed to establish a determined time to get up in the morning, regardless of the amount or quality of sleep during the night. Naps are not allowed during daytime and people must not remain awake in bed for longer than 15 minutes, in case they find it difficult to sleep or to wake up during the night. Regardless of the potential to generate sleep deprivation for some nights, this technique has proven efficient, since employed in the correct fashion and systematically for a minimum of 10 to 15 days<sup>53</sup>.

Another TCC is called Sleep Restriction. This therapy is also based in a pre-established wake up time and works with the concept of sleep efficiency percentage of sleep time in relation to the time of permanence in bed). For instance, patients who wish to wake up at 6h30 AM, but have feeling insomnia when they try to fall asleep at 10PM, are instructed not to go to bed before 1h00AM. This way, they will optimize their sleep efficiency. Little by little, these persons should bring forward, in a slow and progressive fashion, the time to go to bed (for instance, 15 minutes earlier every 4 to 7 days), regarding maintenance of their sleep efficiency of circa 85%. Other behavioral techniques include relaxation and meditation<sup>20</sup>.

A revision study performed by Niet et al.<sup>54</sup> to evaluate efficacy of the relaxation obtained by music for sleep quality of adults with complaints of insomnia, with or without medical comorbidities, conclude that relaxation by music was an efficient aid to improve sleep quality in patients with different health conditions. Assisted musical relaxation had moderate effect in sleep quality for patients with sleep disorder complaints. Most efficient forms of application and most adequate types of music for different populations are still under study. Niet et al.<sup>54</sup> state that no adverse effect were reported with the use of music therapy in the treatment of insomnia. This intervention may be used with no high investments in treatment and material and is cheap and readily available.

Regarding efficient psychological treatments for insomnia, a meta-analysis performed by Murtagh DR & Greenwood K<sup>55</sup> tried to identify effi-

ent psychological treatments for insomnia. They concluded that psychological interventions produce reliable and long lasting benefits for the treatment of insomnia. It seems that active treatments are superior to placebo therapies, but they did not differ much. Gains of the treatment for a period of sleep latency were higher for the clinically referred patients and for people with insomnia who were not regular users of sleeping medicines.

Benzodiazepines and correlate drugs for patients with insomnia subjected to palliative treatments

Insomnia, a subjective complaint of inadequate sleep, associated to bad performance in daily activities, is a common problem. Benzodiazepines are, nowadays, the most commonly used pharmacological treatment for such a complaint<sup>52</sup>. They are considered useful for occasional use and for short term therapies (up to four weeks), but prolonged use is not recommended due to potential problems regarding tolerance, dose increase, psychological and physical dependency. There is no consensus on the use of these medicines in patients with progressive and incurable diseases, that may require sleep aids for many weeks, while their health worsens.

Reviewers<sup>52</sup> of studies designed to evaluate effectiveness and safety of benzodiazepines or agonists of the benzodiazepine receptor such as Zolpidem, Zopiclone or Zaleplon, for insomnia in patients subjected to palliative treatments concluded that, even though a wide search was performed, there were no evidences of random controlled studies. It was not possible to reach any conclusion regarding the use of benzodiazepines in patients subjected to palliative treatment.

Hypnotics, either benzodiazepines or not, increase the GABAergic transmission linking to a specific region of the complex proteic receptor GABA-A. These agents, though, present different degrees of tolerance, dependency and undesirable alterations in sleep architecture. Agents acting specifically increasing GABA endogenous action, more specifically in the gabaergic-galaninergic system of VLPO must produce adequate therapeutic effects with lesser side effects. The agent gaboxodol, a direct GABA-A agonist still in development, presents hypnotic effects with increase of delta sleep. Pregbalin is a new class of ansiolitic, but with an action mechanism different from benzodiazepines, not ac-

ting on GABA-A and GABA-B receptors. Acting in the mechanisms of activity of the calcium channel, pregbalin hampers the pre synaptic liberation of excitatory neurotransmitters such as glutamate, aspartate, P substance in regions of the limbic system such as the hypocamp, the amygdala, cyngulus, producing ansiolitic effects and the increase of delta sleep, being also a potential hypnotic agent in patients with fibromyalgia<sup>56</sup>.

### *Excessive somnolence*

In order to treat excessive somnolence associated to some medical conditions such as narcolepsy, the obstructive sleep apnea syndrome (breathing pauses during sleep) and sleep disorders related to work shifts, modaphinil, a recent drug, is an agent promoting vigil, acting mainly as a noradrenergic agonist inhibiting the gabargic activity of VLPO<sup>23</sup>.

### **Discussion**

Climacteric includes not only the symptoms deriving from estrogenic deficiency, but, most of all, a wide context that contemplated the woman inserted in a social medium, in which inter relationships of diverse natures are sustained, in order to fulfill all their potential for creation and construction<sup>57,58</sup>.

Sleep disorders are a common complaint of women during menopause. Women during the transition for menopause, or after menopause present sleep problems with a frequency much higher than younger women in pre menopause<sup>19, 30</sup>, while others did not show a significant association between stages of menopause transitions and objective sleep parameters<sup>12, 59</sup>.

Women during climacteric presenting hot flashes present an increase of stage 4 and a decrease of sleep efficiency and of REM periods, when compared to women who report no hot flashes<sup>37</sup>, and this may suggest that hormonal state is due to hot flashes or if the hormonal instability would cause the hot flashes and sleep alteration simultaneously<sup>60</sup>. The author states that eight of every nine patients during post menopause wake up at night due to hot flashes, what was not presented in pre menopause.

Among the probable causes of insomnia and sleep disorders associated to menopause, it is possible to outline the occurrence of vasomotor

symptoms (like hot flashes, night sweats), the presence of depression and respiratory disorders during the sleep (such as sleep apnea) beyond chronic pain<sup>34, 61</sup>.

Regarding the use of benzodiazepines in the treatment of insomnia, there were no randomized controlled studies that would fulfill inclusion criteria<sup>56</sup>. Thirty seven studies were considered, but all were excluded from the review<sup>56</sup>. Regardless of the wide search performed, there were no evidence of randomized controlled studies. It was not possible to reach any conclusions regarding the use of benzodiazepines for patients in palliative treatments.

### Conclusion

Even though the prevalence of insomnia and the association of insomnia and menopause has been well described, there are not sufficient works with evidence. Understanding the neurobiology of sleep opens a wide potential for new functional, etiological and pharmacotherapeutic models of the cycle sleep/vigil and mental disorders.

Sleep disorders during the menopausal transition and post menopause may be aggravated by nocturnal hot flashes or depressive symptoms, but may also occur in their absence.

Menopause was independently associated to insomnia after the adjustment for confusing factors such as age, income and depression. Perimenopause showed significant association to a dramatic increase in the risk of insomnia, but there was no significant association for post menopause.

Studies with hormonal therapies suggest a subjective improvement of sleep and wellbeing in symptomatic women. The use of non-benzodiazepine hypnotics and behavioral cognitive techniques present proved efficacy for the management of insomnia. Some alternative treatments may also improve insomnia, especially due to the relief of vasomotor complaints.

The major conclusion is that insomnia shows significant association to menopausal transition. Insomnia prevalence increases by the transition from premenopause to perimenopause but not in post menopause.

In order to deepen the prospective study it is necessary to investigate the influence of menopause on insomnia.

Among other factors, speculations debate high psychiatric comorbidities for affective and anxiety disorders among women may contribute to a higher occurrence of insomnia. Authors disagree regarding periods in which high hormonal variability occur, such as climacteric phase, may be related to a higher incidence of insomnia. They perceive, nevertheless, that data previously mentioned do not coincide with those from other researchers that show a deficit in the quality of sleep and higher occurrence of insomnia among women during peri and post menopause. Respiratory sleep disorders among women seem to have consensus among authors that hypoestrogenism may be a significant factor for these disorders. Menopausal transition is a period of higher risk for the development of depressive, vasomotor and insomnia symptoms, even though they are not solely caused by hypoestrogenism.

It is possible to conclude that there is a high prevalence of sleep disorders during post menopause, especially insomnia, apnea and periodical movements of the legs, and that, during this phase of life, there is a decrease in the quality of sleep. There is an important correlation between sleep and cognitive disorders and these are associated to diverse factors other than the usual hormonal problems of this phase. Symptoms and signs of abnormalities during middle age should not be primarily attributed to menopause before excluding other problems that may be causing sleep and cognitive disorders. Analysis of available studies revealed a tendency to deterioration of the quality of life among women during climacteric, particularly in the domains related to sleep disorders, depressive moods and anxiety. Health professionals who attend women in the menopausal transition must incentive healthy habits, as well as promote nutritional habits and physical exercise as part of a healthy lifestyle and as important factors to maintain health during climacteric.

### References

1. Freedman RR. Hot flashes: behavioral treatments, mechanisms, and relation to sleep. *Am J Med.*; 118 Suppl 12B:124S-130S. *Arch Women's Mental Health.* 2005; 10(5):247-57.
2. Parry BL, Martínez LF, Maurer EL, López AM, Sorenson D, Meliska CJ. Sleep, rhythms and women's mood. Part II. Menopause. *Sleep Med Rev.* 2006;10(3):197-208.

3. Lorenzi DRS, Baracat EC, Saciloto B, Padilha-Jr I. Fatores associados à qualidade de vida após menopausa. *Rev assoc med bras* 2006; 52(5): 312-7.
4. Hachul HC, Bittencourt LRA, Soares JM, Tufik S, Baracat EC. Sleep in post-menopausal women: Differences between early and late post-menopause. *European Journal of Obstetrics & Gynecology and Reproductive Biology* - July 2009 Vol. 145, Issue 1, Pages 81-84.
5. Pien GW, Sammel MD, Freeman EW, Lin H, DeBlasis TL. Predictors of sleep quality in women in the menopausal transition. *Sleep*; 31(7): 991-9, 2008 Jul 1.
6. Greendale GA, Wight RG, Huang MH, Avis N, Gold EB, Joffe H, Seeman T, Vuge M, Karlamangla AS. Menopause-associated symptoms and cognitive performance: results from the study of women's health across the nation. *Am J Epidemiol.* 2010 Jun 1;171(11):1214-24. Epub 2010 May 4.
7. Dijk DJ; Groeger JA; Stanley N; Deacon S. Age-related reduction in daytime sleep propensity and nocturnal slow wave sleep. *SLEEP* 2010;33(2):211-223.
8. Guyton AC, Hall JE. Estados da atividade cerebral e sono. In: Guyton AC, Hall JE. *Tratado de Fisiologia Médica*. 10 ed. Rio de Janeiro: Guanabara Koogan; 2002. p.642-5.
9. Fernandes RCL, Silva KS, Bonan C, Zahar SEV, Marinho LRF. Cognitive function in menopausal women evaluated with the Mini-Mental State Examination and Word-List Memory Test. *Cad. Saúde Pública* 2009 Sep ; 25(9): 1883-1893.
10. Buckley T, Schatzberg AF. Methods and compositions for modulation of sleep cycle - US Patent App. 11/707,751, 2007.
11. Backhaus J., Junghanns K., Hohagen F. Sleep disturbances are correlated with decreased morning awakening salivary cortisol (2004) *Psychoneuroendocrinology*, 29 (9), pp. 1184-1191.
12. Young T, Rabago D, Zgierska A, Austin D, Laurel F. Objective and subjective sleep quality in premenopausal, perimenopausal, and postmenopausal women in Wisconsin Sleep Cohort Study. *Sleep* 2003; 26(6):667-72.
13. Olofsson AS, Collins A. Psychosocial factors, attitude to menopause and symptoms in Swedish perimenopausal women. *Climacteric*. 2000; 3:33-42. ->Fatores indicadores da sintomatologia climatérica *Rev Bras Ginecol Obstet.* 2005; 27(1): 12-19.
14. Silva Filho EA, Costa AM. Avaliação da qualidade de vida de mulheres no climatério atendidas em hospital-escola na cidade do Recife, Brasil. *Rev. Bras. Ginecol. Obstet.* 2008 Mar; 30(3): 113-120.
15. Campbell SS, Murphy PJ. The nature of spontaneous sleep across adulthood *Journal of Sleep Research* Volume 16, Issue 1, p. 24-32, March 2007.
16. Deecher DC, Dorries K. Understanding the pathophysiology of vasomotor symptoms (hot flushes and night sweats) that occur in perimenopause, menopause, and postmenopause life stages. *Arch Womens Mental Health.* 2007; 10(5):247-57.
17. Maganhin CC, Carbonel AAF, Hatty JH, Fuchs LFP, Oliveira-Júnior IS, Simões MJ et al. Efeitos da melatonina no sistema genital feminino: breve revisão. *Rev. Assoc. Med. Bras.* 2008 June; 54(3): 267-271.
18. Vigeta SMG. Alterações do sono e menopausa: uma revisão da literatura. *Cienc Cuid Saude* 2007 Jul/Set;6(3):377-383.
19. Shin C, Lee S, Lee T, Shin K, Yi H, Kimm K. And Cho, N. (2005), Prevalence of insomnia and its relationship to menopausal status in middle-aged Korean women. *Psychiatry and Clinical Neurosciences*, 59: 395-402.
20. Soares C N. Insônia na menopausa e perimenopausa: características clínicas e opções terapêuticas. *Rev. psiquiatr. clín.* 2006 33(2): 103-109.
21. NAMS. *The Menopause Practice: A Clinician's Guide*. USA: NAMS, 2004.
22. Backhaus J, Born J, Hoeckesfeld R, et al. Midlife decline in declarative memory consolidation is correlated with a decline in slow wave sleep. *Learn Mem.* 2007;14:336-341
23. Togeiro SMGP, Smith AK. Métodos diagnósticos nos distúrbios do sono. *Revista Brasileira de Psiquiatria*, São Paulo, v. 27, n.1, 2005.
24. Roth T, Zammit G, Kushida C, Doghramji K, Mathias SD, Wong JM, Buysse DJ. A new questionnaire to detect sleep disorders. *Sleep Medicine* 2002;3:99-108.
25. Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). *The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research.* *Psychiatry Research*, 28, 193-21
26. Zomer, J., Peled, R., Rubin, A. H., & Lavie, P. (1985). *Mini Sleep Questionnaire (MSQ) for screening large populations for EDS complaints.* In W. P. Koella, E. Ruther, & H. Schulz (Eds.), *Sleep* (pp. 467-470). New York: Gustav Fischer Verlag.
27. Partinen M, Gislason T. Basic Nordic Sleep Questionnaire (BNSQ): a quantified measure of subjective sleep complaints. *J Sleep Res* 1995;4 (suppl.1): 150±5.
28. Cheng MH, Hsu CY, Wang SJ, Lee SJ, Wang PH, Fuh JL. The relationship of self-reported sleep disturbance, mood, and menopause in a community study. *Menopause: September 2008 - Volume 15 - Issue 5 - pp 958-962.*
29. Poyares D, Aloe F, Rizzo GNV, Minhoto G, Pinto Junior LR, Bezerra MLS, et al. I Consenso Brasileiro de Insônia. *Hypnos.* 2003;4(Supl 2):5-39.
30. Dennerstein L, Smith AM, Morse C, Burger H, Green A, Hopper J, et al. Menopausal symptoms in Australian women. *Med J Aust.* 1993;159(4):232-6. 1B
31. Hachul HC, Bittencourt LRA, Haidar MA, Tufik S, Baracat EC. Prevalência de distúrbios do sono na pós-menopausa, *Rev Bras Ginecol Obstet.* 2005; 27(12): 731-6.
32. Nappi RE, Nijland EA. Women's perception of sexuality around the menopause: Outcomes of a European telephone survey. *Eur J Obstet Gynecol Reprod Biol.* 2008;137:10-16.

33. Polo-Kantola P, Erkkola R, Irjala K, Helenius H, Pullinen, Polo O. Climacteric symptoms and sleep quality. *Obstet Gynecol.* 1998; 94:219-24. Fatores indicadores da sintomatologia climatérica *Rev Bras Ginecol Obstet.* 2005; 27(1): 12-19.
34. Joffe, H, Hall JE, Soares CN, Hennen J, Reilly CJ, Carlson K, Cohen LS. Vasomotor symptoms are associated with depression in perimenopausal women seeking primary care. *Menopause: November 2002 - Volume 9 - Issue 6 - pp 392-398.*
35. Chokroverty, S. *Sleep disorders medicine: basic science, technical considerations, and clinical aspects / UK: Sudhansu Chokroverty. -3rd ed. 2009.*
36. Freeman EW, Sammel MD, Lin H, Gracia CR, Pien GW, Nelson DB, Sheng L. Symptoms associated with menopausal transition and reproductive hormones in midlife women. *Am J Obstet Gynecol.* 2007; 110: 230-40.
37. Shaver JL, Zenk SN. Sleep disturbance in menopause. *J Womens Health Gend Based Med.* 2000;9(2):109-18.
38. Daltro CHC, Fontes FHO, Santos-Jesus RGPB, Araújo LMB. Obstructive sleep apnea and hypopnea syndrome (OSAHS): association with obesity, gender and age. *Arq Bras Endocrinol Metab.* 2006 Feb; 50(1): 74-81.
39. Martins AB, Tufik S, Moura SMGPT. Síndrome da apnéia-hipopnéia obstrutiva do sono. *Fisiopatologia. J. bras. pneumol.* 2007 Fev ; 33(1): 93-100.
40. Fry, June M. Treatment modalities for narcolepsy *Neurology* 1998 50: S43-48.
41. Honda Y. Clinical features of narcolepsy: Japanese experience. In: Honda Y, Juji T (eds). *HLA in Narcolepsy.* Springer-Verlag, Berlin, 1988; 24-57. 3B
42. Lin L, Faraco J, Li R, Kadotani H, Rogers W, Lin X, Qiu X, Jong PJ, Nishino S, Mignot E. The Sleep Disorder Canine Narcolepsy Is Caused by a Mutation in the Hypocretin (Orexin) Receptor 2 Gene. *Cell - 6 August 1999 Vol. 98, Issue 3, pp.365-376.*
43. Purdie D, Green A, Bain C, Siskind V, Ward B, Hacker N, Quinn M, Wright G, Russell P, Susil B. Reproductive and other factors and risk of epithelial ovarian cancer: an Australian case-control study. *Survey of Women's Health Study Group. Int J Cancer.* 1995 Sep 15;62(6):678-684.
44. Cistulli PA, Barnes DJ, Grunstein RR, Sullivan CE. Effect of short-term hormone replacement in the treatment of obstructive sleep apnoea in postmenopausal women. *Thorax Volume 49, Issue 7 1994; 49: 699-702.*
45. Polo-Kantola P & Erkkola R. Sleep and the menopause. *Menopause Vol 10, Number 4 Int* 2004;10:145-150. Pp. 145-150. 3A
46. Soares CN. Insomnia in women: an overlooked epidemic? *Archives of Women's Mental Health Volume 8, Number 4, 2005.*
47. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, Jackson RD, Beresford SA, Howard BV, Johnson KC, Kotchen JM, Ockene J. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA.* 2002 Jul 17;288(3):321-33.
48. Soares CN. Hormones and mental health: where do we stand in the post-WHI era?. *Rev. Bras. Psiquiatr.* 2003 Oct; 25(4): 198-199.
49. Taylor M. Alternatives to HRT: an evidence-based review. *Int J Fertil Womens Med* 48(2):64-8, 2003.
50. Cervena K, Dauvilliers Y. et al. Effect of cognitive behavioural therapy for insomnia on sleep architecture and sleep EEG power spectra in psychophysiological insomnia. *J Sleep Res* 13(4):385-93, 2004.
51. Mahady GB. Black cohosh (*Actaea/Cimicifuga racemosa*): review of the clinical data for safety and efficacy in menopausal symptoms. *Treat Endocrinol* 4(3):177-84, 2005. 2C
52. Antonijevic IA, Stalla GK. et al. Modulation of the sleep electroencephalogram by estrogen replacement in postmenopausal women. *Am J Obstet Gynecol* 182(2): 277-82, 2000.
53. Chesson LA, Littner M, Davila D, MacDowell WA, Grigg-Damberger M, Hartse K, Johnson S, Wise M. Practice Parameters for the Use of Light Therapy in the Treatment of Sleep Disorders. *SLEEP, Vol. 22, No. 5, 1999.*
54. Niet G, Tiemens B, Lendemeijer B, Hutschemaekers G. Music-assisted relaxation to improve sleep quality: meta-analysis. *Journal of Advanced Nursing* 2009;65(7) :1356-1364.
55. Murtagh DR, Greenwood KM. Identifying effective psychological treatments for insomnia: a meta-analysis. *Journal of Consulting and Clinical Psychology* 1995;63(1) :79-89.
56. Hirst A, Sloan R. Benzodiazepines and related drugs for insomnia in palliative care. *Cochrane Database Syst Rev.* 2002;(4):CD003346. Review.
57. Utian WH. Quality of life (QOL) in menopause. *Maturitas.* 2007;57(4):100-2.
58. Lindh-Åstrand L, Hoffmann M, Hammar M, Kjellgren KI. Women's conception of the menopausal transition--a qualitative study. *J Clin Nurs.* 2007;16(3):509-17.
59. Regestein QR, Friebely JE, Shifren JL, Scharf MB, Wiita B, Carver J, Schiff I. Self-reported sleep in postmenopausal women. *Menopause: March/April 2004 - Volume 11 - Issue 2 - pp 198-207.*
60. Manber R, Armitage R. Sex steroids, and sleep: a review. *Sleep.* 1999;22(5):540-55.
61. Krystal AD, Edinger J, Wohlgenuth W, Marsh GR. Sleep in peri-menopausal and post-menopausal women, *Sleep Medicine Reviews, Volume 2, Issue 4.*

## Corresponding Author

Sandra Dircinha Teixeira de Araújo Moraes  
 University of São Paulo,  
 Medicine College, Department of Gynecology,  
 General Hospital,  
 Brazil,  
 E-mail: sandradircinha@gmail.com

# Burdens perceived by the family caregivers of cancer patients receiving outpatient chemotherapy and family functions: a cross-sectional study

Zeynep Güneş<sup>1</sup>, Hüsnüye Çalışır<sup>1</sup>, Ayşe Özkan<sup>2</sup>, Gülsüm Orhan<sup>2</sup>

<sup>1</sup> Assistant professor, Adnan Menderes University School of Health, Aydın, Turkey,

<sup>2</sup> Hospital of Adnan Menderes University, Aydın, Turkey.

## Abstract

**Background:** Long-term illnesses and their treatment may change the roles of family members; providing care to a patient with cancer can create emotional and social burdens and affect family relationships.

**Aim:** The present study had two main purposes: (1) to identify factors that affect the sense of burden felt by family members caring at home for cancer patients, receiving outpatient chemotherapy in Turkey; and (2) to examine the relationships between family functioning and caregiver burden and socio-demographic factors.

**Methods:** A cross-sectional descriptive study carried out in Aydın, located in the Western Province of Turkey. The sample number was determined as 46 according to the power analysis, and the study was completed with 102 patients' relatives. Interviews were conducted in the caregiver's home. We used multiple linear regression analysis (enter method) to determine the independent predictors of caregiver burden and family functions.

**Findings:** High caregiver burden scores were associated the caregiver having lower education (Regression coefficient beta = 8.632, 95% CI = 1.082-16.182). Caregivers who reported high burden had unhealthy family functioning in the roles, affective responsiveness, affective involvement, behaviour control and general functioning domain.

It was found out that financial difficulties had a negative impact on family roles. Our main study showed that financial difficulties had a positive effect on their problem-solving skills.

**Conclusions:** Caregiver burden were associated with a low level of education. Family caregivers of cancer patients, in relation to their per-

ceived burden, have problems in communication, roles, affective responsiveness, affective involvement, behaviour control and general functioning.

**Key words:** cancer, family caregivers, family functioning, burden, nursing

## Background

The family is conceptualized as a living open system [1]. A family system have elements (family structure) and there are relationships between the elements (family functioning) [1,2]. Family functioning is multidimensional, with several processes characterizing the family unit as a whole such as cohesiveness, flexibility, affective and instrumental communication, behavioural control, and so on [2].

Family members may be called on to provide primary care at home when a patient receives aggressive or disabling treatment in an outpatient setting [3,4,5]. Family caregivers are essential supporters of cancer patients who are staying at home, since they provide practical and emotional help and care [6]. Referred to as informal caregivers, family caregivers provide a complex array of support tasks that extend across physical, psychological, spiritual, and emotional domains. This care affects the caregiver significantly in physical, mental, social and economic aspects. Providing care for disabled older adults has been described as a stressful experience that may erode the physical and psychological health of the caregiver. The overall impact of physical, psychological, social, and financial demands of caregiving has been termed caregiver burden [4,6,7-10]. Numerous studies have focused on the burden of care experienced by family members living with cancer patients [4,6,7-10]. Haley reported that care



giving may have a negative effect on the caregiver's mental and physical health and may entail social and economic costs [6]. Patient characteristics (e.g. age and gender), the demographic characteristics of the caregiver (e.g. age, gender, relatives status, health status) [8,10], perceived social support, number of informal hours of care [11] and lower socioeconomic status [9] are among the factors believed to influence the experience of caregiver burden.

Caregivers with high levels of burden reported greater family dysfunction in communication and roles, regardless of their relatives to the patient (i.e. spouse or child) [1]. Also, it produces an overload of tasks and it usually changes the functional dynamics of the family. The literature reports that illness may have a significant impact on family development, structure, and/or functioning [1,2]. Tremont et al. reported that caregivers with prior good family functioning had significantly less strain and burden compared with caregivers with poor family functioning [12]. Family functioning was identified as a factor that might impact on families' depression and anxiety [13]. Kissane et al. found that 71% of families in their study had greater levels of psychosocial morbidity as a result of poor family functioning [14]. Care giving may have a strong influence on family relationships; therefore, assessment from a family-centered perspective is important to determine the function of the family [15].

The present study had two main purposes: (1) to identify factors that affect the sense of burden felt by family members caring at home for cancer patients receiving outpatient chemotherapy in Turkey; and (2) to examine the relationships between family functioning and caregiver burden and socio-demographic factors.

## Material and Methods

### *Design of Study and Participants*

This study was conducted with the care giving family members of patients receiving outpatient anticancer chemotherapy at a research and application hospital in the province of Aydın, located in Western Anatolia. Research data was collected between October 2007 and April 2009. We performed a cross-sectional study because this design studies characteristics of a phenomenon in a population and the relationship between different

variables at a given point in time. This study is based on previous cross-sectional studies about this topic performed in other countries and our country [11,16,17]. The participant sampling number was determined as a minimum of 46 as a result of power analysis and the study was completed with 102 relatives of patients. A sample of 46 subjects, each responding to 24 items, achieves 90% power to detect the difference between the coefficient alpha under the null hypothesis of 0.90 and the coefficient alpha under the alternative hypothesis of 0.95 [19] using a two-sided F-test with a significance level of 0.05. There was significant relationship between communication and burden ( $r=0.274$ ;  $power=0.752$ ) [19]. The relatives of patients who received chemotherapy treatment at least once and were willing to participate in this research were included in this study. The relatives of the patients in the terminal period were not included in the research. This study was conducted in patients with newly diagnosed.

### Data Collection Instruments

Caregiver burden was measured using the Zarit Burden Interview. Family functioning was measured using the FAD.

#### *Zarit Burden Scale (ZBI):*

The ZBI is a 22-item self-administered questionnaire assessing burden associated with functional/behavioural impairments and home care context. The questions refer to the care giver/patient relationship and evaluate the caregiver's health condition, psychological well-being, finances, and social life. The caregiver burden was evaluated by means of the total score obtained from the sum total of questions. The reliability of the original version was excellent ICC (intraclass correlation coefficient = 0.71;  $\alpha = 0.91$ ) [20]. The validity and reliability of the scale in Turkish was tested by İnci and Erdem [19]. The retest reliability of the scale was .90 and the Cronbach's alpha value was 0.95.

#### *Family Assessment Device (FAD):*

The FAD is a self-reported questionnaire which measures subjects' family functioning along seven dimensions, namely, problem solving, communication, roles, affective responsiveness, affective

involvement, behaviour control and general functioning [21]. The scores over 2.00 for each subscale indicate an unhealthy movement related to family function. The effectiveness (validity) and reliability scale of the FAD was carried out by Miller et al. [21]. The effectiveness and reliability of the FAD for Turkish families was tested by Bulut [22]. The reliability study of the scale in Turkey gave a significant result at the  $p < 0.001$  level in terms of both internal consistency and point invariance (stability). For each subscale, the Cronbach's-alpha coefficient was calculated between 0.38 and 0.86 [22].

### Data Collection

A pre-interview was carried out with the relatives of patients receiving outpatient chemotherapy at the Medicine and Health Sciences Research and Application Hospital of Adnan Menderes University, and an appointment was requested to have an interview at their homes. Interviews were conducted in the caregiver's home. Data collection forms were filled in during face-to-face interviews with the family caregivers at their homes. Completion of questionnaires required approximately 30 minutes (interval: 20-40 mins).

### Ethical Considerations

Ethical permission for the study was given by the Ethical Board of the Faculty of Medicine, Adnan Menderes University. Permission for the study was obtained from the chief physician of the hospital. The relatives of the patients included in this research were informed about the study and their written consent was obtained from those who accepted to participate. Nothing was paid to the participants for their participation in this research.

### Statistical Analysis

All analyses were carried out using the Statistical Package for the Social Sciences 15.0 (SPSS Inc., Chicago, IL, USA) for Windows. In the research, the socio-demographic features of the patients' relatives, their kinship degrees to the patient and status to help the daily living activities of the patients are given as numbers and percentages.

The multiple linear regression (enter method) analysis method was used to determine the burden perceived by family caregivers of cancer patients, and the factors affecting the family functionality. The independent variables analysed with multiple linear regression were the families' financial problems, degree of kinship with patients, the caregivers' education levels, age and gender, and the caregivers' burden. The independent variables analysed with multiple linear regression were the family's financial problems, degree of kinship with patients, the caregivers' education levels, caregivers' burden, and the age and gender of the caregivers for family functioning. The discrete variables in the study were included in the regression analysis by coding them as "dummy variables", and continuous variables were analysed with their original values. In the analysis, participants' genders, educational levels, financial problems due to disease, and the level of kinship with the patients were transformed into "dummy" variables; "males", "the participants who have received education for 11 or more years", "the participants who do not have financial problems" and "close relatives providing care to the patient" were coded as "0" and were transformed into dummy variables. Values of a  $p < 0.05$  were considered statistically significant.

### Findings

#### *Descriptive features of the family caregivers and status to help their patients*

The age average of the caregiver relatives of the patients receiving chemotherapy was  $47.15 \pm 16.08$  (interval: 15-82). Most of the caregivers of the patients receiving outpatient chemotherapy were as women (84.3 %) and married (82.4 %). Also, it was determined that more than half of the caregivers were primary school graduates (57.8 %) and housewives (57.8 %), and 2/3 of the caregivers were the spouse of the patient. Almost all of the family caregivers (98 %) that participated in our research had social security.

The caregivers were asked whether they helped the patients receiving outpatient chemotherapy at a chemotherapy unit in their daily living activities or not, and it was determined that more than half of the caregivers (55.9%) helped with the daily living ac-

tivities of the patients. The caregivers of the patients were asked the question, "What daily activities of your patient do you help with?" It was determined that family caregivers provide assistance mostly for activities like feeding, excretion and bathing.

Table 1. Characteristics of family caregivers (n=102)

Descriptive characteristics	
Age (mean $\pm$ SD, years)	47.15 $\pm$ 16.08 (15-82)
Gender (n, %)	
Female	16 (15.7)
Male	86 (84.3)
Educational level (n, %)	
Secondary school or less	34 (33.3)
High school or more	68 (66.7)
Financial problems (n, %)	
Yes	45 (44.1)
No	57 (55.9)
Status of living in the same house with patient (n, %)	
Yes	93 (91.2)
No	9 (8.8)
The degree of kinship (n, %)	
Spouse	63 (61.8)
Other close relatives	33 (38.2)

### **Burden, family functions and affecting factors**

The multiple linear regression analysis of factors associated with family caregiver burden is shown at Table 2. Low level of education (regression coefficient beta = 8.632, 95% CI = 1.082-16.182) and being spouse of the patient (regression coefficient beta = 5.472, 95% CI = -3.421-14.366) are associated with a higher level of burden (Table 2). There was no relationship between the caregivers' burden scores and the other descriptive characteristic of the caregivers.

In order to examine the relationship between caregiver burden and family functions, Pearson correlation coefficients were computed (Table 3). There was significant correlation between their family functions, like communication, roles, effective responsiveness, affective involvement, behavioural control, general functions of family and caregiver burden.

The factors associated with the family functions of caregivers are shown in Table 4. When multiple linear regression analysis results were considered, it was observed that caregiver spouses had more difficulties compared to other relatives in terms of problem solving (regression coefficient beta = 0.339; 95% CI = 0.068-0.609) and effective res-

Table 2. Factors associated with the sense of burden felt by the caregiver—multiple regression analysis

Variables	Coefficients		t	p	95% Confidence interval for B	
	Beta	S E			Lower bound	Upper bound
Constant	12.637	7.585	1.666	0.099	2.419	27.693
Age (years)	-0.099	0.138	-0.717	0.475	-0.372	0.174
Gender (female)	8.151	4.914	1.659	0.100	-1.602	17.904
Education ( $\leq$ 8)	8.632	3.804	2.269	0.025	1.081	16.182
Financial problems	5.349	3.474	1.540	0.127	-1.547	12.245
The degree of kinship	5.472	4.480	1.221	0.225	-3.421	14.366

Table 3. Correlations between family functions and caregiver burden

Family Functions	Pearson Correlation	2-tailed p
Problem solving	0.028	0.779
Communication	0.274(**)	0.005
Roles	0.384(**)	0.000
Effective responsiveness	0.308(**)	0.002
Effective involvement	0.250(*)	0.011
Behavioural control	0.288(**)	0.003
General functions	0.367(**)	0,000

\*\* Correlation is significant at the 0.01 level (2-tailed).

\* Correlation is significant at the 0.05 level (2-tailed).

ponsiveness (regression coefficient  $\beta = 0.339$ ; 95% CI = 0.044-0.633). It was determined that living with financial problems was a factor affecting the caregivers' roles (regression coefficient  $\beta = 0.191$ ; 95% CI = 0.044). Also, there was a *significant* relationship between financial problems and problem solving [regression coefficient  $\beta = (-0.233)$ ; 95% CI = (-0.444) - (-0.022)].

When Table 4 was analysed, it was seen that the burden perceived by the caregivers was related to the different dimensions of family functionality, like communicating (regression coefficient  $\beta = 0.009$ ; 95% CI = 0.003-0.015), performing their roles (regression coefficient  $\beta = 0.008$ ; 95% CI = 0.003-0.012), affective responsiveness (regression coefficient  $\beta = 0.080$ ; 95% CI = 0.003-0.015), affective involvement (regression coefficient  $\beta = 0.009$ ; 95% CI = 0.001-0.014), behaviour control (regression coefficient  $\beta = 0.006$ ; 95% CI = 0.002-0.011), and performing their general roles in the family (regression coefficient  $\beta = 0.013$ ; 95% CI = 0.006-0.020).

## Discussion

The purpose of this study was to identify the factors that affect the family functions and burdens of the family caregivers of cancer patients receiving outpatient chemotherapy. Burden is one of the most important problems for caregivers of cancer patients [5,23]. Having a lower level of education (secondary school or less) was associated with a higher level of care giving burden reported by the family caregivers. This result showed that education level affected the burden perception of the caregivers differently, and there was an inverse relationship between the education level and perceived burden. When one has a higher level of education, one is more likely to possess more knowledge about how to deal with a sustained stressful healthcare event, such as caring for a family member with cancer. It was emphasized in the literature that a high education level increased the ability to get formal and informal support [25]. Furthermore, education was a factor

Table 4. Factors associated with family functions of caregiver—multiple regression analysis<sup>a</sup>

Family Functions	Variables	Coefficients		t	p	95% Confidence interval for B	
		Beta	Standard Error			Lower bound	Upper bound
Problem solving	Constant	1.847	0.232	7.950	0.000	1.385	2.308
	Financial problem	-0.233	0.106	-2.193	0.031	-0.444	-0.022
	The degree of kinship	0.339	0.136	2.484	0.015	0.068	0.609
Communication	Constant	1.744	0.242	7.199	0.000	1.263	2.225
	Burden	0.009	0.003	2.837	0.006	0.003	0.015
Roles	Constant	1.740	0.162	10.712	0.000	1.418	2.063
	Financial problems	0.191	0.074	2.573	0.012	0.044	0.338
	Burden	0.008	0.002	3.504	0.001	0.003	0.012
Effective responsiveness	Constant	1.473	0.253	5.828	0.000	0.971	1.975
	The degree of kinship: Spouse	0.339	0.148	2.283	0.025	0.044	0.633
	Burden	0.008	0.003	2.340	0.021	0.001	0.015
Effective involvement	Constant	1.884	0.225	8.382	0.000	1.438	2.331
	Burden	0.009	0.003	2.867	0.005	0.003	0.014
Behavioural control	Constant	1.877	0.175	10.699	0.000	1.529	2.226
	Burden	0.006	0.002	2.785	0.006	0.002	0.011
General functions	Constant	1.343	0.258	5.211	0.000	0.832	1.855
General functions	Burden	0.013	0.003	3.795	0.000	0.006	0.020

<sup>a</sup> The table includes variables of statistical significance  
† CI, confidence interval; SE, standard error.

that improved life quality by increasing positive competing methods, social support and awareness [25]. For that reason, it might be assumed that encountered difficulties and problems might be coped with and solved more easily as the education level increases.

It was determined that spouses had more difficulties in giving emotional reactions compared to close relatives. The cause of this might be that the caregivers might avoid giving emotional responses so as not to upset their partners.

In our study, it was determined that caregiver spouses were less successful than close relatives in problem solving. Cancer diagnosis and cancer treatment are among the most important stressors. It is thought that the problem solving skills of patients' spouses who participated in our study were affected negatively from the stress caused by the disease. It is known that individuals who have psychological problems show insufficient problem solving behaviours. As a matter of fact, psychological problems force individuals' defence mechanisms to be used for dealing with the problems and problem solving skills [12].

Our study showed that living with financial difficulties was a negative factor for the family caregiver's roles. Economic difficulties might have created unwillingness for the family members to perform their roles. A family's financial situation is a key determinant of a member's sense of wellbeing, which could affect family life [26] and family roles [27]. Haley reported that financial inadequacies might disrupt the lifestyles of caregivers [6]. Caregivers who reported a negative financial impact of cancer care were more likely to suffer from the negative health impacts of cancer care [28].

In our study, it was determined that the problem solving skills of family caregivers who lived with financial difficulties were better. One reason for this result is that all medical bills paid by the state in Turkey and this might be alleviated financial hardship due to illness. It is one of the important cultural properties of the Turkish family that all close relatives provide support to the family in a crisis (disease, marriage, death, etc.). This cultural difference might positively affected in the problem solving skills of family caregivers who participated in our study.

Our study showed that it was seen that the caregivers who perceived more emotional and social burdens exhibited unhealthy functions in performing their duties, communicating, giving emotional reactions (expressing emotions such as anger, excitement and sadness), effective involvement, controlling behaviours and performing general roles in family. Results of this study showed that perceptions of burden were significant contributor to the family dysfunction of the caregivers. Similarly, caregivers of dementia patients with high levels of burden reported greater family dysfunction in communication and roles [12]. The reason why the caregivers who participated in our study had difficulties in the stated dimensions of family functionality might be explained by social and emotional overload. It might be assumed that the caregivers had difficulties in expressing their feelings, communicating, performing their roles and general functions because they were emotionally overloaded. Gaugler et al. asserted that the stress that emerges in the caregivers might create unwillingness to performing activities such as shopping, going to somewhere from somewhere, and doing housework [27].

The findings obtained as a result of this study are important in terms of indicating the relationship between family functionality and caregiver burden and being the first study regarding cancer patients' caregivers. There has been no study which has examined the relationship between family functionality and the burden emerging in the family caregivers of cancer patients. However, when the studies carried out [3,4,11,28] are examined, it might be said that the caregivers of cancer patients have problems in different dimensions of family functionality. One study reported that families might be affected by stressors, such as changes in roles and employment and disruptions in schedules (e.g. frequent clinic visits) [6]. Grunfeld et al., employed caregivers reported an increased inability to work regular hours [4]. Inoue et al., in their study, determined weak family function perception in the communication area [28]. Tamayo et al. determined that expressing feelings and continuing housework were key factors which determined caregivers' wellbeing [3].

## Limitations

Several limitations exist regarding this study. The findings of this study might have not shown that burden is a factor affecting family function directly. That is, whether family dysfunction results in greater caregiver burden or whether increased burden causes greater family dysfunction. Regardless of the direction, our findings highlight the importance of including a family assessment and intervention when working with caregivers of cancer patients. This study was a cross-sectional study. It was carried out by going to the houses of patients who received outpatient chemotherapy. Therefore, a full understanding of the effect of cancer on the caregiver is limited. Studying family functioning (and associated moderating variables) in a longitudinal study might be more likely to identify causal relationships.

## Conclusions

The findings obtained as a result of our study indicate the factors related to family functionality and caregiver burden. It was determined that a high educational level is a positive factor which reduces the burden. This study is important since it is one of the first studies to discuss the family functionality and caregiver burden regarding the cancer patients' caregivers. Caregiver spouses and patients' relatives who live with financial problems have difficulties in performing their family roles. Changes occur in the family functions of caregivers of cancer patients and one reason for this change is the emotional and social overloads experienced by the family. In addition to the known relationship between burden and psychological problems, future studies should focus on caregiver burden, family functionality and psychological problems.

## Relevance to clinical practice

Nurses determine the changes in family functions and their reasons are important for the holistic approach. Families are faced with financial, social and psychological problems due to the cancer and cancer treatment process. Families' lives are affected negatively and changes occur in their da-

ily routines. Functional families deal with the financial and psychological problems they face and solve the problems more easily. Therefore, nurses must continue to work hard to focus not only on the disease and its symptoms, but also on the impact of the illness on the day-to-day living of the patient with cancer and their family. Finally, the family needs to be considered when developing the nursing plan. Family assessment instruments that allow the provider to evaluate the family and its ability to adapt to stress might be helpful in predicting the ability of the family to adapt to stressful events.

## List of abbreviations

CI: confidence interval

SE: standard error

FAD: Family Assessment Device

## Authors' contributions

Study design: ZG, HÇ, AÖ, GO; data collection: ZG, HÇ, AÖ, GO; manuscript preparation: ZG, HÇ, and data analysis: ZG and power analysis: Mevlüt Türe

## Acknowledgements

The authors are grateful to all the family caregivers. The authors wish to thank MT for power analysis.

## References

1. Wright LM, Bell JM. Retrospective--nurses, families, and illness: a new combination. *Journal of Family Nursing* 2004, 10(3):2-11.
2. Patterson JM. Understanding family resilience. *Journal Of Clinical Psychology* 2002, 58(3): 233-246.
3. Tamayo GJ, Broxson A, Munsell M, Cohen MZ. Caring for the caregiver. *Oncology Nursing Forum* 2010, 37(1): 50-57.
4. Grunfeld E, Coyle D, Whelan T, Clinch J, Reyno L, Earle CC, Willan A, Viola R, Coristine M, Janz T, Glossop R. Family caregiver burden: results of a longitudinal study of breast cancer patients and their principal caregivers. *The Canadian Medical Association Journal* 2004, 170(12): 1795-1801.

5. Wilkinson AM, Lynn J. Caregiving for advanced chronic illness patients. *Techniques In Regional Anesthesia And Pain Management* 2005, 9(3):122-132.
6. Haley WE. Family caregivers of elderly patients with cancer: understanding and minimizing the burden of care. *J Support Oncol* 2003, 1(2): 25-29.
7. Longo CJ, Fitch M, Deber RB, Williams A P. Financial and family burden associated with cancer treatment in Ontario Canada. *Support Care Cancer* 2006, 14(11): 1077-1085.
8. Rees J, O'Boyle C, MacDonagh R. Quality of life: impact of chronic illness on the partner. *Journal of The Royal Society of Medicine* 2001, 94(11): 563-566.
9. Yusuf A, Adamu A, Nuhu FT. Caregiver burden among poor caregivers of patients with cancer in an urban African setting. *Psycho-Oncology* 2011, 20(8):902-905.
10. Karlikaya G, Yukse G, Varlibas F, Tireli H. Caregiver Burden In Dementia: A study in the Turkish population. *The Internet Journal of Neurology* 2005, 4(2).
11. Chappell NL, Reid C. Burden and wellbeing among caregivers: examining the distinction. *The Gerontologist* 2002, 42(6): 772-780.
12. Tremont G, Davis JD, Bishop DS. Unique contribution of family functioning in caregivers of patients with mild to moderate dementia. *Dementia Geriatric Cognitive Disorders* 2006, 21: 170-174.
13. Edwards B, Clarke V. The psychological impact of a cancer diagnosis on families: the influence of family functioning and patients' illness characteristics on depression and anxiety. *Psycho-Oncology* 2004, 13(8): 562-576.
14. Kissane DW, McKenzie M, McKenzie DP, Forbes A, O'Neill I, Bloch S. Psychosocial morbidity associated with patterns of family functioning in palliative care: baseline data from the Family Focused Grief Therapy controlled trial. *Palliative Medicine* 2003, 17(6): 527-537.
15. Illingworth N, Forbat L, Hubbard G, Kearney N. The importance of relationships in the experience of cancer: A re-working of the policy ideal of the whole-systems approach. *European Journal of Oncology Nursing* 2010, 14(1): 23-28.
16. Gözüüm S, Akçay D. Response to the needs of Turkish chemotherapy patients and their families. *Cancer Nursing* 2005, 28(6): 469-575.
17. Chan CWH. Managing caregiver tasks among family caregivers of cancer patients in Hong Kong. *Journal of Advanced Nursing* 1999, 29(2): 484-489.
18. Ho SC, Chan A, Woo J, Chong C, Sham A. Impact of Caregiving on Health and Quality of Life: A Comparative Population-Based Study of Caregivers for Elderly Persons and Noncaregivers. *J Gerontol A Biol Sci Med Sci.* 2009,;64(8):873-9.
19. İnci FH, Erdem M. Adapting the Caregiving Burden Scale to Turkey, its validity and reliability. *Journal of Anatolia Nursing and Health Sciences* 2008, 11(4): 85-95. (In Turkish).
20. Zarit SH, Reever KE, Bach-Peterson J. Relatives of impaired elderly: Correlates of feelings of burden. *Gerontologist* 1980, 20(6): 649-55.
21. Miller IW, Epstein NB, Bishop DS, Keitner GI. The McMaster Family Assessment Device: reliability and validity. *Journal of Marital and Family Therapy* 1985, 11(4): 345-356.
22. Bulut I. *The Handbook of Family Evaluation Scale.* Ankara: Öz-Güzeliş Print House; 1990.
23. Grov EK, Fosså SD, Oystein Sørebo, Dahl AA. Primary caregivers of cancer patients in the palliative phase: a path analysis of variables influencing their burden. *Social Science & Medicine* 2006, 63(9):2429-2439.
24. Pinquart M, Sörensen S. Gender differences in caregiver stressors, social resources, and health: an updated meta-analysis. *Journal of Gerontology: Psychological Sciences* 2006, 61(1): 33-45.
25. Awadalla AW, Ohaeri JU, Gholoum A, Khalid AOA, Hamad HMA, Jacob A. Factors associated with quality of life of outpatients with breast cancer and gynecologic cancers and their family caregivers: a controlled study. *BMC Cancer* 2007, 19(7): 102.
26. Ishii-Kuntz M, Gomel CN, Tinsley BJ, Parke RD. Economic hardship and adaptation among Asian American families. *Journal of Family Issues* 2010, 31(3): 407-420.
27. Gaugler JE, Linder J, Given CW, Kataria R, Tucker G, Regine WF. Family cancer caregiving and negative outcomes: the direct and mediational effects of psychosocial resources. *Journal of Family Nursing* 2009, 15(4): 417-444.
28. Inoue S, Saeki T, Mantani T, Okamura H, Yamawaki S. Factors related to patient's mental adjustment to breast cancer: patient characteristics and family functioning. *Support Care Cancer* 2003, 11(3):178-184.

Corresponding Author  
Zeynep Güneş,  
Adnan Menderes Üniversitesi,  
Aydın Sağlık Yüksekokulu,  
Aydın,  
Turkey,  
E-mail: zeynep\_adu@hotmail.com

# Playgrounds in Novi Sad (Serbia) and their influences on children's health and development

Milena Krkljes<sup>1</sup>, Marija Jevtic<sup>2</sup>

<sup>1</sup> University of Novi Sad, Faculty of Technical Sciences, Serbia,

<sup>2</sup> University of Novi Sad, Faculty of Medicine, Serbia.

## Abstract

Playgrounds are spaces in urban environments where children spend most of their free time. Continuous and various games in the open, with numerous physical and emotional reactions, have great significance for their health. The importance of playgrounds is based on possibilities for children to realize different needs for their proper psychophysical development. The aim of this research was to explore what kinds of playgrounds are adequate for children according to their development levels. Focusing on playgrounds in the urban area of Novi Sad (Serbia), the paper analyzes different playgrounds and sport fields. The analyzed examples are differently positioned, shaped and various in used elements, as well as in the overall quality of surroundings. Play opportunities and problems within playgrounds were identified and documented in order to determine possible strategies and recommendations to improve their quality and provide children with healthy and secure environments. Upon analyzing playgrounds in Novi Sad, conclusions were made that the unified need of children for play does exist in diversified places and that all spaces have certain influence on children's development and health. There is an obvious lack of adequate playgrounds, which would fully satisfy modern children's needs.

**Key words:** children, health, development, play, playgrounds, environment

## Introduction

Playing is considered as one of the most important activities in children's life. Both indoor and outdoor play have important role for their health (Jevtić et al. 2000, Jevtić et al. 2002). Playgrounds and other play fields in urban fragments of the city have essential importance for proper psychophys-

cal development. Places where children spend their time and develop their abilities should be carefully analyzed and designed. Therefore, the concern about playgrounds is the research core of various professionals who deal with problems of children.

Complex and artificial environments of today's cities where children grow up have fewer and fewer places that are appropriate for these young age groups, offering them insufficient opportunities to freely investigate their surroundings and find about the world around them with their own senses. Numerous children-centred scientists consider that nowadays children have less freedom to walk around without parental supervision (Weller and Bruegel, 2009) and that cramped quarters for moving and meeting with other children have as a result specific isolation from real life, intensified by an effect of hypnovision and other mediums of artificial information (Kamenov, 1989). In this way, children are deprived of possibilities for their own authentic experience, which is important in their development.

Regarding the benefits that children's outdoor play has on their overall health and development, the specified public playgrounds should be appropriately designed and the freedom of independent activities and movements should be the goal toward which children oriented professionals strive. Several studies in different European cities have already shown that the quality of play on public playgrounds remains beneath the desired standard (Huttenmoser and Meierhofer, 1995). All of these spaces can become child-friendly environments that promote exploration and environmental learning, different activities and social interactions, by adequate shaping of physical characteristics of playgrounds and by allowing children to express themselves freely in creation and control of their spaces (Chatterjee, 2005, p. 17). Only in this way, play-spaces can become appropriate for overall children's de-



velopment. The complexity of these play areas, as well as significance of playgrounds stressed in many works by authors of different professions (medicine, psychology, pedagogy...), requires the use of careful analyses in all research phases.

### **The aim of the research**

This paper analyzes different playgrounds and play fields in the city of Novi Sad (Serbia). The analyzed examples are differently positioned, shaped and various in used elements and materials, as well as in the overall quality of surroundings. It reviews questions and problems children face with during their daily play in different public areas. The aim of the research was to identify, document, point out play opportunities and problems within these playgrounds in order to determine possible strategies and recommendations for improving their quality, and provide children with healthy and secure development.

### ***Play as children's main activity***

Children's play includes a range of behaviours through which they explore and understand their surroundings. Unfortunately, the awareness in more urbanized nations and the understanding that play is fundamental to a child's health and development was insufficient to significantly improve the policy for play provision and to provide high-quality playgrounds for many children (Hughes, 1990).

One of basic children's rights is "to rest and leisure, to engage in play and recreational activities appropriate to age of the child and to participate freely in cultural life and the arts... to participate fully in cultural and artistic life and shall encourage the provision of appropriate and equal opportunities for cultural, artistic, recreational and leisure activity" (The Convention on the Rights of the Child, 1989). Following the CRC and giving the children rights in matters affecting them, Skivenes and Strandbu suggested four procedures that should be followed to ensure children's participation: children's opportunity to form their opinions, to express their viewpoints, children's arguments to be taken seriously and to be informed about made decisions (Skivenes and Strandbu, 2006).

Children's play includes different physical, cognitive, creative, emotional and social aspects. It re-

presents one of the most important activities during their growing up and development. As it is concluded in study of the effects of physical exercise on behaviours in children, active engagement in physical activity encourages acquisition and development of conventional norms of behaviour (Tubic and Golubovic, 2010). By playing different games children experience different emotional reactions, they explore and understand their environments which results in creating special relationships with them (DeBord and Amann, 2005). Certain fields of psychology and pedagogy, engaged in different aspects of children's play, think of it as the basic type of child activity, as it reflects the whole neuro-physical state of a child, and its biological and physical needs (Maletic, 1970). The theory that sees play as the central activity during childhood is generally accepted. It also emphasizes the importance of play in any child's intellectual development, as presented by the findings of the cognitive theory of child's play, which confirm the connection between the way they play and their intelligence (Kamenov, 1989). Gross's theory from 1899 indicates a need to procure children with an opportunity to play, primarily for health and healthy movements, providing them with playgrounds (according to Maric, 1979). The play has a key role in proper development. Longo has stated that play includes spontaneous activities of children, which have a direct impact on their experience about the world around them (Longo, 2005). As Moore has stated, cognitive development might be seen in transactional terms, because children develop through a series of transactions with the socio-physical environment, suggesting giving a child possibilities to explore, discover, initiate, etc. in physical environment as a medium (Moore, 1985, p. 30).

Apart from physical, cognitive, creative and emotional aspects, play also includes a social one (Jevtić, 2009). Children who were not playing outside with their friends were restricted in their social relationships. The assumptions of some scientists that family and school as institutions are the only adequate surroundings for children have negative consequences and the result is neglecting the social importance of play in different surroundings. In his research, Moore noted that because of such an opinion we could see inferiority and confusion of children in interaction with people of different age and social groups (Moore, 1999).

### *Healthy and adequate play spaces*

From the child's perspective, space can be defined as a collection of different structural elements whose relations form an entity. Maybe even more important is the definition of space as sequences of experiences and events. Children recognize space as series of activities connected with a particular place, but only after certain experiences can create their own image of that space (Krklješ, 2009). Continuous and various movements in open space, richness in physical and emotional reactions are important factors of children's development. It is widely accepted that live-environment parameters influence growth, development, reproduction and general condition of human organism (Stojisavljevic et al., 2009). Therefore, playgrounds, as places where children spend most of their time, have important role to provide a quality environment for their healthy life.

According to Christian Norberg-Schulz, space can be defined using five concepts: pragmatic space of physical activities, perceptual space of direct orientation, existent space that represents the stable image of people's environment, cognitive space of physical world and abstract space of pure logical relations (Norberg-Schulz, 1974). This differentiation can be used to define what public space for children should look like in the future.

It is widely noticed that, as Eliana Riggio states "children in wealthier communities often live in a world rigidly organized by adults with little opportunity for playing and socializing freely with their peers. Young people usually have no possibilities to express their specific needs and for proposing alternatives from the perspective of a child" (Riggio, 2002, p. 46). On the other side, Roger Hart pointed in his research that even if they often play in unsafe and unsanitary conditions "children in many of the world's poorest neighbourhoods have more freedom to play outdoors close to their homes than children in middle-class areas of the same cities or in the high-income nations" (Hart, 2002, p. 135). Not only playgrounds near housing units are important for children's play, but also the pre-school centres should offer improved movement-requiring educational program. In many different countries, lack of playing facilities and inappropriate environment is one of the major problems to organise more appropriate play activities within these institutions (Fallah et al., 2011).

From experiences of play spaces' designers, it is important to understand how children appreciate spaces in order to meet both the concerns and needs of adults and those of the children. Children can make a dialogue with space: by senses (of sight, hearing, smell, taste and touch) which helps children to perceive space; by psycho-mobility (climbing, running, jumping) which enables children's development and coordination of their own body in different spaces; by symbols, which are in a domain of creativity and enable children to perceive world through imitation before they are able to demonstrate their own ideas; by interrelations, as a result of direct contact with other children and enable comprehension of social interaction (Heintz, 2004). As their spatial cognition includes many different sensory experiences, they need various open spaces with constant possibility for their creative play.

Creating challenging environments is one of the problems to be solved in order to create "a physical environment that makes sense" for children (Lennard and Crowhurst Lennard, 1992, p.58).

The overall importance of this study comes from the fact that even though developed societies understand importance of children's play for their health, open space is used for building development. In many European countries the response to children's needs is often limited to the provisions of traditional forms of equipment such as swings, slides and roundabouts, ignoring the fact that how play takes place and where it takes place are, as Huges stated, two major factors that influence the effectiveness of play (Hughes, 1990).

### **Methodology**

The study was conducted in all urban fragments of the city of Novi Sad, both in the inner city and in suburbs, which are contrasting in terms of morphology. Socially and ethnically, these areas are mostly equitable. The paper is concerned with two aspects of playgrounds valorisation. First one relates to the spatial and design characteristics, and the other to the children's spatial experiences of playgrounds. In both of them, the emphasis is placed on their impact on children's health and development.

In the first part of the research, basic criteria set for analyses and valorisation of playgrounds is defined (Krklješ, 2007):

- Location (in the direct vicinity of the kindergarten, school or housing area...);
- Accessibility for all potential users, especially for disabled children;
- Safety of children in playgrounds;
- Spaciousness for various activities and games;
- High quality (in the sense of natural light, wind protection and adequate vegetation);
- Hygienic conditions;
- Appropriate equipment (in the sense of used materials, shapes and dimensions);
- Durability and sustainable development of a playground (possibilities for flexible changes in modern tendencies and needs of children).

As there are different age groups of children at playgrounds, a differentiation was made into the following categories:

- Play areas for children aged 1 to 3 (always accompanied by adults);
- Play areas for children aged 3 to 7;
- Play areas for children aged 7 to 14;
- Play areas for children aged 14 to 19.

Apart from previously listed set of criteria for valorisation of playgrounds, diversity and dimensions of equipment were key parameters for analyses of suitability for different age groups of children according to the level of their development.

The given set of criteria has been used in analyses of the playgrounds. Fieldwork was conducted between 2007 and 2009 throughout the year, in order to determine the presence of children and the quality of the analyzed spaces during various weather conditions. Regarding the purpose of the study, survey research is used combined with visual analyses of playgrounds (observation method). Questionnaires were used as data gathering tools, to evaluate viewpoints and thoughts of the responding children. The questionnaire consisted of two parts that feature of spatial and design characteristics and spatial experiences. During the research 140 playgrounds and play areas were analysed, of which 41 were in kindergarten yards and 99 were in housing areas or other public spaces. Apart from playgrounds within kindergartens and sport fields within schoolyards, all other research-

ed areas were chosen by the overall observation of the mostly visited spaces in the city. As part of the study, 231 children (aged 3-15) were randomly chosen at playgrounds to answer the questions and 86 adults who were accompanying children (aged 1-3) have completed the questionnaire. Through the questionnaire a number of issues about play spaces, such as their location, size, elements for play, environmental values, children's interests, freedom, etc. were explored. Questions were asked to provide an overall insight into the influence of playground's quality on children's health and development.

### The results and discussion

The results of playgrounds' analysis in the city of Novi Sad, confirmed the hypothesis that there is a connection between the quality of certain types of playgrounds and children's interest to play over there. It has confirmed the fact that various equipment and appropriate surrounding encourage children to play which affected their healthier development.

In the city of Novi Sad, according to the data from the Health Status of the Novi Sad population 2008 there are 323,708 inhabitants, 15.6 % or 50,544 are children age 0-15. The estimated number of children from three to seven is 17,101 or 5.3 % (Jevtić, 2006). Having in mind the fact that proper growth and development of a child requires spending time outdoors, as well as the importance of physical activity being the significant factor in decreasing the health risk in the adult population, the existence and proper attitude towards children's playgrounds represent an important part of the future health situation of the population and its maintenance.

Most of the analysed playgrounds were built within open spaces near the multi-family buildings. Some of the researched examples have been redesigned during the past two years, but most of them are still the same as at the time when they were constructed. As some of them date from the seventies and the eighties of the last century, it is clear that they are in bad condition and obsolete. During the research, some of play areas were redesigned, new elements were positioned and new greenery was planted. In addition, some play areas, which were previously neglected, are designed as

playgrounds or sport fields for older children. The investment in playgrounds and new equipment was funded by the City Council and Public Enterprise for City Construction and Development. Similar actions are widely recognised in many different studies in European cities (Horelli, 1998; Nordström, 2010).

Through the research, in a relation to the specific characteristics of places with various attractive and interesting play elements, different types of playgrounds are defined:

- Playgrounds equipped with different elements for play. These places offer, but also impose, certain kinds of physical games and activities. They are usually located near children's institutions such as kindergartens and schools and near housing buildings. Few of them are located in the city's parks.
- Green open spaces in urban blocks, which enable children to imagine and create games by their own rules. Most of such spaces are not equipped with play elements, or with any other elements of urban furniture, but are favourite places for children to play in greenery in their own way. These places are usually allocated from heavy traffic and children feel free and safe to play. Also, their parents find these areas appropriate for children's play without their supervision, which is meant to be one of the most important criteria for defining child-friendly playground (Haikkola et al. 2007; Nordström, 2010). The apparent fact is that parents are very concerned about children's safety, not only on playgrounds, but also in the other public places.
- Sports fields - places that are planned and designed for recreation and various sport activities for children. They are located near or in schoolyards or in open spaces near housing buildings. Unfortunately, sport fields are usually equipped with minimum elements for basketball or football. No other equipment such as benches, drinking fountain, canopies, etc. could be seen on sport fields.

Analysed playgrounds are generally intended for children aged three to seven, who are most common users of these spaces. Sometimes, in the

areas without play spaces for older children, they use playgrounds in an inappropriate way. That is a shortcoming pointed out by children and adults, as it causes conflicts between different generations of children.

At most of playgrounds, different play equipment is made of wood, metal or plastic materials, in bright colours, which should enable children to develop and improve their psychophysical abilities. However, there is a serious problem as many of the analysed playgrounds are poorly looked after or even ruined (as shown in Figure 1), which makes them less attractive for everyday play and dangerous for children's health. Some of them are also unsuitable places because of their inappropriate hygienic conditions. There is a significant problem of dirty playgrounds and a complete lack of toilets near play areas.



*Figure 1. Ruined playground, which is dangerous for children's health*

Some playgrounds in the Novi Sad have been recently renovated. New play equipment and adequate surfaces in accordance with the necessary aspects of child's safety have been provided. Although the selection of new elements and equipment with the highest quality and design standar-

ds have great importance regarding playgrounds, children who were included in the study clearly stated in their interviews that they are more attracted to the playgrounds, which offer various and challenging play. It is clear from the study that children prefer playgrounds with arranged greenery and some other natural elements, such as water, sand, etc. Children also think that playgrounds with different structures for jumping or running made of recycled materials, are more interesting than ordinary one. Their interests are more oriented towards playgrounds where they can freely organise different games. These playgrounds are also adequate for children of various ages, as they encourage their imagination and healthy physical development. Children have noticed that some kindergarten yards do not even have basic play equipment, but that they play various games thanks to their imagination and from an effort of teachers to design equipment with minimum resources by using, as shown in Figure 2.



Figure 2. Play elements of recycled materials

One of the most significant problems noticed in the study is that disabled and non-disabled children do not have equal possibilities for access and use of playgrounds. Even though accessible play spaces are important for social inclusion of disabled children and their families, the environmental barriers usually obstruct them to participate in all activities. Most of accompanying persons who were interviewed in this study point to the fact that good play spaces should enable all children to play together and use play equipment, which should be designed for them. Parents of disabled children mostly stress the importance of physical activiti-

es for their children's health and improvement of their psychophysical condition. Same as in a similar study (Dunn and Moore, 2005), parents of disabled children pointed to the need for careful design of playgrounds because the accessibility to the spaces can be easily spoiled by poor detail. They stressed the lack of shelters and other necessary elements of urban furniture, what makes public playgrounds less favourite places to come.

Through interviews with older children, age 7-19, the main problem is recognized in a shortage of spaces, which are properly designed for sport activities. As Novi Sad is a city under social and economic transition, with expressive urban growth and fast urban transformation, there is an obvious lack sport fields. Most of the existing ones are neglected, some of these are ruined with certain broken elements such as hoops and goal constructions even dangerous for children's play. Almost none of them have dressing rooms, canopies and toilets (Figure 3). Insufficient hygienic condition at sport fields is one possible health risks for children, who play over there, and certainly bad example for their health education.



Figure 3. Sport field in the urban block with high-rise housing buildings

Important part of the questionnaire in the study refers to the materials of play elements. Children have pointed out that they prefer certain traditional materials such as wooden elements, which are not always the best choice for play equipment. As wood is not compact and smooth, sometimes might cause some small injuries. Children think that the use of standard prefabricated plastic elements makes playgrounds boring after some time. On the other side, parents showed their satisfaction with

plastic elements on playgrounds as they find them safe and attractive for children's play. For parents most important characteristic of playground and play equipment is overall safety in the games and the ability to design attractive equipment. Although playing equipment should be designed to encourage active play, the choice of elements should satisfy the highest safety standards. As there is no public committee to create guidelines for public playgrounds' safety, a number of analyzed places could be marked a risky environments, mostly because of broken elements or equipment installed over hard surfaces. Even though city government should carefully consider the question of children playgrounds' safety, the experiences from the United States shows that too much concern for safety might become a paranoid attempt to create no-risk environments without physical challenge and without possibilities for children to learn how to manage their own safety by engaging in appropriate risk taking (Hart, 2002).

As the purpose of playgrounds is not only physical play, but also some aspects of interaction among children, which is related to their psychical development and health, some questions in analysis referred to possibilities for social interaction at such places. The interaction between children on playgrounds is stated to be good, but there is a problem for children with disabilities. Most of them are excluded from play with other children, both for difficulties with accessibility to the playgrounds and their non-acceptance from other children. Such situation has bad influence on both positive attitude and healthy psychophysical development of disabled children.

### Conclusion

Upon analyzing many playgrounds in Novi Sad, we can conclude that the unified need of children for play does exist in diversified places and that all of such spaces have certain influence on children's development and health in different ages. Open spaces have fewer and fewer attractive content, which would satisfy modern children's needs. Moreover, there is an obvious shortage of spaces for play in some urban areas. In addition, some playgrounds are neglected and uninteresting for children.

However, doing research on playgrounds in kindergartens of Novi Sad, we can conclude that there are a number of social and psychophysical aspects and their influences on children lives. So, we should ask ourselves do we create proper places for children and what can we do to make playgrounds more appropriate for children's overall healthy outdoor play?

If we accept facts that perceptions and needs of children considerably differ from those of adults and that children need freedom to create their own games, we just have to offer them inspiring places with everyday challenges suitable for their different levels of development, age and gender. At the same time, play spaces must be safe and designed according to the highest predefined safety standards. There is also a significant need to design places for children that will be in line with most of the recommendations for overall sustainable development (Jevtic, 2011).

Being that careful designing process of play areas is rather seldom, playgrounds, which are necessary for children's proper psychophysical development, are frequently neglected. Therefore, we have to consider the needs of all different age and gender groups of children and try to create challenging play areas, which would be safe and full of cosy spaces. The selection of play elements is very important. One of important characteristics of all play equipment should be their challenging role in children's play. The other one refers to the choice of materials used for playgrounds, both for play elements and ground. Use of prefabricated products must not make playgrounds boring for children, as there is the risk that they might try to find some more attractive and unusual places for play that are usually dangerous. The functional characteristics of playgrounds should also be appropriate for different age groups of children in order to encourage their development. As they all need to be and feel safe, the important aspect in the process of playground's design is to make sense of enclosure and to protect children from potential negative external influences.

Since children are the part of population who can't independently materialize their needs and wishes, our efforts should be focused on possibilities to create places for them based on a concept of "child friendly cities", which has been developed

to ensure that city governments consistently make decisions in the best interests of children (Riggio, 2002), especially in terms of the right of all young citizens to walk safely in the streets, on their own, meet friends and play, have green spaces for plants and animals, live in an unpolluted and sustainable environment, etc (Krklijes, 2011). Children should have play spaces where they can experience the world and perform different activities. We must make an effort to create environment with direct approach to play equipment and everyday challenges suitable for children's different levels of development, age and gender.

A significant problem is noticed in the lack of financial support and investments to create cosy environments and interesting playgrounds with affordable elements within playgrounds. The importance of equable network of playgrounds all around the city comes from the fact that in different child-oriented studies (Weller and Breugel, 2009), such as this one, most parents stress their fear about possible risk if their children have to go far away from living surroundings to find appropriate play area. Most young children do not even have the autonomy and freedom to go unaccompanied over different parts of the city.

Even though institutions stress the importance of children's rights, one of the problems that can be recognised through interviews is that children do not recognise their role in the community. They do not have almost any part in designing activities and therefore have no sense of full belonging to the playgrounds or identifications with other groups of children. Such a feeling might be the reason why children devastate playgrounds and feel like a strangers there. The recommendation to both community and designers of playgrounds is to try to synchronise their work in order to try to create child-friendly environments, which will ensure better living conditions in the city for all children.

### Acknowledgement

The paper was done within the project "Optimisation of architectural and urban planning and design in function of sustainable development in Serbia" (TR36042) funded by the Ministry of Education and Science, Republic of Serbia. The authors also acknowledge the financial support of

the Ministry of Education and Science of Serbia, within the project "Biosensing Technologies and Global System for Continuous Research and Integrated Management" (No.43002).

### References

1. Jevtić M, Vesković M, Čonkić Lj, Bikit I, Krmar M, Slivka J, Žikić N. *Indoor Radon Survey in Novi Sad. Archive of Oncology, Institute of Oncology Sremska Kamenica; September 2000; 8/3: 137-138.*
2. Jevtić M, Vesković M. *Health Risk due to Exposures to Radon of Novi Sad Population. Central European Journal of Occupational and Environmental Medicine. 2002; 8(2-3): 221-226*
3. Weller S, Bruegel I. *Children's 'Place' in the Development of Neighbourhood Social Capital. Urban Studies 2009; 46 (3): 629-643.*
4. Kamenov E. *Intelektualno vaspitanje kroz igru, Beograd: Zavod za udzbenike i nastavna sredstva, Sarajevo: Svjetlost OOUR Zavod za udzbenike i nastavna sredstva; 1989.*
5. Huttenmoser M, Meierhofer M. *Children and Their Living Surroundings: Empirical Investigations into the Significance of Living Surroundings for the Everyday Life and Development of Children. Children's Environments 1995; 12(4): 1-17.*
6. Chatterjee S. *Children's Friendship with Place: A Conceptual Inquiry. Children, Youth and Environments 2005; 15(1): 1-26.*
7. Hughes B. *Children's Play - A Forgotten Right. Environment and Urbanization 1990; 2 (2): 58-64.*
8. *The Convention on the Rights of the Child UN General Assembly resolution 44/25; 1989.*
9. Skivenes M, Strandbu A. *A Child Perspective and Children's Participation. Children, Youth and Environments 2006; 16(2): 10-27.*
10. Tubić T, Golubović S. *The effects of physical exercise on externalizing and internalizing behaviors in children. HealthMED 2010; Volume 4 (4): 750-758.*
11. DeBord K, Amann N. *Benefits of Play in Children: Age Specific Interventions. NC State University, <http://www.ces.ncsu.edu/depts/fcs/human/disas4.html>; 2005.*
12. Maletic S. *Znacaj decje igre i decja igralista, Beograd: Partizan; 1970.*

13. Maric A. *Prostorna organizacija igre fizički ostecene dece u uslovima savremenog stanovanja*, Beograd: Institut za arhitekturu i urbanizam; 1979.
14. Longo M. *Children and Play*, Ohio State University, <http://ohioline.osu.edu/hyg-fact/5000/5297.html>; 2005.
15. Moore HL. *The Designed Environment and Cognitive Development: A Brief Review of Five Domains of Research*. *Children's Environments* 1985; 2 (2): 26-33.
16. Jevtić M. *Održivi razvoj, urbana ekologija i zdravlje populacije. Rad za užu specijalizaciju, decembar 2009*. Medicinski fakultet, Univerzitet u Novom Sadu
17. Moore HL. *The Health of Children and Young People: A New Agenda*. *Health Education* 1999; 99 (4): 161-169.
18. Krklješ M. *Dečja igrališta u okviru predškolskih ustanova kao faktori pravilnog psiho-fizičkog razvoja dece*. *Nauka + Praksa* 2009; 12(1): 93-96.
19. Stojisavljević D, Jusupović F, Mirilov J, Danojević D, Jandrić Lj, Kristoforović-Ilić M, Kudumović M. *Environment impact to the health behavior of schoolchildren*, *HealthMED* 2009; Volume 3 (2): 149-154.
20. Norberg-Schulz C. *Existence, space and architecture*. New York: Praeger; 1974.
21. Riggio E. *Child Friendly Cities: Good Governance in the Best Interests of The Child*. *Environment and Urbanization* 2002; 14 (2): 45-58.
22. Hart R. *Containing Children: Some Lessons on Planning for Play From New York City*. *Environment and Urbanization* 2002; 14 (2): 135-148.
23. Fallah Z, Janani H, Mohammadian F, Mallahi A, Jamali SS. *A Survey on Children Plays and Movement preferences in Pre-school Centers*. *HealthMED* 2011; Volume 5 (2): 327-333.
24. Heintz D. *D'espaces et d'enfants, Dossier: Petite enfance*. *T & a* 2004; 473: 19-27.
25. Lennard H, Crowhurst LS. *Children in Public Places: Some Lessons From European Cities*. *Children's Environments* 1992; 9(2): 56-75.
26. Krklješ M. *Future of Public Spaces for Children*, 51st IFHP World Congress, International Federation for Housing and Planning, <http://www.ifhp2007copenhagen.dk/Components/GetMedia.aspx?id=80effcbc-1d34-4972-ae20-38657bf3c6f2>; 2007.
27. Jevtić M. *Zdravlje i lokalni održivi razvoj in Lokalni održivi razvoj - izazovi planiranja razvoja u gradovima i opštinama Srbije*, ed. dr Slobodan Milutinović, *Stalna konferencija gradova i opština* 2006; 73-119.
28. Horelli L. *Creating child-friendly environments: case studies on children's participation in three European countries*. *Childhood* 1998; 5: 225-239.
29. Nordström M. *Children's Views on Child-Friendly Environments in Different Geographical, Cultural and Social Neighbourhoods*. *Urban Studies* 2010; 47 (3): 514-528.
30. Haikkola L, Pacilli MG, Horelli L, Prezza M. *Interpretations of Urban Child-Friendliness: A Comparative Study of Two Neighbourhoods in Helsinki and Rome*. *Children, Youth and Environments* 2007; 17(4): 319-351.
31. Dunn K, Moore M. *Developing Accessible Playspace in the UK: What They Want and What Works*. *Children, Youth and Environments* 2005; 15(1): 331-353.
32. Jevtić M. *Javno zdravlje. poglavlje u Putokaz ka održivom razvoju. Nacionalna strategija održivog razvoja*, priručnik, Beograd 2011; 96-109.
33. Krklješ M. *Deca i javni prostori grada*. U: Kurtović-Folić N., ur.: *Zbornik radova: Unapređenje strategije obnove i korišćenja javnih prostora u prostornom i urbanističkom planiranju i projektovanju*, Departman za arhitekturu i urbanizam, Fakultet tehničkih nauka, Novi Sad 2011: 105-122.

Corresponding Author

Milena Krklješ,  
University of Novi Sad,  
Faculty of Technical Sciences,  
Serbia,  
E-mail: milena.krkljes@gmail.com



## Appendix: Tables with results from the questionnaire

Table 1. Results from the children's questionnaire

Urban settlement	Novo Naselje	Satelit	Telep	Liman	Grbavica	Centar	Podbara, Salajka	Bulevar, Rotkvarija	Detelinara, Sajmište
Area	188,35 ha	51,21 ha	353,61 ha	189,31 ha	151,68 ha	147,15 ha	225,56 ha	213,33 ha	224,41 ha
Number of children in the study	34	22	26	32	21	31	24	22	19
Percentage of children who go alone to playgrounds	76 %	68 %	69 %	69 %	66 %	74 %	79 %	68 %	73 %
Percentage of children who participated in conflicts with other age groups	29 %	18 %	31 %	53 %	14 %	35 %	16 %	13 %	21 %
Percentage of children who play in kindergarten yards	53 %	28 %	77 %	50 %	71 %	65 %	29 %	40 %	63 %
Positive characteristics of play areas	Large inner yards, greenery	Greenery	/	Large inner yards, greenery	/	Greenery, Dunavski park	/	Numerous sports facilities	/
Disadvantages of play areas	Lack of sports facilities and well equipped playgrounds, abandoned greenery	Lack of well equipped playgrounds, bad street lightening	Lack of sports facilities and well equipped playgrounds	Devastated sports facilities and playgrounds	Lack of sports facilities and well equipped playgrounds, abandoned greenery	Lack of large green inner yards	Lack of sports facilities and well equipped playgrounds	Devastated sports facilities and playgrounds	Lack and devastation of sports facilities and playgrounds

Table 2. Results from the parent's questionnaire

Urban settlement	Novo Naselje	Satelit	Telep	Liman	Grbavica	Centar	Podbara, Salajka	Bulevar, Rotkvarija	Detelinara, Sajmište
Area	188,35 ha	51,21 ha	353,61 ha	189,31 ha	151,68 ha	147,15 ha	225,56 ha	213,33 ha	224,41 ha
Number of parents in the study	11	11	10	13	8	11	8	8	6
Percentage of parents satisfied with children's playgrounds	73 %	36 %	40 %	54 %	38 %	64 %	50 %	63 %	67 %
Percentage of parents satisfied with children's safety	55 %	36 %	30 %	46 %	25 %	36 %	38 %	38 %	50 %
Positive characteristics of play areas	Large inner yards, quietness, greenery, safety	Quietness, greenery, safety	Nice kindergarten yards	Large inner yards, quietness, greenery, playgrounds and sport fields	Playgrounds, greenery	Greenery, various playgrounds	/	Various sport fields	/
Disadvantages of play areas	Lack of sport facilities and well equipped playgrounds abandoned greenery	Lack of well equipped playgrounds, bad street lightening	Lack of sports facilities and well equipped playgrounds	Devastated sports facilities and playgrounds lack of urban furniture	Lack of sports facilities and well equipped playgrounds abandoned greenery	Lack of large green inner yards, close to the traffic	Lack of sports facilities and well equipped playgrounds	Devastated sports facilities and playgrounds	Lack and devastation of sports facilities and playgrounds, lack of urban furniture

# Effect of quadriceps and ankle plantar flexor muscle fatigue on balance of elderly women

Fatemeh Islami<sup>1</sup>, Zynolabedin Fallah<sup>1</sup>, Soolmaz Mahdavi<sup>1</sup>, Amin Farzaneh Hesari<sup>1</sup>, Hamid Janani<sup>2</sup>

<sup>1</sup> Department of physical Education, Gorgan Branch, Islamic Azad University, Gorgan, Iran,

<sup>2</sup> Department of physical Education, Tabriz Branch, Islamic Azad University, Tabriz, Iran.

## Abstract

This study aims at investigating the effect of the fatigue of quadriceps and ankle plantar flexors on balance performance in active female elderly. The population of the study consisted of the active female elderly in Gorgan city who took regular exercise three times a week. From among the population, 20 subjects, who had no history of injuries in their lower extremity over the past 5 years or injuries which prevented them from doing Berg balance test, participated in the study voluntarily. Descriptive statistics was used to account for the participants' mean and standard deviation of age, height and weight as well as their scores on Berg balance test. Dependent samples t test was used to examine the significance of difference in the participants' scores on BERG balance test before and after inducing fatigue in each group. Independent samples t test was used to assess the difference in the effects of fatigue program in two different limbs (knee and ankle) on the participants' balance. The results showed that balance performance of the active female elderly weakens after, as compared to before, the implementation of fatigue protocol. The findings also revealed that the fatigue of quadriceps reduces the balance performance of female elderly more significantly than the fatigue of ankle plantar flexors does.

**Key words:** fatigue, balance, quadriceps, ankle plantar flexors, the elderly

## Introduction

Adherence to the standards of hygiene and increase in life expectancy has led to increase in the number of elderly in the society. Besides ethical issues, not only should the elderly enjoy adequate physical, mental and social health as the senior citizens, but they should also be efficient and productive both socially and economically, as a rule (Laurence,

2007; Caylan, 2011). Therefore, it is of utmost importance to prevent and overcome the disabilities of the elderly, identify their problems and diagnose the individuals who are vulnerable to these problems. Loss of control and falls are a threatening problem in the elderly, which results in changes in their life quality and high costs of the care of them. Besides, it may cause physical, mental and socio-economic problems and even death in the elderly (Bal, 2001; Gribble, 2004). One of the factors preventing falls in the elderly is to maintain the optimal performance of the muscles operating in the lower extremity joints. Considering the elderly's disinclination for participating in long-term sport activities, it is crucial to determine the effects of the fatigue of operating muscles in different joints on the elderly's balance, which may be a help to designing exercises that can delay the muscular fatigue. Aging and reduction in physical activities cause disorders in lots of physiological functions including sensorimotor functions, which may result in the lack of postural control and vulnerability to injuries in the elderly (Beers, 2000). Reduction in postural control endangers the safety of the elderly in doing daily and sport activities, which may account for reduction of activities and the consequent disorders in the elderly.

Fatigue is one of the commonest feelings we experience in our daily life. However, due to the variety of meanings associated with it including exhaustion, physical (muscular) fatigue and mental fatigue, it is difficult to offer a comprehensive definition of it. From among the variety of fatigue types, muscular fatigue, caused by physical activity, occurs in different parts of neuromuscular control including the central nervous system, neuromuscular control as well as muscles, which leads to muscle malfunction and vulnerability to injuries following fatigue (David, 2004; Kiliç, 2011). In the literature, the sources of muscular fatigue are divided into two categories of peripheral and cen-

tral sources. Peripheral factors refer to disorder in guiding the shakes of muscular fibers as well as the process of contraction (McComas, 1996). Central factor refers to the brain's lack of activating motor neurons and break in the information chain from brain to motor neurons to muscle (Miura, 2004).

With regard to reduction in fatigue threshold time and the consequent reduction in the capacity of physiological organs as well as in postural control as a result of neuromuscular control disorders, the elderly are frequently reported to have suffered injuries due to lack of adequate postural control and falls following daily activities or sport competitions when the occurrence of fatigue is quite probable (Balogun, 1994; Hashim, 2011). Therefore, researchers have paid attention to the investigation of factors affecting postural control including fatigue in the elderly. A review of the literature on the effects of fatigue on balance performance reveals the significant definite impact of muscular fatigue on balance performance (Gribble, 2004; Vuillerom, 2006). However, most of the previous studies on the effects of fatigue on balance have studied young athlete and non-athlete participants (Ochsendorf, 2000; Yaggie, 2002; Sasaki, 2007). Few studies done on the elderly so far have used isokinetic and isometric fatigue protocols which do not bear any resemblance to daily and sport activities. Besides, the relative role of the effects of lower extremity muscles fatigue on the reduction of postural control has not yet been identified. Considering this and the importance of maintenance of health in the elderly and hypothesizing that the fatigue of different lower extremity muscles plays variable roles in reducing postural control, the present study aims at comparative investigation of the effects of the fatigue of quadriceps and ankle plantar flexors on balance performance in the elderly.

## Methodology

The design of the research is quasi-experimental. The population of the study consisted of the active female elderly in Gorgan city who took regular exercise three times a week. From among the population, 20 subjects, who had no history of injuries in their lower extremity over the past 5 years or injuries which prevented them from doing Berg balance test, participated in the study voluntarily.

In order to select the participants, the research methodology was explained to the elderly who were doing fitness exercises in Gorgan city gyms. Then a questionnaire was used to assess the history of lower extremity injuries in the volunteers. Subsequently, those with the history of serious injuries in the lower extremity over the past 5 years and those with inadequate physical conditions to do the balance test or participate in the fatigue program were excluded from the research. Afterwards, the participants were informed of the procedures and stages of doing the test. In order to facilitate the administration of the test and implementation of fatigue programs in the two limbs under similar conditions, the participants were divided into 4 groups. The test was administered over 4 weeks. As to the procedure, for example, the first 5 participants arrived at the test location (body building gym) to use the equipment for reinforcing lower extremity muscles on Sunday at 10 A.M. The participants' weight and leg length (i.e. from anterior superior iliac spine to inner ankle) were measured. Following a brief re-explanation of test procedures, the participants began practicing the Berg test during which one maximal repetition of knee extension and ankle plantar flexion exercises were measured in the participants. Afterwards, the participants' warm-up exercises (5-10 minutes of stretch and jogging) began. Next, the participants did the 14 items of Berg test while the researcher recorded their scores. Then, the participants went on the equipment for the reinforcement of quadriceps and did the knee extension exercise with 50% maximum repetition- which was previously calculated and added to the equipment resistance – up to 50 repeats. When the participants could not continue the exercise in the first set in any repeat, the fatigue protocol was stopped and the Berg test was administered. But, if they could complete the first 50 repeats in the first set, they were to continue doing the protocol following a 4-minute rest. 72 hours later (i.e. the time interval needed to remove the fatigue in knee extensors), these 5 subjects came to the test location again. Similar to the protocol for inducing fatigue in knee extensors, the participants did ankle plantar flexion exercise at the stop of which the Berg test was administered. Over the following weeks, all the testing stages were carried out for other groups in the same way.

### Procedure for inducing fatigue

In order to induce fatigue in quadriceps and ankle plantar flexors, the participants were asked to do knee extension and ankle plantar flexion exercises on the equipment for the reinforcement of quadriceps (to induce fatigue in the knee) and on the equipment for the reinforcement of ankle plantar flexors (to induce fatigue in the ankle), respectively. They were to do the exercises in two 50-repeat sets with 50% one maximal repetition and 4 minutes interval between the sets. The magnitude of one maximal repetition is calculated via the formula:  $IRM = \frac{\text{the weights lifted}}{1 - 0.02 (\text{repeat})}$ . The premise is that fatigue occurs when the participants fail to continue the repeats. In order to induce fatigue in two different limbs (i.e. quadriceps and ankle plantar flexors), the test was administered with 72 hours interval and under similar conditions as far as possible.

Descriptive statistics was used to account for the participants' mean and standard deviation of age, height and weight as well as their scores on Berg balance test. Dependent samples t test was used to examine the significance of difference in the participants' scores on BERG balance test before and after inducing fatigue in each group. Independent samples t test was used to assess the difference in the effects of fatigue program in two different limbs (knee and ankle) on the participants' balance.

### Results

Regarding participants' anthropometric data, their mean age, weight and height were  $64.09 \pm 4.19$ ,  $61.15 \pm 3.13$  and  $16.26 \pm 3.58$ , respectively.

According to table 1, the balance test means score has decreased in the active female elderly after, as compared to before, the implementation of fatigue protocol. Considering the level of significance in the table, it may be concluded that the decrease is statistically significant. In other words, the fatigue of quadriceps ( $t=7.93$ ,  $P<0.001$ ) and ankle plantar flexors ( $t=7.93$ ,  $P<0.001$ ) significantly decreases the balance performance.

Based on the results of table 2, the fatigue of quadriceps decreases the balance performance in the female elderly more significantly than the fatigue of ankle plantar flexors does ( $t=4.86$ ,  $P<0.001$ ).

### Discussion and conclusion

Loss of balance and falls can expose the elderly to acute problems. A common result of falls, particularly in the elderly with osteoporosis, is the fractures of spine vertebrae, pelvis, thigh-bone and wrist. The complexity of these problems may bring about such adverse consequences as spending high medical costs, dependence on others, immobility, lifestyle change (low activity) and over caution. Falls in the elderly depends on a variety of factors the most important of which include lifestyle, family problems, socio-economic status, diseases and the use of medicines.

Table 1. Results of t test comparing the means of balance test before and after the implementation of fatigue protocol

Balance test		Statistic	Mean	Std. Deviation	Df	T	Sig.
Quadriceps muscle fatigue	Before test		52.90	1.99	19	7.93	0.00
	After test		47.55	2.25			
Ankle plantar flexor muscle fatigue	Before test		53.55	1.50	19	3.50	0.00
	After test		50.90	3.02			

Table 2. Results of t test comparing the balance test mean scores in the quadriceps and ankle plantar flexors after the implementation of fatigue protocol

Variable	Statistic	Deferent Mean	Std. Deviation	df	T	Sig.
The fatigue of quadriceps		47.55	2.25	19	-4.86	0.00
The fatigue of ankle plantar flexors		50.90	3.02			

The study revealed that balance performance reduces in the active female elderly after, as compared to before, the implementation of fatigue protocol. As well, the fatigue of quadriceps decreases the balance performance more significantly than the fatigue of ankle plantar flexors does.

Salavati (2002) reported that inducing fatigue in the individuals with chronic low back pain may result in higher body sway in response to external turbulence. He also suggested that the frontal plane is more affectable than the sagittal. Besides, the dependence of these individuals on their eyesight for the maintenance of balance could be inferred via the intensification of sways when they closed their eyes, which may be attributed to the difference in balance-keeping strategies. Vuillerom et al (2004) investigated the effects of the fatigue of spine extensors on postural control in healthy young people. Their results showed that, after inducing fatigue, the intensification of COP sways occurred in the two anterior-posterior and lateral-internal planes. They also reported that the induction of fatigue in the torso extensors provokes more COP sways in the anterior-posterior plane than in the lateral-internal plane. Karl (2004) investigated the effects of vision and the topical fatigue of lower extremity muscles on postural control. He reported that the induction of topical fatigue in lower extremity muscles, both with open and closed eyes, decreases postural control. Ledin et al (2004) investigated the effects of the fatigue of posterior tarsal muscles on the body sways in healthy people during bipedal standing. They found that fatigue may reduce the muscular strength and delay the start of movement.

## References

- Bal, R., Socoth, T., Jacobson, K. Comparison of static and dynamic posture graphy in young and older normal people. *J Athl Train*, 2001; 42(4), 405-412.
- Balogun, J., A., Akindede, K., A., & Nahinlola, J. Age-related changes in balance performance. *Diabil Rehabil*, 1994; 16, 58-62.
- Beers, M., Borkow, R. *The Merck Manual of Geriatrics*. Merck Research Laboratories, Whitehous Station, New Jersey, USA. 2000.
- Berg, K. Balance and its measure in the elderly: A review. *Physiotherapy Canada*, 1989; 41: 240- 6.
- Caylan, A., Aydemir, I., Dagdeviren, N. Evaluation of health related quality of life among perimenopausal Turkish women, *HealthMED*, 2011; 5(4), 741-752
- David, J., Joan, R., Arnold, H. *Skeletal muscle from molecules to movement*. Human kinetic, 2004; 87-93.
- Gribble, P., Hertel, J., Denegar, C., Buckley, W. The effects of fatigue and chronic ankle instability on dynamic postural control. *J Athl Train*, 2004; 39(4), 29-32.
- Hashim HA, Golok F, Ali R. Profiles of exercise motivation, physical activity, exercise habit, and academic performance in Malaysian adolescents: A cluster analysis. *International Journal of Collaborative Research on Internal Medicine & Public Health*. 2011; 3(6):416-428.
- Karl, F., & Ian, J. Effect of fatigue on single-leg hop landing biomechanics. *J Athl Train*, 2006; 22(4), 28-32
- Kiliç, M., Eryilmaz, G. The determination of women's fatigue levels in the third trimester of pregnancy and in the postpartum period. *HealthMED*, 2011; 5(4), 826-830
- Laurence, ZR. Falls in older people: epidemiology, risk factors and strategies for prevention. *Age & Aging*, 2006; 35(2): 37- 41.
- Ledin T, Fransson PA, Magnusson M. Effects of postural disturbances with fatigued triceps surae muscles or with 20% additional body weight. *Gait & Posture*; 2004; 19(2):184-93.
- McComas, A. *Skeletal Muscle: Form and Function*. Champaign, IL, Human Kinatics, 1996; 57-67.
- Miura, K., Ishibashi, Y., Tsuda, E. The effect of local and general fatigue on knee proprioception. *Arthroscopy*, 2004; 20(4), 18-414.
- Ochsendorf, D., T., Mattacola, C., G., Arnold, B., L. Effect of orthotics on postural sway after fatigue of the plantar flexors and dorsiflexors. *J Athletic Train*, 2000; 35(1), 26-30.
- Salavati, M. Impairment of postural control in patients with chronic low back pain and spinal stabilization exercises its influence. Thesis University of Tehran, 2003.
- Sasaki, R., Urabe, Y., Tanaka, K. Assessing balance with the Star Excursion Balance Test in elderly. *Physiotherapy*. 2007; 93(1): 443.
- Vuillerom, N., & Dmetz, S. The magnitude of the effect of calf muscles fatigue on postural control during bipedal quiet standing with vision depends on the eye-visual Target distance. *Gait & Posture*, 2006.
- Yaggie, J., McGregor, S. Effect of isokinetic fatigue on the maintenance of balance and postural limits. *Arch Phys Med Rehabil*, 2002; 83, 28-221.

Corresponding Author  
Fatemeh Islami,  
Department of physical Education,  
Gorgan Branch,  
Islamic Azad University,  
Gorgan,  
Iran,  
E-mail: islami.fa@gmail.com

# Comparison of efficacy of letrozole and clomiphene citrate in ovulation induction for women with polycystic ovarian syndrome

Hakan Nazik<sup>1</sup>, Yakup Kumtepe<sup>2</sup>

<sup>1</sup> Department of Obstetrics and Gynaecology, Adana Numune Education and Research Hospital, Adana, Turkey,

<sup>2</sup> Department of Obstetrics and Gynaecology, Atatürk University Medical Faculty, Turkey.

## Abstract

**Background:** A prospective, controlled clinical trial was performed at university hospital and comprised 98 patients (120 cycles) with PCOS.

**Aim(s):** To compare the efficacy of letrozole and clomiphene citrate in ovulation induction for women with polycystic ovarian syndrome (PCOS).

**Methods:** Patients were divided into three groups. Patients receiving ovulation induction for the first time randomly established to the first two groups and were treated with 100 mg/day clomiphene citrate (1st group) or 2.5 mg/day letrozole (2nd group). The 3rd group consisted of patients who failed to ovulate after CC treatment and 2.5 mg/day of letrozole was given. Main outcome measures were number of mature follicles, ovulation and pregnancy rate (PR).

**Results:** There were no significant differences between the 1st and 2nd groups with respect to number of mature follicles ( $1.02 \pm 0.83$  vs.  $0.83 \pm 0.68$ ), and in group 1 and 2 the number of mature follicles were significantly greater than group 3 ( $0.4 \pm 0.25$ ). There were no significant differences between the 1st and 2nd groups with respect to ovulation rate (72.5% vs. 70%), and in both groups ovulation rate were greater than group 3 (37.5%). The pregnancy rate was 20% in group 1 and 17.5% in group 2 without significant differences, while pregnancy was not detected in group 3.

**Conclusions:** 2.5 mg/day letrozole is as effective as clomiphene citrate for ovulation induction in patients with PCOS.

**Key words:** Letrozole, clomiphene citrate, PCOS, ovulation induction

## Introduction

Polycystic Ovary Syndrome (PCOS) is a chronic anovulatory disease, a common cause of infertility that affects 4-6% of women during their reproductive age (1). For years, clomiphene citrate (CC) has been the most frequently used oral agent to induce ovulation in patients with PCOS. CC is cost effective, easy to monitor, and enables good ovulation (60-90%); however, the rate of pregnancy in patients treated with CC is low (10-40% per cycle) (2). The reason behind this is thought to be the anti-estrogenic effects CC has on the endometrium and endocervix (3). 20-25% of women are CC-resistant and do not ovulate (4). The next step for patients is gonadotropin. Gonadotropin is an agent which is expensive, hard to apply, causes ovarian hyperstimulation and increased multiple pregnancy risk in anovulatory patients with PCOS (5).

Mitwally and Casper (6) were the first to suggest the use of aromatase inhibitors, used in treating breast cancer, as an alternative oral agent to CC in ovulation induction (7). Letrozole is an oral aromatase inhibitor that prevents estrogen synthesis; this action is specific and reversible. By blocking estrogen production, aromatase inhibition temporarily eliminates the negative feedback effect created on the hypothalamic-hypophyseal axis, increases FSH production, and stimulates follicle development (8).

The aim of the present study is to assess the role of letrozole in ovulation induction and compare its efficacy with CC with respect to ovulation and pregnancy rates in women with PCOS.

## Materials and method

This study was conducted on 98 PCOS patients (120 cycles) applied to the Infertility Polyclinic

of Atatürk University Medical Faculty (Erzurum, Turkey) between December 2005 and March 2007. Ethical approval was obtained from the institutional review board of Atatürk University Medical Faculty in order to conduct this study.

The diagnosis of PCOS was based on the 2003 Rotterdam criteria (9). Patients who had ovarian or adnexial surgery, hypothyroidism, hyperprolactinemia, bilateral tubal occlusion diagnosed with hysterosalpingography and unexplained infertility were excluded from the study. Sperm was examined according to World Health Organization-1999 criteria, and according to Kruger Strict criteria in terms of morphology (10). No male factor was detected in the two normal spermograms conducted fortnightly. The day 3 hormonal profile and a transvaginal ultrasound (USG) were performed to all patients (Aloka-SSD  $\alpha$ 10; Tokyo, Japan). Patients with follicles greater than 10 mm was excluded the study.

There were three study groups in this study. The patients receiving ovulation induction for the first time were randomly allocated using a computer random list into first and second groups: CC group (33 patients, 40 cycles) and letrozole group (31 patients 40 cycles) respectively. CC-resistant patients who failed to ovulate when taking 50, 100, and 150 mg/day of CC during successive cycles, added non-randomly to the category of group three (34 patients, 40 cycles).

Withdrawal bleeding was achieved using oral 10-mg medroxyprogesteron acetate for 6 days before stimulation for patients with oligomenore. 100 mg/day oral CC (Gonaphene®; Organon İlaçları A.Ş., Turkey) was administered to the 1st group, 2.5 mg/day oral letrozole (Femara®; Novartis Pharma AG, Basel, Switzerland) was administered to the 2nd and 3rd groups from day 3 to day 7 of menstruation. A month long break was given in the treatment to allow CC to leave the body in the 3rd group. After 3 days of the last treatment day patients were examined with transvaginal USG; the diameter of the follicle and the thickness of the endometrium were recorded. Follicles were measured with USG daily or every other day until the diameter of the follicle reached  $\geq 17$  mm. Human chorionic gonadotropin (hCG) (10.000 IU, intramuscular) was given on the day the mature follicle developed. Patients were rec-

ommended to have scheduled intercourse. All patients had an ultrasound on the second day after the hCG, and the ovulation was assessed. The serum hCG concentration was determined 15 days after the hCG injection in the absence of menstruation for diagnosis of pregnancy.

### Statistical analysis

The main outcome measures were the rate of ovulation and pregnancy. Statistical analysis was accomplished on a personal computer by using statistical program for social sciences version 12.0 (SPSS 12.0, demo, SPSS Inc. Chicago, Illinois). Normality of variables was analyzed and normally distributed variables in three groups were compared with One-Way ANOVA test. For post-hoc comparison Bonferroni test was used. Proportions were analyzed using the chi-square test. Results were expressed as mean and standard error of the mean. Statistical significance level was set at 5%.

### Results

The patients in group 2 were found to be significantly younger and have shorter duration of infertility the other two groups although the patients had been grouped randomly (Table 1). However, the BMI, the hormone values on 3rd day of menstruation were similar. This illustrates that the patients are homogeneously distributed among the three groups.

A summary of the responses of all three groups to the treatment protocols were depicted in Table 2. There were no significant differences between the 1st and 2nd groups with respect to the number of mature follicles (respectively,  $1.02 \pm 0.83$  vs.  $0.83 \pm 0.68$ ;  $P=0.40$ ), and in groups 1 and 2 the number of mature follicles were significantly greater than group 3 ( $0.4 \pm 0.25$ ;  $P=0.001$ ). The estradiol ( $E_2$ ) levels in group 2 (241 pg/mL) and group 3 (212 pg/mL) were significantly lower than group 1 (455 pg/mL;  $P<0.001$ ). There were no significant differences between groups 1 and 2 with respect to endometrial thickness (8.60 and 8.22 mm, respectively), and endometrial thickness in these groups was significantly higher than group 3 (7.01 mm;  $P=0.032$ ). There were no significant differences between the 1st and 2nd groups with respect to



Table 1. The Characteristics and Endocrine Status of Patient Groups

	Group 1 (n=33)	Group 2 (n=31)	Group 3 (n=34)	P value
Age (Year)	27.80±6.18	25.55±4.45 <sup>a</sup>	28.70±4.96	.025
BMI (kg/m <sup>2</sup> )	25.90±4.80	24.66±3.57	25.48±4.86	.447
Duration of Infertility (year)	4.40±3.58	3.40±3.04 <sup>a</sup>	5.45±3.66	.032
<b>Hormonal profile<sup>b</sup></b>				
E <sub>2</sub> (pg/mL)	56.06±26.64	57.04±29.36	58.75±25.42	.905
FSH (mIU/mL)	5.36±1.77	6.19±2.42	6.22±1.90	.107
LH (mIU/mL)	7.39±3.58	6.16±3.48	7.71±4.30	.162

<sup>a</sup>Statistically different from the other two groups ( $P<0.05$ )

<sup>b</sup>Measurements were taken on day 3 of menstruation.

Table 2. The Effects Different Ovulatory Drugs on the Parameters

	Group 1 (n = 33)	Group 2 (n = 31)	Group 3 (n = 34)	P value
The number of follicles on the day of hCG ( $\geq 17$ mm)	1.02±0.83	0.83±0.68	0.4±0.25 <sup>a</sup>	.001
E <sub>2</sub> (pg/mL) on hCG day	455±203.37 <sup>a</sup>	241±230.43	212±94.38	<.0001
End. thickness (mm)	8.22±2.89	8.60±2.93	7.01±1.85 <sup>a</sup>	.032
Ovulation rate (%)	72.5 (29/40)	70.0 (28/40)	37.5 <sup>a</sup> (15/40)	.001
Pregnancy rate (%)	20.0 (8/40)	17.5 (7/40)	0.0 <sup>a</sup> (0/40)	.012

<sup>a</sup>Statistically different from the other two groups ( $P<0.05$ )

ovulation rate (72.5% vs. 70%), and both groups' ovulation rate were greater than group 3 (37.5%;  $P=0.001$ ). The pregnancy rate was 20% in group 1 and 17.5% in group 2 without significant differences, while pregnancy was not detected in group 3 ( $P=0.012$ ). There was one twin pregnancy in group 1, one abortus in group 1 and 2. No important side effects were seen in letrozole-treated patients except slight gastrointestinal complaints.

## Discussion

In the present study, CC and letrozole were administered to the women with PCOS, who had never used any treatment for ovulation induction before. In addition letrozole was administered to women who failed to ovulate after CC treatment. The clinical parameters were compared in order to determine whether or not letrozole can be used as an alternative to CC in ovulation induction and it was found that 2.5 mg/day letrozole is not better, but an alternative to clomiphene citrate for ovulation induction.

CC, known to achieve desired ovulation as a result of peripheral anti-estrogenic effect and not to achieve desired pregnancy rates, has been used to

induce ovulation in anovulatory patients. Aromatase inhibitors, used as adjuvant treatment in treating breast cancer for many years, were suggested as an alternative oral drug to CC (6). Aromatase inhibitors enable the hydroxylation of androstenedione to estrone, and testosterone to estradiol, and inhibit the last step in estrogen metabolic reactions that restrict rate. Aromatase inhibition blocks estrogen production, temporarily eliminates the negative feedback effect created on the hypothalamic-hypophyseal axis, increases FSH production, and stimulates ovarian follicle development (11). The most commonly used agent for this purpose is letrozole; almost completely absorbed after taken orally, has a short half-life (45 hours), and mild side effects (12). The fact that letrozole has no peripheral anti-estrogenic effects brought about the idea that maybe pregnancy rates would increase if used as an alternative to CC; hence, why it was started to be used in ovulation induction (6). After initial use, it was tried by numerous researchers worldwide, in conventional ovulation induction or IVF treatment, either on its own or combined with gonadotropin; it proved to be as effective as CC, or more effective in terms of ovulation and pregnancy rates (2).

There are a limited number of studies that compare letrozole and CC in ovulation induction applied to patients with PCOS (4, 6, 13-19). One of the basic aims of ovulation induction in anovulatory patients is to provide unifollicular development. The argument is that in women with PCOS who have been on treatment for ovulation induction for the first time, letrozole provides an advantage of monofollicular development when compared with CC (8, 9, 15, 18). Additionally, it has been shown that CC-resistant women produce more mature follicles when receiving letrozole (4, 6, 16, 17). In this study, there were no significant differences between the 1st and 2nd groups' number of mature follicles (Table 2). The ovulation rate (37.5%) in group 3 supports that more mature follicles are obtained for women who failed to ovulate with CC. It is a known fact that  $E_2$  levels on hCG day give us an idea of the quality of follicular development. In all similar clinical experiments, the  $E_2$  levels on hCG day for letrozole-treated women are significantly lower than those of CC-treated women (4, 6, 13-18). The total and per follicle  $E_2$  levels on hCG day for group 2 and group 3 (letrozole-treated) were measured 50.2% and 45.9% lower than group 1 (CC-treated) (Table 2). It is a known fact that  $E_2$  values on hCG day are lower because letrozole restricts the hydroxylation of peripheral androgens to estrogens (11). However, there are no existing studies that have analyzed the interaction between this negative effect and pregnancy rates.

According to clinical studies, the endometrium thickness is higher (4, 6, 13, 14, 17), or similar (15), in the letrozole group in comparison to the CC group. In this study, while there were no significant differences between the 1st and 2nd groups' endometrial thickness, in group 3 was significantly thinner (Table-2).

It is a known fact that clomiphene citrate achieves 60%-90% ovulation rates but does not achieve high pregnancy rates (10%-40% per cycle) in ovulation induction (2). According to clinical studies, the ovulation rate of letrozole-treated women with PCOS, receiving ovulation induction treatment for the first time, is higher (13, 17), or similar (15, 18, 19), than the ovulation rate of CC-treated women (15, 18, 19). Additionally, the ovulation rate of CC-resistant women receiving letrozole is higher (range 70%-90%) (4, 6, 14, 16).

In this study, the ovulation rates in groups 1 and 2 were 72.5% and 70%, respectively (Table 2); this result complies with two clinical studies (15, 18). However, the ovulation rate in group 3 (37.5%) (CC-resistant, letrozole-treated) was lower than the ovulation rate obtained in similar studies (4, 6, 14, 16).

According to clinical studies, the pregnancy rates in PCOS patients receiving letrozole for the first time is higher (13, 17), or similar (15, 18, 19) than those receiving CC, and the pregnancy rate increases in CC-resistant women receiving letrozole (18.8%-25.9%) (4, 6, 14, 16). In this study, the pregnancy rate was 20% in group 1 and 17.5% in group 2 without significant differences, but no pregnancy was detected in the CC-resistant group 3 (Table 2). The measured reproduction parameters do not explain why group 3 patients did not become pregnant.

A meta-analysis, summing up the presently available literature published recently (20). The aim of this meta-analysis was to systematically compare the clinical efficacy and safety of letrozole with clomiphene citrate for ovulation induction in women with PCOS. In this meta-analysis letrozole was associated with a number of lower mature follicles per cycle compared with clomiphene citrate. There were no significant differences in pregnancy, abortion and multiple pregnancy rate between the CC and letrozole. This study's conclusion was 'letrozole is as effective as clomiphene citrate for ovulation induction in patients with PCOS'.

In conclusion, this study investigated whether or not 2.5 mg/day letrozole was an alternative drug to CC in the ovulation induction of anovulatory patients. The letrozole was found to be as effective as CC in PCOS patients receiving ovulation induction for the first time. As opposed to the results of previous studies, the ovulation rate for the CC-resistant group in this study was significantly lower, and there were no pregnancies, which is the fundamental success criteria. The fact that 2.5 mg/day of letrozole was unsuccessful in the CC-resistant women, leads us to believe that it is not a better drug than CC.

## References

1. Franks S. Polycystic ovary syndrome. *N Engl J Med* 1995;333:853-861
2. Hananel H, Casper RF, Tulandi T. A new era in ovulation induction. *Fertil Steril* 2006;85:277-84
3. Li TC, Warren MA, Murphy C, Sargeant S, Cooke ID. A prospective, randomised, cross-over study comparing the effects of clomiphene citrate and cyclofenil on endometrial morphology in the luteal phase of normal fertile women. *Br J Obstet Gynaecol* 1992;99:1008-1013.
4. Mitwally MF, Casper RF. Use of aromatase inhibitor for induction of ovulation in patients with an inadequate response to clomiphene citrate. *Fertil Steril* 2001;75:305-9.
5. Hamilton-Fairley D, Franks S. Common problems in induction of ovulation. *Baillieres Clin Obstet Gynaecol* 1990;4:609-25.
6. Mitwally MF, Casper RF. Aromatase inhibition: a novel method of ovulation induction in women with polycystic syndrome. *Reprod Technol.* 2000;10:244-247.
7. Broodie AM, Njar VJ. Aromatase inhibitors and breast cancer. *Semin Oncol* 1996;46:4823-6.
8. Mitwally M, Casper R. Aromatase Inhibitors in ovulation induction. *Semin Reprod Med* 2004;22:61-78.
9. The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril* 2004;81:19-25
10. Kruger TF, Coetsee K. The role of sperm morphology in assisted reproduction. *Hum Reprod Update.* 1999 Mar-Apr;5(2):172-8. Review
11. Casper RF, Mitwally MF. Aromatase Inhibitors for Ovulation Induction. *J Clin Endocrinol Metab* 2006;91:760-771.
12. Buzdar A, Howell A. Advances in aromatase inhibition: clinical efficacy and tolerability in the treatment of breast cancer. *Clin Cancer Res* 2001;7:2620-2635
13. Atay V, Cam C, Muhcu M, Cam M, Karateke A. Comparison of letrozole and clomiphene citrate in women with polycystic ovaries undergoing ovarian stimulation. *J Int Med Res.* 2006;34:73-76.
14. Begum MR, Quadir E, Begum A, Begum RA, Begum M. Role of aromatase inhibitor in ovulation induction in patients with poor response to clomiphene citrate *J Obstet Gynaecol Res.* 2006;32: 502-6.
15. Bayar U, Basaran M, Kiran S, Coskun A, Gezer S. Use of an aromatase inhibitor in patients with polycystic ovary syndrome: a prospective randomized trial. *Fertil Steril.* 2006;86:1447-51.
16. Al-Omari, Sulaiman WR, Al-Hadithi N. Comparison of two aromatase inhibitors in women with clomiphene-resistant polycystic ovary syndrome. *Int J Gynaecol Obstet.* 2000;85:289-291.
17. Begum MR, Ferdous J, Begum A, Quadir E. Efficacy of aromatase inhibitor and clomiphene citrate in induction of ovulation in polycystic ovarian disease (PCOD). *Fertil Steril* 2009;92:853-7.
18. Badawy AM, Aal IA, Abulatta M. Clomiphene citrate or letrozole for ovulation induction in women with polycystic ovarian syndrome? A prospective randomized trial. *Fertil Steril* 2009;92:849-52.
19. Baruah B, Roy KK, Rahman SM, Kumar S, Sharma JB, Karmakar D. Endometrial effects of letrozole and clomiphene citrate in women with polycystic ovary syndrome using spiral artery Doppler. *Arch Gynecol Obstet* 2009;279:311-314.
20. He D, Jiang F. Meta-analysis of letrozole versus clomiphene citrate in polycystic ovary syndrome. *Reprod Biomed Online.* 2011;23(1):91-6.

### Corresponding Author

Hakan Nazik,  
 Department of Obstetrics and Gynecology,  
 Adana Numune Education and Research Hospital,  
 Adana,  
 Turkey,  
 E-mail: drhakannazik@gmail.com

# Transitory tubal dysfunction during vasoactive therapy

Dejan Rancic<sup>1</sup>, Olivera Dunjic<sup>2</sup>, Ivana Pesic<sup>2</sup>, Vesna Stojanovic<sup>3</sup>

<sup>1</sup> ENT Clinic, Clinical Center of Nis, Medical faculty, University of Nis, Serbia,

<sup>2</sup> Institute of Pathophysiology, Medical faculty, University of Nis, Serbia,

<sup>3</sup> Medical faculty, University of Nis, Serbia.

## Abstract

There is an increased tendency to optimize therapy and therapeutic procedures in patients with hearing loss - from those with weakened hearing (patients with a Sensorineural Hearing Loss) to those with acute deafness (Sudden Deafness). Increasing attention is due to the side effects in the application of vasoactive therapy in these patients. The expected positive effects (a hearing enhancement) can be monitored but also the effects that are not initially visible.

The study was conducted in the tertiary health institution. We followed two groups of patients with hearing difficulties that have successively occurred in a period of last 5 years. The patients were followed clinically (otoscopy), audiometrically (pure tone audiometry) and by an impedance-metric method (tympanometry and acoustic reflex). We followed a total of 20 patients of both genders. Two types of infusion therapy were used. A continuous vasoactive therapy was applied to the patients of the first group. The patients of the second group were treated with increasing and decreasing doses of vasoactive infusions. With both groups ampoules of pentoxifyllin (Trental), xantinol nicotinate (Complamin), glucocorticoids (Dexason), vitamin B1 (Aneurin) and ascorbic acid (Vitamin C) were administered.

There was a significant success in treatment of the observed patients groups, especially by using a combined therapy (with increasing and decreasing doses of xantinol nicotinate).

**Key words:** sensorineural hearing loss (SNHL), acute deafness (SD), vasoactive therapy.

## Introduction

Hearing impairment is a handicap for the patient and the further progression of the disease depends on how pronounced the hearing loss is.[1]

With the gradual loss of hearing the patients adapt to this disability with various efforts, but patients with acute deafness experience an especially pronounced anxiety. Acute deafness is considered to be a hearing disorder that manifested itself in a few hours or days (up to 72h), where the tonal audiometry recorded the hearing loss of at least 30 dB at three or more successive frequencies. Time lost before the beginning of treatment has a crucial influence on the outcome of treatment.[2-4]

Besides corticoids which are now recommended for these conditions (but which also have restrictions with long-term application), medications that are intended to cause vasodilation, better oxygenation and improvement of metabolic activity, are also in use. Most common medications used for this purpose are: pentoxifyllin, xantinol nicotinate, nifedipine, cinnarizine, dihydroergotamine mesilate, corticoids, B-vitamins and antioxidants. With their individual but also synergistic effect they manage to ameliorate the hearing loss.[2, 4-7]

The aim of this study was to highlight the advantages of two therapeutic schemes for the group of patients with sensorineural hearing loss and the group of patients with acute hearing loss. We also aimed to indicate the occurrence of clinical and impedance-metric findings during therapy.

## Patients and methods

Patients were divided into two experimental groups. The first group consisted of those patients with sensorineural hearing loss (SNHL), while the other group considered patients with sudden deafness (SD). The study was conducted in a tertiary health institution. We included the total of 40 patients, 18 female and 21 male.

Patients were followed otoscopically, audiometrically (tonal audiometry) and using impedance-

ce-metric methods (tympanometry and stapedial reflex) on admission, in the middle of treatment and at discharge.

The first group (patients with SNHL) received a continuous infusion therapy of 300 mg xantinol-nicotinate in 2 mL solution, 100 mg pentoxiphillin in 5 mL solution and ascorbic acid and B-complex dissolved in 500 ml isotonic solution (NaCl 0.9%).

The second group (patients with SD) received a daily increasing dose of xantinol-nicotinate up to 12 ampoules (2 mL solution per ampoule) per day and then the dose was reduced to the one ampoule until the final application of the therapy.

Using tonal audiometry we followed 125 - 250 Hz, 0.5 - 2 kHz and 2 - 8 kHz frequencies. The improvements in dB were also followed. Impedance-metric values were determined according to the changes in volume (ccm) and pressure (dPa).

The data were compiled with the software package GraphPad Prism 4. Descriptive statistics were reported as mean (x) and standard deviation for continuous data. Comparison of the variables among the experimental groups was made with one-way ANOVA (Kruskal-Wallis test) and t-test. A value of  $p < 0.05$  was considered statistically significant.

## Results

Applied therapeutic procedures have led to hearing improvement in both groups of patients but different final effect. Hearing improvements in the first group for these frequencies was 125-500 Hz,  $x = 12.7$  dB; for frequencies 0.5 - 2 kHz,  $x = 15.9$  dB

and for frequencies 2-8 kHz,  $x = 18.4$  dB (**Table 1**). Improvement in group of SD patients was audiometrically not found for the frequencies of 125-250 Hz,  $x = 19.3$  dB; the frequencies of 0.5 - 2 kHz,  $x = 17.8$  dB and the frequencies of 2-8 kHz,  $x = 19.4$  dB (**Table 1**). At the maximum dosage, this group recorded the changes in tonal audiometry that resembled the catarrh of Eustachian tube (**Table 2**). These changes were resistant to treatment with nasal decongestants, and the standard doses of corticosteroids. Tympanometric examination demonstrated a reduction of 93.4% in static compliance in SD patients ( $x = 0.27$  with SD 0.05) and a flattened look of the tympanometry curve (A apl) (**Graph 1**).

In comparison of the effects from applied therapeutic schemes in the examined patients, we had found certain regularities in audiometric and impedance-metric findings (**Table 3**).

During the application of increasing and decreasing dosages we observed a characteristic otoscopic findings: the emergence of more pronounced hyperemia localized in *pars flaccida* of the tympanic membrane with a definite or easily shortened light reflex. This appearance of the tympanic membrane occurred from 5 to 8 days from the application of vasodilators in SD patients group.

Table 1. Tabulation of hearing improvements in patients from both experimental group at the end of treatment; SNHL – Sensorineural Hearing Loss, SD – Sudden Deafness

\*SD vs. SNHL,  $p < 0.05$

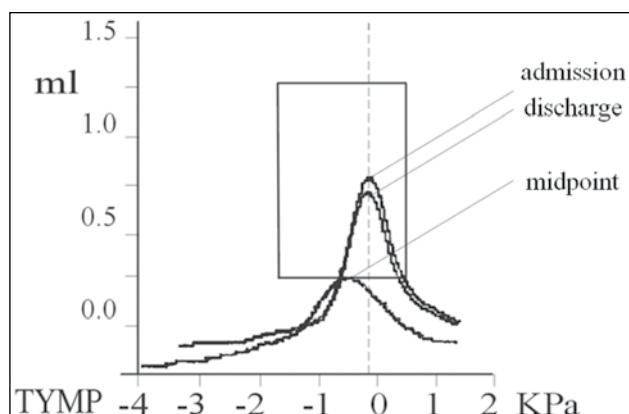
frequency(Hz)	125 - 500 Hz	0.5 - 2 kHz	2 - 8 kHz
SNHL Group	12,7 dB SD 4,1	15,9 dB SD 7,4	18,4 dB SD 3,2
SD Group	19,3 dB* SD 2,3	17,8 dB SD 5,3	19,4 dB SD 2,4

Table 2. Tabulation of hearing improvement in patients with acute hearing loss (SD) during the maximum dosages (in the midpoint of the treatment)

frequency (Hz)	125 - 500 Hz	0.5 - 2 kHz	2 - 8 kHz
SD group	- 9,7 dB SD 3,7	16,1 dB SD 2,1	17,6 dB SD 2,8

Table 3. Showing changes in audiometric findings during vasoactive therapy application; (A = air conductivity, B = bone conductivity, T = tympanogram, SR = stapedia reflex), \**p*<0.05

	DG	ISP.	Admission	Midpoint	Discharge
AUDIO AND IMPEDANCE-METRIC FINDINGS	acute deafness	audiom	A unilateral.mixed. B unilateral.mixed.	A conductivity worsened B unmeasured	A improved (>19dB) B improved (>18dB)
		imped	T normal SR +	T * flattened SR + (+/-)	T normal SR +
	SENZORINEURAL HEARING LOSS	audiom	V sens.-neur.bilateral. B sens.-neur.bilateral.	V sens./mixed. B sens.-neur.	V improved (>16dB) B improved (>14dB)
		imped	T normal SR +	T * mini.flattened SR +	T normal SR +



Graph 1. Changes of the tympanometry curve at the beginning (type A), during the application of the maximum dosage (A apl.) and at the discharge (type A)

**Discussion**

We observed differences in the effectiveness of the applied therapy protocols between patients with hearing loss - from those with weakened hearing (patients with a Sensorineural Hearing Loss, SNHL) to those with acute deafness (Sudden Deafness, SD).

Since the acute deafness is one of the otorhinolaryngology emergencies, we used the standard recommended therapy.[8, 9] Better results provided from examinations of SD group (Table 1, Table 2) are probably the consequence of the constant increase of xantinol-nicotinate in the serum

and its effect on reducing the peripheral resistance with reduction of the cerebral blood flow.[10] Pentoxiphylline has its own contribution by increasing the flexibility of erythrocytes.[11] This was presented with its ability to change the diameter of erythrocytes (which allows the transfer of oxygen through the capillary narrowings of less than 7 microns), inhibits thrombocytes aggregation and reduces blood viscosity.[11] Synergistic action of applied medications together with the antiedematous effect of corticoids on the peripheral neurons, improves the main activity at the receptor.[12, 13]

In acute deafness (SD) the essence of diseases pathway is in the ischemia of the entire cochlea, or of any of its parts, as a primary receptor. The longer the ischemia lasts the more uncertain the recovery will be due to the loss of viability of the cells that make up the organ of Corti.[13-15] In sensorineural hearing loss (SNHL) the process causing the condition is still present to a lesser extent. Perhaps the cochlea was exposed to affection of different ethiological faktor for a longer period of time (hypoxia, infection, endotoxins, autoimmune reactions).[16-18]

Audiometric testing in the mid-point of the treatment with vasoactive therapy indicated the improvement, but during the otoscopy we noted a slight hyperemia of the tympanic membrane with a slightly reduced light reflex. Tympanometry had shown a lower level of maximum compliance

and, depending on the improvement, the findings are accompanied by the stapedial reflex of variable quality (defined as present, reduced, absent) (Table 3). In the midpoint of the application of the therapy we observed a volume change in the middle ear, i.e., a static compliance (Table 5). It was shown with reduced values but the previous values will return with the reducing of the xantinol-nicotinate dosage. It should be underlined that the tumors of the pontocerebral angle are followed by the impaired hearing or the complete loss of hearing and that this symptom occurs in 85-95% of patients and, consequently, it is of great importance to do a AEP (Acoustic evoked potentials) before the administration of the vasoactive therapy.

Given the specificity of the venous blood vessels of the upper body, especially of the head and neck, that are without the developed valves and cerebral arteries with no tunicae muscularis, we can determine that the hyperemia of blood vessels and the mucous membrane at the level of the Eustachian tube and the middle ear is directly related to the described changes. The feeling of pressure in the ears, the existence of small conductive hearing deficit and impaired hearing during speech, although the tonal audiometry showed an objective hearing improvement, may be explained by mucosal edema at the level of the middle ear and tube.[19]

The hyperemia which is observed in this period, and which is most evident in pars flaccida supports the repeatedly overflowed blood vessels of the mentioned regions. This is also an explanation for the pathophysiological changes normally resistant to the application of corticoids and local intranasal decongestants. These findings completely disappeared a couple of days after the intensive therapy is disrupted and a tympanometric and otoscopic findings become completely normal. The findings of the altered appearance of the tympanic membrane (with redness in the pars flaccida) were present in all patients treated with increasing and then decreasing doses of xantinol-nicotinate. Similar changes can be observed with neurologic patients on intensive chemokinetic therapy. [20]

It was found that in patients from the SNHL group, there are no clinical or tympanometric changes while the audiometrically verified improvement shows lower average values of  $x = 12.8$  dB. Greater improvement verified by audiometry findings, and

which has been observed in the group with SD, leaves the possibility of applying this therapeutic scheme and its use in sensorineural hearing loss that is not due to chronic infection or tumor destruction in the middle and inner ear.[21-24]

## Conclusions

In the summary, we experienced in both groups hearing improvements and changes caused by implementation of vasoactive therapy. A greater hearing improvement was reported in the group that received first increasing and then decreasing dosages of xantinol-nicotinate. In this group of patients we observed the occurrence of otoscopic, audiometric and tympanometric changes. The consistency in the appearance of otoscopic changes in the shape of redness in the pars flaccida may be a valuable otoscopic sign - a sign of vasodilator and chemokinetic saturation.

## References

1. Chau, J.K., et al., *Systematic review of the evidence for the etiology of adult sudden sensorineural hearing loss. Laryngoscope*, 2010. 120(5): p. 1011-21.
2. Vergison, A., et al., *Otitis media and its consequences: beyond the earache. Lancet Infect Dis*, 2010. 10(3): p. 195-203.
3. Steinert, R., [Sudden deafness today--a review]. *HNO*, 1986. 34(11): p. 453-60.
4. Van Geert, G., [Sudden deafness]. *Rev Med Brux*, 1997. 18(4): p. 149-51.
5. Glasziou, P.P., M. Hayem, and C.B. Del Mar, *Antibiotics for acute otitis media in children. Cochrane Database Syst Rev*, 2000(2): p. CD000219.
6. McAleer, M., *Communicating effectively with deaf patients. Nurs Stand*, 2006. 20(19): p. 51-4.
7. *Steroids for bacterial meningitis in children? Drug Ther Bull*, 2007. 45(12): p. 93-5.
8. Chen, C.Y., C. Halpin, and S.D. Rauch, *Oral steroid treatment of sudden sensorineural hearing loss: a ten year retrospective analysis. Otol Neurotol*, 2003. 24(5): p. 728-33.
9. Ghosh, A. and R. Jackson, *Best evidence topic report. Steroids in sudden sensorineural hearing loss. Emerg Med J*, 2005. 22(10): p. 732-3.

10. Herrschaft, H., [Therapy of inadequate cerebral circulation]. *Nervenarzt*, 1976. 47(11): p. 639-50.
11. Chodynicka, B., H. Laudanska, and T. Reduta, [Application of pentoxifylline to treatment of leg ulcers: a Polish multicenter study]. *Pol Merkur Lekarski*, 1999. 6(36): p. 322-5.
12. Gaeyvi, M.D., T.V. Sankina, and G.V. Nagornaia, [Effect of pentoxifylline and xanthinol nicotinate on the overall blood pressure and tonus of cerebral and peripheral vessels]. *Farmakol Toksikol*, 1984. 47(1): p. 53-7.
13. Zivic, L., D. Zivic, and S. Stojanovic, [Sudden hearing loss--our experience in treatment with vasoactive therapy]. *Srp Arh Celok Lek*, 2008. 136 (3-4): p. 91-4.
14. Ota, Y. and M. Oda, Lesion site in sudden deafness: study with electrocochleography and transiently evoked otoacoustic emission. *Acta Otolaryngol*, 1999. 119(1): p. 33-41.
15. Cadoni, G., et al., Magnetic resonance imaging findings in sudden sensorineural hearing loss. *J Otolaryngol*, 2006. 35(5): p. 310-6.
16. Tapia, M.C., et al., [Auditory neuropathy]. *An Esp Pediatr*, 2000. 53(5): p. 399-404.
17. Beutner, D., et al., Risk factors for auditory neuropathy/auditory synaptopathy. *ORL J Otorhinolaryngol Relat Spec*, 2007. 69(4): p. 239-44.
18. Brookes, G.B., Immune complex-associated deafness: preliminary communication. *J R Soc Med*, 1985. 78(1): p. 47-55.
19. Givens, G.D. and M.F. Seidemann, Acoustic immittance testing of the Eustachian tube. *Ear Hear*, 1984. 5(5): p. 297-9.
20. Glasscock, M.E., 3rd, et al., A systematic approach to the surgical management of acoustic neuroma. *Laryngoscope*, 1986. 96(10): p. 1088-94.
21. Haberkamp, T.J. and H.M. Tanyeri, Management of idiopathic sudden sensorineural hearing loss. *Am J Otol*, 1999. 20(5): p. 587-92; discussion 593-5.
22. Selesnick, S.H. and R.K. Jackler, Atypical hearing loss in acoustic neuroma patients. *Laryngoscope*, 1993. 103(4 Pt 1): p. 437-41.
23. Stewart, M.G., Outcomes and patient-based hearing status in conductive hearing loss. *Laryngoscope*, 2001. 111(11 Pt 2 Suppl 98): p. 1-21.
24. Watanabe, E., et al., Neurophysiologic monitoring in posterior fossa surgery. II. BAEP-waves I and V and preservation of hearing. *Acta Neurochir (Wien)*, 1989. 98(3-4): p. 118-28.

Corresponding Author  
 Dejan Rancic,  
 ENT Clinic,  
 Clinical Center of Nis,  
 Medical faculty,  
 University of Nis,  
 Nis,  
 Serbia,  
 E-mail: dsrancic@gmail.com



# Study of bacterial contamination of keyboard and mouse in a medical school computer center

Manijeh Mehdinejad<sup>1</sup>, Azar Dokht Khosravi<sup>1,2</sup>, Marjan Afzali<sup>3</sup>, Ali Zarei Mahmoudabadi<sup>2,4</sup>

<sup>1</sup> Dept. of Microbiology, School of Medicine, Iran,

<sup>2</sup> Infectious and Tropical Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences (AJUMS), Ahvaz, Iran,

<sup>3</sup> Public Health Division, AJUMS, Iran,

<sup>4</sup> Dept. of Medical Mycology, AJUMS, Ahvaz, Iran.

## Abstract

The Present study was carried out with the aim to investigate the microbial colonization of computer keyboards and mice in our medical school computer center.

In total, 56 samples were collected from surfaces of multiple-user computers in daily open-access, student computer center of School of Medicine. Two samples were taken by sterile swab from each computer keyboard and mouse and were put in trypticase soy broth. The specimens were subcultured onto blood agar and MacConkey agar after initial incubation at 37 °C. The confirmatory standard biochemical tests were then performed to identify the grown bacteria on the culture media.

All the key boards and 26 (96.29%) out of total tested computer mice were contaminated with at least two kinds of bacteria. CoNS was the most common contaminated bacteria recovered from computer keyboards (36.5%) and mice (38.8%). Other isolated bacteria were Diphtheroids, *Bacillus* spp., and Enterobacteriaceae as the least isolates bacteria. *S. aureus* was detected on the 5 keyboards and 4 mice.

In conclusion, this study has shown the multiple-user computer keyboards and mice as potential reservoir for microbial contamination, some of which are of importance in transmission the nosocomial infections between medical students and patients in hospital wards.

**Key words:** keyboard, mouse, multiple-user computer, bacterial contamination

## Introduction

Computers have been commonly used for multiple purposes in our occupational, recreational and residential environments. In the university en-

vironment, students have been used the computers for regular access to Internet, and use of e-mail and ordinary word processing. Most universities have developed multiple-user “computer laboratories” for general student access. As the popularity of such facilities increases, there is a need to recognize that computer equipment may act as a reservoir for the transmission of potentially hazardous or pathogenic microorganisms (Anderson and Palombo, 2009).

The transmission of nosocomial infections through hospital and medical and dentistry school computer users have been documented in Previous studies (Man et al., 2002; Schultz et al., 2003; Palenik and Hughes, 2005).

The surfaces of computer keyboards and mice are often contaminated with nosocomial pathogens and when those are coming into contact with hands can serve as vehicles for infection transmission (Kramer et al., 2006).

The common bacteria that are commonly present on keyboards are coagulase-negative staphylococci (CoNS), diphtheroids and *Bacillus* spp (Fukada et al., 2008), however, meticillin resistant *Staphylococcus aureus* (MRSA) is also reported in some studies (Rutala et al., 2006). Several investigations have been done on contamination of computer keyboards in various hospital wards due to importance of nosocomial infections (Bures et al. 2000; Hartmann et al., 2004), since some harmful bacteria can survive for >24 h on computer keyboards and keyboards in hospitals may therefore contribute to cross-transmission of bacteria (Devine et al., 2001; Wilson et al., 2005). However little work is done on computers in use by students in medical schools computer centers located outside the hospital environment. The pre-

sent study therefore was carried out with the aim to investigate the microbial colonization of computer keyboards and mice in our medical school.

## Methods

In this study, 56 samples were collected from surfaces of multiple-user computers (28 keyboards and 28 mice) in daily open-access, student computer center of School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. All computers had been in use for a period of 1 to 5 years. Sample collection was performed in the afternoon and at least 6 hours after the commencement of computer operating hours. For sampling cotton swabs inserted in sterile trypticase soy broth tubes were used.

Two samples were taken by direct contact of swabs and moving over each computer keyboard especially space bar, enter keys and mouse and were put in trypticase soy broth and immediately transferred to the microbiology department. A control, 'field blank' swab that was briefly exposed to the air in computer center was also collected.

The specimens were incubated at 37°C for 18-24 hours and were subcultured onto blood agar and MacConkey agar on the consecutive day. The culture media were examined after 24 hours of incubation. Colony characteristics were studied and

Gram's staining, microscopic examination and confirmatory biochemical tests were performed to identify the grown bacteria (Forbes et al., 2007).

## Results

All the computer keyboards and mice in the center showed bacterial contamination. All the keyboards and 26 (96.29%) out of total tested computer mice were contaminated with at least two kinds of bacteria. The total number of bacteria recovered from computer keyboards and mice was 74 and 67 respectively. On the surface of majority of computer keyboards two (27%) and three (60.8%) species of the bacterial normal flora were grown. The rate of bacterial growth on computer mice were 37.8% for two species and 44.5% for 3 species (Table 1).

The isolated bacteria from computer keyboards and mice and the bacterial total count are shown in Table 2. CoNS was the most common contaminated bacteria recovered from computer keyboards (36.5%) and mice (38.8%). Other isolated bacteria were Diphtheroids, *Bacillus* spp., and Enterobacteriaceae as the least isolates bacteria. *S. aureus* was detected on the 5 keyboards and 4 mice and is a well known bacterium to cause nosocomial infections. The recovered bacteria from control blank swab was the same as sample tests except for lower bacterial count and none detection of *S. aureus* strain.

Table 1. Type and total count of bacteria isolated from computers.

Type of isolates	No. of isolated bacteria	
	Keyboard	mouse
one bacterium	0 × 1 = 0	1 × 1 = 1
two bacteria	10 × 2 = 20	14 × 2 = 28
three bacteria	15 × 3 = 45	11 × 3 = 33
four bacteria	3 × 4 = 12	2 × 4 = 8
Total	74	67

Table 2. Microorganisms identified on computer keyboards and mice

Microorganisms	keyboard, No.(%)	mouse, No. (%)	Total
*CoNS	27 (36.5%)	26 (38.8%)	53
Diphtheroids	18 (24.3%)	17(25.4%)	35
<i>Bacillus</i> species	15 (20.3%)	14(20.9%)	29
<i>Micrococcus</i> species	6 (8.1%)	5(7.4%)	11
<i>Staphylococcus aureus</i>	5 (6.75%)	4 (6%)	9
Enterobacteriaceae	3 (4.05%)	1(1.5%)	4
Total	74 (100%)	67 (100%)	141

\* *Coagulase-Negative Staphylococci*

## Discussion

Medical students are in close contact with patients in clinical wards in teaching hospitals, so they may act as a reservoir of microorganisms gains from computer keyboards and mice and transmit the organisms to patients. Besides the computer keyboard and mouse represent a high contact area for all staff, who may spread the organism without direct patient contact (Neely and Sittig, 2002).

In this study, we investigated the number and nature of contaminating microorganisms on the keyboards and mice of multiple-user computers located in computer center of School of Medicine. Several studies have indicated the contamination of computer keyboards and mice with pathogenic bacteria in hospitals and health care settings. In these investigations apart from normal flora, there are reports of detecting MRSA as potential pathogen in nosocomial infections (Kassem et al., 2007; Bures et al., 2000).

In our study the contamination rate of keyboard was high and this shows that microbial contamination also occurs on computer equipments located outside the hospitals and in an environment that is not directly connected to hospital. However most of isolated bacteria in our study was normal flora with CoNS as the most common isolated bacteria. In similar studies conducted in a tertiary care center and in a hospital, CoNS was reported as the major isolated organism at the rate of 100% and 96.7% respectively (Rutala et al., 2006; Dogan et al. 2008) which was higher than our findings. This may be due to existence of higher rate of bacterial contamination in hospital environment. Although, the rate of isolated *S. aureus* in our study was in concordant to their results as 6% which was lower than 17.4% reported rate of *S. aureus* isolation in another recent study (Lu et al., 2009). In the only investigation we have found on literature review which was conducted on computers in a university setting, the high bacterial contamination rate in multiple-user computers was reported which was similar to our findings (Anderson and palombo, 2009). Further study is needed to compare the bacterial contamination of multiple-user computers with the academic staff single-user computers in point of view of bacterial count and nature.

The ideal way for elimination or minimizing the risk of transmission from contaminated keyboards and mice would be performance of hand hygiene before and after use of computers, however this may be impractical and can not be checked for a great number of daily users. So the desired way might be use of a suitable disinfection on a regular basis as has been suggested by other investigations (Rutala et al., 2006).

In conclusion, this study has shown the multiple-user computer keyboards and mice as potential reservoir for microbial contamination, some of which are of importance in transmission the nosocomial infections between medical students and patients in hospital wards.

## Acknowledgements

We are grateful to the staff of computer center of School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran, for their collaboration in sample collection.

## References

1. Anderson G, and Palombo EA. (2009). *Microbial contamination of computer keyboards in a university setting. Am. J. Infect. Control.* 37(6):507-509.
2. Man GS, Olapoju M, Chadwick MV, Vuddamalay P, Hall AV, Edwards A, Kerr. (2002). *Bacterial contamination of ward-based computer terminals. J. Hosp. Infect.* 52(4):314-315.
3. Schultz M, Gill J, Zubairi S, Huber R, and Gordin F. (2003). *Bacterial contamination of computer keyboards in a teaching hospital. Infect. Control Hosp. Epidemiol.* 24:302-303.
4. Palenik CJ, and Hughes EA. (2005). *Microbial contamination of computer keyboards and mice present in dental clinics. Am. J. Infect. Control.* 36:E23.
5. Kramer A, Schwebke I, Kampf G. (2006). *How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. BMC Infectious Diseases.* 6: 130-137.
6. Neely AN, Sittig DF. (2002). *Basic microbiologic and infection control information to reduce the potential transmission of pathogens to patients via computer hardware. J Am Med Inform. Assoc.* 9(5):500-508.

7. Fukada T, Iwakiri H, and Ozaki M. (2008). Anaesthetists' role in computer keyboard contamination in an operating room. *J. Hosp. Infect.* 70: 148-153.
8. Rutala WA, Matthew S. White MS, Gergen MF, and Weber DJ. (2006). Bacterial contamination of keyboards: Efficacy and functional impact of disinfectants. *Infect. Control Hosp. Epidemiol.* 27(4): 372-377.
9. Bures S, Fishbain JT, Uyehara CFT, Parker JM, and Berg BW. (2000). Computer keyboards and faucet handles as reservoirs of nosocomial pathogens in the intensive care unit. *AJIC.* 28 (6): 465-470.
10. Hartmann B, Benson M, Junger A, Quinzio L, Rohrig R, Fengler B, Farber UW, Wille B, and Hempelmann G. (2004). Computer keyboard and mouse as a reservoir of pathogens in an intensive care unit. *J. Clin. Monitor. Computing.* 18: 7-12.
11. Devine J, Cook RPD, and Wright EP. (2001). Is methicillin-resistant *Staphylococcus aureus* (MRSA) contamination of ward-based computer terminals a surrogate marker for nosocomial MRSA transmission and hand washing compliance? *J. Hosp. Infect.* 48:72-75.
12. Wilson APR, Hayman S, Folan P, Ostro PT, Birkett A, Batson S, Singer M, Bellingan G. (2005). Computer keyboards and the spread of MRSA. *J. Hosp. Infect.* 9:390-392.
13. Forbes BA, Sahm DF and Weissfeld AS. (2007). *Bailey and Scott's Diagnostic Microbiology: A textbook for isolation and identification of pathogenic microorganisms, 11th ed., The Mosby Company, St. Louis.* pp. 378 -422.
14. Lu PL, Siu LK, Chen TC, Ma L, Chiang WG, Chen YH, Lin SF, and Chen TP. (2009). Methicillin-resistant *Staphylococcus aureus* and *Acinetobacter baumannii* on computer interface surfaces of hospital wards and association with clinical isolates. *BMC Infect. Dis.* 1:9:164-170.
15. Kassem II, Sigler V, and Esseili MA. (2007). Public computer surfaces are reservoirs for methicillin-resistant staphylococci. *The ISME Journal.* 1: 265-268.

*Corresponding Author*

Azar D. Khosravi,  
Dept. of Microbiology,  
School of Medicine,  
Ahvaz Jundishapur University of Medical Sciences,  
Ahvaz,  
Iran,  
E-mail: khosraviaz@yahoo.com

# Age, Puberty, Sport Participation, Body Mass Index and Aerobic Capacity In Turkish Adolescents

*Murat Ozsaker*

School of Physical Education and Sport, Adnan Menderes University, Aydın, Turkey

## Abstract

This study was performed to investigate the relationship between 1 mile (1609 m) running-walking test performance and body mass index (BMI) in 12-14 years of age children at 6<sup>th</sup>, 7<sup>th</sup> and 8<sup>th</sup> grades of primary education. The study included a total of 1006 voluntary students (529 male and 477 female). After taking body weight and height measurements of students, Body Mass Index (BMI) values were calculated. One mile (1609 m) running-walking test was applied to determine aerobic capacities of children. Correlation and regressions statistical analyses were performed to investigate the relationship between BMI and 1 mile running-walking test. Statistical analyses demonstrated a statistically significant and positive relationship between BMI and 1 mile running-walking test ( $r = .319$ ,  $p = .000$ ).

**Key words:** Aerobic capacity, Body mass index, Adolescence, Sport Participation, Obesity

## Introduction

Obesity is an important health problem that occurs due to the increases in fat tissue with higher energy intake than consumption and could cause social, psychological and serious medical disorders (1,2).

Overweight and obesity are regarded as indicators for many chronic diseases, high blood pressure, psychological disorders, cardiovascular diseases, digestion disorders, cancer, respiratory illness, and skin diseases (3,4,5) and cause considerable economic problems to countries (6).

Obesity, an extension of sedentary lifestyle, is generally accompanied with low physical activity (7, 8, 9, 10) and the rates continue to rise (11, 10,12, 13).

All kinds of physical activities require energy consumption. The interaction between physical ac-

tivity and energy consumption is quite effective on the occurrence of obesity (14, 15); in addition, low physical activity could be seen as a result of obesity. Individuals who lead physically inactive lifestyle or become inactive are more prone to obesity than more active people. Inactivity is observed as a reason for obesity, and then obesity causes inactivity, which results in vicious circle (8).

Several studies (9,16,17) reported that non-school computer use and screen time-composite measures of TV, video games, computers (18), unhealthy eating and excess weight (19, 20), television viewing habits (21) may lead to obesity. Also, due to the inadequate physical activity that is accepted as the cause of obesity in Turkey and the world (22), the rate of obese children, youth and adult gradually increases (23), and this rate is expected to double by 2040 if no precaution is taken (24).

Aerobic endurance is described as resistance of the organism against fatigue during the long-time physical activities. The level of this resistance is largely dependent on the quality of the cardiovascular system and respiratory system. Repeating the exercises many times depends on the use of the cardiovascular system and respiratory system (25).

Aerobic capacity is regarded to be in relation with especially the health of cardiovascular system (26). The researches conducted point out that acceptable levels of aerobic capacity (cardiovascular suitability) are associated with lower risk for coronary heart diseases, obesity, diabetes, high blood pressure, some cancer types and other health problems among the adults and it is said that acceptable levels of aerobic capacity decrease disease related risk factors and fatigue (27, 28).

One of the methods that can be used to determine the physical activity level is the measurement of aerobic capacity. There are different tests to measure aerobic capacity like one mile running-walking

test, 20 m shuttle running test etc. (29). In this study, one mile running/walking test was performed to measure aerobic capacity levels of children.

Body composition can be determined by certain techniques like underwater weighing, skin fold thickness measurements for subcutaneous fat evaluation.

However, the value known as Body Mass Index (BMI) related to body weight and height measurements is found by division of weight by squared height ( $BMI = \text{body weight (kg)} / \text{height}^2 \text{ (m)}$ ) (30). It is one of the common methods used for determining whether the individual has obesity disorder and the level of obesity. BMI is a reliable, easy to measure, cheap and favorite method preferred in studies including large number of participants (31, 32, 33, 34).

For all these reasons, this study aims to determine the relationship between body mass indices and aerobic capacities of Turkish children aged 12-14 in the secondary stage of primary education.

### Material and Method

This study included a total of 1006 voluntary students and was composed of 529 males and 477 females (sedentary: 710, sportive: 296). Children were attending the secondary stage of primary education randomly selected from 4 different state schools in Izmir. In addition, individuals with serious health problems (cardiac disease, cancer etc.) were excluded from the study. All the permissions required for the study were granted from children, their families, directorate of education affiliated by primary schools and the university where the researcher was employed.

### Collection of Body Mass Index Values

Height measurements of participants were taken as cm by a measuring tape fixed on wall at anatomic standing, on bear feet with adjacent heels, with bated breath, head on frontal level, and upper head plate in contact with vertex point. (35). Body weight measurements were taken as kg by a Tefal trademark electronic bascule with t-shirt and short on, bear feet and anatomic standing position (35). Body weight and height values were registered to personal information forms and then formulated ( $BMI = \text{Body Weight (kg)} / \text{height}^2 \text{ (m)}$ ). BMI

values of participants were calculated by the division of body weight with squared height.

### Cardiovascular endurance

Cardiovascular endurance of students were determined by 1 mile (1609 m) running-walking test. Students were asked to complete a predetermined distance of 1 mile (1609 m) as soon as possible and they were accordingly motivated. With the start command, students started to run and the duration was recorded by chronometer (36,37,38). Male students and female students were sorted into two separate groups of 15 and were tested in the athletics tract in a stadium near the school for 1 mile (1609 m) running-walking test in accordance with the protocols.

### Analysis of data

Statistical analysis of data was made by SPSS 15.0 statistical packet software for Windows. Primarily, descriptive statistics of BMI and aerobic capacities of students were performed. Secondly, Pearson correlation analysis was applied to determine the degree of linear relationship between BMI and 1 mile running-walking test and basic linear regression analysis was made for detailed investigation of this relation. Significance level of the analyses were set to  $p < 0.01$ .

### Findings

The mean scores, standard deviations and correlations of 1 mile (1609 m) running-walking test and BMI were given in Table 1. The mean scores of female students in 1 mile (1609 m) running-walking test was 11.45, while the mean score of male students was 9.24 ( $F: 19.210, p < .01$ ); on the other hand, considering the physical activity status, the mean score of individuals leading a sedentary life was 11.35 and the mean score of physically active ones was 7.93 ( $F: 68.983, p < .01$ ). Furthermore, the results of the Pearson correlation analysis demonstrated a statistically significant and positive relation between BMI and 1 mile (1609 m) running-walking test ( $r = .319, p < .01$ ).

$\beta$  coefficients in regression analysis were given in Table 2. One unit increase in BMI means 0.192 sec increase in 1 mile (1609 m) running-walking

Table 1. The means, standard deviations and Pearson correlation between BMI and 1 mile running-walking test

		age	x	sd	1mile running-walking test	BMI (kg/m2)
1 mile running-walking test(minute/second)	Female	12 age	12.96	2.35	-	.319*
		13 age	17.73	2.30		
		14 age	11.95	1.86		
	Male	12 age	10.48	2.09		
		13 age	10.41	2.04		
		14 age	9.54	1.80		
BMI (kg/m)2	Female	12 age	19.47	3.28	.319*	-
		13 age	20.92	4.18		
		14 age	20.88	3.65		
	Male	12 age	19.33	4.01		
		13 age	20.25	3.81		
		14 age	20.51	3.49		

\*p < .01

Table 2. Basic linear regression analysis results

Predictive	B	SD	β	R	R2	t	p
BMI	.192	.017	.257	.738	.545	10.98	.000*
Age	-.525	.081	-.152			-6.504	.000*
Gender	1.807	.126	.333			14.390	.000*
Physical activity status	-2.946	.137	-.505			-21.576	.000*
*p < .01							

duration, while one year increase in age means 0.525 sec decrease in 1 mile (1609 m) running-walking duration. Females had 1.807 sec of higher increase than males, and sportive individuals decreased 1 mile (1609 m) running-walking time by 2.946 sec compared to sedentary individuals. These four variables explain 54.5% of the variances of 1 mile (1609 m) running time (R<sup>2</sup>=0.545).

**Discussion and Conclusion**

The aim of this study is to determine the relationship between aerobic capacity (1 mile running-walking test) and Body Mass Index (BMI) of children aged 12-14 attending to the second stage of the primary education.

As the cost of the advantages brought by sedentary lifestyle and technology, the rate of many disorders reached incredible levels especially in children compared to the past. Physical activity remains low as in many age groups (9, 39) and obesity rates continue to rise (10, 11,12, 13).

There has been a tremendous fight against inactivity and obesity crisis that threatened life in the

last century (40). This inactivity crisis is especially important in the pediatric population as recent data from the Canadian Health Measures Survey (9) suggest that only 7% of children and youth aged 6-19 years participate in at least 60 minutes of moderate- to vigorous-intensity physical activity per day, thus meeting the current physical activity guidelines from Canada (18), the U.S. (41), the U.K (42), Australia (43) and the World Health Organization (44). All these data show that lower physical activity and sedentary behaviors cause many different physiologic and psychological diseases to increase (45, 46).

For this reason, many studies performed to determine the relationship between Body Mass Index and aerobic capacity reported that over amount of body fat has negative effect on the performances in 20 m shuttle running and 1 mile running-walking tests (47, 48,49, 50, 51, 52, 53). The findings of the present study supported the results in literature.

Correlation and regression statistical analyses made in the study indicated a slight and negative relationship, and this relation was found statistically significant as in many previous scientific

studies performed in the past (51,52,53,54,55,56). The findings of the present study are compatible with the results in the literature.

Kamtsios and Digelides (2007) performed a study to measure BMI and aerobic capacities by 20 m shuttle running test of children at 5<sup>th</sup> and 6<sup>th</sup> grades of primary education and their results indicated a significant relation between two variables and BMI values of children decreased with higher levels of aerobic capacities (57). Similarly, Stratton et al. (2007) investigated the relationship between BMI and cardiovascular fitness levels of children aged 9-11 for 6 years and reported a significant relation between these two variables, and BMI levels increased with age, while cardiovascular fitness levels decreased(56). Similarly, the results of the present study indicated that BMI levels increased with age.

On the other hand, Agbuğa et al. (2007) carried out a study to determine the relationship between BMI and 20 m shuttle running test results of children aged 8-12 and reported a low and negative relation (53), and they concluded the relation was statistically significant. In the presents study, a positive and statistically significant relation was observed between BMI and 1 mile running test.

Pekel et al. (2006) investigated the relation between anthropometric characteristics and physical fitness parameters related to performance of female and male children aged 10-13, and reported that 1 mile running time increased in parallel with BMI, and thus the performance was negatively affected (58). Moreover, Sağlam et al. (2002) found no significant relation between the 20 m shuttle running test scores of primary school students (59). In the present study, it was determined once again that overweight and over body fat had negative effect on children. Furthermore, the regression analysis results indicated the effects of BMI, age, gender, and physical exercise on aerobic endurance ( $R^2=0.545$ ).

As the result of Janz et al. (2002), it was emphasized that improvements in cardiovascular suitability among pubertal children in the early and medium periods had positive effects on their blood pressures. It was said that age-related increases in systolic blood pressures of the children who improved their cardiovascular suitability were lower. Meanwhile, it is possible to conclude that efforts

made to increase children's cardiovascular suitability help them enter adolescent period with more healthy cardiovascular profiles(60).

Lately, there have been significant decreases in the aerobic test performances of the adolescents and pubertal children; which is –it is said- caused by adaptation of sedentary life style due to technological advancements, easy access to energy-rich foods and decreased physical activity levels in the society (61). And also, the fact that maximal oxygen consume (max VO<sub>2</sub>) is associated with risk factors of cardio vascular diseases (CVD) emphasizes more measurement of cardiovascular suitability among children and adolescents.

In conclusion, rapidly advancing technological developments and the spread of sedentary lifestyle in the society resulted in decreases in physical activity levels of especially children and adults, and therefore, caused body mass index to increase. According to several studies; sedentary behavior (assessed primarily through increased TV viewing) for more than 2 hours per day was associated with unfavorable body composition, decreased fitness, lowered scores for self-esteem and pro-social behavior and decreased academic achievement among school-aged children and youth (5-17 years). Besides, many studies report a positive correlation between sedentary life style and risk factors associated with health (62). With the results of the study we conducted, it was observed that children tended to give up running without completing the test due to the inactive life style determined by one mile running test and girls tended this more. It may be thought that the reason behind this result was that particularly girls led a sedentary life style in the Turkish culture.

Movements and physical activities in every stage of life -starting from childhood, especially in schools- become quite necessary for physically and spiritually healthier societies.

## References

1. Şarbat G, Demirkol M. *Obesit, Aysel Ekşi (Ed.): I am not ill, Nobel medicine printing. 441-450, 1999.*
2. Cinaz P, Bideci A. *Obesity: Günöz H, Öcal G, Yordam N, Kurtoğlu S (Ed.). Pediatric endocrinology, 1<sup>st</sup> edition, pediatric endocrinology and auxology association 1. Kalkan Printing.487–505, 2003.*



3. Health implication of obesity. National Institutes of Health Consensus development Conference statement: *Ann Intern Med.* 103: 1073-1077, 1985.
4. Parizakava J, Hills A. *Children obesity: Prevention and treatment*, CRC press 2000.
5. Fisch RD, Blick MK, Ulstrom R. Obesity and leanness at birth and their relationship to body habitués in later childhood. *Pediatrics.* 56: 521-528,1975.
6. Finkelstein EA, Fiebelkorn IC, Wang GG. National medical spending attributable to overweight and obesity: How much, and who's paying? *Health Affairs.* 3: 219-226, 2003.
7. Durukan P. *Evaluation of physical activities and psychosocial factors on obesity. Specialty Dissertation, Ankara, 2001.*
8. Gedik O. Obesity and environmental factors. *Turkish J Endocrinology and Metabolism.* 7(2): 1-4. 2003.
9. Colley RC, Garriguet D, Janssen I, Craig C, Clarke J, Tremblay MS. Physical activity of Canadian adults: Accelerometer results from the 2007-2009 Canadian Health Measures Survey, In *Health Rep. Volume 22, Statistics Canada, Catalogue no. 82-003-XPE:(1), 2011.*
10. Tremblay MS, Shields M, Laviolette M, Craig CL, Janssen I, Connor-Gorber S. Fitness of Canadian children and youth: Results from the 2007-2009 Canadian health measures survey. In *Health Rep. Volume 21. Statistics Canada, Catalogue no. 82-003-XIE): (1), 2010.*
11. Shields M, Tremblay MS, Laviolette M, Craig CL, Janssen I, Connor Gorber S. Fitness of Canadian adults: results from the 2007-2009 Canadian Health Measures Survey. In *Health Rep. Volume 21. Statistics Canada, Catalogue no. 82-003-XPE; (1), 2010.*
12. Flegal KM, Carroll MD, Ogdenand CL, Curtin LR. Prevalence and trends in obesity among US adults. 1999-2008 *JAMA.* 303(3):235-41, 2010.
13. Walls HL, Magliano DJ, Stevenson CE, Backholder K, Mannan H, Shaw J, Peeters A. Projected progression of the prevalence of obesity in Australia. *Obesity (Silver Spring), Epub. Dec 13, 2010.*
14. Peker İ, Çiloğlu F, Buruk Ş, Bulca Z. Biochemistry of exercise and obesity, *Istanbul Nobel Medical Printin.* 83-97, 2000.
15. Sothern MS, Gordon ST. Prevention of obesity in young children. *A Critical Challenge for Medical Professionals. Clinic Pediatri.* 42: 101-111, 2003.
16. *Active healthy kids canada. Healthy habits start earlier than you think report card on physical activity for children and youth. Toronto: Activ Healthy Kids Canada, 2010.*
17. LeBlanc AG, Saunders TJ, Larouche R, Colley RC, Goldfield G, Tremblay MS. Relation between sedentary behaviours and health outcomes in childrenand youth. *Joint Meeting of the North American Society for Pediatric Exercise Medicine and the European Group for Pediatric Work Physiology Annual General Meeting, Sep 22-26,; Niagara-on-the-Lake, ON. (abstract), 2010.*
18. Tremblay MS, Warburton DER, Janssen I, Patterson DH, Latimer AE, Rhodes RE, Kho ME, Hicks A, LeBlanc AG, Zehr L, Murumets K, Duggan M. *New Canadian physical activity guidelines. Appl Physiol Nutr Metab.* 36:36-46, 2011.
19. Hancox RJ, Milne BJ, Poulton R. Association between child and adolescent television viewing and adult health: a longitudinal birth cohort study. *The Lancet.* 364(9430):257-262, 2004.
20. Barr-Anderson D, Larson N, Nelson M, Neumark-Sztainer D, Story M. Does television viewing predict dietary intake five years later in high school students and young adults? *Int J Behav Nutr Phys Act.* 6(1):7, 2009.
21. Carson V, Pickett W, Janssen I. Screen time and risk behaviors in 10 to 16 year-old Canadian youth. *Prev Med.* 52(2):99-103, 2009.
22. Centers for Disease Control and Prevention CDC. *Physical activity and good nutrition. Essential elements to prevent chronic diseases and obesity. 2001.* <http://www.cdc.gov/nccdphp/dnpa/dnpaaag.htm>
23. Centers for Disease Control and Prevention CDC. *Promoting better health for young people through physical activity and sports. A report to the President. 2006.* [http://www.cdc.gov/healthyyouth/physicalactivity/promoting\\_health/](http://www.cdc.gov/healthyyouth/physicalactivity/promoting_health/)
24. Wagner P. *Trimming the fat: Poor diet and inactivity hurt children and state's future, Texas Comptroller's Office. Fiscal News.* 5: 23, 2004.
25. Özer D, Özer K. *Motor Development among the Children. Nobel Printing 3<sup>rd</sup> Edition. Ankara.* 183-186, 2004.
26. Leger L. *Aerobic Performance in Docherty, D. (Ed): Measurement in Pediatric Exercise Science. Human Kinetics USA.* 183-223, 1996.
27. Freedson PS, Cureton KJ, Heath GW. Status of field-based fitness testing in children and youth. *Preventive medicine.* 31:77- 85, 2000.

28. U.S. Department of health and human services physical activity and health. A Report of the surgeon general, U.S. Department of health and human services. Centers of disease control and prevention. National center for chronic disease prevention and health promotion. The present's council on physical fitness and sports, 1996. ([www.cdc.gov/nccdphpsgr/sgr.htm](http://www.cdc.gov/nccdphpsgr/sgr.htm)).
29. Welk GJ, Morrow JR, Falls HB (Eds.). *Fitnessgram reference guide*. Dallas, TX: The cooper institute, 2002.
30. Weinstein AR, Sesso HD, Lee IM, Rexrode KM, Cook NR, Manson JE. The joint of physical activity and body mass index on coronary heart disease risk in women. *Arch Intern Med*. 168(8):884-90, 2008.
31. Raustorp A, Pangrazi RP, Stahle A. Physical activity level and body mass index among schoolchildren in out-hospital Sweden. *Acta Paediatrica*. 93:400-404, 2004.
32. Tudor-Locke C, Pangrazi RP, Corbin CB, Rutherford WJ, Vincent SD, Raustorp A. BMI-referenced standards for recommended pedometer-determined steps/day in children. *Preventive Medicine*. 38:857-864, 2004.
33. Özer MK. *Physical Suitability: Nobel printing, Ankara*. 173-230, 2006.
34. Heyward VH, Wagner DR. *Applied body composition assessment: Human Kinetics Books*. 3-105, 2004.
35. Lohman TG, Roche AF, Marorell R. (Eds.) *Anthropometric standardization reference manual: Human kinetics books, Champaign: IL, 1988*.
36. Corbin CB, Pangrazi RP. Are american children and youth fit, *research quarterly for exercise and sport*. 63 (2): 96-106, 1992.
37. *Fitnessgram /activitygram references guide*. The cooper institute, Dallas. 9-17, 2008. (<http://www.fitnessgram.net/FG-59-68.pdf>)
38. Trimmer R, Trimmer J. *Fitness testing in schools: american alliance for health, physical education, recreation and dance (AAHPERD) Physical best test*, 2003. [http://www.sportsci.org/encyc/drafts/Fitness\\_AAHPERD.doc](http://www.sportsci.org/encyc/drafts/Fitness_AAHPERD.doc)
39. Troiano R, Berrigan D, Dodd K. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exerc*. 40:181-8, 2010.
40. Olshansky SJ, Passaro DJ, Hershow RC, Layden J, Carnes BA, Brodt J, Hayhick L, Butler RN, Allison DB, Ludwig DS. A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med*. 352:1138-45, 2005.
41. *Physical activity guidelines advisory committee. Physical activity guidelines advisory committee report*. Washington, DC: U.S. Department of Health and Human Services, 2008.
42. Bull FC, Expert Working Groups. *Physical activity guidelines in the U.K.: Review and recommendations*. Leicestershire, UK: School of Sport Exercise and Health Sciences. Loughborough University, 2010.
43. Okely AD, Salmon J, Trost SG, Hinkley T. *Discussion paper for the development of physical activity recommendations for children under 5 years*. Australian Government Department of Health and Ageing, 2008.
44. World Health Organization. *Global recommendations on physical activity for health*. Geneva. Switzerland. World Health Organization, 2010.
45. Treuth MS, Catellier DJ, Schmitz KH, Pate RR, Elder JP, McMurray RG, Blew RM, Yang S, Webber L. Weekend and weekday patterns of physical activity in overweight and normal-weight adolescent girls. *Obesity (Silver Spring)*. 15(7):1782-8, 2007.
46. Owen N, Bauman A, Brown W. Too much sitting: a novel and important predictor of chronic disease risk? *Br J Sports Med*. 43(2):81-3, 2009.
47. Ruiz A, Sherman NW. Associations between Hispanic children's attitudes toward physical activity, fitness variables, and aerobic capacity. *Tahperd J.1*: 8-11, 2005.
48. Saygin Ö, Polat Y, Karacabey K. The effect of movement trainings on physical suitability features. *F.U. Health Sciences J*. 19(3): 205-212, 2005.
49. Suminski RR, Ryan N, Jackson AS, Poston WS, Foreyt JP. Measuring aerobic fitness of hispanic youth, ages 9 to 12 years. *Medicine and science in sports and exercise*. 31:318,1999.
50. Rowlands AV, Eston RG, Ingledeu DK. Relationship between activity levels, aerobic fitness and body fat in 8- to 10-yr-old children. *J Applied Physiology*. 86(4):1428-1435, 1999.
51. Cureton KJ, Boileau RA, Lohman TG, Misner JE. Determinants of distance running performance in children: Analysis of a path model. *Research Quarterly*. 48, 270-279, 1977.
52. Ihaz F, Finn KJ, Meszaros J, Zsidegh M. Does a modified progressive aerobic cardiovascular endurance run test protocol benefit overweight children? *Research Quarterly for Exercise and Sport*. 77 (Suppl.), A19. 2006.

53. Agbuga B, Konukman F, Yılmaz İ, Köklü Y, Alemdaroğlu U. Evaluation of the correlation between aerobic capacity and bmi of the children aged 8-12. *Sports Sciences Journal Hacettepe J Sport Sciences*.18 (3): 137-146, 2007.
54. Lloyd LK, Bishop PA, Walker JL, Sharp KR, Richardson MT. The influence of body size and composition on fitnessgram test performance and the adjustment of fitnessgram test scores for skinfold thickness in youth. *Measurement in Physical Education and Exercise Science*.7: 205- 226, 2003.
55. Nassis GP, Sidossis LS. Central and total adiposity are lower in overweight and obese children with high cardiorespiratory fitness. *European J Clinical Nutrition*.59: 137-141, 2005.
56. Stratton G, Canoy D, Boddy LM, Taylor SR, Hackett AF, Buchan IE. Cardiorespiratory fitness and body mass index of 9-11-year-old English children: A serial cross-sectional study from 1998 to 2004. *Int J Obesity*.31(7): 1172-1178, 2007.
57. Kamtsios S, Digelides D. Physical fitness, nutritional habits and daily locomotive action of 12-years children with different body mass index. *Inquiries in Sport & Physical Education*. 5(1): 63 – 71, 2007.
58. Pekel HA, Bağcı E, Güzel NA, Onay M, Balcı ŞŞ, Pepe H. Evaluation of antropometric features and physical suitability test results associated with performance among the children playing sports. *Kastamonu Education J*. 14:299-308, 2006.
59. Sağlam F, Rakıcioğlu N, Karağaoğlu N, Hazır T, Cinemre A, Tınazcı C. State of physical suitability and alimentation of the primary school children. *Hacettepe J Sport Sciences*. 13: 2-21, 2002.
60. Janz KF, Dawson JD, Maroney LT. Increases in physical fitness during childhood improve cardiovascular health during adolescence: The Muscatine Study. *Int J Sports Medicine*. 23:15-21, 2002.
61. Tomkinson GR, Leger LA, Olds TS, Cazorla G. Secular trends in the performance of children and adolescents (1980-2000). An analysis of 55 studies of the 20m shuttle run test in 11 countries. *Sports Medicine*. 33(4):285-300, 2003.
62. Tremblay MS, LeBlanc AG, Kho ME, Saunders TS, Larouchel R, Colley RC, Goldfield G, Gorber SC. Systematic review of sedentary behaviour and health indicators in school-aged children and youth. Tremblay et al. *Int J Behavioral Nutrition and Physical Activity*. 8(98):2-22, 2011.

*Corresponding Author*

*Murat Ozsaker*

*School of Physical Education and Sport,  
Adnan Menderes University,*

*Aydın,*

*Turkey,*

*E-mail: muratozsaker@yahoo.com*

# Patient assessment of the quality of standard and one day approach to a diagnostic of a couple infertility

*Aleksandra Trninic Pjevic, Vesna Kopitovic, Artur Bjelica, Irena Bujas, Mirko Pjevic, Djordje Ilic*

Department for Human Reproduction, Clinical Centre of Vojvodina, Novi Sad, Serbia

## Abstract

**Introduction:** Patient satisfaction is extremely important, as it turned out in all the previous analyses, as all the patients with the problem of a couple infertility are exposed to a stress, which they themselves ranked very highly, and it has not only personal, but also other effects on the relationships in a marriage. Clinical implementation of a new, contemporary approach to the diagnostic of a couple infertility (hormones, semen analysis, ultrasonography, hysteroscopy and transvaginal laparoscopy) requires also quality assessment of undertaken procedures by patients.

The aim of this study was to evaluate the quality of undertaken diagnostic- therapeutic procedures by the patients.

**Methods:** In each group, there were 70 patients younger than 38 years with the impossibility of achieving pregnancy after 12 months. Our study group consists of patients who underwent one-day diagnostic procedure, and in the control group were patients in whom some of the standard methods of diagnostic were performed, and thus they were offered the possibility of complete diagnostic and subsequently evaluation of the existing problems, as well as possible therapeutic solutions.

**Results:** There is a statistically significant difference in satisfaction with overall time needed until obtaining the final medical results after undergoing investigation of a couple infertility, ( $\chi^2$   $p < 0.001$ ) in favor of a study group. The analysis indicates that the patients in the study groups, who were subjected to one-day approach to a diagnostic of a couple infertility, significantly better assessed the organization of the procedures undertaken, ( $\chi^2$   $p < 0.001$ ). The average rating of the organization of the undertaken procedures is 3.37 in the study group and 2.7 in the control group (grades 1-4). A total of almost 90% of the patients of the study groups committed themself-

ves to the organization as good or very good, unlike the control group where 25% of patients stated that organization is not good.

**Conclusions:** The high level of satisfaction with regard to the invested time, organization as well as the cost-effectiveness speaks in favor of supporting the concept of "one-day diagnostic", whereas the acceptance by patients is one of the main parameters of the evaluation of a diagnostic method or approach.

**Key words:** infertility, laparoscopy, vagina, hysteroscopy, diagnostic

## Introduction

The best approach to the treatment of a female infertility includes optimal time and procedure in order to avoid superficial or too extensive and too early treatment. Unfortunately, in the field of a couple infertility diagnostic and adequate treatment are often unjustifiably and to a great extent delayed.

The length of a couple infertility is a major parameter in determining the optimal time for a routine investigation and the initiation of a treatment. It is assumed that the longer this period, the lower the probability of conception, but, on the other hand, the investigations are not advised before at least one year of failing to achieve pregnancy.

The individual approach, based on the age, the length of a marriage, data on the regularity of the menstrual cycle, the previous gynecological diseases and operations, determines the time for the initiation of an endoscopic and general evaluation of a female infertility.

As for one stop fertility management (1-3), based on a modern and highly sophisticated technique, it involves a complete evaluation of the female reproductive system in a fast, highly reliable and a secure manner. The methods of one day diagnostic

of infertility (including transvaginal ultrasound, hysteroscopy and transvaginal laparoscopy) provide valid and effective information about the problem of a couple infertility, and thus are a good predictor of fertility in the couple, showing high specificity and sensitivity compared to the standard methods. It is considered that in addition to a better tolerance and less invasiveness, as well as its safe application, this approach will be used as an investigation of the first order in infertile couples.

Therefore, patient satisfaction is extremely important as it turned out in all the previous analyses, as all the patients with the problem of a couple infertility are exposed to a stress, which they themselves ranked very highly, and it has not only personal, but also other effects on relationships in marriage. Clinical implementation of a new, contemporary approach to the diagnostic of a couple infertility requires also quality assessment of the undertaken procedures by the patient.

Aim of this study was to evaluate the quality of the undertaken diagnostic - therapeutic procedures by patients.

## Methods

The study included 140 patients with subfertility. Of these, 70 patients belonged to the study group and 70 to the control group. All the patients were younger than 38 years, while a partner semen analysis was regular.

The investigation was carried out prospectively and partly prospectively whilst retrospectively in the control group, in cases where patients underwent diagnostic by any of the standard methods (including hormonal analysis, semen analysis, HSG and / or laparoscopy and / or hysteroscopy).

The criteria for the inclusion in the study group of this investigation were: inability to achieve pregnancy after at least 12 months of unprotected intercourse, and the criteria for the exclusion from the study group of this investigation were: the previous diagnostic with the standard methods (HSG, laparoscopy, hysteroscopy), the previous surgery, the presence of an ultrasonic visible pathology in the small pelvic (simplex cysts larger than 3 cm, not simplex cysts, intramural myomas greater than 5 cm).

The criteria for inclusion in the control group of this investigation were: the impossibility of

achieving pregnancy after at least 12 months of unprotected sexual intercourse, the early diagnostic of a standard approach (HSG, laparoscopy and hysteroscopy).

Our study group consists of female patients who were assessed suitable for submission to a one-day diagnostic procedure (for obtaining general information about the patient, length of marital infertility, menstrual cycle pattern, the previous eventually carried out diagnostic and therapeutic procedures). They came at the scheduled appointment bringing the results of hormone analysis and semen analysis of their husbands. After transvaginal ultrasound examination, hysteroscopy and transvaginal laparoscopy were performed under general intravenous anesthesia, according to the standard procedure described in the literature (1-3).

The fallopian tube patency was checked by inserting the Foley balloon catheter (8 fr) into the uterine cavity through which the diluted solution of methylene blue dye was instilled. Medical findings obtained upon performing transvaginal laparoscopy were being entered into the database alongside the respective result of the possible pathohistological examination.

All results obtained during the examination were exposed to a female patient or a couple. Taking into account the previously taken results a further plan of action was formed, and subsequently potential therapeutic guidelines and expected possibilities of a conception in individual cases were presented. If one day investigation proved the necessity of abdominal surgical approach, surgery was scheduled.

The control group consists of patients with the problem of a couple infertility, selected after obtaining details that some of the standard methods of diagnostic were carried out, and thus they were offered the possibility to complete the diagnostic evaluation and subsequently the evaluation of existing problems and possible therapeutic solutions. All the data of the previous studies were obtained from medical records and were introduced into the database.

Data from the questionnaires and the results of the performed diagnostic and therapeutic procedures were recorded in a specially designed database and further processed on a computer using an ACCESS database and statistical programs in EXCEL. During statistical analysis, obtained by

these investigations, the following statistical methods were used: univariate statistical methods (absolute number, number of respondents, mean, median, standard deviation), multivariate statistical methods (multifactorial analysis), tests of statistical significance: student t-test, parametric X<sup>2</sup>-test.

**Results**

The average age of patients in the study group was 31.47 ± 3.83 years (24-37) and 31.61 ± 3.28 years (24-37) in the control group. There was no significant difference in the age of patients in both the study and control group (p = 0.813).

Groups Analysis of patients by level of education showed the following results, which are shown in Table 1. There was a statistically significant difference in the distribution of the level of education in groups (χ<sup>2</sup> p = 0.035).

Patients' satisfaction with the quality of the diagnostic-therapeutic procedures was assessed by the questionnaire survey.

*Question: How satisfied are you with the information you had got from the doctor before starting the diagnostic procedure?*

The answers are presented in the tables, for both groups, Table 2. There was not any statistically significant differences in the degree of satis-

faction with the information from doctors in both groups (χ<sup>2</sup> p = 0.752), and the average score of the obtained information was 3.45 in the study and 3.77 in the control group (grades from 1-4).

*Question: How are you satisfied with the care and attention given during diagnostic - therapeutic procedures?*

This question was significantly most often responded by patients in both groups with satisfied, 78.6% in the study and 71.5% in the control group.

*Question: How satisfied are you with the length of time spent to obtain the final diagnostic - therapeutic results of your marital infertility?*

There is a statistically significant difference in satisfaction with overall time spent to obtain the final investigation results of a marital infertility, (χ<sup>2</sup> p < 0.001) in favor of the test group, Figure 1.

*Question: How would you assess the organization of the diagnostic procedures undertaken?*

The analysis shows that the patients of the study group, who were subjected to one-day access to diagnostic of a couple infertility, significantly better assessed the organization of the procedures undertaken, (χ<sup>2</sup> p < 0.001), Figure 2. The average rating of the organization of undertaken procedures is 3.37 in the study, and 2.7 in the control group

Table 1. The distribution of education in the study and control group

	Groups		Total
	Tested group	Control group	
Primary (%)	4 (5,7%)	6 (8,6%)	10 (7,1%)
Secondary (%)	23 (32,9%)	38 (54,3%)	61 (43,6%)
High (%)	20 (28,6%)	14 (20,0%)	34 (24,3%)
University (%)	23 (32,9%)	12 (17,1%)	35 (25,0%)
TOTAL	70 (100%)	70 (100%)	140 (100%)

Table 2. Satisfaction with the information provided from a physician, before starting the diagnostic-therapeutic procedures

	Groups		Total
	Tested group	Control group	
Very dissatisfied (%)	0 (0%)	0 (0%)	0 (0%)
Unsatisfied (%)	3 (4,3%)	2 (2,9%)	5 (3,6%)
Satisfied (%)	32 (45,7%)	36 (51,4%)	68 (48,6%)
Verysatisfied (%)	35 (50,0%)	32 (45,7%)	67 (47,9%)
TOTAL	70 (100%)	70 (100%)	140 (100%)

(grades 1-4). A total of almost 90% of the patients of the study group committed themselves to the organization as good or very good, unlike the control group where 25% of patients stated that organization is not good.

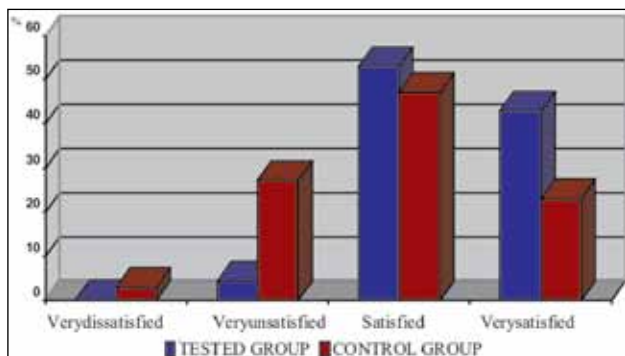


Figure 1. Satisfaction with overall time spent to get final investigation results of a marital infertility

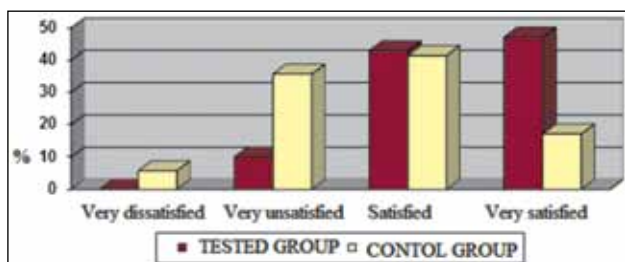


Figure 2. Assessment of the organization of the undertaken procedures

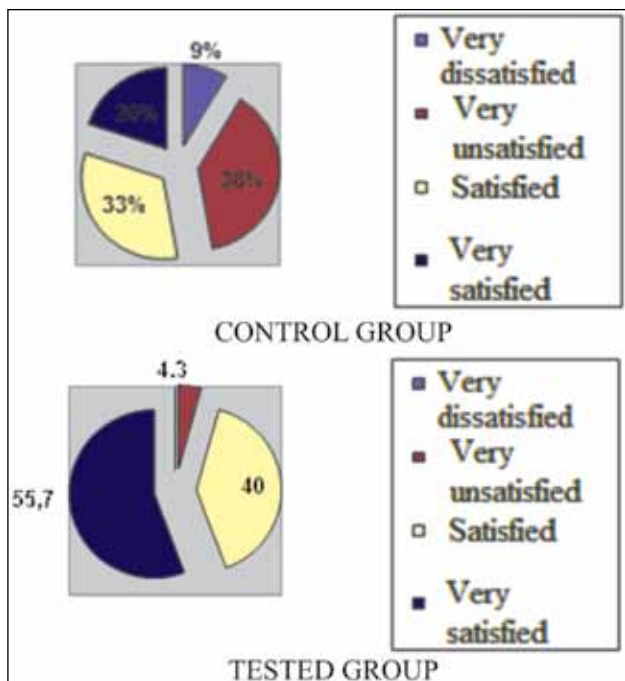


Figure 3. Satisfaction with the cost of diagnostic procedures undertaken in relation to the invested time

*Question: How would you assess the cost of diagnostic procedures undertaken in relation to the time needed for the final diagnostic?*

A significantly higher satisfaction was found with the cost of diagnostic procedures undertaken in relation to the invested time in the study group ( $\chi^2 p < 0.001$ ). Many as 55.7% said very satisfied in the study group, while 38.6% were dissatisfied in the control group (Figure 3).

### Discussion

In the late eighties and early nineties of the last century, investigations of a patient's satisfaction in the field of diagnostic and treatment of infertility were carried out, and they showed dissatisfaction present in the various aspects (the method of conducting research, the lack of emotional support). Then, Sauter and associates in the UK, in 1998, and Schmidt in Denmark, in 2003 conducted a new investigation in relation to a patient's satisfaction with the diagnostic and treatment of a couple's infertility, as well as in relation to their expectations (4-6).

The analysis of female patients by level of education showed a statistically significant difference in the distribution of the level of education in groups ( $\chi^2 p = 0.035$ ). Evidently, the dominant majority (54.3%) of patients in the control group were of high school education. In the study group there were significantly more patients with a high, and a higher level of education. This probably indicates that these patients get more informed through the media, where this method of "one day" diagnostic was promoted in our surroundings in 2006. They are perhaps more demanding in relation to the applied diagnostic investigation, insisting on a modern and an efficient approach. It is certain that they are likely users of the Internet where the information about the new methods spread quickly, pointing out where it is undertaken and what are the benefits. On the official website of the Clinical Centre, Department of Obstetrics and Gynecology there is a section dedicated to "one-day" diagnostic of a married couple's infertility.

There was not any statistically significant differences in the degree of satisfaction with the information-giving obtained from the doctors in both groups, and the average score of the information given was 3.45 in the study group and 3.77 in

the control group (grades 1-4). Furthermore, the analysis shows the existence of the satisfaction with the care and attention given during the diagnostic- therapeutic procedures (78.6% declared themselves satisfied with the study and 71.5% in the control group).

According to the literature data, one might expect that in the control group, and among female patients with lower levels of education and qualifications, exist greater degree of satisfaction with medical services (Hall and Dorman, 1990) (7).

In accordance with the citations by Souter and Schmidt, satisfaction was recorded with the provided care and attention during the diagnostic and treatment (in their citations 87% said to be satisfied or very satisfied) and our results coincide with their citations. As it has been confirmed in all studies, our female patients ranked most highly :information and explanation given and the attitude of the doctor is surprisingly. Furthermore, our patients have expressed their highest grades in surprisingly positive 50% of cases in the study group, and 45.7% in the control group with regard to the information and explanation given. This differs significantly from the results of the extensive studies in the UK where 25% said they had received no or little information about their problems and possibilities of diagnostic and reasons for its implementation.

There is a statistically significant difference in the satisfaction in respect to overall time needed to obtain the final results of a couple infertility investigation, ( $\chi^2 p < 0.001$ ) in favor of the study group. Patients who have undergone the process of diagnostic and eventual treatment of the “one day” approach declared themselves in the 52.9% as satisfied and 42.9% as very satisfied with the time they needed until the completion of investigation and treatment. On the other hand, the patients in the control group almost 30% declared themselves dissatisfied on this issue, which is very understandable considering the length of their examination and treatment.

According to the literature, the same number (30%) considered that the length of the investigation is too long, and these are patients in whom the standard approach to diagnostic and treatment of a couple infertility was applied. All this leads to the advantages of the new concepts of a diagnostic and treatment of infertility, which in addition to a greater efficiency implies a higher patient satis-

faction. Female patients in the study group significantly better assessed the organization of the undertaken procedures with average grade of 3.37, as opposed to 2.7, as the patients in the control group assessed. A total of almost 90% of the patients of the study groups committed themselves to the organization as good or very good, unlike the control group where 25% of patients stated that organization is not good. It appears that in the standard approach, according to the “step by step” system patients learn retrogradely that previous results, although accurate, in fact, were not sufficient and that more tests followed. Therefore, it is the source of a frustration, discontent and gaining the impression that this is a bad organization in the approach to infertility investigation, but basically it is a standard concept, which now in the era of a fast and modern living does not meet expectations. The estimation of the cost of diagnostic procedure undertaken in relation to the time you needed for the final diagnostic showed significantly higher satisfaction in the study group. As many as 55.7% in the study group said they were very satisfied, while 38.6% in the control group were dissatisfied . This is another argument in favor of establishing of the one day approach to a diagnostic of a married couple infertility.

Patient satisfactions extremely important, as it turned out in all the previous analyses that all the patients with the problem of a couple infertility are exposed to a stress, which they themselves ranked very highly, and it has, not only personal, but also other effects on the relationships in a marriage. Just the stress of bearing a problem of infertility is deteriorating during a number of medical examinations (4-6), especially if they are accompanied by a lack of an explanation, assertiveness and empathy from the medical staff. So, it is also with this perspective important, to provide such an approach to the problem of infertility, which will not only aggravate stress and move a couple away from the further attempting to identify and solve the problem but also partners away from each other. A high level of satisfaction with regard to the invested time, organization and cost effectiveness suggests support for the concept of “one-day” diagnostic, whereas the acceptance by patients is one of the main parameters in the evaluation of onedagnostic method or approach (8-9).



## Conclusions

There is a high level of satisfaction with the information given by the physician, as well as with the provided care and attention, which is considered very important among patients with the problem of a marital infertility, during the diagnosis and treatment.

A high level of satisfaction with regard to invested time, organization as well as cost effectiveness of their time suggests support for the concept of "one-day diagnostic", since the acceptance by patients is one of the main parameters in the evaluation of a diagnostic method or approach.

## References

1. Gordts S, Campo R, Puttemans P, Verhoven H, Gianaroli L, Brosens J and Brosens Ivo. Investigation of the infertile couple: a one-stop outpatient endoscopy approach. *Human Reproduction* 2002; 7:1684-87
2. Taylor A, Sharma M, Al Khouri A, Goumenou A, Tsirkas P, Scot P, Magos A. Investigation of infertility: One stop fertility clinic. *British Medical Journal* 2002; 325: 1116.
3. Magos A, Al Khouri A, Scot P, Taylor A, Sharma M, Buck L, Chapman L, Tsirkas P, Kailas N, Mastrogamvrakis G. One stop fertility clinic. *Journal of Obstetrics and Gynecology* 2005; 25:153-59.
4. Souter VL, Penney G, Hopton JL, Temleton AA. Patients satisfaction with the management of infertility. *Hum Reprod* 1998;13:1831-1836.
5. L. Schmidt, B.E. Holstein, J. Boivin, H. Sångren, T. Tjørnhøj-Thomsen, J. Blaabjerg, F. Hald, A. Nyboe Andersen, and P.E. Rasmussen. Patients' attitudes to medical and psychosocial aspects of care in fertility clinics: findings from the Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme. *Hum. Reprod.* 2003;18: 628-637.
6. L. Schmidt, B.E. Holstein, J. Boivin, T. Tjørnhøj-Thomsen, J. Blaabjerg, F. Hald, P.E. Rasmussen, and A. Nyboe Andersen. High ratings of satisfaction with fertility treatment are common: findings from the Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme. *Hum. Reprod.* 2003; 18: 2638-2646.
7. Hall JA. and Dornan MC. Patients sociodemographic characteristics as predictors of satisfaction with medical care: a meta-analysis. *Soc Sci Med* 1990;30:811-818.
8. ESHRE Capri work shop group. Optimal use of infertility diagnostic test and treatments. *Hum Report* 2000; 15:723-732.
9. Gordts S, Campo R, Rombauts L et al. Transvaginal hydrolaparoscopy as an outpatient procedure for infertility investigation. *Hum Reprod* 1998;13:99-103.
10. Trninić Pjević A. Transvaginal endoscopy in one-stop fertility investigation: our experience, *HealthMED* 2010; 4(4): 720-727.

Corresponding Author,  
Aleksandra Trninić Pjević,  
Department for Human Reproduction,  
Clinical Centre of Vojvodina,  
Novi Sad,  
Serbia,  
E-mail: [aleksandra.trninic\\_pjevic@yahoo.com.sg](mailto:aleksandra.trninic_pjevic@yahoo.com.sg)

# Syntax of social life in postpartum depression: Mother-child interaction

*Luiz Carlos de Abreu<sup>1</sup>, Alberto Olavo Advincula Reis<sup>1</sup>, Modesto Leite Rolim Neto<sup>1,2,3</sup>, Nádia Nara Rolim Lima<sup>3</sup>, Jesus de Souza Cartaxo<sup>3</sup>, Elizabeth Alves Silva<sup>3</sup>, Saulo Araujo Teixeira<sup>2</sup>, Cícero Hedilberto Pereira Filgueiras Macedo<sup>2</sup>*

<sup>1</sup> Postgraduation Program in Public Health, Universidade de São Paulo, Brazil,

<sup>2</sup> Department of Medicine, Universidade Federal do Ceará, Brazil,

<sup>3</sup> "Suicidology" Research Group, Universidade Federal do Ceará, Brazil.

## Abstract

**Purpose:** Understand the difficulties and experienced of individuals suffering from postpartum depression, related to mood disturbances, the mother-child bond and its repercussions in the meanings established for the experience of being a mother.

**Methods:** Forty-one patients were interviewed, with ages ranging from 20 to 49 years, from a total of 106 attended at the Primary Care Unit, in the interior of the state of Paraíba, Brazil. A sample of 21 women was selected, presenting an inclusion profile, propitious to mapping postpartum depression. The eligible patients were referred by two PSF (Health Family) teams (one each from the urban and rural zones), aimed at diagnosing the psychic disturbance of the perperium. They were accompanied by a psychologist and all signed an informed consent form. A field diary supported the information recorded. Beck's Depression Inventory complemented the inclusion and follow-up of the patients. The data were analyzed statistically.

**Results:** We confirmed the findings of the most recent studies that infant abandonment in the postpartum period occurs in situations where multiple and serious factors add up, such as misery (86.7%), little schooling (67%), lack of a support network (36.5%), estrangement of the mother's family relations (12%) and lack of paternal involvement (91.5%).

**Conclusion:** The feeling of psyching pain and suffering, resulting from postpartum depression, is the most emphasized by women (87%) because it triggers the greatest discomfort, due to the difficulty in overcoming it.

**Key words:** mother-child bond; postpartum depression; narratives; psychic illness.

## Introduction

Hear other's narratives, from complaint to symptoms, involves a series of abstract and practical ways that conflux to more diverse and different ways to comprehend words, voices, images, asks, pains, illnesses and psychic sufferings. It references in the context of informants<sup>[1]</sup> and in the perspective of what we see as disease.

The employing of oral narratives for patients with postpartum depression make possible to translate the dynamic of their life histories and recurrent discourses of events and living significations. Nowadays, studies disclose that 10% a 20% of parturient women develop postpartum depression<sup>[2,3]</sup>. Probably, maternal psychopathologies antecedents and previous puerperal psychiatric disturbs can act as risk factors<sup>[2,4,5,6,7,8]</sup>.

We tried to translate, during postpartum period, the effects that arose of patient's deep stigmas. They needed proximity to what made them inhabit themselves, quaking their own references of child and maternity and the sense of disease could offer to comprehension of pregnancy and life histories that came from this route.

In this direction, we faced movements of messaging construction. These messages tried to translate the superposition of symptoms and the space of necessities and recurrences, making possible to outline the nature of rejecting on mother-children bond<sup>[1]</sup>. We tried to classify those aspects that appeared as disease, specially on composing the seriousness of symptoms and their reflexes to patients and their familiar units<sup>[9]</sup>.

This classification was made by searching in the arduousness and difficulties lived by patients with postpartum depression, by decoding their memories of speeches, conflicts, complaints and symptoms,

through the look for treatment. We identified the necessity of questioning the disease and the prescriptions employed, especially when they become obscure and put in risk their own speech.

Basing on this reflection, we tried to select, between the patients of a healthcare center located on Alto Sertão, the driest region of Paraíba, northeast Brazil, the difficult found by women, by manifesting pain and psychic illness, by outlining the presence of disease and finding linkage between personal experiences and what this makes possible on developing actions and behaviors in their relationship with newborns. It was fundamental on this process to realize that disease process involves subjective experiences of physical and emotional changes, making spaces of mess in peoples' conducts on mobilizing words and editing their meaning register.

Recognize this experience allows us to comprehend the articulation between places occupied by women, along their pregnancies, establishing the course of their wishes, their contacts, their voices, and giving them intentions that represents giving off, absence and desertion with themselves and the others. In this aspect, the gap between what we know and what we do is lethal<sup>[10,11,12]</sup>.

Disease incorporates the reality of what have been lived for presenting a new way of perceiving the world surrounding them, starting from their greater or minor absorption of this reality, in managing social life through their own life story, in a course of wishing to translate some truths by what is not said in living with disease. Being recorded, these histories become accessible to multiple readers, opening new interpretation possibilities<sup>[1]</sup>.

We aimed to know the arduousness of daily practices lived by patients with postpartum depression, as a disturb of humor, at mother-children bond and its reflexes on significations and meanings for the experience of maternity.

## Methods

Was intended to create narratives for social research, reconstructing events, starting from informant's perspective<sup>[12]</sup>, as much directly as possible, looking for "what" and "who" involved on recontextualization<sup>[13]</sup> of what provokes, when said, an own manner to translate the narrated si-

tuation. It is fundamental, on this process, not to lose the way people talk about their lives, the employed language and the links they made<sup>[14]</sup>.

As a method to data generation, we fixed our attention on using narrative interviews. This process made us able to establish a particular relationship with social cartography, helping us to search, find and outline, graphically and abstractly, narratives<sup>[15,16]</sup>.

We interviewed 41 patients, with aging starting from 20 to 49 year-old, from a total quantity of 106 users of a basic healthcare unit located in Paraíba, northeast Brazil, along two years of surveying. A sample group of 21 of them was chosen for presenting compatible profiles to postpartum depression tracking. Chosen patients must be from two selected healthcare units with suspected postpartum depression, must be under psychic treatment and sign the free consent and permission term. A logbook recorded important data of indices, symptoms, effects and reactions to pharmacological prescription.

For data caption we used narrative interviews, done by researcher. Beck's inventory for depression completed the criteria for inclusion or exclusion and patients watching. Our procedures were designed by the approval given by the official council for ethics in research from Universidade Federal do Rio Grande do Norte, free consent and permission term, individual interviews, integral interview transcription, detailing of verbal expressions, dividing material on indexed and non-indexed, establishing similarities and designing collective trajectories.

Theme analysis<sup>[17,18]</sup> and social cartography<sup>[19]</sup> were guidelines to graphic and abstract interpretations of narratives.

## Results

A particular characteristic of this female population is the manner they describe postpartum depression. For them, depression is a "nervous sickness" or "disease of nerves", because they learned to call it this way. So the terms "nerves" or "nervous system" acquires new meanings of subjective lived situations, for these women. DSM-IV criteria for depression accepts those terms like common expressions to Latin-American people

to call this state of vulnerability facing some circumstances or experiences that generates pain or anxiety<sup>[20,21]</sup>.

In their narratives, patients use to manage their own expressions of social relationships, comparing senses and significations of their reality, like: "firing branches", "withered rose", "color-changing chameleon", just to cite some of them. Narratives, therefore, create a field for collective attitudes, legitimating certain identities and conducting people to take positions according to their cultural profile<sup>[1]</sup>.

The symbols they venerate constitute a determinant factor on translating the children rejection, especially when they relate: "when fire blows out, nothing remains, everything is ashes", "garden with withered flowers is not a garden". The perspective of mother is disclosed by pain and psychic illness. We can infer that terms like "ashes", "dry", "fire" and "blow out" translate their feelings, linking them to spaces of affection and emotion, like the negation of legitimating the newborn. We confirmed the recent finds in most of researches<sup>[22]</sup> of child abandon in postpartum period happens in situations with it occurs in addition to poverty (86,7%), lack of formal education (67%), lack of public services (36,5%), damaged relationships between them and their mothers (12%) and absence of child's father (91,5%).

However, the opportunity of telling their own histories makes these women the opening of spaces in which they can expose their pathologies and turn familiar what seems strange. In this scenario, the interpretation of diseases course make viable to find possible territories of "pain" and "illness" of being<sup>[23]</sup>.

We outlined three groups of symptoms starting of Beck's Depression Inventory: light, medium and serious. 21 patients have confirmed the diagnosis of postpartum depression. Three of them presented light symptoms, seven of them presented medium symptoms and eleven of them disclosed serious clinical signals. Other diseases had an statistic association index ( $p=0,013$ ). Symptoms of serious depression, besides of living in rural areas were predominant (80% or more).

History of psychopathologies in family was positive for 40% of patients. Half of total had been unsatisfied of pharmacological treatment that doctors prescribed. Five patients presented suicide ideation and one of them actually attempted to suicide.

## Discussion

Pain and psychic illness feelings that come from postpartum depression are the most focused by women (87%) because it is what unleashes most of discomforts, by its difficult domination. While corporal symptoms are palpable, tolerable, psychic illness is endless, permanent and make patients need to tell and retell their histories related to uncertain process of their disease. The illness of being them carry<sup>[23]</sup> is a factor that unleashes social exclusion, because it affects interpersonal relationships. From it becomes a conflict of enunciates: Why me? What fault has my child? Until this feeling are going to follow me? I want to see nobody! Am I sick of nerves? This way, patients with postpartum depression establish their trajectories starting from the illness they feel, notably through past-to-past, past-to-present and present-to-present relationships.

Therefore, depression configures, on puerperal period, a fragilized emotional situation, making necessary to alert that pain patients feel and talk about is a signal of what body feels, of what mind experiences. Suffering is the immediate reflex of this pain. Rejection as immediate reaction provokes weird sensations, the translation of strange, as a moment when pain and psychic illness achieve their most important insertion on reality of decrypting what you feel and what you live<sup>[24,25]</sup>. Love is maintained in obscure position, maybe to open its doors and recover the necessary enchantment to the sense life can give to comprehension of maternity.

## References

1. Silva, D.G.V., Mercedes, T. *Narrativas como técnica de pesquisa em enfermagem. Revista Latino Americana de Enfermagem* 2002; 5:423-432.
2. Ribeiro, C.S. *Depressão Pós-parto e Relação Mãe e Filho. PsiquWeb* 2002; [online] disponível em: <http://gballone.sites.uol.com.br/colab/carmem.html>.
3. Stein, A., Gath, D.H., Bucher, J., Bond, A., Day, A., Cooper, P.J. *The relationship between postnatal depression and mother-child interaction. British Journal of Psychiatry* 1991; 158: 46-52.
4. Gozzano, J.O.A., Politi, P., Abib, S.C.V., & Oliveira, S.M.P.B. *Estado de depressão e ansiedade em puérperas. Jornal Brasileiro de Psiquiatria* 1989; 38(2): 59-61.

5. Meltzeres, K.R. Puerperal mental illness, clinical features and classification: A study of 142 mothers-and-baby admissions. *British Journal Psychiatry* 1985; 147: 647-654.
6. Mcneil, T.F. A prospective study of post partum episodes. *Acta Psychiatrica Scandinavica* 1986; 74:205-216.
7. Seger, C.P. A controlled study of postpartum mental illness. *Journal of Mental Science* 1960; 106: 214-230.
8. Tetlow, C. Psychosis of child bearing. *Journal of Mental Science* 1955; 101:629-639.
9. Ricouer, P. *Tempo e narrativa*. Campinas: Papyrus, 1994.
10. Jamison, K.R. *Uma mente inquieta: memórias de loucura e instabilidade de humor*. São Paulo: Martins Fontes, 1996.
11. Jamison, K.R. *Quando a noite cai: entendendo o suicídio*. Rio de Janeiro: Gryphos, 2002
12. Jovchelovitch, S., Bauer, M.W. Entrevista narrativa. In Bauer, M.W., Gaskell, G. (Eds.), *Pesquisa qualitativa com texto, imagem e som: Um manual prático*. Petrópolis, RJ: Vozes, 2002; 90-113.
13. Bernstein, B. *The structuring of pedagogic discourse*. Londres: Routledge, 1990.
14. Spencer, J. *The usefulness of qualitative methods in rehabilitation: Issues of meaning of context and of change*. *Archives Physical Medicine and Rehabilitation* 1993; 74: 119-126.
15. Abell, P. (1987). *The syntax of social life: The theory and method of comparative narratives*. Oxford: Oxford University Press.
16. Abell, P. (1993). *Some aspects of narrative method*. *The Journal of Mathematical Sociology*, 18, 93-134.
17. Mayring, P.H. *Qualitative inhaltsanalyse: Grundlagen und Techniken*. Basel: Beltz, 1983.
18. Minayo M.C.S. *O desafio do conhecimento: Pesquisa qualitativa em saúde*. São Paulo/Rio de Janeiro: Hucitec/ABRASCO, 1994.
19. Santos, B.S. *Uma cartografia simbólica das representações sociais*. *Revista Crítica de Ciências Sociais* 1988; 24: 139-172.
20. *DSM-IV. Manual diagnóstico e estatístico de transtornos mentais*. Porto Alegre: Artes Médicas, 1995.
21. Jacques, M.G., & Wanderley, C. *Saúde mental e trabalho: Leituras*. Petrópolis: Vozes, 2002.
22. Falceto, O.G., Quinalha, A.F., Tetelbom, M., Maltz, F., Campos, M.T., & Sanchez, P. (1994). *Abandono infantil no pós-parto imediato: estudo de casos*. *Revista de Psiquiatria do Rio Grande do Sul* 1994, 16(1): 80-88.
23. Peres, U.T. *Depressão e melancolia*. Rio de Janeiro: Jorge Zahar Editores, 2003.
24. Cacilhas, A.A. *Considerações sobre a comunicação e o vínculo mãe-bebê e correlações com o trabalho psicoterápico*. *Revista de Psiquiatria do Rio Grande do Sul* 1993;, 15(3): 227-233.
25. Scochi, C.G.S., Lima, R.A.G., Delácio, L.B., Morais, G.R. *O conhecimento de puérperas sobre o cuidado com o recém nascido: avaliação da influência da internação em uma maternidade de um hospital-escola*. *Revista Brasileira de Enfermagem* 2002; 45(1): 36-43.

Corresponding Author  
 Luiz Carlos de Abreu  
 University of São Paulo,  
 Brazil,  
 E-mail: luizcarlos@usp.br

# Dietary and other factors as risks of hyperemesis gravidarum

Gul Kiziltan<sup>1</sup>, Mendane Saka<sup>1</sup>, Perim Turker<sup>1</sup>, Aydan Ercan<sup>2</sup>

<sup>1</sup> Baskent University, Health Science Faculty, Department of Nutrition and Dietetics, Ankara, Turkey,

<sup>2</sup> T.C. İstanbul Bilim University, School of Health, Department of Nutrition and Dietetics, İstanbul, Turkey.

## Abstract

**Aim:** To evaluate the dietary and other factors on the risk of hyperemesis gravidarum (HG) during pregnancy.

**Method:** A case-control study was conducted on thirty women with hyperemesis gravidarum and 30 women without hyperemesis gravidarum admitted to Women Health Care Clinic in Ankara over 3-months period. Dietary (total energy, total fat, saturated fat, monounsaturated fat and polyunsaturated fat intakes) and non-dietary (prepregnancy body mass index, previous history of HG, parity, gravidity, education level, employment and smoking status) factors were evaluated on the risk of hyperemesis gravidarum (HG).

**Results:** Cases and controls were similar with respect to education levels, employment status, gravidity number and smoking habits. Frequency of previous history of hyperemesis gravidarum was significantly higher in women with HG than the women without HG ( $p < 0.05$ ). The odds ratio for the women with hyperemesis history was 0.7 (95% CI 0.6, 0.9). There were no statistically significant associations with energy (OR = 2.0; 95% CI 0.7, 5.9), total fat (OR = 1.2; 95% CI 0.4, 3.3) and saturated fat (OR = 2.0; 95% CI 0.7, 5.9) intakes and HG.

**Conclusion:** Despite, previous history of hyperemesis gravidarum had a significant effect on the risk of HG, the etiology of the HG in pregnancy is still unclear because, hyperemesis gravidarum most probably is a disease with a complicated etiology, with several independent and interdependent risk factors.

**Key words:** hyperemesis gravidarum, etiology, dietary factors

## Introduction

Nausea and vomiting of pregnancy are a known and common symptom of pregnancy affecting 50

% to 90 % of pregnant women.<sup>[1]</sup> Hyperemesis gravidarum (HG), intractable nausea and vomiting, is rare but more serious. The incidence of HG shows large variations between different countries and settings. The prevalence of hyperemesis varies from 0.5 to 3.2% and the condition is the most common cause of hospitalization during the first half of pregnancy<sup>[2,3]</sup>. Hyperemesis gravidarum are characterized by prolonged intractable vomiting leading to severe fluid and electrolyte imbalance, ketonuria and weight loss of 5 % or more.<sup>4</sup> Hepatic, renal and neurological damage has been reported for the untreated condition. The typical onset is between 4 and 8 weeks of gestation, continuing to about 14 to 16 weeks of gestation.<sup>[5,6]</sup>

The exact etiological mechanism leading to HG is far from fully understood. However, the occurrence of hyperemesis gravidarum coincides closely with the gestational age when human chorionic gonadotropin ( $\beta$ hCG) production is at its peak. Hyperemesis gravidarum is also more frequently associated with multiple pregnancies and their higher  $\beta$ hCG levels.<sup>[7]</sup> Some patients with hyperemesis gravidarum have major elevations of total thyroxine (TT4) and free thyroxine (FT4) in the first trimester. Elevated FT4 associated with suppressed TSH levels may be present in up to 60 % of women presenting with hyperemesis gravidarum. Whether HG is caused by hyperthyroidism<sup>[8,9]</sup>, a hyperestrogenic state associated with hyperstimulation by  $\beta$ hCG<sup>[10]</sup>, and/or other mechanisms is still not known.

It is known that social factors are associated with hyperemesis gravidarum. Women living in overcrowded or unfamiliar circumstances were found to be more likely to suffer from HG than the others.<sup>[11]</sup> Other studies have investigated the impact of parity, smoking and body weight. A low body mass index (BMI) has been shown to be associated with hyperemesis gravidarum.<sup>[12]</sup> In

the small amount of epidemiologic research that has been conducted, the role of diet as an etiologic factor has received scant attention. A case-control study showed that prepregnancy high daily intake of saturated fat increases the risk of severe hyperemesis gravidarum.<sup>[13]</sup> In an other study, the study findings suggest that a healthy diet that includes vegetables and fish are associated with a lower risk of developing hyperemesis<sup>[14]</sup>

We conducted this case-control study for the reason of to evaluate the factors on the risk of HG in Turkish pregnant women.

## Methods

### *Participants*

The study was carried out at a private Women Health Care Clinic in Ankara between October 2009 and January 2010. Thirty women with hyperemesis gravidarum and 30 women without hyperemesis gravidarum were enrolled in the study. Ethics approval was obtained before the commencement of the study. Each patient gave informed consent to the study. The hyperemesis gravidarum was defined as prolonged nausea and vomiting during pregnancy that required hospitalization before 25th week of pregnancy. Women with urinary tract infection, diabetes mellitus, pancreatitis and thyroid disorder, were excluded from the study. Gestational age was based on the last menstrual period and ultrasonographic examination in all subjects. Personal information, including lifestyle, educational level, occupation, gravidity and smoking habits were collected via a questionnaire by face to face.

### *Body Mass Index (BMI)*

Pre-pregnancy BMI was calculated as weight in kg divided by height in meters squared using self-reported pre-pregnancy weight and height. Current weight was measured by dietitians and BMI was calculated from the same equation. The mean BMI values were evaluated by World Health Organization (WHO) classification.<sup>[15]</sup>

### *Dietary intake*

Participants completed a self-administered semi quantitative food frequency questionnaire. This food frequency questionnaire was admini-

stered with reference to the participant's average diet during the year just before her pregnancy. The food consumptions were analyzed using the Nutrient Data Base Program (BEBIS).

### *Statistical analysis*

The statistical analyses were performed with SPSS version 13.0 for Windows. Comparison between normal pregnant women and patients with hyperemesis gravidarum were performed with the Mann-Whitney *U* test. Logistic regression analyses were conducted to test for statistical differences between the groups when the dependent variables were dichotomous. The relative risks were calculated as crude odds ratio (OR) with 95% confidence intervals (CIs). Differences were considered significant with a probability value of  $p < 0.05$ .

## Results

The age and the physical characteristics of the study population were presented in Table 1. The mean ages for cases and controls ( $\pm$  standard deviation) were similar ( $25.1 \pm 4.23$  years and  $25.2 \pm 3.54$  years, respectively). The average pre-pregnancy body mass index for cases was  $23.8 \pm 2.14$  kg / m<sup>2</sup>, for controls was  $23.5 \pm 2.24$  kg/m<sup>2</sup>. These differences between groups were not statistically significant ( $p > 0.05$ ). Present values of BMI for cases and controls were  $23.7 \pm 3.01$  kg /m<sup>2</sup> and  $24.5 \pm 2.66$  1kg /m<sup>2</sup>, respectively. And the differences between groups were statistically significant ( $p < 0.05$ ). During pregnancy the women with hyperemesis lost  $4.52 \pm 1.52$ kg body weight, the women without hyperemesis gained  $2.95 \pm 1.92$  kg body weight ( $p < 0.05$ ). The mean gestational age of the women with and without hyperemesis was  $7.7 \pm 1.70$  weeks and  $7.1 \pm 1.48$  weeks respectively.

Table 2 represented the association between non-dietary risk factors and hyperemesis gravidarum. Cases and controls were similar with respect to education levels and employment status. Gravidity number and smoking habits were also similar in groups. Frequency of previous history of hyperemesis gravidarum was significantly higher in women with HG than in women without HG ( $p < 0.05$ ). The odds ratio for the women with hyperemesis history was 0.7 (95 % CI 0.6, 0.9).

Table 1. Age and physical characteristics of the women with and without hyperemesis gravidarum

	Women with hyperemesis gravidarum (n=30)		Women without hyperemesis gravidarum (n=30)	
	Mean	SD	Mean	SD
Age (year)	25.1	4.23	25.2	3.54
Body weight (kg)*	63.4	5.36	66.6	7.04
BMI (kg/m <sup>2</sup> )*	23.7	3.01	24.5	2.66
Prepregnancy body weight (kg)	64.0	5.48	63.8	7.91
Prepregnancy BMI (kg/m <sup>2</sup> )	23.8	2.14	23.5	2.24
Weight change (kg)*	-4.52	1.44	2.95	1.92
Gestational age (weeks)	7.7	1.70	7.1	1.48
Parity	1.4	0.77	1.2	0.43

\* $p < 0.05$ 

Table 2. Logistic regression-derived crude odds ratio (OR) and 95% confidence limits (95% CI) for the association between non-dietary risk factors and hyperemesis gravidarum

Characteristics	Women with hyperemesis gravidarum (n=30)		Women without hyperemesis gravidarum (n=30)		OR	95% CI
	n	%	n	%		
Education						
≤ High school	25	83.3	26	86.6	0.9	0.2-3.8
College	5	16.7	4	13.4		
Employed						
Yes	4	13.3	3	10.0	1.1	0.3-5.3
No	26	86.7	27	90.0		
Gravidity						
Primigravida	11	36.7	9	30.0	0.8	0.3-2.3
Multigravida	19	63.3	21	70.0		
Smoker						
Yes	4	13.3	7	23.3	0.5	0.1-2.1
No	26	86.7	23	76.7		
Hyperemesis history						
Yes	14	46.7	1	3.3	0.7	0.6-0.9
No	16	53.3	29	96.7		
BMI (prepregnancy)						
< 22	10	33.3	6	20.0	1.7	0.6-5.5
≥ 22	20	66.7	24	80.0		

The estimates of the effect of energy and fat intake on the risk of HG were shown in Table 3. We observed no statistically significant associations with energy (OR = 2.0; 95% CI 0.7,5.9), total fat (OR = 1.2; 95% CI 0.4, 3.3), saturated fat (OR = 2.0; 95% CI 0.7,5.9) intakes and HG.

## Discussion

Approximately, four million women in the United States and 350,000 women in Canada experience nausea and vomiting of pregnancy (NVP). Hyperemesis gravidarum (HG), a severe form of nausea and vomiting, affects one in 200 pregnant women. Among Asian women the incidence and severity of HG appears greater than in women of



Table 3. Logistic regression–derived crude odds ratio (OR) and 95% confidence limits (95% CI) for the association between dietary risk factors and hyperemesis gravidarum

Nutrient*	Cases (n=30)		Control (n=30)		OR	95% CI
	n	%	n	%		
Total energy intake						
< 2052 kcal‡	20	66.7	15	50.0	2.0	0.7, 5.9
> 2052	10	33.3	15	50.0		
Total fat						
< 72 gm‡	15	50.0	14	46.7	1.2	0.4, 3.3
> 72	15	50.0	16	53.3		
Saturated fat						
< 25 gm‡	10	33.3	15	50.0	2.0	0.7, 5.9
> 25	20	66.7	15	50.0		
Monounsaturated fat						
< 25 gm‡	15	50.0	15	50.0	1.0	0.4, 2.9
> 25	15	50.0	15	50.0		
Polyunsaturated fat						
< 17 gm‡	16	53.3	14	46.7	1.3	0.5, 3.8
> 17	14	46.7	16	53.3		

\* Average daily intake of each nutrient is dichotomized by the approximate median of the control distribution

‡ Referent

European origin.<sup>[16,17,18]</sup> Unfortunately we have no data on the incidence of HG in Turkey.

Risk factors vary among different populations. Genetic and socioeconomic differences may have a role in the pathogenesis. In a study it was reported that NVP was significantly associated with low educational level and low-income level.<sup>[19]</sup> In a large prospective multicenter study of pregnant women vomiting (excluding HG) occurred in 56 % of women and was more common in the first pregnancy, in younger women, in women with fewer than 12 years of education, in nonsmokers and in obese women.<sup>[20]</sup>

Previous research has implicated nulliparity, young age, and low education as factors that increase the risk of HG or lower-grade nausea and vomiting during pregnancy.<sup>[21,22]</sup> In our study, women expecting their first baby (parity 0) had a decreased risk for hyperemesis, parity 3 showed a lower or than parities 1-2. On the other hand, socioeconomic factors (low education level, employment status) had no significant effects on the risk of HG.

Nausea and vomiting in one pregnancy have been associated with an increased risk of nausea and vomiting in a subsequent pregnancy. Women with a previous diagnosis of hyperemesis may be

more likely to get the diagnosis in the second pregnancy, compared with women with no previous hyperemesis.<sup>[22]</sup> Furthermore, about one-third of multigravidas with hyperemesis gravidarum admitted to the hospital were reported to have been treated in hospital for the same condition in a previous pregnancy.<sup>[23]</sup> Finding in our study was the increased risk of recurrent hyperemesis in women who had hyperemesis in the previous pregnancy.

Women with HG are at risk of malnutrition. Weight loss of more than five percent of prepregnancy weight has been associated with retarded fetal growth.<sup>[24]</sup> In recent studies it was shown that hyperemesis infants are born earlier and weight less.<sup>[25,26]</sup> The women with hyperemesis gravidarum in our study had lost 6.5 % of their body weight. We found a significantly higher percentage of prepregnancy underweight women who developed hyperemesis as compared to a control group of women without hyperemesis. BMI was lower in the hyperemetic patients in the late first trimester, but there was no statistically difference before pregnancy. In our findings the relative risk for developing hyperemesis in underweight subject was 1.44. Lagiou et al<sup>[27]</sup> also have found that pre-pregnancy BMI was not an important determinant of reported nausea during

first trimester with or without vomiting. It is possible that with larger numbers, these differences might reach significance.

It was previously hypothesized that women with below normal pre-pregnancy BMI would experience a lesser degree of nausea and vomiting due to a stronger maternal anabolic drive to fat accumulation.<sup>[28]</sup> Our findings do not support this hypothesis, because pregnant women in all BMI categories (underweight or overweight) with hyperemesis gravidarum had severe vomiting (>5 times/day). The findings of a study were parallel to our results.<sup>[29]</sup>

A previous study showed that maternal smoking before pregnancy was a significant protective factor against NVP even after consideration of maternal age, parity and working situation.<sup>[30]</sup> Our results do not indicate that tobacco smoking reduces the risk of HG. Also in other studies found no overall association between smoking and NVP, but among women who smoked, a relationship was seen between the amount smoked and NVP.<sup>[31,32,33]</sup>

Other non-dietary factors, serum beta-hCG levels, prolactin, thyroid hormones, serum electrolyte or blood gases, as risks of HG has been mentioned previously in the literatures<sup>5,26,32,33</sup>. Our study did not include these analyses; it is a limitation of this study.

Dietary factor such as a high daily intake of primarily saturated fat before pregnancy was reported to cause a higher risk for HG only in a study conducted by Signorella et al.<sup>[13]</sup> The mechanism was defined as saturated fat lead to increase circulating levels of estrogen. A positive correlation between intakes of PUFA and umbilical cord oestriol concentration was reported in a more recent study, in which long-chain omega-3 fatty acids were significantly negatively correlated with oestriol concentration.<sup>[34]</sup> In a study published in 2009, no association was found between fat intake and oestriol concentration during pregnancy.<sup>[35]</sup> In present study the women with hyperemesis had high fat intake before pregnancy than controls, and it was significantly different. But we found no association with saturated fat remained a risk factor for HG.

In conclusion, we found no evidence that maternal age, pre-pregnancy BMI, smoking, social status (education level, employment status) and dietary fat are important determinants of HG. Only previous history of hyperemesis grava-

rum had a significant effect on the risk of HG. The etiology of the HG in pregnancy is still unclear. Because hyperemesis gravidarum most probably is a disease with a complicated etiology, with several independent and interdependent risk factors. Moreover, these factors may play different roles in different populations.

## References

1. Eliakim R, Abulafia O, Sherer DM. Hyperemesis gravidarum: a current review. *Am J Perinatol* 2000;17:207-218.
2. Vikanes, AV, Grjibovski A, Vangen S, et al. Variations in prevalence of hyperemesis gravidarum by country of birth: a study of 900,074 births in Norway, 1967-2005. *Scand J Public Health* 2008;36:135-142..
3. Bennett T, Kotelchuck M, Cox C, et al. Pregnancy-associated hospitalizations in the United States in 1991 and 1992: a comprehensive view of maternal morbidity. *Am J Obstet Gynecol* 1998; 178:346-354.
4. Tsang I, Katz V, Wells S. Maternal and fetal outcomes in hyperemesis gravidarum. *Int J Gynecol Obstet* 1996; 55:231-5.
5. Goodwin TM, Montoro M, Mestman JH, et al. The role of chorionic gonadotropin in transient hyperthyroidism of hyperemesis gravidarum. *J Clin Endocrinol Metab* 1992; 75:1333-1337.
6. Al-Yatama M, Diejomaoh M, Nandakumaran M, et al. Hormone profile of Kuwaiti women with hyperemesis gravidarum. *Arch Gynecol Obstet* 2002;266: 218-222.
7. Ballabio M, Poshychinda M, Ekins RP. Pregnancy-induced changes in thyroid function, role of human chorionic gonadotropin as putative regulator of maternal thyroid. *J Clin Endocrinol Metab* 1991; 73: 824-831.
8. Glinoeer D, Nayer P de, Bourdoux P, et al. Regulation of maternal thyroid during pregnancy. *J Clin Endocrinol Metab* 1990; 71:276-287.
9. Krentz AJ, Redman H, Taylor KG. Hyperthyroidism associated with hyperemesis gravidarum. *Br J Clin Pract* 1994; 48:75-6.
10. Depue RH, Bernstein L, Ross RK, et al. Hyperemesis gravidarum in relation to estradiol levels., pregnancy outcome and other maternal factors: a seroepidemiologic study. *Am J Obstet Gynecol* 1987; 156: 1137-41.
11. Douchar N. Nausea and vomiting in pregnancy a review of the problem with particular regard to psychological and social aspects. *Br J Obstet Gynaecol* 1995; 102:6-8.

12. Rochelson B, Vohra N, Darvishzadeh BA, et al. Low prepregnancy Ideal Weight: Height Ratio in Women with Hyperemesis Gravidarum. *J Reprod Med* 2003; 48: 422-424.
13. Signorello LB, Harlow BL, Wang S, et al. Saturated fat intake and the risk of severe hyperemesis gravidarum. *Epidemiology* 1998; 9:636-640.
14. Hagen M, Vikanes A, Brantsaeter A.L, et al. Diet before pregnancy and the risk of hyperemesis gravidarum. *Br J Nutr* 2011; 1-7.
15. WHO/FAO. Diet, nutrition and the prevention of chronic diseases. Report of a joint WHO/FAO expert consultation. WHO Technical Report Series 916. Geneva, World Health Organization 2003.
16. Mazzotta P, Maltepe C, Navoiz Y, et al: Attitudes, management and consequences of nausea and vomiting of pregnancy in the United States and Canada. *Int J Gynecol Obstet* 2000; 70:359-65
17. Koch KL, Frissora CL. Nausea and vomiting during pregnancy. *Gastroenterol Clin N Am* 2003; 32: 201-234.
18. van Oppenraaij RH, Jauniaux E, Christiansen OB, et al. Predicting adverse obstetric outcome after early pregnancy events and complications: a review. *Hum Reprod Update* 2009; 15:409-421
19. Price A, Davies R, Heller SR, et al. Asian women are at increased risk of gestational thyrotoxicosis. *J Clin Endocrinol Metab* 1996; 81:1161-3.
20. Fairweather D: Nausea and vomiting in pregnancy. *Am J Obstet Gynecol* 1968; 102: 135-175.
21. Klebanoff MA, Koslowe PA, Kaslow R et al. Epidemiology of vomiting in early pregnancy. *Obstet Gynecol* 1985; 66:612-6.
22. Hod M, Orvieto R, Kaplan B, et al. Hyperemesis gravidarum. E review. *J Reprod Med* 1994: 39:605-12.
23. Cedergren M., Brynhildsen J., Josefsson A., et al. Hyperemesis gravidarum that requires hospitalization and the use of antiemetic drugs in relation to maternal body composition. *Am J Obstet Gynecol* 2008; 198: 412-415.
24. Broussard CN, Richter JE. Nausea and vomiting of pregnancy. *Gastroenterol Clin North Am* 1998; 27: 123-51.
25. Trogstad LIS, Stoltenberg C, Magnus P, et al. Recurrence risk in hyperemesis gravidarum. *BJOG* 2005; 112: 1-5.
26. Gross S, Librach C, Cecutti A. Maternal weight loss associated with hyperemesis gravidarum. A predictor of foetal outcome. *Am J Obstet Gynecol* 1989; 160: 906-9.
27. Lagiou P, Tamimi R, Mucci LA, et al. Nausea and vomiting in pregnancy in relation to prolactin, estrogens and progesterone: a prospective study. *Obstet Gynecol* 2003; 101(4):639-44.
28. Bailit JL. Hyperemesis gravidarum: Epidemiologic findings from a large cohort. *Am J Obstet Gynecol* 2005; 193:811-4.
29. Ben-Aroya Z, Lurie S, Segal D, et al. Association of nausea and vomiting in pregnancy with lower body mass index. *Eur J Obstet Gynecol and Repro Biol* 2005; 118:196-198.
30. Vilming B, nesheim BI. Hyperemesis gravidarum in a contemporary population in Oslo. *Acta Obstet Gynecol Scand* 2000; 79:640-643.
31. Huxley RR. Nausea and vomiting in early pregnancy: its role in placental development. *Obstet Gynecol* 2000; 95(5):779-82.
32. Gadsby R, Barnie-Adshead AM, Jagger C. A prospective study of nausea and vomiting during pregnancy. *Br J General Pract* 1993; 43:245-8.
33. Kallen B, Lundberg G, Aberg A. Relationship between vitamin use, smoking, and nausea and vomiting of pregnancy. *Acta Obstet Gynecol Scand* 2003; 82:916-920.
34. Nagata C, Iwasa S, Shiraki M, et al. Association of maternal fat and alcohol intake with maternal and umbilical hormone levels and birth weight. *Cancer Sci* 2007; 98:869-873.
35. Lof M, Hilakivi-Clarke L, Sandin SS, et al. Dietary fat intake and gestational weight gain in relation to estradiol and progesterone plasma levels during pregnancy: a longitudinal study in Swedish women. *BMC Womens Health* 2009; 9:10.

Corresponding Author  
 Gul Kiziltan,  
 Baskent University,  
 Health Sciences Faculty,  
 Department of Nutrition and Dietetics,  
 Baglica Kampusu,  
 Ankara,  
 Turkey,  
 E-mail: gkizilta@baskent.edu.tr

# Predictive markers for one-year outcome in patients with Stemi treated with primary Percutaneous Coronary Intervention (PCI)

Nebojsa Krstic<sup>1</sup>, Milan Pavlovic<sup>1</sup>, Goran Koracevic<sup>1</sup>, Aleksandar Stojkovic<sup>1</sup>, Svetlana Pavlovic<sup>2</sup>

<sup>1</sup> Clinic of Cardiovascular Diseases of the Clinical Centre in Nis, Nis, Serbia,

<sup>2</sup> Center for anesthesiology and reanimation, Clinical Center Nis, Serbia.

## Abstract

**Objective:** The objective of this study was to investigate prognostic significance of markers of necrosis and inflammation, echocardiographic parameters and risk factors for coronary heart disease, for one-year outcome (death, recurrent MI, repeated percutaneous coronary intervention-PCI, surgical revascularization) after primary PCI, which was used as a measure of treatment in patients with acute myocardial infarction with ST-elevation (STEMI).

**Patients and Methods:** The study included 116 patients with STEMI (72 males and 44 females, aged  $63.35 \pm 10.33$ ), treated with primary PCI. Check up of patients, in order to investigate prognostic significance of the markers of inflammation (fibrinogen, CRP, leukocytes), the markers of necrosis (Tn I, CPK, CKMB, CKMB mass), echocardiographic parameters (EF, EED, ESD) and risk factors of coronary heart disease (age, sex, hypertension, diabetes mellitus, hyperlipidemia, obesity, smoking) compared to one-year outcome (death, recurrent MI, repeated PCI, surgical revascularization), was conducted through telephone interviews and ambulance controls.

**Results:** Most commonly registered intra-hospital complications were angina pain, ECG dynamics and hemodynamic instability, while the most common complications within a year of hospitalization were: death, recurrent MI and angina pain. It was shown that CRP is a predictor of one-year recurrent MI (OR 1.11, 95% CI 1.002 to 1.23;  $p < 0.05$ ), leukocytes count is a predictor of the need for repeated PCI (OR 1.36; 95% CI 1.08-1.7;  $p < 0.01$ ), EF is a predictor of recurrent MI (OR 0.99; 95% CI 0.89-0.99;  $p < 0.05$ ) and the need for surgical revascularization (OR 0.91; 95% CI 0.82-0.99;  $p < 0.05$ ), while age, male gender, hypertriglyceridemia, dia-

betes mellitus and smoking are predictors of death, whereas age is an independent risk factor of death (OR 1.62; 95% CI 1.14-2.31;  $p < 0.01$ ) and recurrent MI (OR 1.11; 95% CI 1.03-1.19;  $p < 0.01$ ).

**Conclusion:** Based on the results of this study, it can be concluded that CRP is a predictor of recurrent MI, the leukocytes count is a predictor of the need for repeated PCI, EF is a predictor of recurrent MI and a need for surgical revascularization, while age, male gender, hypertriglyceridemia, diabetes mellitus and smoking are predictors of death within one year of STEMI and primary PCI treatment.

**Key words:** STEMI, PCI, one-year outcome, and in-hospital and post-hospital complications

## Introduction

Cardiovascular diseases are the leading cause of morbidity and mortality in developed countries and in developing countries, with a tendency of significant increase in recent decades. Cardiovascular mortality annually worldwide is estimated at 12 million.

Primary percutaneous coronary intervention (pPCI) is a therapy of choice for the management of patients with acute ST-elevation myocardial infarction (STEMI). Despite the very low incidence of major adverse cardiovascular events (MACE) after contemporary pPCI, certain categories of patients with STEMI still have an adverse forecast. It is noteworthy that the risk of adverse outcomes is highest within the first 30 days after infarction (1).

Primary PCI can be applied in patients with contraindications to fibrinolytic therapy, and it proved to be effective in opening occluded coronary arteries in relation to fibrinolytics. According to the recommendations, primary PCI should be

used in patients with STEMI and in patients with newly developed left bundle branch block within 12 hours of symptom onset, and in patients within 12 to 24 hours of the complication onset in cases of severe heart failure, heart rhythm disorders, and proven persistent ischemia (2).

Intra-hospital and one month mortality was higher in patients with STEMI compared with NSTEMI ACS (2.99 vs. 5.26%) but there was worse 7-year mortality rate than STEMI patients (3).

These results support the invasive management of patients with acute coronary syndromes to reduce short-term case fatality. Identification of patients at risk for major adverse cardiovascular events (MACE) might help selecting candidates for aggressive treatment or early discharge after primary percutaneous coronary intervention (pPCI).

There are several key pathogenetics mechanisms involved in MACE occurrence in short and long term follow up. They can be connected with endothelial dysfunction and atherosclerotic processes (inflammation, cardiovascular risk factors, glycoregulation), severity of occlusion (location and number of occluded vessels, spreading of occlusions), level of cardiac necrosis (biomarkers of cardiomyocyte necrosis), functional performance of cardiovascular system (ejection fraction, heart failure, blood pressure) and preparation of PCI (time to PCI, type of stent, technique, etc..) (4).

Successful reperfusion sometimes is not associated with a decrease in infarct size and with repairing of the regional and global contractile function of the left ventricle, usually due to untimely started therapy or reocclusion (in 10 to 25% of cases) (5), but its benefit is reflected in a significant reduction of one-year mortality. It is important not only to achieve reperfusion, but also to maintain adequate flow through the reperfused coronary artery in order to improve left ventricular function and even survival. Optimal water flow rate in 90 minutes is achieved in 50% of patients who receive fibrinolytic therapy, while in patients treated with primary PCI, it is even greater (6).

The aim of this research was to examine the prognostic significance of the markers of necrosis and inflammation, echocardiographic parameters and traditional risk factors for coronary heart disease in relation to one-year outcome (death, recurrent MI, repeated PCI, surgical revascularization)

after primary PCI, which is applied as a measure of treatment of patients with STEMI.

### **Patients and methods**

A prospective study included patients with STEMI, hospitalized in the Coronary unit at the *Clinic of Cardiovascular Diseases of the Clinical Centre in Nis*, in the period from May 1, 2009 to December 31, 2009. The sample consisted of 116 patients with STEMI (72 males and 44 females) treated medically and with primary PCI within 12 hours of early symptoms.

Clinical checkup of the patients, *electrocardiographic*, and echocardiographic and *coronography* examination were conducted at the Clinic of Cardiovascular Diseases, and basic laboratory tests, markers of necrosis, markers of inflammation and markers of renal function were determined at the Center of Medical Biochemistry, Clinical Center in Nis.

### **Clinical examination**

Immediately after admission at the Coronary unit, the patients were subjected to thorough clinical examination, which included examination of all systems and organs, with a particular emphasis on the function of cardiopulmonary system, on determining the values of arterial blood pressure, pulse rate, degree of nutritional status, comorbidities present, existing and threatening complication of MI. Arterial blood pressure is expressed as the average of 3 consecutive measurements on the left hand, with the patient still in the sitting position. Heart rate is determined by the digital method, palpation a. radialis. Body mass index (BMI) is defined as the ratio of body weight and body height squared.

### **Electrocardiogram examination**

In all patients with STEMI, a 12-lead ECG was registered within at the latest 10 minutes of arrival at the emergency department of the Clinic. ECG was routinely recorded immediately after primary PCI, after 6 and 24h of intervention, while in case of repeated complications, ECG dynamics was observed serially. A continuous ECG monitoring was constantly carried out during the patients' stay at the Coronary unit.

***Echocardiographic examination***

Echocardiographic examinations of the patients involved in the study were carried out at the beginning and during hospitalization, using two-dimensional transthoracic methods on the device for echocardiographic examination Vivid 4, GE. Ejection fraction (EF) was determined by the method of Simpson.

***Basic laboratory tests***

Basic biochemical tests were performed on multichannel biochemical analyzer (Olympus ® Chemistry Immuno AU400e Analyser), using the original Olympus reagents. Glucose was determined by enzymatic UV test with hexokinase. Total cholesterol was determined by Chod-PAP method, employing the enzymatic color test using cholesterol esterase. HDL cholesterol was determined by immuno-inhibition method, using the enzymatic color test, and by using anti-human HDL antibodies. LDL cholesterol was calculated by Friedwal's formula. Triglycerides were determined by GPO-PAP method, using enzymatic color test, i.e. after enzymatic hydrolysis of lipase. Urea was determined by GLDH method, using kinetic UV test. Creatinine was measured by kinetic color test. AST and ALT were determined by kinetic UV test.

Troponin I (TNI) was determined on AxSYM analyzer (Abbott), by using the original AxSYM Troponin I ADV immunoassays, by using "sandwich" technique with monoclonal anti-human anti-cTnI antibodies (7). Creatine kinase was determined on the Olympus analyzer by using original Beckman Coulter kinetic UV test. Creatine kinase isoenzyme MB (CKMB) was determined on the Olympus analyzer, by using the original Beckman Coulter immuno-inhibition enzyme test (8), whereas CKMB mass was determined on AxSYM analyzer (Abbott), by using the original AxSYM CK-MB immunoassays, by using "sandwich" technique with monoclonal anti-human anti-CKMB antibodies (9).

Values of C-reactive protein (CRP) were determined by immunoturbidimetric method on the Olympus system, using normal applications (0.2 to 480 mg/L), and using latex particles coated with anti-human CRP antibodies. Fibrinogen was determined by immunoturbidimetric method by using Parfontier's saturated solution.

***Determination of renal function markers***

Glomerular filtration rate was calculated using the MDRD (Modification of Diet in Renal Disease equation) formula (10).

***Investigation of intra-hospital complications***

Of particular importance for the study was to investigate intra-hospital complications, including recurrent angina pain, ST segment dynamic and T-wave on ECG, increase in TnI and / or in CKMB, hemodynamic instability, the occurrence of malignant heart rhythm disorders, disorders of circulation, bleeding, anemia and acute major coronary events (death, recurrent MI, repeated PCI, surgical revascularization).

***Coronary angiography***

Urgent invasive strategy was used in all patients involved in the research program within 12 hours of symptom onset. Coronary angiography was performed with the use of the Seldinger technique, i.e., coronary tree was recorded routinely, by using standard projections. Primary revascularization strategy included percutaneous transluminal angioplasty of coronary artery with or without stenting responsible lesions, according to the coronography findings.

***Investigation of post-hospital complications***

Checkup of the patients included in study, with the aim of examining post-hospital complications (death, recurrent MI, re-hospitalization for unstable angina, repeated PCI and surgical revascularization), was conducted during routine ambulance controls, medical records examination and through telephone interviews, a year after hospitalization.

The results were analyzed by means of the statistical analysis program (SPSS 12.0 Inc., Chicago, Illinois, USA and Sigma Stat 3.5). The values of the studied parameters were determined by descriptive analysis and shown as mean  $\pm$  standard deviation, i.e., median with maximum and minimum values or the absolute value of the percentage. Predictive value of the studied parameters was investigated by univariate and multivariate logistic regression analysis. The value  $p < 0,05$  is considered as statistical significant.

## Results

There were 116 patients included in the study, 72 males (62.07%) and 44 females (37.93%), average age  $63.35 \pm 10.3$  years. The parameters of clinical examination at admission are shown in Table 1.

The main cardiovascular risk factors at admission were: arterial hypertension, hypercholesterolemia, hypertriglyceridemia, multi-vessel coronary disease and family burden of cardiovascular disease. The frequency of cardiovascular risk factors is shown in Table 2.

Average values of basic biochemical parameters, including markers of necrosis, inflammation and renal function are shown in Table 3.

According to their medical history, patients were admitted to the Clinic within 30 minutes to 10 hours from onset of the symptoms, while the average time from admission to intervention procedure was less than 1 hour. Findings of coronary angiography are shown in Table 4.

The highest incidence among post-hospital complications was noted in relation to death, recurrent MI and recurrent angina pain. The results are shown in Table 5.

Table 1. The results of clinical examination at admission

	Patients (n=116, 100%)
<b>heart rate:</b>	
sinus rhythm (n,%)	112 (96,55)
atrial fibrillation (n,%)	4 (3,45)
<b>heart rate (beats / min)</b>	75,60 ± 15,08
<b>blood pressure:</b>	
<b>systolic</b> (mmHg)	139,43 ± 20,07
<b>diastolic</b> (mmHg)	85,71 ± 13,01
<b>ejection fraction (%)</b>	48,17 ± 12,45
<b>BMI (kg/m<sup>2</sup>)</b>	27,46 ± 3,39

Data are presented as n (%) or mean±SD;

Table 2. Cardiovascular risk factors at admission

	Patients (n=116, 100%)
<b>Risk factors for coronary disease</b>	
+ 65 years (n,%)	48 (41,38)
hypertension (n,%)	96 (82,76)
hypercholesterolemia (n,%)	86 (74,14)
hypertriglyceridemia (n,%)	76 (65,52)
overweight (n,%)	56 (48,28)
obesity (n,%)	26 (22,41)
diabetes mellitus (n,%)	36 (31,03)
smoking	
non-smoker (n,%)	48 (41,38)
ex-smoker (n,%)	22 (18,97)
active smoker (n,%)	46 (39,66)
<b>Personal medical history</b>	
angina pectoris (n,%)	58 (50,0)
myocardial infarction (n,%)	24 (20,69)
multi-vessel disease (n,%)	82 (70,69)
PCI (n,%)	16 (13,79)
surgical revascularization (n,%)	0 (0)
congestive heart failure (n,%)	10 (8,62)
anemia (n,%)	8 (6,89)
<b>Family medical history for CVD</b>	86 (74,14)

Data are presented as n (%)

Table 3. Basic biochemical tests at admission

	Patients (n=116, 100%)
glycemia at admission (mmol/L)	8,96 ± 3,32
glycemia (mmol/L)	7,59 ± 2,82
total cholesterol (mmol/L)	6,15 ± 1,65
HDL-cholesterol (mmol/L)	1,24 ± 0,36
LDL-cholesterol (mmol/L)	4,21 ± 1,32
triglycerides (mmol/L)	2,32 ± 1,84
AST (U/L)	53,00 (7,00-611,00)
ALT (U/L)	27,00 (8,00-281,00)
hemoglobin (g/L)	135,46 ± 18,52
hematocrit (%)	41,23 ± 4,66
erythrocytes (x 10 <sup>12</sup> /L)	4,52 ± 0,54
<b>Markers of necrosis</b>	
Tn I (ng/ml)	4,77 (0,08-16,50)
CPK (U/L)	443,50 (26,00-7275,00)
CKMB (U/L)	64,74 (5,10-560,90)
CKMB mass (U/L)	29,60 (1,00-778,00)
<b>Markers of inflammation</b>	
CRP (mg/L)	5,30 (0,90-235,70)
fibrinogen (g/L)	5,24 ± 1,52
leukocytes (x 10 <sup>9</sup> /L)	12,07 ± 3,29
<b>Markers of renal function</b>	
urea (mmol/L)	6,83 ± 3,23
creatinine (µmol/L)	104,72 ± 45,33
GFR (ml/min/1,73m <sup>2</sup> )	63,47 ± 19,04

Data are presented as mean±SD or median (maximum-minimum values)

Table 4. Findings of coronary angiography

	Patients (n=116, 100%)
pain to room time (min)	150,0 (30,0-600,0)
room to ballon time (min)	50,0 (10,0-420,0)
number of affected blood vessels:	
1	46 (39,66)
2	42 (36,21)
3	28 (24,14)
responsible lesions:	
LAD	62 (58,49)
Cx	18 (15,52)
RCA	36 (31,03)
periprocedural complications	40 (34,48)

Data are presented as n (%) or median (maximum-minimum values)

Table 5. Post-hospital complications

	Patients n=116 (100%)
Fatal outcome	24 (20,69)
Recurrent MI	22 (18,97)
Repeated PCI	14 (12,07)
Surgical revascularization	4 (3,45)
Recurrent angina pain	18 (15,52)
Second act	14 (12,07)
Export	4 (3,45)
Total complications	100 (86,22)

Data are presented as n (%)

Table 6. The predictive role of examined markers on defined clinical outcomes

	Fatal outcome	Recurrent MI	Repeated PCI	CABG
<b>Necrosis</b>				
Tn I	-	0.58 (0.15-2.18)	0.34 (0.03-4.17)	0.58 (0.15-2.18)
CPK	1.0 (0.9-1.3)	1.0 (0.93-1.2)	1 (0.78-1.21)	1 (0.94-1.01)
CKMB	1.0 (0.99-1.01)	1.01 (0.97-1.01)	1 (0.99-1.01)	1.0 (0.99-1.01)
CKMB mass	0.89 (0.72-1.11)	0.89 (0.72-1.1)	0.82 (0.64-1.05)	-
<b>Inflammation</b>				
CRP	1.05 (0.96-1.14)	1.12 (1.01-1.2) <sup>C</sup>	0.99 (0.97-1.02)	0.98 (0.92-1.06)
Fibrinogen	0.82 (0.51-1.32)	0.96 (0.65-1.43)	1.09 (0.7-1.69)	1.10 (0.57-2.14)
Leukocytes	1.01 (0.85-1.2)	1.22 (1.03-1.4) <sup>C</sup>	1.36 (1.08-1.7) <sup>B</sup>	1.08 (0.79-1.46)
<b>Cardiovascular risk factors</b>				
Age	1.10 (1.05-1.2) <sup>A</sup>	1.08 (1.03-1.14) <sup>B</sup>	1 (0.94-1.06)	0.96 (0.87-1.07)
Sex	2.89 (1.15-7.27) <sup>C</sup>	1.47 (0.57-3.76)	1.26 (0.4-3.91)	1.66 (0.2-12.2)
Hypertension	1.85 (0.62-5.49)	1.08 (0.32-3.63)	0.77 (0.16-3.7)	7.02 (0.86-10.1)
Hypercholeste-rolemia	1.06 (0.37-2.97)	1.72 (0.53-5.56)	0.41 (0.12-1.3)	7.88 (0.52-9.32)
Hypertriglyce-ridemia	0.16 (0.05-0.44) <sup>A</sup>	0.32 (0.12-0.85) <sup>C</sup>	0.48 (0.15-1.5)	1.0 (0.65-3.25)
Obesity	0.79 (0.30-2.06)	0.66 (0.25-1.78)	1.04 (0.3-3.58)	8.28 (0.4-10.5)
Diabetes mellitus	2.83 (1.12-7.15) <sup>C</sup>	5.72 (2.1-15.4) <sup>A</sup>	1.8 (0.57-5.63)	2.29 (0.3-16.9)
Smoking	0.27 (0.10-0.69) <sup>B</sup>	0.32 (0.12-0.85) <sup>C</sup>	0.93 (0.3-2.88)	1.0 (0.25-1.89)
Thrombus	3.8 (1.16-12.39) <sup>C</sup>	2 (0.69-5.74)	0.72 (0.21-2.4)	0.74 (0.1-5.48)
<b>ECHO findings</b>				
EF	0.98 (0.86-1.2)	0.98 (0.89-0.99) <sup>C</sup>	1.05 (0.98-1.1)	0.9 (0.82-0.99) <sup>C</sup>

Data are presented as OR (95%CI), (univariate logistic regression analysis), <sup>A</sup>p<0,001; <sup>B</sup>p<0,01; <sup>C</sup>p<0,05

The predictive role of examined parameters (markers of necrosis, inflammation, renal function markers and cardiovascular risk factors) for defined clinical outcomes is shown in Table 6. Myocardial necrosis markers did not show a significant predictive role for clinical outcomes after primary PCI in patients with STEMI. CRP and the leukocytes count represent risk factors of recurrent MI and repeated PCI. The risk of mortality is particularly related to age, male gender, hypertriglyceridemia, diabetes mellitus, smoking, and angiographic findings by examining blood clot. The risk of recurrent MI is particularly related to age, hypertriglyceridemia, diabetes mellitus, and smoking. EF is shown as a protective factor for recurrent MI and surgical revascularization

## Discussion

Reperfusion therapy as primary PCI is efficient, not only in terms of opening occluded coronary arteries, but also in terms of significantly better survival in patients with STEMI, compared to fibrinolytic therapy. This fact is supported by the results of a meta-analysis of several major randomized studies (11, 12).



The main clinical finding at admittance was overweight and obesity of STEMI patients with other cardiovascular parameters within the range of optimal values (Table 1). BMI itself had no impact on in-hospital and late mortality in patients undergoing primary PCI for AMI (13), which is in concordance with obtained results. Obesity paradox described by some investigators (14) is not seen in conducted study (Table 6).

Hypertension, hypercholesterolemia, multi vessels disease and positive family history for CVD were presented in more than two third of patients with STEMI at admittance (Table 2). This is in line with results from similar investigation conducted in Poland where average age of patients was  $59.9 \pm 13.3$  years and main prevalent risk factors for CVD included arterial hypertension (51.8%), hypercholesterolaemia (54.5%), smoking (51.8%) and diabetes (22.3%) (15). The values of inflammatory and metabolic risk factors (Table 3) are within the range observed in other studies.

Findings of coronary angiography are shown in Table 4. The average time from admission to intervention procedure was less than 1 hour (Table 4), which is in concordance with other similar facilities. The proportion of patients with one, two or three occluded vessels is similar, with dominance of occluded LAD (Table 4).

At checkup, conducted after a year of hospitalization, the highest incidence among post-hospital complications was noted in relation to the fatal outcome (20.69%), and recurrent MI (18.97%). The frequency of other clinical outcomes is showed in Table 5. In similar study two-year mortality was 6.1% (15), the discrepancy in high mortality registered in this study could be in part explained by higher prevalence of risk factors, late presentation of patients together with low accessibility to early PCI. These were responsible for the high amount of patients with complicated STEMI course despite good adherence to clinical guidelines.

One of the main objectives of this study was to investigate the predictive value of different biomarkers in one-year outcome of the patients with STEMI treated with primary PCI, as these markers reflect different pathophysiological mechanisms of cardiac damage.

The research has shown that inflammatory biomarkers, above all, CRP and leukocyte count are

associated with recurrent MI (Table 6). Our results are in agreement with the study of Mariani et al., which showed that leukocytosis on admission was associated with reduced epicardial blood flow, higher CK release, more frequent development of LV remodeling, congestive heart failure and adverse outcomes (16).

As ACS consists of multi-factorial disorders, based on a complex pathophysiological mechanisms which include not only thrombotic, but also inflammatory processes (17, 18). Several randomized studies have indicated a significant predictive value of certain systemic inflammatory markers for the occurrence of future cardiovascular events, including the most studied CRP, but also, leukocytes count, fibrinogen, cell adhesion molecules, and cytokines and complement components (19, 20). Of particular importance for the patients with STEMI is to determine the dynamics and the serial measurement of CRP, the predictive value of which has been examined both in relation to intra-hospital and short-term prognosis, as well as in relation to long-term prognosis after coronary artery bypass grafting. (21,22). Based on the results of the study conducted by Dimitrijevic and his associates, it was shown that CPR, measured after 24-72 h from the onset of complications, stands for an independent predictor of 1-year outcome in patients with STEMI, unlike CRP at hospital admission (23,24).

The results of previous studies have shown that TnI is a leading marker to predict short-term (within 30 days) risk of death and recurrent MI, but also a significant risk predictor within one year from the occurrence of ACS and afterward (25). However, based on this study results none of the examined necrosis markers, including TNI, CPK, CKMB, and CKMB mass, did not showed significant predictive value for defined clinical outcomes (Table 6).

It has been shown that the risk of recurrent MI is related to age, hypertriglyceridemia, diabetes mellitus, and smoking, and the results have isolated age as an independent risk factor of re-infarction; with an increase in age, the risk of fatal outcome and recurrent infarction within one year of hospitalization increases 1.1 times (Table 6). The age of the patients represents an independent risk factor of death. It has been shown that with an

increase in age, the risk of fatal outcome within a year of hospitalization increases 1.623 times. The increased mortality with age in patients undergoing PCI for STEMI reflects comorbidity and suboptimal procedural outcomes rather than any age effect per se (26).

The results of several major studies that have examined the difference between the sexes in terms of survival after hospitalization in patients with STEMI, have pointed to a higher rate of intra-hospital mortality, but also to a higher rate of post-hospital complications in females, because of old age at hospital admission, higher frequency of comorbidity and lower frequency of revascularization treatment procedures (27). But there are opposite findings that gender difference is not important factor in late outcome after PCI in STEMI patients (28). The results of this study, however, indicated that the male gender was a significant risk predictor of fatal outcome within a year of hospitalization with STEMI and primary PCI treatment, which confirmed the conflicting results found in the literature on this issue, even after adjustment according to the demographic and clinical characteristics of the patients.

Hypertriglyceridemia, diabetes mellitus and smoking are associated with high rates of adverse events in patients with ACS, especially with fatal outcome and recurrent ischemic cardiac events within 1-year period of observation (Table 6). Based on the published results, the estimated incidence of diabetes among the patients hospitalized for MI is approximately 10-20% and shows a tendency to a constant increase (29). The studies that followed established that the risk of death, in patients with diabetes due to coronary disease but without being previously diagnosed with MI, is the same as the risk in non-diabetic patients being previously diagnosed with MI (30), which is why diabetes is considered equivalent to coronary artery disease for the future MI and death from cardiovascular causes (31). According to the Swedish Coronary Angiography Angioplasty Registry (SCAAR), long-term mortality is not only greater in patients with diabetes compared to non-diabetic patients, but it also increases in time (32). The results of GUSTO-I study (33) pointed out to a significantly higher overall mortality within 30 days of STEMI in patients with diabetes compared to non-diabetic

patients (10.5% compared to 6.2%). Global Registry of Acute Coronary Events (GRACE registry) ruled out diabetes as a risk factor of fatal outcome within 6 months of MI (34).

Smoking is considered a major cardiovascular risk factor, especially when it comes to the patients with STEMI, especially those of young age and female gender (35). On the basis of obtained results, smoking is also assessed as one of the leading predictors of death and recurrent MI within one-year period of observation (Table 6).

The results of numerous studies have shown that EF value of left ventricular, determined immediately after PCI, is a strong predictor of long-term survival of patients hospitalized with STEMI. The research results of Rasoul and his associates, which included a sample of 4732 patients with STEMI, showed that within 30 days of hospitalization in the patients with STEMI and PCI, 4.6% of them died, while among those who survived, 2.8% of them died within a year. Age, Killip class, multi-vessel disease, and EF were estimated as the most significant predictors of death within one year. Predictive value of EF less than 30% has been confirmed, both in relation to outcome after 30 days, and in relation to one-year outcome (29). It was found that the average value of EF, established during hospitalization, and immediately after PCI, represents a significant protective factor. An increase in EF decreased the risk of re-infarction 0.94 times, while the risk of re-hospitalization, due to the need for surgical revascularization within one year, was 0.906 times lesser (Table 6). Thrombolysis in myocardial infarction (TIMI) 3 flow predicted a good outcome, whereas recurrent ischemia in hospital, prior aspirin therapy and discharge creatinine predicted a poor outcome; age alone was not an adverse prognostic factor. (26).

According to the results of this study, it can be concluded that CRP is a significant predictor of recurrent MI, the leukocytes count is a predictor of the need for repeated PCI, EF is a predictor of recurrent MI and a need for surgical revascularization, while age, male gender, hypertriglyceridemia, diabetes mellitus, and smoking are predictors of death, whereas age is an independent predictor of death and recurrent MI within one year of STEMI and primary PCI treatment.

## References

1. Adabag AS, Therneau TM, Gersh BJ, Weston SA, Roger VL. Sudden death after myocardial infarction. *JAMA* 2008;300(17):2022–2029.
2. 2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update) A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2009, 120:2271-2306.
3. García-García C, Subirana I, Sala J, Bruguera J, Sanz G, Valle V, et al. Long-Term Prognosis of First Myocardial Infarction According to the Electrocardiographic Pattern (ST Elevation Myocardial Infarction, Non-ST Elevation Myocardial Infarction and Non-Classified Myocardial Infarction) and Revascularization Procedures. *Am J Cardiol.* 2011;108(8):1061-1067.
4. Valgimigli M, Airoldi F, Zimarino M. Stent choice in primary percutaneous coronary intervention: drug-eluting stents or bare metal stents? *J Cardiovasc Med (Hagerstown)*. 2009;10 Suppl 1:S17-26.
5. Lincoff AM, Topol EJ. Illusion of reperfusion: does anyone achieve optimal reperfusion during acute myocardial infarction? *Circulation* 1993;87:1792-1805.
6. Grines CL, Cox DA, Stone GW, et al. For the Stent Primary Angioplasty in Myocardial Infarction Study Grup. Coronary angioplasty with or without stent implantation for acute myocardial infarction. *N Engl J Med* 1999;341:1949-1956
7. Painter PC, Cope JY, Smith JL. Reference information for the clinical laboratory. In: Burtis CA, Ashwood ER, eds. *Tietz textbook of clinical chemistry*. Philadelphia: WB Saunders Company, 1826 pp, 1999.
8. Horder M, Elser R, Gerhardt W, Mathieu M, Sampson EJ. International Federation for Clinical Chemistry. Scientific division committee on enzymes: Approved recommendation on IFCC methods for the measurement of catalytic concentration of enzymes. Part 7. IFCC method for creatini kinase. *Eur J Clin Chem Biochem* 1991;29(7):435-456.
9. Primus FJ, Kelley EA, Hansen HJ, et al. "Sandwich"-type immunoassay of carcinoembryonic antigen in patients receiving murine monoclonal antibodies for diagnosis and therapy. *Clin Chem* 1988;34:261-264.
10. Levey AS, Greene T, Kusek JW, Beck GJ. A simplified equation to predict glomerular filtration rate from serum creatinine. *J Am Soc Nephrol* 2000;11:155.
11. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomized trials. *Lancet* 2003;361:13–20.
12. Jackson G. Primary angioplasty in acute myocardial infarction—the preferred option, but time is of the essence. *Int J Clin Pract* 2006;60:379.
13. Kosuge M, Kimura K, Kojima S, Sakamoto T, Ishihara M, Asada Y, et al. Japanese Acute Coronary Syndrome Study (JACSS) Investigators. is not seen in conducted study Impact of body mass index on in-hospital outcomes after percutaneous coronary intervention for ST segment elevation acute myocardial infarction. *Circ J.* 2008 Apr;72(4):521-525.
14. Kang WY, Jeong MH, Ahn YK, Kim JH, Chae SC, Kim YJ, et al. Korea Acute Myocardial Infarction Registry Investigators. Obesity paradox in Korean patients undergoing primary percutaneous coronary intervention in ST-segment elevation myocardial infarction. *J Cardiol.* 2010;55(1):84-91.
15. Kaluzay J, Remisova S, Pontuch P. Management and two-year prognosis of patients with acute myocardial infarction in a community hospital toward the end of thrombolytic era. *Bratisl Lek Listy.* 2006; 107(1-2): 34-39.
16. Mariani M, Fetiveau R, Rossetti E, et al. Significance of total and differential leukocyte count in patients with acute myocardial infarction treated with primary coronary angioplasty. *Eur Heart J* 2006; 27: 2511–2515.
17. Blake GJ, Ridker PM. C-reactive protein and other inflammatory risk markers in acute coronary syndromes. *J Am Coll Cardiol* 2003;41(4 Suppl S):37S-42S.
18. Mulvihill NT, Foley JB. Inflammation in acute coronary syndromes. *Heart* 2002;87:201-204.
19. Pearson TA, Mensah GA, Alexander RW, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice. A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation* 2003;107:499-511.
20. Biasucci LM. CDC/AHA Workshop on Markers of Inflammation and Cardiovascular Disease: Application to Clinical and Public Health Practice: clinical use of inflammatory markers in patients with cardiovascular diseases: a background paper. *Circulation* 2004;110:e560-567.
21. Bruneti ND, Troccoli R, Correale M, Pellegrino PL, Di Biase M. C-reactive protein in patients with acute coronary syndrome: correlation with diagnosis, myocardial damage, ejection fraction and angiographic findings. *Int J Cardiol* 2006;109:248-256.

22. Suleiman M, Khatib R, Agmon Y, et al. Early inflammation and risk of long-term development of heart failure and mortality in survivors of acute myocardial infarction predictive role of C-reactive protein. *J Am Coll Cardiol* 2006; 47: 962-968.
23. Dimitrijevic O, Đoric Stojcevski B, Ignjatovic S, Majkic Singh N. Serial Measurements of C-Reactive Protein After Acute Myocardial Infarction in Predicting One-Year Outcome. *Int Heart J* 2006; 47: 33-842.
24. Kuch B, von Scheidt W, Kling B, Heier M, Hoermann A, Meisinger C. Differential impact of admission C-reactive protein levels on 28-day mortality risk in patients with ST-elevation versus non-ST-elevation myocardial infarction (from the Monitoring Trends and Determinants on Cardiovascular Diseases [MONICA]/Cooperative Health Research in the Region of Augsburg [KORA] Augsburg Myocardial Infarction Registry). *Am J Cardiol* 2008; 102(9):1125-1130.
25. Lindahl B, Diderholm E, Lagerqvist B, Venge P, Wallentin L. Mechanisms behind the prognostic value of troponin T in unstable coronary artery disease: a FRISC II substudy. *J Am Coll Cardiol* 2001; 38: 979-986.
26. Hiew C, Williams T, Hatton R, Narasimhan S, O'Connor S, Baker F, et al. Influence of age on long-term outcome after emergent percutaneous coronary intervention for ST-elevation myocardial infarction. *J Invasive Cardiol*. 2010;22(6):273-277.
27. Bufe A, Wolfertz J, Dinh W, et al. Gender-based differences in long-term outcome after ST-elevation myocardial infarction in patients treated with percutaneous coronary intervention. *J Womens Health* 2010;19(3):471-475.
28. Yu L, Le-feng W, Xin-Chun Y, et al. Gender differences in efficacy of primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction. *Chinese Medical Journal* 2008;121(23):2374-2378.
29. Aguilar D, Solomon SD, Kober L, et al. Newly diagnosed and previously known diabetes mellitus and 1-year outcomes of acute myocardial infarction: the VALsartan In Acute myocardial iNfarcTion (VALIANT) trial. *Circulation* 2004; 110: 1572-1578.
30. Haffner SM, Lehto S, Ronnema T, Pyorala K, Lakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998;339(4):229-234.
31. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106(25):3143-3421.
32. Norhammar A, Lagerqvist B, Saleh N. Long-term mortality after PCI in patients with diabetes mellitus: results from the Swedish Coronary Angiography and Angioplasty Registry. *EuroIntervention* 2010;5(8):891-897.
33. Mak KH, Moliterno DJ, Granger CB, et al. Influence of diabetes mellitus on clinical outcome in the thrombolytic era of acute myocardial infarction: GUSTO-I Investigators (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries). *J Am Coll Cardiol* 1997;30(1):171-179.
34. Fox KA, Dabbous OH, Goldberg RJ, et al. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). *BMJ* 2006;333(7578):1091.
35. Björck L, Rosengren A, Wallentin L, Stenestrand U. Smoking in relation to ST-segment elevation acute myocardial infarction: findings from the Register of Information and Knowledge about Swedish Heart Intensive Care Admissions. *Heart* 2009; 95(12): 1006-1011.

## Corresponding Author

Nebojsa Krstic,  
 Clinic of Cardiovascular Diseases of the Clinical  
 Centre in Nis,  
 Nis,  
 Serbia,  
 E-mail: dr\_nebojsa\_krstic@yahoo.com

# The effects of group solution– focused therapy on depression and completion of treatment in patients with chronic hepatitis B

Jinous Arvand<sup>1</sup>, Abdollah Shafiqabadi<sup>2</sup>, Mohammad Reza Falsafinejad<sup>3</sup>, Mohammad Reza Zali<sup>4</sup>

<sup>1</sup> PhD of Counseling, Faculty of Human Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran,

<sup>2</sup> Full Professor, Faculty of Human Sciences, Allameh Tabatabaie University, Tehran, Iran,

<sup>3</sup> Assistant Professor, Faculty of Human Sciences, Allameh Tabatabaie University, Tehran, Iran,

<sup>4</sup> Full Professor, Research Center for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

## Abstract

**Background and Aim:** Hepatitis B may be associated with several psychiatric disorders and decrease quality of life of affected patients. This study was conducted to assess the effects of group solution– focused therapy (SFT) on reducing depression and increasing their completion of treatment among patients with chronic hepatitis B.

**Methods and Materials:** This experimental study was performed on married patients with chronic hepatitis. They were randomly assigned to interventional group (n=11) and control group (n=11). Interventional group received solution focused therapy for 7 sessions, each session 2 hours once a week, but control group was observed without any psychotherapy interventions. At the beginning and immediately after ending study, both groups were evaluated by Beck depression inventory (BDI) for evaluating depression and completion of therapeutic regimen prescribed by clinician.

**Results:** At the end study, Mean score of depression was statistically different between SFT and control groups ( $p=0.02$ ). Also, SFT stimulates patients to complete treatment, so that all patients of SFT group take regularly therapeutic regimen during study and there was significant difference between two groups, regarding completion of treatment ( $p=0.006$ ). Analysis of covariance (ANCOVA) was completed to control for pretest differences on depression and showed significant differences between groups on the depression ( $p=0.001$ ).

**Conclusion:** Overall, using solution- focused therapy could be an efficient technique in helping and supporting patients with chronic hepatitis B to cope with depression and completion medical treatments.

**Key words:** Chronic hepatitis B, Solution– focused brief therapy, Depression Completion of treatment.

## Introduction

Hepatitis B is a common infectious disease with 2 billion people infected worldwide, and 350 million chronic HBV carriers. It is a national health problem in Iran and it is estimated that 2.14% of Iranian population is affected by HBV infection (1, 2). Chronic somatic diseases increase the risk of psychological distress compared with healthy people. Psychological manifestations are in many forms, including having problem to cope with essential adaptations, emotional symptoms such as nervousness and definite psychiatric disorder, such as depression (3). Hepatitis B, as a chronic disorder, may be associated with several psychiatric disorders and decrease quality of life of affected patients. Ebrahimi Daryani et al, (2008) revealed higher prevalence of psychiatric disorder than general population add detected depression in 30%, anxiety in 6%, functional impairment in 6%, and somatic abnormalities in 8% of Iranian HBV carriers. Besides, 36 patients had at least one psychiatric disorder (4). In the other hand, disabilities originated from chronic disorder and associated psychiatric problem may affect several aspects of human life. One of the most important consequences of these problems is the patients' compliance to take prescribed medications and complete therapeutic regimens. Psychotherapy, such as solution– focused therapy, may help these patients to resolve psychiatric problems, increase quality of life and completion of therapeutic regimens.

Solution-focused therapy highlights the client's strong points and resources, aiding the person apply the skills and strategies that he or she has used effectively in the past. Solution-focused therapists work under the hypothesis that clients have the answer to their own problem and the abilities and resources required to achieve it. Treatment starts with determine what the client wants and how he or she will know whether a successful outcome has been reached. It focuses of solving problem, instead of only concentrating the problem. It has high importance as an introductory and frequently satisfactory intervention and can be used with to other treatments (5, 6). This therapy is frequently used in patients suffering from somatic diseases. Cockburn, et al evaluated variables associated with the psychosocial adjustment of work hardening program participants when exposed to solution-focused psychotherapy. They found that solution-focused therapy, in conjunction with work hardening protocols, is effective for patients when developing effective coping responses to the stressors associated with orthopedic rehabilitation (7). To our information, there was no study to evaluate efficiency of solution-focused therapy on patients with chronic hepatitis B. So, we conducted this study to assess the effects of group solution-focused brief therapy on reducing depression and increasing their completion of treatment among patients with chronic hepatitis B.

## Methods and Materials

### *Subjects*

This experimental study was performed on married patients with chronic hepatitis referred to a private office in Tehran, Iran. Those who had HBsAg positivity for at least 2 years and currently receiving therapeutic regimen for hepatitis B were included in the study. The study was described for patients and after getting informed consent, they were randomly assigned to interventional group (n=11) and control group (n=11). Interventional group received solution focused therapy for 7 sessions, each session 2 hours once a week, but control group was observed without any psychotherapy interventions. Patients who refused to complete study, involved by major stressors, such as divorce, etc, and or having other severe somatic

or psychiatric disorders were excluded from study. At the beginning and immediately after ending study, both groups were evaluated by Beck depression inventory (BDI) for evaluating depression and completion of therapeutic regimen prescribed by clinician.

### *Solution focused therapy*

Group solution focused therapy was performed in 7 sessions, each 2 hours once a week. In the first session, the therapist determined what the person is hoping to get from the session, what the routine and everyday details of the patient's life would be like, what the patient is currently performing or has done in the past that might play a role to these hopes and what might be different if the patient made one very small step to achieve these hopes. Following sessions started by asking, 'What is better?' If there were improvements, even for a little time, they asked: what was different, who noted, how it occurred, what strengths and resources the patient used to change.

### *Measurement tools*

*Beck Depression Inventory.* BDI is a 21-item scale which determines the occurrence and intensity of various somatic, emotional, and cognitive features of depression. Internal consistency and concurrent validation are well documented for the scale (8). Higher total scores represent more severe depression. Scores above 16 are considered indicative of clinical depression; scores 16-30 minor depression, score 31-46 moderate depression and scores 47-63 major depression (9).

Completion of treatment was categorized into three groups of bad with no beginning of treatment, moderate with partially and good with complete taking therapeutic regimen.

### *Statistics*

Data are present as mean  $\pm$  standard deviation for numerical and frequency (percent) for categorical data. Data were analyzed by chi-square test and independent sample t- test using SPSS Ver.13. Univariate analysis of variance was used to investigate interaction of age and sex with mean scores of depression and control groups. Also, analysis of covariance (ANCOVA) was completed to control for pretest differences on depression and DAS scores.

## Results

22 patients with chronic hepatitis B were studied in two groups of intervention with mean age of  $38.1 \pm 5.9$  (8 males, 3 females) and control with mean age of  $37.6 \pm 5.2$  (8 males, 3 females). There were no significant differences between sex and age of two groups.

At the beginning of study, of 11 people of SFT group, 7 had no depression, 1 mild depression and 3 moderate depression, while in control group, 4 had no depression, 4 mild depression, 1 moderate depression and 2 severe depression ( $p=0.13$ ). Mean Score of depression was not statistically different between 2 groups. Table 1 compares variables between 2 groups at the beginning study. As it is seen, completion of treatment was no significant different between two groups before study.

SFT and control groups were re-evaluated by aforementioned tools at the end study. In the SFT group, 9 patients had no depression and 2 acquired score of mild depression. No moderate or severe depression was observed. 4 normal, 3 mild depression, 2 moderate and 2 severe depression were detected in control group. Frequency of depression was not significantly different between two groups ( $p=0.11$ ), but mean score of depression was statistically different between SFT and control groups ( $p=0.02$ ). Also, SFT stimulates patients to complete treatment, so that all patients of SFT group take regularly therapeutic regimen during study and there was signifi-

cant difference between two groups, regarding completion of treatment ( $p=0.006$ ) (table 2).

Since there were differences in post term scores, an analysis of covariance (ANCOVA) was completed to control for pretest differences on depression. There were significant differences between groups on the depression ( $p=0.001$ ) when controlling for pretest scores. Univariate analysis of variance showed that age and sex had no significant effects and interactions on mean scores of depression of SFT and control groups.

## Discussion

This study showed that SFT is an effective psychotherapy technique to improve depression and persuade patients to complete medical treatments. Psychological care is progressively more accepted as an essential part of the comprehensive care of the patients with chronic diseases. Life disturbances, diminished quality of life, and fear of disease recurrence or progression may also make psychological disorders. Solution focused therapy (SFT) is a relatively new method of psychotherapy and counseling that persuade clients to obtain positive changes in their lives, and construct on resources, strong point and pre-existing changes (10-12).

Hansen et al found that severity of somatic diseases is associated with high prevalence of psychological disorders (13). Ormel et al. revealed that mental illness is dissimilar in patients with 16 chronic somatic diseases, however, after contro-

Table 1. Comparison of variables among two groups at the beginning study

Variables		Interventional group (n=11)	Control group (n=11)	p-value
Depression*		$9.4 \pm 9.4^{\ddagger}$	$14.6 \pm 13.1$	0.29
Completion treatment				0.3
	Good	5(45.5) <sup>§</sup>	4(36.4)	
	Moderate	1(9)	4(36.4)	
	Bad	5(45.5)	3(27.2)	

\*Depression score by Beck depression inventory; <sup>‡</sup>mean $\pm$ standard deviation; <sup>§</sup>Number (%)

Table 2. Comparison of variables among two groups at the end of study

Variables		Interventional group (n=11)	Control group (n=11)	p-value
Depression*		$3.6 \pm 4.8^{\ddagger}$	$14.8 \pm 13.5$	0.02
Completion treatment				0.006
	Good	11(100) <sup>§</sup>	4(36.4)	
	Moderate	0	4(36.4)	
	Bad	0	3(27.2)	

\*Depression score by Beck depression inventory; <sup>‡</sup>mean $\pm$ standard deviation; <sup>§</sup>Number (%)

ling for disability and personality characteristics of patient, these variations were dissolved (14). It is shown that physical disease characteristics can be responsible for psychological diseases and low functionality. Also, their social and relationship difficulties may explain the differences in different presentations of psychological manifestations (3).

In a study on Iranian patients with hepatitis B carriers, Ebrahimi Daryani et al found that psychiatric disorders are one of the main problems in these patients and they are often socially isolated and have a poor quality of life (4). This recommends using counseling and different techniques of psychotherapy to improve patients' conditions. SFT has shown encouraging effects in the treatment of depression (15-18) In a research on a small group study (n=10) with pre-test, post-test self assessment scales Beck Depression Inventory (BDI), efficacy of solution focused therapy on subjects with moderately to severely depressed was evaluated. Mean average improvement of 55.12%, in the range of 19.23% (lowest improvement) to 93% (highest improvement) was observed (19).

This study showed that SFT persuade s patients to continue regularly therapeutic regimen. We observed that SFT can improve patients' quality of life, lower occurrence and severity of psychological problems, such as depression, and also diminish marital maladjustment. These findings may explain that SFT can change patients mind to improve life expectancy and complete the treatment.

The limitation of this study was relatively low sample size of both groups, but selection of control groups that was comparatively similar with SFT group at the beginning study encourages us to trust the findings. Also, it provides preliminary evidence on the probable advantages of SFT in decreasing psychosocial consequences of chronic hepatitis B.

In conclusion, this study showed significant efficacy of group solution– focused brief therapy on reducing depression and increasing their completion of treatment in patients with chronic hepatitis B. So, we recommend considering counseling and psychotherapy, especially SFT as a brief and short- term method, in patients with chronic hepatitis B, particularly those who suffer from psychiatric disturbances.

## Reference

1. Zali MR, Mohaghegh Shalmani H. *The changing epidemiology of hepatitis B in Iran. Gastroenterol Hepatol Bed Bench.* 2010; 3(1): 1-4.
2. Alavian SM, Hajarizadeh B, Ahmadzad- Asl M, Kabir A, Bagheri- Lankarani K. *Hepatitis B infection in Iran: a systematic review. Hepatitis Monthly.* 2008; 8(4): 281-294.
3. Verhaak PFM, Heijmans MJWM, Peters L, Rijken M. *Chronic disease and mental disorder. Social Science and Medicine.* 2005; 60(4): 789-797.
4. Ebrahimi Daryani N, Bashashati M, Karbalaieian M, Keramati MR, Ebrahimi Daryani N, Shadman Yazdi AA. *Prevalence of psychiatric disorders in hepatitis B virus carriers in Iranian charity for hepatic patients support (December 2004-August 2005). Hepatitis Monthly.* 2008; 8(3): 201-205.
5. Iveson C. *Solution- focused brief therapy. Advances in Psychiatric Treatment.* 2002; 8: 149–157.
6. Berg IK, Miller SD. *The miracle method: A radically new approach to problem drinking.* New York: Norton; 1995.
7. Cockburn JT, Thomas FN, Cockburn OJ. *Solution- focused therapy and psychosocial adjustment to orthopedic rehabilitation in a work hardening program. J Occupational Rehabilitation.* 1997; 7: 97-106.
8. Beck A, Ward C, Mendelson M, Mock J, Erbaugh J. *An inventory for measuring depression. Archives of General Psychiatry.* 1961; 4: 53-63.
9. Harrell T, Ryon N. *Cognitive-behavioral assessment of depression: Clinical validation of the automatic thoughts questionnaire. Journal of Consulting and Clinical Psychology.* 1983; 51: 721-725.
10. Berg IK. *Family- based services: a solution- focused approach.* New York: Norton and Company; 1994.
11. O'Hanlon WH, Weiner- Davis M. *Family therapy: concepts and Methods.* 4th ed. Boston: Allyn and Bacon; 1989.
12. Selekman MD. *Pathways to change: brief therapy solutions with difficult adolescents.* New York: Guilford; 1993.
13. Hansen MS, Fink P, Frydenberg M, Oxhoj M, Sondergaard L, Eriksen M. *Mental disorder in medical inpatients and the association to severity of illness, self rated physical disability and health perception. Psychosomatics* 2001; 42: 41–47.



14. Ormel J, Kempen GJMJ, Penninx BWJH, Brilman EI, Beekman ATF, Sonderen E. Chronic medical conditions and mental health in older people: Disability and psychosocial resources mediate specific mental health effects. *Psychological Medicine* 1997; 27: 1065–1077.
15. Linssen F. *Solution focused therapy for anxiety and depression. A controlled study.* Berlin, Germany: European Brief Therapy Association; 2005.
16. Lee MY, Greene GJ, Mentzer RA, Pinnell S, Niles D. Solution- focused brief therapy and the treatment of depression: a pilot study. *Journal of brief therapy.* 2001; 1: 33-49.
17. Sundstrom SM. *Single- session psychotherapy for depression: It is better to focus on problems or solution? [Dissertation]* Ames: Iowa State University; 1993.
18. Knekt P, Lindfors O. *A randomized trial of the efficacy of four forms of psychotherapy on depression and anxiety disorders: designs, methods and results on the effectiveness of short- term psychodynamic psychotherapy and solution- focused therapy during a one- year follow- up.* Helsinki, Finland: The Social Insurance Institution; 2004.
19. Hanton P. *Moderate to severe depression. Solution Focused Research review.* 2008; 1(1): 16-24.

*Corresponding Author*

*Jinous Arvand,  
Faculty of Human Sciences,  
Research and Science Campus,  
Islamic Azad University,  
Tehran,  
Iran,  
E-mail: jinusarvand@yahoo.com*

# The effects of web-based childbirth education program on activities of daily living of pregnant women

Kerziban Yenil<sup>1</sup>, Ümran Sevil<sup>2</sup>

<sup>1</sup> Dokuz Eylül University School of Nursing, Izmir, Turkey,

<sup>2</sup> Ege University School of Nursing, Izmir, Turkey.

## Abstract

**Purpose:** This study was conducted for the purpose of investigating the effect of a web-based pregnancy counseling and childbirth educational program on pregnant women's activities of daily living.

**Methods:** This is a quasi-experimental study. The web site: '<http://web.deu.edu.tr/gebelik>' was used in the education, counseling and data collection stages of the study. The study sample consisted of 32 pregnant women in their 12th-26th week of pregnancy. Individual counseling and a two-week standard education were given to the pregnant women who participated in the study. In the data collection, forms developed by the researcher were used to determine the pregnant women's activities of daily living (ADL). The pregnant women were assessed before education (BE), as well as one (OM) and two months (TM) after education.

**Results:** The pregnant women's ADL scores steadily increased ( $p < .001$ ). This result shows that web-based childbirth education and counseling program has a positive effect on pregnant women's ADLs.

**Conclusions:** Web-based childbirth education and counseling can be provided to pregnant women by nurses and midwives.

**Key words:** "Internet", "Counseling", "Pregnancy", "Activities of Daily Living"

## Introduction

Becoming a parent is one of the most important decisions made in a person's life. Pregnancy is the first stage in the parenthood role (1). Mothers-to-be experience both physical and psychosocial changes in the prenatal, childbirth and postnatal periods. These changes make it necessary for pre-

gnant women to make changes in their ADLs. It is necessary for individuals to develop new coping strategies for adapting to these situations (2). For families to be able to cope with these types of crises, they begin searching for information to help them adapt to ADLs that change in the prenatal period. For this reason, future mothers and fathers receive counseling from health care facilities, read books and magazines, and participate in preparation for childbirth classes (3).

In recent years, major changes have been experienced in science and technology. In Turkey, as in the rest of the world, the number of computer and internet users is rapidly increasing. According to 2009 data from the Turkish Statistical Institute (TSI), 34% of the internet users are in Turkey. Of these, 45.1% use internet to find health related information (4).

Significant changes experienced in technology and people's interest in this has also increased health care workers' interest in this subject. Computer-based education programs for ill and well individuals began to be developed. This has brought a new dimension to the understanding of classic education and counseling (5).

In place of classic face-to-face education or education with educational booklets, the use of the internet as an interactive method provides a rapid and low cost educational environment that allows for concomitant use by one individual and many individuals for as much time as they want for counseling (6, 7, 8, 9). In a variety of research studies, web-based individual/patient education has been shown to be beneficial (9, 10, 11). In parallel with the technological advancements, the rate of pregnant women participating in the traditional childbirth education has recently decreased, while their tendency to obtain information from internet has increased (12).

Nurses, who are important members of the health care team, cannot ignore the effectiveness of these developments. Changes and improvements in information technology provide a new dimension to education and counseling, the most important nursing roles. These nursing roles are extremely important for pregnant women and their families to be able to adapt and appropriately cope with difficulties they experience (2). Larsson (2007) performed a study in Sweden and demonstrated that the majority of the pregnant women (84%) followed up in polyclinic benefitted from web and used internet 62 times a month on average (13).

Based on this information, the **purpose of this study** was to investigate the effect of Web-based pregnancy counseling and childbirth education programs (WEBCEP) on pregnant women's ADLs.

### Conceptual Framework

ADLs is a nursing model developed by Nancy Roper in 1976 and later improved by Winifred Logan, and Alison J. Tierney in 1980. This model focuses on daily living activities changing between complete dependency and complete independency based on age, condition, and environment during lifetime. ADL model provides individual interference plan by determining diagnosis and priorities, which is the initial step of nursing (14, 15).

Pregnancy is a period of rapid changes in which both fetus and mother are physically and emotionally affected (1).

The rapid changes are especially effective on daily living activities of mother. Pregnant women need education and counseling from nurses to accommodate these changes. Roper defined life as the period from fecundation to death. Living activities consist of 12 items in total (15). Living activities are given below, and a sample is provided for how each living activity is affected in pregnancy.

**Ensuring safety:** It aims to provide safe continuance of living activities and performance of required protecting activities (14). Changing gravity center increases falling tendency of pregnant women. Therefore, pregnant women should be taught to use body mechanics properly and safety precautions should be taken (16). **Communication:** It helps to determine the communication pattern of nurse, individual /patient and family (14).

Ambiguities fear and anxiety during pregnancy might negatively affect the communication within the family (1).

**Breathing:** It helps to define respiration activity, indispensable for life, and the factors effective on respiration (14). Ventilation is more needed to meet the increasing need for oxygen during pregnancy. Pregnant women experience difficulty in respiration due to the pressure of growing uterus on diaphragm in the further months of pregnancy (1).

**Nutrition:** It is one of the principle activities of life. It aims to define individual nutrition by age periods and factors effective on nutrition (14). Pregnant women should make changes in nutrition in order to meet the requirements of their own and fetus compared to period before pregnancy (17).

**Elimination:** It aims to assess the intestinal and bladder functions( 14). Frequent widdling and constipation could be observed during pregnancy depending on the hormonal and mechanical effects ( 16).

**Personal Cleanliness and Dress:** It helps to determine the personal cleaning and clothing behaviors and effective factors (14). Due to the rapid increase in weight gain, changes in body, and higher risks (e.g. varicose, lordosis) during pregnancy, pregnant women should carefully choose all their clothes and shoes (1).

**Controlling temperature:** It involves determining and evaluating the body heat (14).

**Exercise:** It aims to assess personal activity and mobility (14). Exercise is recommended for many problems experienced during pregnancy (16, 18, 19).

**Working and playing:** It involves determining the individual activities of working (current and future profession), entertainment and relief (14). They should maintain the changes in daily living activities they make during pregnancy.

**Sexuality:** The activity of expressing sexuality provides a wider perspective by expressing sexual activity, masculinity and femininity as well as determining factors effective on the perception of body (14). As long as there is no problem in pregnancy, no change is expected in sexual life. However, couples generally avoid intercourse for fear of infection and harming baby (1, 16).

**Sleep:** It aims to detect the factors effective on regular sleep pattern and sleep of individuals (14).

Sleeplessness problems are experienced due to the increasing movements of baby, frequent widdling, discomfort due to baby pressure, difficulty in respiration, and inability to take the regular sleeping position (20).

**Death:** It takes part in the model because the dying patient and relatives are in need of supporting approaches and there is an end for other activities (14).

## Methods

### Design

The research was conducted as a quasi-experimental study. The quasi-experimental time series design of pretest and posttest in a single group was used. The research was conducted on the web site: <http://web.deu.edu.tr/gebelik> (Figure 1)



Figure 1. Home Page

### Sample

After the web page was created, all (6-40 week) pregnant women who made request from the web page were given counseling by e-mail. The research population was comprised of 161 pregnant women who became members by accessing the web page between year 2005-2006. Of these pregnant women, 62 wanted to receive on-going education. 32 of these 62 pregnant women were taken into the sample as they were in their 12th-26th week of pregnancy, completely filled out all three forms and were healthy and not a risky pregnancy. Those with multiple pregnancy, a chronic illness or pregnancy-related complications were excluded from the sample.

The reason for including 26 weeks or less pregnant women into the sample was related to the research method. The final test was planned three

months after the beginning of the education; for this reason, women in pregnancies over 26 weeks and women who delivered before the final test were not included in the study. The women who requested on-going education and who were not yet at their 12th week of pregnancy were explained the purpose of the study and asked to wait until their 12th week.

To be able to continue with the on-going education, it was necessary for the pregnant women to be good computer users and to have access to the internet at home or work.

The sample size was calculated using NCSS Pass Program. At the end of the study, the power of the study was calculated based on the data obtained. The pregnant women's ADL total scores were considered as the primary outcome. Repeated measures one way analysis of variance was used for power analysis. The power of the study was found 99.9% ( $\alpha = 0.05$ ,  $n = 32$ , before education (BE) ADL score average:  $4.1 \pm 1.4$ , one month after the end of the educational program (OM) ADL total score average:  $6.4 \pm 1.3$ , two months after the end of the educational program (TM) ADL total score average:  $6.8 \pm 1.4$ , effect size = 1.19).

### Measurement

Form 1: This form needed to be completed by all the pregnant women or their husbands. It contains 19 questions for the purpose of obtaining the pregnant women and their husbands' sociodemographic characteristics.

Form 2: This form needed to be completed by pregnant women who participated in the WE-BCEP. The form had 16 items which were directed at determining whether or not the pregnant women experienced minor discomforts.

Form 3: This form was developed by the researcher taking advantage of the Activities of Daily Living (ADL) Model, developed by Nancy Roper, Winifred Logan and Alison J. Tierney. Roper, Logan, and Tierney's ADL model has a total of 12 items (Roper et al., 1990). The researcher selected from eight items affected in pregnancy and created a new form, Form 3. The four items from ADL that were not included were communication, body temperature control, working and playing, and death. The basic reason for removing these items was that they would not have an effect from the

internet and thinking that examining the death-related item in pregnancy would not be appropriate.

Form 3 was developed to determine the pregnant women's ADLs and their appropriate and inappropriate behaviors in response to frequently encountered discomforts and the Web-based education education's effect on these behaviors. The pregnant women completed this form three times: before education, one month and two months after the end of the educational program.

A few questions (2-5 ) were asked for defining each living activity. For the definition of eight fields investigated in the study, a total of 32 questions were asked, 22 of which were designed as multiple choice questions for the purpose of determining the pregnant women's appropriate and inappropriate behaviors. The pregnant women could mark more than one answer to these questions. These questions were scored by giving one point for every correct answer and zero points for every incorrect answer. One question was written in a table format in which the women could mark the amount of food consumed daily from each food group. This table was scored by giving one point for every appropriate amount selected for every food group and giving zero points for every amount that was excessive or insufficient. The maximum score possible from the ADLs is 75. In the findings, the scores of the pregnant women were converted and given out of 10 to make them easier to read and interpret.

There was one open-ended question on Form 3 that asked the pregnant women's height, pre-pregnancy weight and their weight at the time they completed the form. According to their pre-pregnancy Body Mass Index (BMI), their appropriate weight gain was evaluated. The weight that should be gained according to BMI before pregnancy is shown in Table 1 (17).

These values are accepted as the basis for evaluating whether or not they gained the appropriate weight according to month of pregnancy. For the

calculation of BMI, height and weight values were used based on the statement of pregnant women.

After the preparation of forms, opinions of three professors in women's health and nursing field were asked. Cronbach alpha coefficient was found 0.89 in reliability test on ADLs total scores.

## Research Implementation

**Creation of Web Page:** Taking advantage of Dokuz Eylül University's web hosting services, a web page was created on the World Wide Web. Windows software program was used in the preparation of the information. Because all of the internet procedures hosting have Linux management system, this management system was used to create the page. When the Web page was created PHP Script Language and HTML were used. Support and guidance were received from a computer technician and computer education and instruction technology were employed in the page design and preparation. The content of the web page was formed by the authors, and opinions of three professors in women's health and nursing field were taken.

On the home page, there are three buttons on the left: "New Registration," "Member Log-on," and "Who is XXXX?" The system was run by opening the sub-topics.

**Conducting Counseling and Education:** By filling out the new registration form (Form 1), any pregnant woman could become a member and receive counseling about subjects of interest to them during pregnancy. These pregnant women were sent to the counseling section of the web page where they could write about a topic for which they wanted counseling. The researcher answered these questions within maximum 48 hours by sending information to their email address.

Pregnant women who wanted to participate in the WEBCEP ongoing education program were given a planned two-week education program. On Monday of every week were sent a new topic was

Table 1. Prepregnancy BMI and Weight Needed to be Gained During Pregnancy

BMI Before Pregnancy	Diagnosis	Weight (in kg) Needed to be Gained During Pregnancy
<19.8	Low	12.5-18
19.8-26	Normal	11.5-16
>26	High	7-11.5
>29	Obese	£ 6

sent by e-mail . If they had any questions about the topic, they were answered by e-mail by Friday of that week.

Educational topics in WEBCEP:

1st Week: Nutrition in pregnancy,

- What is nutrition?
- Nutrition groups
- Importance of nutrition in pregnancy
- Adequate and balanced nutrition in pregnancy
- Foods and beverages that should be avoided in pregnancy

2nd Week: ADLs in pregnancy and precautions for common complaints.

- Changes in mother's body
- Clothing in pregnancy
- Working life in pregnancy
- Computer use in pregnancy
- Pregnancy and traveling
- Sexual life in pregnancy
- Exercise in pregnancy

In addition to the standard WEBCEP, the pregnant women were also given individual counseling about what they needed to do for minor complaints they identified on Form 2 and for inappropriate behaviors that were identified on Form 3.

#### ***Data Collection Method***

All of the forms sent to the pregnant women from the web page were connected to the researcher's e-mail. All of the pregnant women who wanted to be a member of the web page and who agreed to participate in the study completed the new registration form (Form 1) found on the home page of the web page. Member pregnant women were sent to their e-mail address a user's name and password determined by the experts who designed the web page. Together with the user's name and password, information was sent about how they could take advantage of these services. All pregnant women who wanted to take advantage of the on-going educational service used their user name and password to get access to the other forms from the home page log-on for members. Pregnant women who completed Form 2 and Form 3 were sent the first educational topic to their e-mail address on the same day. Within the first

48 hours individual counseling was given to the pregnant women according to the information on the form. After completing the 2-week educational program, the pregnant women were reminded by e-mail to complete Form 3 again one month and two months after finishing the education. The forms were completed by the pregnant women on the web page. At the beginning of the forms, information was given about how to complete them. Counseling was provided by e-mail when they felt a need. Pregnant women and their spouses who completed the educational program and filled out the forms three times were sent a "Model Soon-to-be-Parent Certificate" designed by the researcher to their mail address.

#### ***Data Analysis***

The SPSS 15.0 packet program was used for statistical analysis of all findings obtained by the data collection tools. The sociodemographic and obstetric characteristics of participant pregnant women and their husbands were given as percentage. In the examination of the effect of the WEBCEP on pregnant women's ADLs, repeated measures One Way Analysis of Variance was used. The appropriateness of weight gain from the time before education was given until two months after the conclusion of the educational program was tested using McNemar test.

#### ***The Ethical Dimensions of the Study***

Permission was received from Ege University School of Nursing Scientific Ethics Committee prior to beginning the research.

#### ***Study Limitation***

A control group could not be established because the pregnant women only filled out the data collection forms without any interference or education on the internet. This was the limitation of the study.

#### **Results**

The sociodemographic and obstetric characteristics of the participants are shown in Table 2. The mean age of the research participant pregnant women was 28.8 years and their husbands' mean age was 31.1 years. It was determined that

the pregnant women and their husbands had high educational levels and high income levels, and the majority of the pregnant women were employed. The current pregnancy was the first for 84.4% of the women and 87.5% did not have any living children.

When the status of receiving information about pregnancy was examined, it was determined that 87.5% of the pregnant women received information, and the sources of their information was their physician for 68.3%, books and magazines for 65.6%, and other web pages for 59.4%.

*Table 2. Sociodemographic and Obstetric Characteristics of Pregnant Women and Spouses*

Characteristic	Total (n=32)
<b>Age Mean</b> ( $\bar{x} \pm SD$ )	28.8 (3.1)
<b>Women's Educational Level</b>	
High school	1 (3.1)
University	25 (78.1)
Postgraduate education	6 (18.8)
<b>Employment Status</b>	
Employed	26 (81.2)
Not employed	6 (18.8)
<b>Husband's Mean Age</b> ( $\bar{x} \pm SD$ )	31.1 (3.9)
<b>Husbands' Educational Level</b>	
High school	4 (12.5)
University	17 (53.1)
Postgraduate education	11 (34.4)
<b>Income Status</b>	
Income less than expenses	4 (12.5)
Income and expenses balanced	18 (56.3)
Income more than expenses	10 (31.3)
<b>Week of Pregnancy (at first registration)</b>	
12-19 week	18 (59.4)
20-26 week	14 (40.6)
<b>Number of Living Children</b>	
0	28 (87.5)
1	4 (12.5)
<b>Status of Having Received Information about Pregnancy</b>	
Received	28(87.5)
Have not received	4(12.5)
<b>Distribution of information source* n=28</b>	
Physician	22(68.3)
Nurse	2(6.3)
Books and Magazines	21(65.6)
Preparation for Childbirth class	1(3.1)
Other Web Pages	19(59.4)

\*Data include making more than one selection.

The results obtained for the pregnant women's total and subcategory ADLs are given in Table 3. The pregnant women's ADL subcategory and total scores were examined with repeated measures one way analysis of variance. Statistically significant differences were found in all of the subcategories of ADL. Bonferroni corrected t test was used to determine the source of differences, whether they were originated from BE, one month or two months after the conclusion of educational program measurements.

In the advanced analysis with the pregnant women's nutrition, personal cleanliness-dress and ADL total scores significant differences were determined between all three measurements. The scores in these two subcategories and the total ADL were seen to steadily increase. In the advanced analysis of the pregnant women's scores from the ensuring safety, breathing, elimination, sexuality, and sleep subcategories, significant differences were determined between BE and OM and between BE and TM. There was no significant difference between OM and TM. The scores at both measurements after completion of education were found to be higher than the BE scores. In the advanced analysis of the pregnant women's scores in the exercise subcategory, a statistically significant difference was found between BE and TM ( $p=.02$ ). However, no significant difference was found between the BE and OM scores ( $p=.06$ ), or between the OM and the TM scores ( $p=1.0$ ).

If the pregnant women's weight gain was normal according to their BMI, it was described as normal, if more or less, it was described as inappropriate. In the results of the pregnant women's weight gain, evaluated according to their BMI, at the pre-education and two months post-education times, 46.9% of the women had an appropriate weight gain at the pre-education time period, but the rate of appropriate weight gain increased to 78.1% 3 months later. According to the McNemar analysis, the difference was determined statistically significant ( $p=.02$ ) (Table 4).

## Discussion

The subcategory scores that increased the most compared to the other subcategories were the nutrition, personal cleanliness and dress subcategory.

Table 3. Comparison of the Pregnant Women's ADL Subcategory Scores BE, OM, and TM

Activities of Daily Living	BE	OM	TM	F/P	Difference Over Time
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$		
1. Ensuring safety	4.2±2.3	6.7±1.6	7.1±1.8	25.31 .00	a<b,c
2. Breathing	1.72±1.9	6.1±2.3	6.7±2.1	272.756 .00	a<b,c
3. Nutrition	3.9±1.3	6.3±1.5	6.8±1.4	65.528 .00	a<b<c
4. Elimination	5.5±2.9	7.2±1.6	7.5±2.1	10.115 .00	a<b,c
5. Personal Cleanliness and Dress	4.2±1.8	6.4±1.9	6.9±1.8	40.472 .00	a<b<c
6. Exercise	3.5±4.3	5.2±4.7	5.2±4.2	46.209 .00	a,b<c
7. Sexuality	4.9±2.4	6.3±2.6	6.3±2.0	264.132 .00	a<b,c
8. Sleep	2.9±2.3	6.1±2.2	5.8±2.5	227.181 .00	a<b,c
Total Score	4.1±1.4	6.4±1.3	6.8±1.4	76.221 .00	a<b<c

a= Score BE b= Score OM c= Score TM

Table 4. Evaluation of Pregnant Women's BE and TM Weight Gain According to BMI

Appropriateness of Weight Gain	Two Months After Completion of Education		Total	McNemar P
	Appropriate	Inappropriate		
	n	n	n	
<b>Before Education</b>				
Appropriate	12 (37.5)	3 (9.4)	15 (46.9)	P= .02
Inappropriate	13 (40.6)	4 (12.5)	17 (53.1)	
Total	25 (78.1)	7 (21.9)	32 (100)	

ries. Nutrition in pregnancy is important in many cultures. In Turkish culture as well, great significance is given to nutrition during pregnancy. The value given to nutrition in Turkish culture is shown in various beliefs. Importance is given to various foods and others are avoided for the infant who will be born to be intelligent, pretty and not handicapped (21, 22). The personal cleanliness and dress subcategory for ADLs, as with nutrition, is another topic that is given importance in society. What a pregnant woman should wear, and her hygienic and self-care needs are given importance by pregnant women and their families. For this reason, it is thought that these topics were better assimilated by the pregnant women after completing the education and re-reading it. The finding that the pregnant women continued to benefit from the

information in these areas after the completion of the educational program is an encouraging result from the standpoint of the effectiveness and usability of the education.

In the results of the pregnant women's weight gain evaluated according to their BMI at the pre-education and two months post-education times, 46.9% of the women had an appropriate weight gain at the pre-education time period, but the rate of appropriate weight gain increased to 78.1% three months later ( $p = .02$ ). The increase in number of pregnant women who had appropriate weight gain after the educational program may be related to the high educational level of the pregnant women who participated in the education and their being at the appropriate age for childbirth. In various studies, a correlation was observed be-



tween pregnant women's appropriate weight gain and their educational level (23, 24).

The least affected ADLs subcategory after education was exercise. The education of pregnant women covered the importance of exercise, areas to be considered, actions to be not taken, and necessary information about exercises suitable for pregnant women like walking, aerobic, etc. However, the exercises that can be done during pregnancy were not explained with pictures. Because of possible injury that could be caused by incorrect exercise, the exercise diagrams were not shown for ethical concern. For this reason, the pregnant women may have been less affected from this education. In addition, exercise not being a habit in the pregnant women's work lives and normal pregnancy lives could create a difficulty. In a previous study, women who exercised before pregnancy (39%) were determined to continue exercising during pregnancy. In the same study, pregnant women were found to consider rest and relaxation to be more important than exercise (96%) (18). In a study by Okumuş et al. (2002), after education, 12.3% of the participants were found to make exercises regularly three times a week (3).

Statistically significant differences were found between the pregnant women's BE, OM and TM ADL total scores. In the advanced analysis, significant differences were determined between the three time periods. The pregnant women's ADLs steadily increased.

In a study by Herman et al. (2005), web-based social support was provided for low income women. The women were determined to be pleased with the social support they received (11).

In a study by Adler and Zarchin (2002), an on-line communication method was used for social support for women who were on bedrest at home because of their risk for early delivery (10). All of the women stated that this method helped them cope at home. Lagan et al. (2010) reported in their studies that the information obtained from the web was stated to be effective on the decision of 84% of internet user pregnant women (25).

In a study performed on pregnant women in England, the majority of midwives (86%) was reported to share information with pregnant women and this sharing was effective on the decisions of most women (67%) (26).

The results obtained from this study show that pregnant women can benefit from a two-week educational program, and that education and counseling has a positive effect on pregnant women's ADLs. The steady increase in total score shows that the pregnant women continued to use the information after the completion of the educational program, which is an encouraging result.

## Conclusions

In conclusion, it was found out that the two week childbirth education program and counseling have positive effects on pregnant women's ADLs. Web-based childbirth education can be considered as an appropriate educational method.

As a result of the research, the following might be recommended for the practitioner nurses:

- Education and counseling can be given to pregnant women by nurses and midwives using the web environment.

Recommendations for researcher nurses:

- The effect of web-based childbirth education on the postnatal period can be investigated.
- Adding a forum section to a web page designed for pregnant women can provide a way for pregnant women to share information with each other. The resulting social support from the web perceived by pregnant women can be examined.
- The effects of web-based pregnancy training program on daily activities of pregnant women could be studied in comparison with control group.

## References

1. Perry, S.E., Hockenberry, M.J., Lowdermilk, D.L. & Wilson, D. (2010). *Maternal child nursing care*. Canada: Mosby Co.
2. Murray, S.S., Mckinney, E.S., & Gorrie, T.M. (2002). *Foundations of Maternal-Newborn Nursing*. (3rd ed.). Philadelphia: Saunders comp.
3. Okumus, H., Mete, S., Aytur, T., Yenil, K., & Demir, N. (2002). *Effectiveness of childbirth education class on labor outcomes*. *Journal of Clinical Sciences & Doctor*, 8, 771-775.

4. Turkish Statistical Institute (TSI). (2009). *Türkiye İstatistik Yıllığı (Turkey's Statistical Yearbook)*. Retrieved January 28, 2011 from <http://www.tuik.gov.tr/yillik/yillik.pdf>
5. Richards, B., Colman, A.W., & Hollingsworth, R.A. (1998). *The current and future role of the internet in patient education*. *International Journal of Medical Informatic*, 50, 279-85.
6. Colvin, J., Chenoweth, L., Bold, M., & Harding C. (2004). *Caregivers of older adults: advantages and disadvantages of internet based social support*, *Family Relation*, 53, 49-57.
7. Soop, A.P., Riet, A., & Berg, M. (2004). *Using information technology for patient education: realizing surplus value?* *Patient Education and Counseling*, 54, 187-195.
8. Partridge, M.R. (2004). *An assessment of the feasibility of telephone and e-mail, consultation in a chest clinic*. *Patient Education and Counseling*, 54, 11-13.
9. Nguyen, H., Kohlman, V., Rankin, H., Slaughter, R., Stulbarg, M.S. (2004). *Internet based patient education and support interventions: a review of evaluation studies and directions for future research*. *Computers in Biology Medicine*, 34, 95-112.
10. Adler, C.L., & Zarchin Y.R. (2002). *The "virtual focus group": using the internet to reach pregnant women*. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 31, 418-427.
11. Herman, J., Mock, K., Blackwell, D., & Hulsey, T. (2006). *Use of pregnancy support web site by low – income African American women*. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 34, 713-720.
12. Romano, A.M. (2007). *A changing landscape: implications of pregnant women's internet use for childbirth educators*. *The Journal of Perinatal Education*, 16, 18-24.
13. Larsson, M.A. (2009). *Descriptive study of the use of the Internet by women seeking pregnancy-related information*. *Midwifery*, 25, 14–20.
14. Roper, N., Logan, W., & Tierney, A. (1990). *The Elements of Nursing a Model for Nursing Based on a Model of Living*. (3rd ed.). Livingstone: Edinburgh Churchill.
15. Healy, P., Timminis, F. (2003). *Using the Roper-Logan-Tierney Model in neonatal transport*, *British Journal of Nursing*, 12 , 792-798.
16. London, M.L., Ladewig, P.W., Ball, J.W., & Bindler R.C.(2003). *Maternal Newborn & Child Nursing, Family Centered Care*. Philadelphia: Printice Hall, p:180-210.
17. Williamson, C.S. (2006). *Nutrition in pregnancy*. *British Nutrition Foundation Nutrition Bulletin*, 31, 28-59.
18. Clarke, P.E., & Gross, H. (2004). *Women's behavior, belief and information sources about physical exercise in pregnancy*. *Midwifery*, 20, 133-141.
19. Smith, S., & Michel, Y. (2006). *A pilot study on the effects of aquatic exercises on discomforts of pregnancy*. *JOGNN*, 35, 315-323.
20. Sahota, P.K., Jain, S.S., & Dhand, R. (2003). *Sleep Disorders in Pregnancy*. *Current Opinion in Pulmonary Medicine*, 9, 477-483.
21. Taş, H. (1996). *Türk Kültüründen Derlemeler (Compilation from Turkish Culture)*, Kültür Bakanlığı Halk Kültürlerini Araştırma ve Geliştirme Genel Müdürlüğü Yayınları, No: 228, Ankara, 190-191.
22. Artun, E. (1998). *Tekirdağ halk kültüründe geçiş dönemleri (Past ages in Tekirdağ public culture)*. *Türk Dünya İncelemeleri Dergisi (Turkish World Studies Journal)*, 9, 1-8.
23. Maddah, M., Karandish, M., Mohammadpour, B., Neyestani, T.R, Vafa, R., & Rashidi, A. (2005). *Social factors and pregnancy weight gain in relation to infant birth weight: a study in public health centers in rasht*. *European Journal of Clinical Nutrition*, 59, 1208-1212.
24. Maddah, M. (2005). *Pregnancy weight gain in Iranian women attending a cross-sectional study of public health centres in rasht*. *Midwifery*, 21, 365-370.
25. Lagan, B.M., et al. (2010). *Internet use in pregnancy informs women's decision making: a web-based survey*. *Birth*, 37, 106-115.
26. Lagan, B.M., Sinclair, M. & Kernohan, G. (2011) *A web-based survey of midwives' perceptions of women using the Internet in pregnancy: a global phenomenon*. *Midwifery*, 27, 273-281.

Corresponding author

Kerziban Yenil,

Dokuz Eylül Üniversitesi Hemşirelik Yüksekokulu,

İnciraltı,

İzmir,

Turkey,

E-mail: kerziban.koyun@deu.edu.tr

# Sensitivity and efficiency of „silent“ phlebothrombosis early detection tests in ambulatory vascular patients

Milan M. Jovanovic<sup>1</sup>, Aleksandra Krstic<sup>2</sup>, Goran Stanojevic<sup>3</sup>, Miroslav Stojanovic<sup>3</sup>, Ivan Ignjatovic<sup>4</sup>, Jovica Jovanovic<sup>5</sup>

<sup>1</sup> Clinical Center of Nis, Vascular Surgery Clinic, Nis, Serbia,

<sup>2</sup> Clinic for Gastroenterohepatology, Clinical Centre of Serbia, Belgrade, Serbia,

<sup>3</sup> Clinic for General Surgery, Clinical Centre, Niš, Serbia,

<sup>4</sup> Clinic for Urology, Clinical Centre, Niš, Serbia,

<sup>5</sup> The Faculty of Medicine, Niš, Serbia.

## Abstract

**Background / Aim:** Early detection of „atypical and silent“ deep venous thrombosis (DTV) would reduce the embolic potential, mortality and disability in this severe disease.

Sensitivity, reliability and efficiency of the protocol for early detection of this, the hardest recognizable, phlebothrombosis in the everyday ambulance work, was the aim of this research.

**Methods:** All ambulatory vascular patients with suspected symptomatic or asymptomatic DTV were included in this two-year prospective study. „DD diagnostic protocol“ (DDdp), based on an estimate of the degree of clinical probability of DTV, DD testing and ultrasound examination of selected patients was applied in D-dimmer (DD) group. Serial ultrasound diagnostic („US diagnostic protocol“ - Usdp) was applied in control group. DTV was excluded in „unlikely“ patients with negative DD results and in „likely“ patients with US and DD negative results. Quarterly monitoring of patients with initially excluded DTV, detected cases with overlooked DTV. Precise evaluation of protocols sensitivity, specificity, predictive value and diagnostic efficiency was based on these results.

**Results:** Overlooked DTV was determined in one patient (0,17%) by using DD test in DDdp, compared to 582 excluded DTV. It was significantly lower compared to group subjected to the USdp, where we determined 7 (1,2%) patients with DTV in group of 581 excluded DTV ( $p < 0.05$ ). Negligible and insignificant difference was found comparing the sensitivity and negative predictive value (NPV) of D-dimmer test and US.

However, NPV, sensitivity and diagnostic efficiency are significantly higher in patients who underwent DDdp in DTV detection.

**Conclusion:** The use of DD test significantly increases the NPV, sensitivity and efficiency of the applied diagnostic protocol for early detection of DTV.

**Key words:** deep vein thrombosis, D-dimer, ultrasonography, sensitivity and specificity.

## Introduction

It is complicated to precisely define the incidence of deep venous thrombosis (DVT) since many cases go unnoticed.<sup>1,2</sup> According to the data of »National Health Research Committee«, annual incidence of DVT amounts to 159 patients in 100.000 healthy population.<sup>1-4</sup> Pulmonary embolism (PE), as its most severe complication, manifests itself in about 1.6% patients with DVT, of which 0.87% have fatal outcomes.<sup>2,5</sup>

More than half patients with DVT (65%) are asymptomatic or having discrete and unspecific clinical symptoms, that do not reduce their morbidity, embolic potential and mortality.<sup>3,6,7</sup> Life threat on the patients with phlebothrombosis not diagnosed and treated on time as well as high rate of disability, that is common cause of post-thrombotic syndrome, highlight the significance of timely diagnosis, particularly important in the cases of 'silent' DVT.<sup>3,8</sup>

Ultrasound (US) diagnostics with its high sensitivity and specificity has been affirmed as a method of choice in diagnosis of DVT and has almost excluded invasive phlebography, that is

now reserved only for a small number of dubious cases.<sup>2,9,10</sup> Significant breakthrough in early detection of DVT was made with the introduction of D-dimer (DD) test, an extraordinary screening test for the exclusion of venous thromboembolism (VTE).<sup>11-16</sup> Negative predictive value of DD test amounts to 100% in clinically unlikely DVT cases, 94% in clinically moderately likely DVT cases, while in highly likely cases it adds up to 87%.<sup>12-15</sup> Diagnosis of DVT, however, cannot be based on this parameter only, but it also requires clinical likelihood rating of the disease, and in some cases US examination.<sup>10,12,16-24</sup>

Early detection of »silent and atypical« forms of DVT and their timely treatment would reduce mortality rate and disability of this severe disease.

The aim of this reserach was to evaluate sensitivity, realiability and efficiency of early detection protocol of the phlebothrombosis that are hardest to detect in everyday ambulance work with vascular patients.

**Methods**

Two-year prospective study included all patients examined in the ambulance for vascular surgery of Clinical Centre Niš, with suspected symptomatic or asymptomatic DVT. Patients with one or more criteria for exclusion were not included in this study: life expectancy < 3 months; age < 18 years; difficult follow-up of patients; DVT diagnosis of the same leg in the past; two-day or longer anticoagulant treatment in the last 30 days, un-critical condition of patients, sudden death, stroke or massive hearth attack during the follow-up.

Upon giving their written approval, suitable patients underwent clinical evaluation of DVT probability using modern Wells clinical model, and the patients with the score < 2 were classified as »unlikely« to develop DVT and those with the score ≥ 2 in the category »likely« to develop DVT.

With the method of randomly selected patients, the patients were randomly selected for control and DD group. All patients in the control group underwent US examination of lower extremity magistrale veins. »Unlikely« patients were excluded as suffering from DVT whose US result was negative, and those »likely« to develop DVT underwent control US, seven days after the initially

negative US result. All patinets in DD group, classified as »unlikely« to develop DVT, underwent DD test after which, in the cases of positive result, underwent US. The patients in DD group, classified as »likely« to develop DVT underwent US first, and in the cases of negative result, they underwent DD test, with the negative test result that meant exclusion from DVT while positive test result indicated control US examination in the follow-up (after 7 days) (Figures 1 and 2).

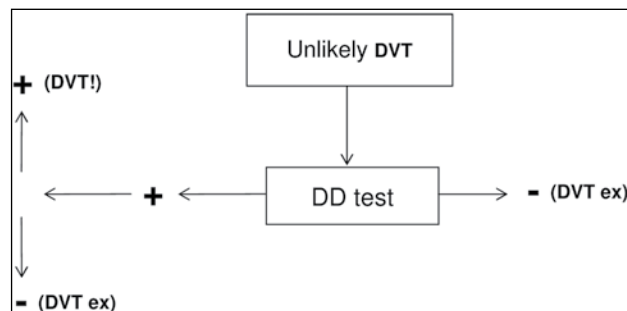


Figure 1. Diagnostic protocol in DD patient group of 'unlikely' to develop DVT

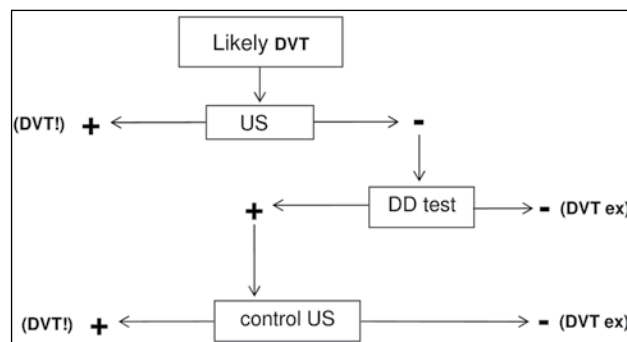


Figure 2. Diagnostic protocol in DD patient group of 'likely' to develop DVT

DVT was excluded in »unlikely« to develop DVT patients with negative DD result as well as in »likely« to develop DVT patients with negative US and DD results. »Unlikely« to develop DVT patients with negative DD test result did not undergo US examination, while all other patiens underwent it. Control US was performed in »likely« to develop DVT patients whose »first« US result was negative and DD positive, while »unlikely« to develop DVT patients underwent it only in the cases of dubious »first« ultrasound (Figure 1 i 2).

In order to evaluate the precision of the applied diagnostic algoritms, that is, the overlooked cases with DVT, the patients who were initially excluded as suffering from DVT were followed in the

period of three months, being advised to visit vascular ambulance or contact their doctors by phone if they develop DVT symptoms. Patients and their relatives were thoroughly informed on the complication and were also given printed guidelines. The state of the patients was evaluated after 7, 30 and 90 days in order to detect possible DVT, that could be foreseen with the applied examination protocol, with all suspected cases evaluated in the above mentioned way.

On the basis of the results of the applied diagnostic protocols, statistical tests, their sensitivity, specificity and predictive values as well as diagnostic efficiency were precisely evaluated.

### Results

In total 1297 patients divided into control (644 patients) and DD (653 patients) groups were analyzed. Fifteen patients from the control group, that is, 10 from DD group were lost, that is, refused to be furtherly examined and followed, with statistical analysis including 1272 patients in total, of whom 62 (9.64%;95%CI=7.12-9.29) in DD group and 55 (8.74%; 95% CI=8.12-9.96) in control group had verified VTE with total prevalence of 9.19% .

Figure 3 shows DVT prevalences in the studied groups in relation to the time of diagnosis.

During the follow-up period 7 (1.2%; 95%CI= 0.21-0.72%) cases of VTE in the series of 581 of excluded DVT (in control group), that is, 1 (0.17%; 95%CI= 0.0-0.3%) in the series of 582 of excluded DVT (in D-dimer group). It has been proven that there are statistically significant differences between the groups in the rates of various VTE manifestations during the follow-up, (0.17% [1 of 582] according to 1.2% [7 of 581]; Fisher exact test:p=0.038; p<0.05) (Figure 1), where 95% CI for the difference of 1.03% is 0.02-0.68%.

The analysis of US results in groups shows very low frequency (4, that is, 0.3%) of falsely negative results, that is, misinterpreted diagnoses, that shows high sensitivity and negative predictive value (NPV) of this diagnostic method, when it comes to the detection of deep venous thrombosis (Table 1).

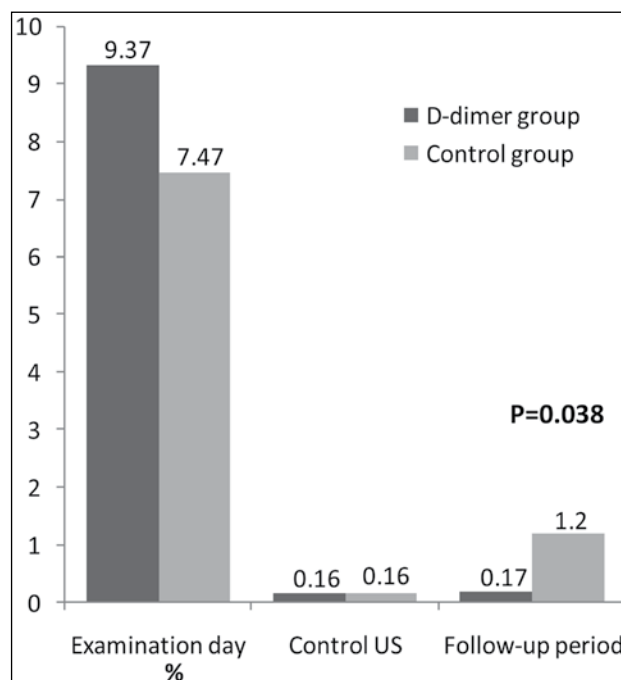


Figure 3. Prevalence (%) DVT in studied groups in relation to the time of diagnosis

Ultrasound as a diagnostic method in detecting DVT is statistically significantly more sensitive in D-dimer group in comparison to the control group of the examined patients (Fisher's exact test=0.0019; p<0.01). The difference in negative predictive ultrasound value amounts to 100%, while it is lower in the control patient group and amounts to 99.4%. This difference is statistically significant (Fisher's exact test=0.0385; p<0.05) (Table 2).

Table 1. Results of US diagnostics in the examined patients

US	'Unlikely' DVT		'Likely' DVT		Total
	D-dimer group	Control group	D-dimer group	Control group	
	n				
Positive	26	20	36	31	113
Negative	454	449	127	125	1155
Falsely negative	0	3	0	1	4
Total	480	472	163	157	1272

Table 2. Sensitivity and negative predictive value of US diagnostics in groups

US	DVT		D-dimer group	Control group
	'Unlikely'	'Likely'		
	← %; 95% CI →			
Sensitivity*	94.94 (91.0-97.0)	98.59 (95.9-99.6)	100 (98.1-100.0)	94.72 (90.3-96.9)
NPV†	99.64 (98.9-99.8)	99.77 (98.3-100.0)	100 (98.9-100.0)	99.4 (98.2-99.9)

\*Sensitivity (D-dimer/ control group) Fisher=0.0019; p<0.01

†NPV (unlikely/likely p>0,05

(D-dimer/ control group) Fisher=0.0385; p<0.05

In comparing of sensitivity and negative predictive value of D-dimer test and ultrasound diagnostics negligible and insignificant difference was noticed (Table 3).

Table 3. Relation of sensitivity and NPV D-dimer and ultrasound diagnostics

	D-dimer test	Ultrasound	Fisher's exact test (p)
	← % (95%CI) →		
Sensitivity	95.1 (82,3-98,9)	96.28 (96.1-98.9)	0.709 (p>0.05; ns)
NPV	99.71 (97,3-100,0)	98.92 (95.7-99.6)	1.000 (p>0.05; ns)

Diagnostic characteristics of the applied D-dimer and ultrasound (control) diagnostic protocol comparatively evaluated in the Table 4.

Negative predictive value and diagnostic efficiency are statistically significantly higher in the

group of the examined patients using D-dimer diagnostic protocol in detecting DVT compared to ultrasound (control) diagnostic protocol, where only ultrasound was used. D-dimer diagnostic protocol is also more sensitive in comparison to ultrasound protocol, with the difference statistically significant for the level p<0.1 (Table 4).

### Discussion

Undeniable ultrasound reliability in diagnosis of DVT confirms the fact that after the common ultrasound finding DVT can be detected in only 0.9% cases.<sup>2,8-11</sup>The results of the two recent studies with the follow-up period of 3 and 6 mont-

Table 4. Comparative evaluation of diagnostic characteristics of the applied diagnostic protocols

Diagnostic characteristics	DD protocol	US protocol	χ <sup>2</sup> test	p
	← % (95%CI) →			
Sensitivity (<0.1)	98.52 (94.9-99.5)	93.92 (91.1-98.2)	3.39	0.059; p>0.05
Specificacy	100.0 (96.7-100.0)	100.0 (94.6-100.0)	-	-
PPV*	100.0 (98.1-100.0)	100.0 (98.6-100.0)	-	-
NPV p<0.05	99.78 (98.8-100.0)	99.3 (98.2-99.1)	3.92	0.041;
Diagnostic efficacy p<0.05	99.77	99.44	3.90	0.043;

\*positive predictive value

hs show even lower frequency of thromboembolic complications evidenced in only 0.6%, that is 0.7% patients with suspected DVT and with normal series ultrasonography result.<sup>2,7-9</sup>

Since it was first described in 1972 by Gaffney, D-dimer has been appreciated as a valuable marker of thromboembolic states.<sup>12-15</sup> Potential value of plasmatic D-dimer as the test for the exclusion of DVT has been evaluated more than a decade. Results of the studies carried out during the last ten years show that negative D-dimer finding may be used to minimise the need for serial ultrasound examinations in the patients suspected with DVT<sup>12-17</sup>, which was also confirmed in this research.

With the introduction of fast, inexpensive and sensitive D-dimer test, the diagnostic procedure in exclusion of DVT has been simplified in great number of patients with clinically suspected disease.<sup>12-18</sup> With this testing the application of ultrasound diagnostics in the patients with 'unlikely' to develop disease has been rationalized.<sup>8-12</sup>

Verified frequency of VTE in the follow-up period of 1.2%, close to earlier referred values (0.6%), shows the reliability and quality of the applied US examination model. The frequency, however, is statistically significantly lower in the group where DD diagnostic protocol was applied and amounts to 0.17%, (in comparison to the total number of patients from this group with excluded DVT).<sup>2</sup>

Ultrasound, as a diagnostic method in detection of DVT, is statistically significantly more sensitive in D-dimer group than in control patient group (Fisher's exact test=0.0019;  $p < 0.01$ ). The difference in negative predictive value of ultrasound diagnostics between the patients with «unlikely» and «likely» thrombosis is not statistically significant. Although the differences when comparing sensitivity and negative predictive value D-dimer test and ultrasound diagnostics are not significant, predictive value of negative ultrasound test in D-dimer group is statistically significantly higher (100%) in comparison to control patient group (99.4%), (Fisher's exact test=0.0385;  $p < 0.05$ ), where these as well as the above mentioned significant differences are certainly the result of diagnostic efficiency of the applied D-dimer test.

The applied DD diagnostic protocol makes the diagnostic procedure simpler and faster, greatly reducing the need for the first and repeated US

examinations, thus significantly reducing the costs and efforts of patients, medical staff and ultrasonographers.<sup>2</sup>

Sensitivity, negative predictive value and diagnostic efficiency is statistically significantly higher in the patient group where D-dimer diagnostic protocol was applied in detecting DVT in comparison to ultrasound protocol where only ultrasound was used, and it should be stated that D-dimer test is a significant precondition of such an effective diagnostic protocol.

## Conclusion

'D-dimer diagnostic protocol', that implies D-dimer testing, clinical evaluation of disease and selective ultrasound diagnostics, thanks to significantly higher sensitivity, NPV and diagnostic efficiency, significantly reduces the possibility of diagnostic error, that is, overlooking of VTE, in comparison to serial ultrasound diagnostics, that is of great importance in early detection of asymptomatic and atypical DVT forms.

## References

1. Bulger CM, Jacobs C, Patel NH. *Epidemiology of acute deep vein thrombosis. Tech Vasc Interv Radiol* 2004; 7(2):50-54.
2. Jovanovic M, Milic D, Djindjic B, Jovanovic J, Stanojevic G, Stojanovic M. *Importance of D-dimer testing in ambulatory detection of atypical and „silent“ phlebothrombosis. Vojnosanit Pregl* 2010;67(7):543-547.
3. Tovey C, Wyatt S. *Diagnosis, investigation, and management of deep vein thrombosis. BMJ* 2003; 326(7400):1180-1184.
4. Bockenstedt P. *D-dimer in venous thromboembolism. N Engl J Med* 2003;349 (13):1203-4.
5. Scarvelis D, Palareti G, Toulon P. *Hemosil D-dimer HS assay in diagnosis of deep vein thrombosis and pulmonary embolism. Results of a multicenter management study. J Thromb Haemostas* 2008;6:1973-5.
6. Marik PE, Plante LA. *Venous thromboembolic disease and pregnancy. N Engl J Med* 2008;359:2025-33.
7. Maksimović Ž. *Bolesti vena. Medicinski fakultet – CIBIF, Beograd, 1998.(Serbian)*

8. Carter D, Olchovsky D, Hagit Y, Langevitz P, Ezra D. Simultaneous deep vein thrombosis and transverse myelitis with negative serology as a first sign of antiphospholipid syndrome: a case report and review of the literature. *Clin Rheumatol* 2006; 25: 756–758.
9. Zlogar DF, Price D, Frazee B. Ultrasonography use in the emergency department: Six-month prospective analysis. *Ann Emerg Med* 2004; 44(4):S113-S113.
10. Birdwell BG, Raskob GE, Whitsett TL, et al. The clinical validity of normal compression ultrasonography in outpatients suspected of having deep venous thrombosis. *Ann Intern Med.* 1998; 128: 1–7.
11. Brown CM, Back M. Factors influencing the yield of duplex testing for lower extremity deep venous thrombosis. *J Vasc Nurs* 2004; 22(2):60.
12. Chan WS, Sanjeev C, Lee A. A red blood cell agglutination D-dimer test to exclude deep venous thrombosis in pregnancy. *Ann Intern Med* 2007;147:165-70.
13. Moerloose P, Palareti G, Aguilar C, Legnani C, Reber G, Peetz D. A multicenter evaluation of a new quantitative highly sensitive D-dimer assay for exclusion of venous thromboembolism. *Thromb Haemostas* 2008;100(3):505-12.
14. Bates SM, Grand'Maison A, Johnston M. A latex D-dimer reliably excludes venous thromboembolism. *Arch Intern Med* 2001; 161:447–453.
15. Kearon C, Ginsberg JS, Douketis J. Management of suspected deep venous thrombosis in outpatients by using clinical assessment and D-dimer testing. *Ann Intern Med* 2001; 135:108-111.
16. Dempfle CE, Zips S, Ergul H. The Fibrin Assay Comparison Trial (FACT): evaluation of 23 quantitative D-dimer assays as basis for the development of D-dimer calibrators. FACT Study Group. *Thromb Haemost* 2001; 85:671–8.
17. Wells PS, Anderson DR, Rodger M, Forgie M, Kearon C, Dreyer J, Kovacs G, Mitchell M, Lewandowski B, Kovacs MJ. Evaluation of D-Dimer in the Diagnosis of Suspected Deep-Vein Thrombosis. *N Engl J Med* 2003; 349(13):1227-1235.
18. Ten CAJ, Toll DB, Buller HR, Hoes AW, Moons KGM, Oudega R, et al. Cost-effectiveness of ruling out deep venous thrombosis in primary care versus care as usual. *J Thromb Haemostas* 2009;7(12):2042-9.
19. Shebel ND, Whalen CC. Diagnosis and management of iliac vein compression syndrome. *J Vasc Nurs* 2005; 23(1): 10–17.
20. Padberg F. Suprainguinal deep venous thrombosis and pulmonary embolism-Common but often silent. *J Vasc Surg* 2003; 37(5):1129-1130.
21. Katz DS, Hon M. Current DVT imaging. *Tech Vasc Interv Radiol* 2004; 7(2):55-62.
22. Theodoro D, Blaivas M, Duggal S, Snyder G, Lucas M. Real-time B-mode ultrasound in the ED saves time in the diagnosis of deep vein thrombosis (DVT). *Am J Emerg Med* 2004; 22(3):197-200.
23. Blättler W, Martinez I, Blättler IK. Diagnosis of deep venous thrombosis and alternative diseases in symptomatic outpatients. *Eur J Intern Med* 2004; 15(5):305-311.
24. Kelly J, Hunt BJ. The utility of pretest probability assessment in patients with clinically suspected venous thromboembolism. *Thromb Haemostas* 2003; 1(9):1888-1896.

Corresponding Author  
 Milan M. Jovanovic,  
 Clinical Center of Nis,  
 Vascular Surgery Clinic,  
 Nis,  
 Serbia,  
 E-mail: milan.m.jovanovic@gmail.com



# Is spinal anesthesia really innocent?

Gökhan Açmaz<sup>1</sup>, Abdullah Boztosun<sup>2</sup>, Hilal Yuvaci<sup>1</sup>, Aylin Inal<sup>3</sup>, Iptisam Ipek Müderris<sup>4</sup>

<sup>1</sup> Department of Obstetrics and Gynecology, Kayseri Training and Education Hospital of Medicine, Kayseri, Turkey,

<sup>2</sup> Department of Obstetrics and Gynecology, Cumhuriyet University School of Medicine, Sivas, Turkey,

<sup>3</sup> Department of Pediatrics, Kayseri Training and Education Hospital of Medicine, Kayseri, Turkey,

<sup>4</sup> Department of Obstetrics and Gynecology, Erciyes University School of Medicine, Kayseri, Turkey.

## Abstract

**Objective:** Evaluating the effects of maternal hypotension, a common complication of spinal anesthesia, on fetus.

**Design:** Prospective observational study.

**Setting:** A total of 46 pregnant women at term who previously had a caesarean section (C/S) were scheduled to undergo elective CS for their second CS and participated in this study. **Patients:** 46 patients were divided into two groups according to hypotension occurrence during spinal anesthesia.

**Interventions:** After all the patients received 1500ml Ringer Lactate solution 15 minutes before induction, the patients whose oxygen saturation became less than 97% received supplemental oxygen. If SBP was 90mm/Hg or less or a decreasing trend was observed during SA, intravenous injections of 2 to 3mg of ephedrine, up to a maximum total dose of 50mg, were administered.

**Main outcome measures:** Age, birth weight, pCO<sub>2</sub>, bicarbonate, ALT, AST, CK, LDH, Apgar scores, pH and babies requiring pediatric help.

**Results:** pH, HCO<sub>3</sub>, PCO<sub>2</sub>, babies requiring pediatric help and Apgar scores were statistically significantly affected by hypotension.

**Conclusion:** In our study, hypotension is the most important factor contributing to acidosis occurrence. Low Apgar scores and increasing rates of pediatrician requirement in patients with hypotension during SA illustrates us that SA has negative impact on short term fetal outcome.

**Key words:** Acid-base assessment; fetal and neonatal status; elective cesarean section; spinal anesthesia

## Introduction

In recent years, many advantages of spinal anesthesia (SA) such as allowing the mother to be awake, minimizing the problems of maternal as-

piration, avoiding neonatal depression associated with general anesthesia have been established. As a result of this situation, SA has gained popularity as the anesthetic of choice for the pregnant patient. However, there are some conflicts among authors about SA used in cesarean sections (CS) for fetal safety because of sympathetic blockage-induced hypotension which can dangerously decrease uteroplacental perfusion.

Hypotension is the most common complication of SA for caesarean section and can threaten the wellbeing of the unborn child. Different incidences of hypotension from 15% (1) to 33%, (2) as reported in the literature, can be due to varying definitions and different methods of measurement. A decrease in maternal arterial blood pressure can influence intervillous flow significantly and prolonged hypotension can result in fetal asphyxia and severe neonatal acidosis. (3)

In literature, interestingly, some of the authors established a strong relationship between drugs and acidosis occurrence. This drug helps treatment of hypotension and is commonly used for hypotension in SA. (4) Despite many protocols preventing from hypotension in SA, sometimes this situation may be unavoidable. Although Gori et al. started the intravenous (i.v.) infusion of 1000mL of lactated Ringer solution forty minutes before the induction of spinal anesthesia to provide volume preload, they detected hypotension in 19 of 23 patients that required ephedrine injection. (5)

Hypotension is one of the most common side effects of SA. The aim of this study was to evaluate the effects of maternal hypotension, which occurred during SA, on fetus. Additionally, we compared the cases complicated with hypotension to uncomplicated cases from the point of cardiac markers and acid-base status of newborns who were delivered at term by elective CS under SA.

## Materials and methods

A total of 46 pregnant women at term (>37 completed weeks and 3 days) who previously had a caesarean section were scheduled to undergo elective CS for their second CS and participated in this prospective observational study. The patients were divided into two groups; patients complicated with hypotension during SA and uncomplicated patients. The study was approved by the institutional ethics committee and all participants signed an informed consent form regarding both CS and anesthetic technique.

After all the patients received 1500ml Ringer Lactate solution 15 minutes before induction, maternal age, CS history, and blood pressure (BP) before induction of anesthesia and at 1-minute intervals from induction to delivery and fetal birth weight were recorded. Patients received supplemental oxygen if oxygen saturation became less than 97%. None of the participants was in labor (defined as the presence of painful, regular contractions associated with a cervical dilatation of 3 cm or greater).

Maternal well-being was monitored by means of electrocardiography, pulse oximetry, and BP recordings before and during the anesthetic procedure. To prevent aorto-caval syndrome, the operating table was placed in the 15° tilt position (the angle was measured using a protractor with a hanging weight). Maternal hypotension was defined as a BP decrease of more than 20% from baseline, and corrected first by increasing the left lateral tilt to 20° and then, if SBP was 90 mm Hg or less or a decreasing trend was observed, by intravenous injections of 2 to 3mg of ephedrine, up to a maximum total dose of 50mg. The duration of hypotension was measured in minutes. Data concerning BP, electrocardiography and oxygen saturation, were recorded in 1-minute intervals until delivery. The Plusmed Plus 8000 monitoring device was used (Contec Medical Systems, Qinhuangdao, Hebei Province, 066004, P.R.China).

After double-clamping the umbilical cord, cord blood (arterial) was obtained using a pre-heparinized syringe Radiometer Pico 50 (Radiometer Medical APS Bronshoj Denmark) to assess the newborn's acid-base status. Measurements were

analyzed immediately using the Radiometer ABL basic 800 blood gas analyzer (Radiometer Medical APS Bronshoj Denmark).

A number of large studies have reported normal values for umbilical cord arterial blood gases. Sykes (6) et al. (n=899), Victory (7) et al. (n=17668) and Helwig (8) et al. (n=16060) studied consecutive term deliveries and found a mean pH of  $7.20 \pm 0.08$ ,  $7.24 \pm 0.07$  and  $7.26 \pm 0.07$  respectively. The description of acidosis was done according to the above criteria as  $\text{pH} \leq 7.2$  accepted to be significant. Respiratory depression was considered as the absence of spontaneous breathing and requirement of artificial respiration for longer than a 5 min period. The serum levels of creatinine kinase (CK) with myocardial specific isoform, aspartate amino transferase (AST), alanine amino transferase (ALT) and lactate dehydrogenase (LDH) were measured and served ruling out perinatale stress confirming in the diagnoses of perinatale asphyxia and myocardial damage. AST, ALT, LDH and CK were measured by radioimmunoassay.

Anesthetic and obstetric procedures were all standardized maneuvers, and all newborns were attended at the time of delivery by a pediatrician. Pediatricians who assigned the Apgar scores and determined the presence of hypotonia were blinded to the anesthetic technique used. Primary resuscitation care was performed by positive pressure ventilation using a mask (FiO<sub>2</sub> range, 0.21–0.35) in cases of transient tachypnoea of the newborn or mild respiratory distress syndrome.

## Statistical analysis

Differences between categorical variables were compared using the chi-squared test. To compare continuous variables, parametric and nonparametric analyses were performed by testing the appropriateness of variables to normal distribution. Differences between groups were evaluated using an unpaired t test or Mann-Whitney U test. Data from the study were evaluated using the statistical SPSS package release 15.0 (SPSS Inc., Chicago, Ill., USA). P-values of < 0.05 were considered statistically significant.

## Results

During study period, 60 women were included in our study after their informed constant for C/S and anesthesia technique. 30 of them constituted hypotensive group and 30 of them constituted normotensive group. 14 infants in hypotensive group, four due to pH level missing, one due to CK level missing, three due to AST level missing and one due to ALT level missing, didn't meet entry criteria. Four mothers were excluded from the study because of maternal DM and one of them because of thyroid disease. Two of in control group were excluded from study because of pH levels missing. Finally, we had 18 patients in hypotensive group and 28 patients in normotensive group. Our results are listed in table and pH, HCO<sub>3</sub>, PCO<sub>2</sub> and Apgar scores are statistically significantly affected by hypotension.

We didn't detect any perintanale asphyxia in either group. None of the infants required endotracheal intubation mechanical ventilation. 7 of the newborns needed pediatrician help and four infants born under SA with maternal hypotension required ventilation with bag and mask. Three of

them were administered neonatal intensive care unit only for observation.

## Discussion

In literature, some of the authors suggested that regional anesthesia be gaining popularity for CS and it is associated with good fetal outcome as demonstrated by higher Apgar scores and neurobehavioral tests. (9-10) Aim of this study was illustrate the short term outcomes of newborns that were born under SA and complicated with hypotension. In this study, we achieved to illustrate relationship between hypotension and acidosis. Additionally, we detected increased requirement of pediatrician help for babies.

Concomitant to our study Müller et al. defined strong relationship between regional anesthesia and fetal acidosis. In their epidemiologic study, they examined 5806 healthy, singleton, uncomplicated term pregnancies and determined that maternal arterial hypotension is by far the most common problem encountered during regional anesthesia for cesarean delivery. They concluded that this may

Table 1. (Evaluation of two groups for age, weight, pCO<sub>2</sub>, HCO<sub>3</sub>, ALT, pH, AST, CK, LDH and Apgar scores)

Variable	Group 1(n=28)	Group 2 (n=18)	P value
Age	27,03 ± 4,37	25,50±5,39	0,295
Birth weight	3246,07±353,02	3226,11±292,11	0,843
pCo2	42,10±4,96	47,88±9,43	0,025
Bicarbonate	24,02±1,59	22,11±3,64	0,048
ALT	17,41±7,59	13,29±6,75	0,067
AST	24,73 (10-56)	22,69 (16-44)	0,612
CK	187,34(62,40-533,80)	196,78 (108-602)	0,928
LDH	280,26 (222-421,30)	311,10 (232-715,40)	0,260
Apgar 1. minute	7,5 (4-8)	8 (8-8)	<0,001
Apgar 5. minute	9,64 (7-10)	8,5 (6-10)	0,038

Mean ± standard deviation ( $\bar{X} \pm s.d$  )

median (minimum-maximum)

Table 2. (Evaluation of two groups for pediatrician help and pH)

Variable	Group 1 n (%)	Group 2 n (%)	P value
Normal babies	27(%71,1)	11(%28,9)	0,004
Babies requiring pediatric help	1(%12,5)	7(%87,5)	
Normal pH	28 (%100)	14 (%77,8)	0,019
Acidotic pH	0 (%0)	4 (%22,2)	

be responsible for higher incidence of acidosis and loss of uteroplacental blood flow. (11)

Some of the authors, interestingly, reported increased umbilical arterial minus venous Pco<sub>2</sub> (A–V Pco<sub>2</sub>) difference after ephedrine administration. (4)  $\beta$ -adrenergic stimulation of fetal lamb with isoproterenol has been shown to produce an initial increase in oxygen consumption and an increase in blood glucose and lactate concentrations. (12) These data suggest that hypotension alone not be responsible for acidosis seen in patients. One possible mechanism of fetal acidemia is not related to the uteroplacental or fetoplacental circulation, but to the ephedrine induced fetal  $\beta$ -adrenergic stimulation, as it crosses the placenta and increases fetal catecholamine levels and heart rate. This situation may increase utilization of glucose and oxygen. All these mechanisms can increase lactate concentrations. Despite therapeutic equivalence, phenylephrine still produces a better acid–base status than ephedrine. Because we don't have phenylephrine in our country, we have to use ephedrine. So, this situation may help occurrence of fetal acidosis. However, it is possible that fetal catecholamine stimulation before delivery might be beneficial. When a  $\beta$ -adrenergic agonist was administered before elective C/S, lower respiratory morbidity, better lung function and reduced risk of hypoglycaemia in the newborn infant was found. (13)

The Apgar score is commonly used for infant condition at birth which is a conventional method for assessing fetal well-being. (14) Although routinely used for immediate evaluation of newborns, Apgar score is a subjective measurement method and its diagnostic value in fetal asphyxia is not significant. (15) In our study, Apgar scores of newborn were affected by hypotension; additionally, we detected increased rates of babies needing pediatrician's help.

None of the biochemical parameters was found to be related with hypotension and we were not able to find any other study about relationship between hypotension occurrence under SA and biochemical parameters for the evaluation of perinatal distress. In our study, it is certain that hypotension is the most important factor contributing to acidosis occurrence. Statistically significant low Apgar scores and increasing rates of pediatrician requirement in patients with hypotension during

SA lead us to believe that SA has negative impact on short term fetal outcome.

### Acknowledgements

We thank the Anesthesiology department of our hospital for their contribution to this research (Gülseren Süer Kaya, Türkan Söyler Altun). We also thank Dr. Faruk Balkaya (English Department of Kayseri Erciyes University) for his contribution to English terms and language.

### References

1. Tarkkila P, Isola J. A regression model for identifying patients at high risk of hypotension, bradycardia and nausea during spinal anesthesia. *Acta Anaesthesiol Scand* 1992;36:554–8.
2. Carpenter RL, Caplan RA, Brown DL, Stephenson C, Wu R. Incidence and risk factors for side effects of spinal anesthesia. *Anesthesiology* 1992; 76:906–16.
3. Wright R, Shnider S: Hypotension and regional anesthesia in obstetrics, in Shnider S, Levinson G (eds): *Anesthesia for Obstetrics* (ed 3). Baltimore, MD, Williams and Wilkins, 1993, pp 397-407
4. Cooper DW, Carpenter M, Mowbray P, Desira WR, Ryall DM, Kokri MS. Fetal and maternal effects of phenylephrine and ephedrine during spinal anesthesia for Cesarean delivery. *Anesthesiology* 2002; 97: 1582–90)
5. Gori F, Corradetti F, Cerotto V, and Peduto VA. Influence of Positioning on Plain Levobupivacaine Spinal Anesthesia in Cesarean Section. *Anesthesiology Research and Practice*. Volume 2010, Article ID 212696, 4 pages doi:10.1155/2010/212696
6. Sykes GS, Molloy PM, Johnson P, Gu W, Ashworth F, Stirrat GM et al. Do apgar scores indicate asphyxia? *Lancet* 1982;1:494–496.
7. Victory R, Penava D, da Silva O, Natale R, Richardson B. Umbilical cord pH and base excess values in relation to adverse outcome events for infants delivering at term. *Am J Obstet Gynecol* 2004;191:2021–8.
8. Helwig JT, Parer JT, Kilpatrick SJ, Laros RK. Umbilical cord acid-base state: What is normal? *Am J Obstet Gynecol* 1996;174:1807–12.
9. Evans CM, Murphy JF, Gray OP, Rosen M. Epidural versus General anesthesia for elective cesarean section. Effect on Apgar score and acid base status of the newborn. *Anesthesia* 1989;44:778-82.)

10. Ratcliffe FM, Evans JM, Neonatal well-being after elective cesarean delivery with general, spinal and epidural anesthesia. *Eur J Anesthesiol* 1993;10:175-81.
11. Mueller MD, Brühwiler H, Schüpfer GK, Lüscher KP. Higher rate of fetal acidemia after regional anesthesia for elective cesarean delivery. *Obstet Gynecol* 1997; 90:131-4.
12. Gournay VA, Roman C, Rudolph AM. Effect of beta-adrenergic stimulation on oxygen metabolism in the fetal lamb. *Pediatr Res* 1999; 45: 432-6.
13. Eisler G, Hjertberg R, Lagercrantz H. Randomised controlled trial of effect of terbutaline before elective caesarean section on postnatal respiration and glucose homeostasis. *Arch Dis Child Fetal Neonatal Ed* 1999; 80: 88-92.
14. Levine EM, Ghai V, Barton JJ, Strom CM. Pediatrician attendance at caesarian delivery: necessary or not? *Obstet Gynecol* 1999; 93(3); 338-40.
15. Marrin M, Paes B. Birth asphyxia. Does Apgar score have diagnostic value? *Obstet Gynecol* 1988; 72: 120-3.

*Corresponding Author*

Gökhan Açmaz,

Department of Obstetrics and Gynecology,

Kayseri Training and Education Hospital of Medicine,

Kayseri,

Turkey,

E-mail: gokhanacmaz@mynet.com

# Neurogenic appendicopathy in pediatric patients: A clinical and histopathological entity

Slobodan Grebeldinger<sup>1</sup>, Branka Radojic<sup>1</sup>, Igor Meljnikov<sup>1</sup>, Michaela Mocko-Kacanski<sup>2</sup>

<sup>1</sup> Clinic for Pediatric Surgery, Institute of Child and Adolescent Health Care of Vojvodina, Novi Sad, Serbia,

<sup>2</sup> Centre for pathology and histology, Clinical Centre of Vojvodina, Novi Sad, Serbia.

## Abstract

**Introduction:** 15-20 % of appendices removed from patients with suspected appendicitis appear normal on histological examination. The cause of pain in such patients is still unknown. There is an increasing evidence of involvement of the enteric nervous system in immune regulation and in inflammatory response of appendix. Neuroproliferation in the appendix, in association with an increase of S-100 protein level may be involved in the pathophysiology of acute right abdominal pain in the absence of an acute inflammation of the appendix. Nerve proliferation and an increased number of endocrine cells are typical for neurogenic appendicopathy (NA). In neurogenic appendicopathy, a large number of proliferating nerves are visualized independently of neurotransmitters by immunohistochemical staining for S-100 protein.

**Aim:** The aim of study was to confirm the neurogenic appendicopathy as a clinical and histopathological entity in pediatric patients.

**Material and methods:** A case-control study included 209 consecutive patients, aged 4-19 years, and underwent appendectomy for suspected appendicitis. All patients were examined clinically, laboratory and by ultrasound. We evaluated the incidence of NA in macroscopically normal specimens from patients presenting the symptoms of acute appendicitis. Neurogenic appendicopathy was diagnosed by S-100 immunohistochemistry and hematoxylin-eosin (H-E) staining in negative appendectomy group. Data obtained from anamnesis, clinical and ultrasound examination, psychological evaluation and postoperative follow-up were analyzed and correlation with the presence of neurogenic appendicopathy is made.

**Results:** Neurogenic appendicopathy was confirmed in 19 patients (9,09%) clinically presented as acute appendicitis and in 19 patients (38%) with negative appendectomy. Negative appendectomy

rate was 23,92%. The clinical signs for diagnosis of NA were antalgic position, ileocecal pain and presence of previous similar problems. The ultrasound signs for NA diagnosis were low US grade, thickness of appendiceal wall < 2mm, without the presence of echogenic and anechogenic content. H-E staining confirmed the NA in 18 cases, while S-100 protein immunohistochemistry confirmed the NA in 19 patients. Neurogenic appendicopathy is a rare histopathological entity that can be detected by standard H-E staining with an accuracy of 94.74%. S-100 protein immunohistochemistry increases the safety of diagnosis. Histological and clinical confirmation of neurogenic appendicopathy in negative appendectomy group requires revision of indication for appendectomy in pediatric patients.

**Conclusion:** Neurogenic appendicopathy is the clinical and histopathological entity and indication for appendectomy in pediatric patients. On this way the part of negative appendectomy declared surgically and therapeutically justified, thus the negative appendectomy rate in the present study was 14.83%. Therefore it is important to analyze a macroscopically normal appendix in patients presenting with symptoms of acute appendicitis.

**Key words:** Neurogenic appendicopathy; Acute Appendicitis; Negative appendectomy, S-100 / Hematoxylin-eosin staining

## Introduction

Suspected acute appendicitis is the leading cause of emergency laparotomy in children. The negative appendectomy rates of 15 to 20% still exist, despite clinical presentation and routine use of diagnostic algorithm. [1,2,3] The etiology of abdominal pain in these patients remains unknown. Neurogenic appendicopathy (NA) is a disease with a "proliferation of neuroendocrine structures in the appendix, associated with pain in the right lower quadrant of the

abdomen and signs of acute appendicitis".[4,5,6,7] It is a state of neurogenic hyperplasia, nerve proliferation and increase the number of endocrine cells in the appendiceal wall. Histologically, it is presented as an increase of sympathetic nerve fibers and schwannoma ganglia cells in submucosa, thickening of the outer muscular layer and occurs in 40% of the "normal" appendices.[8] *Maresch* and *Masson* gave the first description of neurogenic appendicopathy as neuromatous histological lesions of the appendix without signs of acute inflammation. *Pierre Masson* used the term "appendicite neurogene" for a proliferation of nerve fibers resembling a neuroma in the appendix. [4] *Feyrter* suspected that the abnormal communication between the "adeno and neurointestinum" causes neurogenic appendicopathy. Neurovascular crisis is a basic pathophysiological mechanism that leads to irregular peristalses, spasm and hyperemia of appendiceal blood vessels. [9] Studies on animal models indicate the possible role of neuroimmune reactions in chronic and painful inflammation.[10] *Di Sebastiano* and *Buchler* have confirmed that 15 to 25% of appendices in patients operated for suspected acute appendicitis on histological examination seems "normal", where the cause of pain in the abdominal right lower quadrant (RLQ) is unclear. The assumption of the modified contents of neuropeptides in chronic inflammation has led the authors to examine the possible change in peptidergic innervations for substance P (SP), vasoactive-intestinal peptide (VIP) and growth associated protein-43 (GAP-43) using immunohistochemical methods. Neuroproliferation in the appendiceal wall in a state with high levels of SP and VIP may be involved in the pathophysiological mechanism of acute pain in the RLQ without histological confirmation of acute appendicitis. The same authors mark off neuroimmune appendicitis as a pathological entity. [11,12] *Coskun* analyzed the relationship between the enteric nervous system and mast cells in normal and pathological appendix conditions. [13]

On the basis of the proliferation and swelling of axons in the mucosa observed by electron microscopy by *Aubock* and *Ratzenhofer* (1969) [14], *Höfler* (1980) proposed the classification of neurogenic appendicopathy [15,16]:

1) Mucosal NA is the most frequent variant occurring in 10% of all excised appendices.

The immunoreactions for neuron-specific enolase (NSE) and S-100 protein revealed an obviously increased number of nerve fibers in the mucosa, not detectable by current tinctorial stains. The mucosal plexus is markedly enlarged, separating the crypts of the mucosa. There is also an increase of nerve fibers in the innermost layers of the submucosa and, particularly, in the muscularis mucosae. The majority of the proliferated axons visualized by the immunoreactivity of NSE contained substance-P immunoreactivity, particularly those in the innermost mucosal and submucosal layers.

2) Central or axial neuroma occurs after obliteration of the top of the appendix and results in a large central nerve bundle, surrounded in typical cases by the muscularis mucosae. In central neuroma, a close contact of proliferating nerves with Meissner's plexus is obvious.

3) Neuromuscular proliferation is accompanied by a striking proliferation of smooth muscle fibers and axons adjacent to the mucosa or muscularis propria layera resulting in neuromuscular tangles. Immunohistochemical visualization of NSE revealed predominantly peripheral localization of nerve fibers in the neuromuscular tangles. The majority of the axons showed S-100 protein immunoreactivity. Neuromuscular proliferation is not accompanied by inflammation and proliferation of endocrine cells. [16, 17]

The number of endocrine cells in the stroma of the mucosa significantly increased in neurogenic appendicopathy. [18] *Wang* confirmed the presence of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-2 (IL-2) in the submucosa and lamina propria mucosae of appendix in patients clinically presented as acute appendicitis, but histologically classified as "normal" appendix.[19] *Franke* tried to define the preoperative clinical signs that recognize neurogenic appendicopathy as a clinical entity. He evaluated whether simple hematoxylin-eosin (H-E) staining is sufficient for the histological diagnosis of NA. [20, 21] In a previous multicenter study he demonstrated that NA is a histological entity. *Franke* noted that NA is very rare in children, while on basis of anamnesis and clinical examination is not possible preoperatively diagnosed. [20] In spite of use the sophisticated diagnostic methods diagnosis of acute appendicitis remains a

challenge. [22, 23] The fact that 40% of the removed appendices is without signs of inflammation indicates that decision on surgical treatment is a relatively easy. All attempts to establish neurogenic appendicopathy as a new disease entity have so far failed. A reliable preoperative differential diagnosis of NA and AA is not possible and little is known about a potentially distant course of the disease after surgery. [24]

### Objective

The aim of study was to confirm the neurogenic appendicopathy as a clinical and histological entity in pediatric patients.

### Material and methods

**A case-control clinical study was designed and conducted at tertiary care Children hospital. The trial** included 209 patients, aged 4 to 19 years, underwent appendectomy for suspected acute appendicitis. Experimental group included 50 patients underwent appendectomy for clinical suspicion of acute appendicitis in whom macroscopic and pathological findings didn't confirm the inflammation. Thus, the negative appendectomy is defined as an independent variable of research, and then conducted further histological examination by H-E staining and S-100 protein immunohistochemistry.

In the negative appendectomy group mark off two subgroups of patients: with neurogenic appendicopathy (NA) and without neurogenic appendicopathy (NNA). Control group included 159 surgically treated patients in whom acute appendicitis was confirmed histopathologically (AA).

All patients were examined clinically, with laboratory and ultrasound tests performed. Data obtained by medical history, physical examination, psychological evaluation and results of diagnostic procedures were analyzed and the correlation between the presence of neurogenic appendicopathy, clinical findings and diagnostic results has made. Primary variables of interest were divided into categories of demographic data, anamnestic data –abdominal pain duration and localisation, previous similar symptoms, loss of appetite, nausea, vomiting, diarrhea, urinary dis-

comfort, change in stool, fever. Clinical variables included antalgic position, coated tongue, palpation tenderness, guarding RLQ, muscles defance. Laboratory analysis included the number of white blood cells (WBC). The ultrasound examinations were performed in the whole sample. We previously described new ultrasound criteria of acute appendicitis in pediatric patients [25]. Preoperative psychological assessment of patients and their parents were correlated with the presence of neurogenic appendicopathy.

Histopathological analysis of appendix included:

1) Hematoxylin-eosin (H-E) staining. The minimal diagnostic criteria for early AA were focal erosions demarcated by an infiltrate of polymorphonuclear leukocytes, followed by submucosal and transmural inflammation with microabscesses in late stage. NA was diagnosed by H-E staining when a focal collection of pale spindle cells was found in the lamina propria mucosae (mucosal type of NA), or in an obliterated appendix (axial neuroma).

2) S-100 protein immunohistochemistry diagnosed NA by staining perineuronal Schwann cells to confirm the neurogenic nature of the lesion [26].

Clinical course and length of hospital stay, wound healing, the associated pathology and re-operation are observed. Follow up included the presence of pain in the scar in the RLQ of the abdomen, digestive symptoms and re-operation and was conducted for 3 months after discharge.

### Statistical analysis

The data were statistically analyzed using the software package Statistica for Windows ver. 9.1 (StatSoft, 2010). The data of comparative studies examined groups were analyzed by methods of multivariate statistics. The correspondent canonical analysis was used in order to present the impact of the condition, anamnestic, clinical, laboratory and ultrasound parameters to define the difference between the studied groups as well as the mutual influence of the subgroups. The collected data were grouped and presented in tables and graphs. Statistical analysis was performed at the Department of Biology and Ecology, Faculty of Natural Sciences, University of Novi Sad.



**Results**

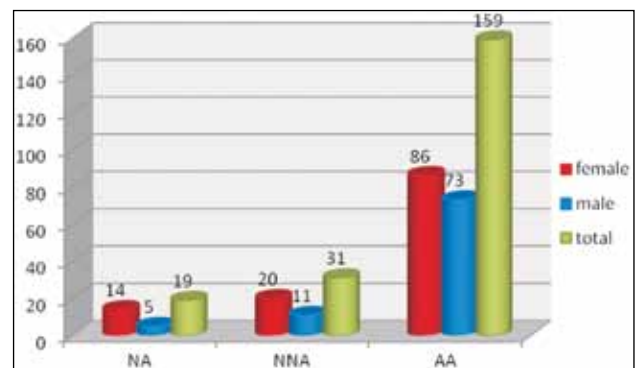
The study included 209 patients aged 4 - 19 years underwent appendectomy. Distribution of patient groups is shown in **Table 1**. Acute appendicitis is intraoperative and histologically confirmed in 159 patients (76%). The negative appendectomy rate initially was confirmed intraoperatively in 50 (24%) patients. After further testing using H-E staining and S-100 protein immunohistochemistry neurogenic appendicopathy was confirmed in 19 patients (9%), while the appendix was without pathological changes in 31 patients (15%). Looking at the distribution within the group of negative appendectomy, NA is present in 38% of macroscopically "normal" appendices. Sex ratio of the sample was 120 girls (57.42%) and 89 boys (42.58%). **Figure 1**. The average age was 11.52 years (NA 12.42, NNA 12.73, AA 11.19 years). **Figure 2**. The highest incidence of acute appendicitis is at the age of 12 to 15 years, while neurogenic appendicopathy usually occurs in the oldest study group of 16 to 19 years. **Figure 3**. Age distribution curve in the analyzed sample was discreetly moved to the right, as a result of increased frequency of older children in the total sample. **Figure 4** correspondent canonical analyses of the effects of demographic data (gender and age) in the tested groups were observed. In the space of first correspondence axis there is a tendency of approaching centroid of older children to the presence of NA, which is important information for the patient's psychological assessment. NNA group is isolated and without effect of relationship with the age and sex. **Figure 5** NA and NNA group is characterized by female sex that allows the effective separation of the first axis, but this is not an absolute characteristic of these groups, which can be seen in the space distribution of the second and third axis in a group is certainly determined by the older population age gradient, indicating that the main score on the population seems population of children aged 16-19 years, mostly female. **Figure 6**.

Clinical examination included a medical history, clinical symptoms and signs. Each of the anamnesis data, clinical symptoms and signs that determine the acute appendicitis were analyzed separately and included in the statistical calculations of clinical judgments. The anamnesis data in-

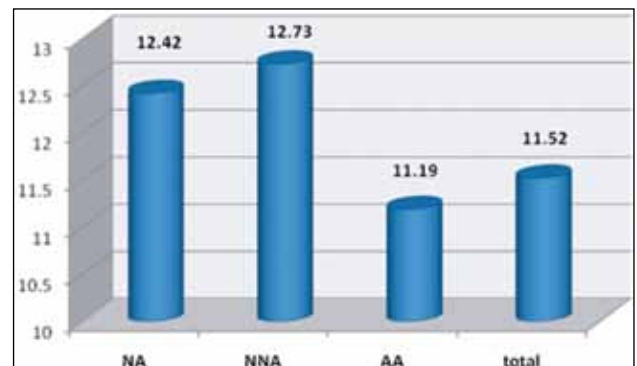
cluded eight symptoms that are in the study group showed a different frequency, and therefore the diagnostic value. A negative trend in the frequencies of occurrence of individual symptoms is noticed. **Table 2, Figure 7**.

*Table 1. Distribution of patients.*

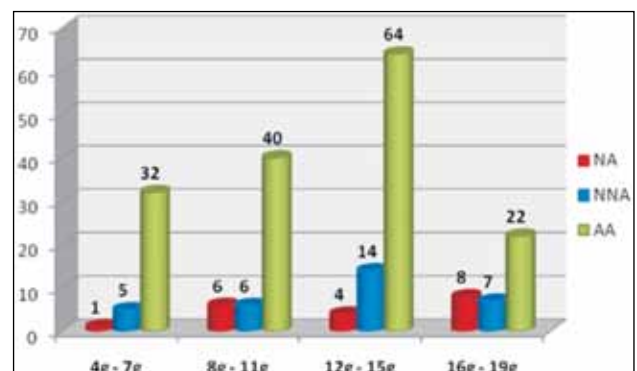
Experimental group	Neurogenic appendicopathy (NA)-19 Without neurogenic appendicopathy (NNA) - 31
Control group	Acute appendicitis (AA) – 159
<b>TOTAL</b>	209



*Figure 1. Sex distribution of patients*



*Figure 2. Average distribution of patients*



*Figure 3. Age distribution of patients*

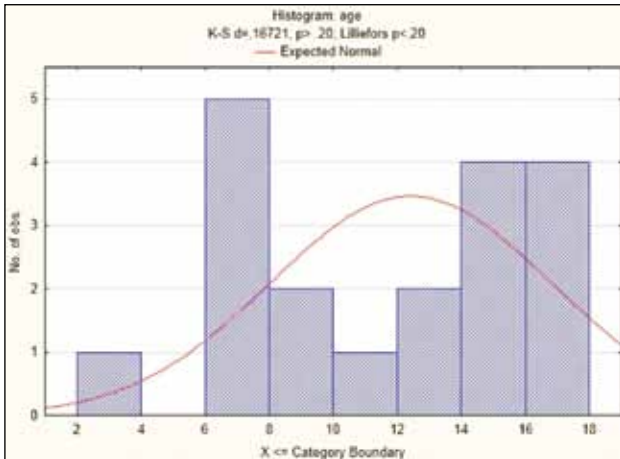


Figure 4. Age distribution in NA group

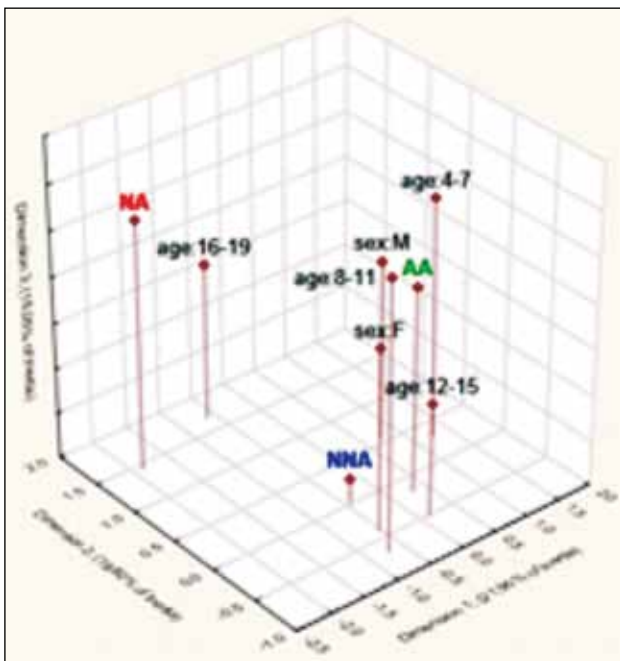


Figure 5. Demographics centroid positions of the analyzed group

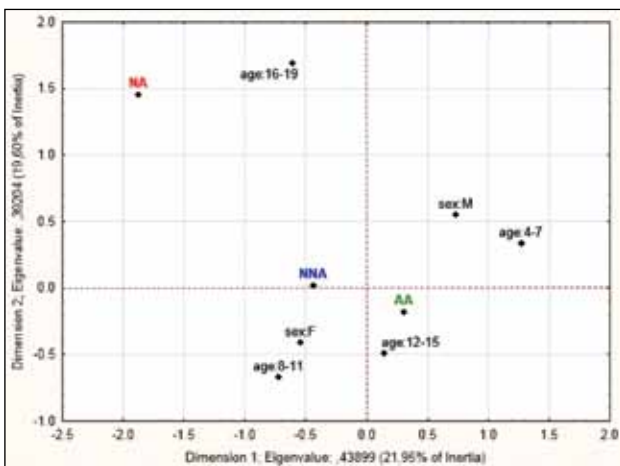


Figure 6. Centroid position of demographic data in the first and second correspondence axes space

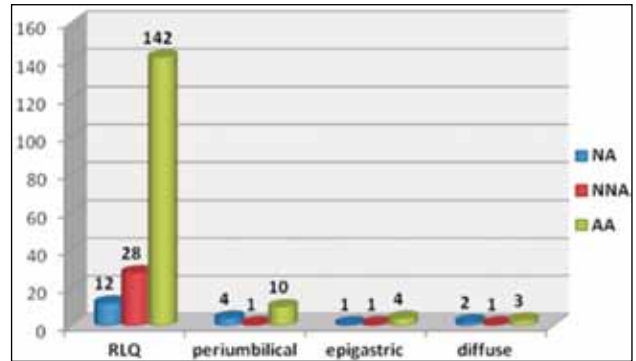


Figure 7. Localization of pain in the analyzed group

The effect of psychological evaluation does not show a clear determination to the appropriate study group. The psychological assessment is unobtrusive feature of the patients who cooperate effectively during diagnostic and anamnestic procedures, while striking is a psychological profile of patients who are not willing to cooperate and oriented towards the NNA group. Girls aged 16-19 years and 8-11 years were mostly psychologically and with the striking absence of cooperation. **Figure 8, Figure 9** Schedule of corresponding feature groups of patients studied in relation to elements of psychological characteristics and anamnestic and demographic data, indicate that the neurogenic appendicopathy directly correlated with previous similar problems, especially in older girls. **Figure 10**

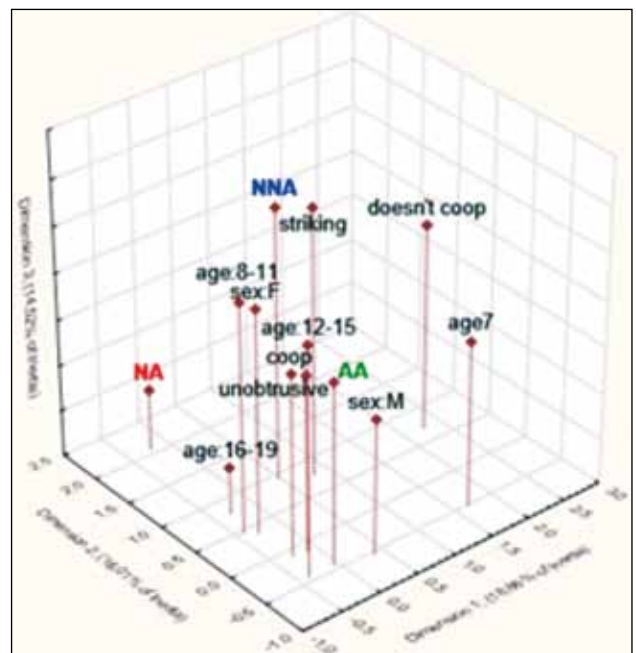


Figure 8. Psychological evaluation results.

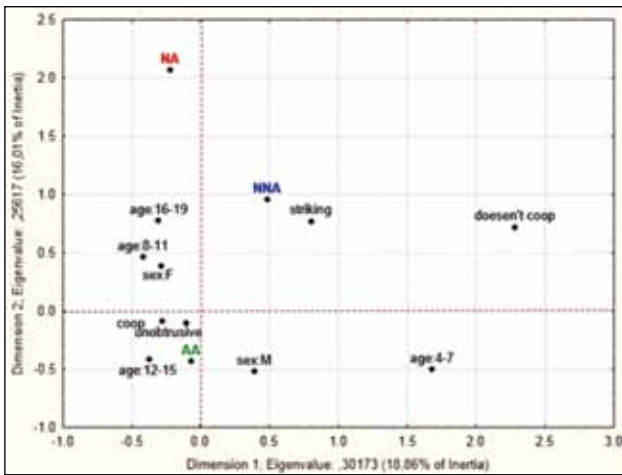


Figure 9. Psychological evaluation of patients and the degree of cooperation.

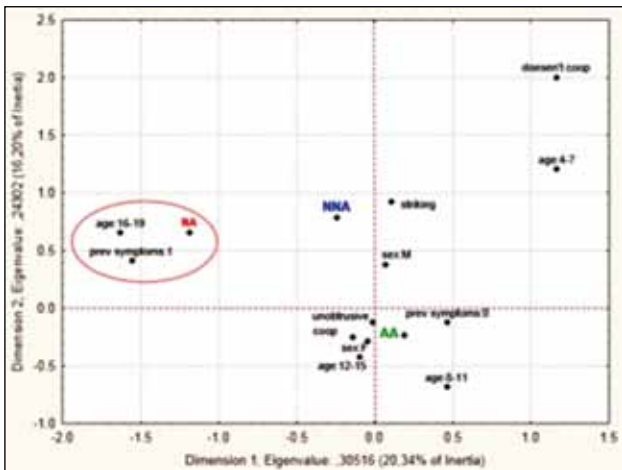


Figure 10. Psychological evaluation, patients cooperation and previous problems.

Results of clinical signs in all groups are shown in **Table 3**. When analyzing the elements of physical examination there has been more pronounced in patients with antalgic position in the NA and AA groups Ileocoecal pain as the central character in AA and NA groups from NNA group separation. It has a set of properties, among them the muscle defance. Diffuse muscle defance could indicate the presence of acute appendicitis, and its absence is uncertain nature of the intermediary position depending on the load level corresponding axis. NA was highly correlated with the presence of previous similar symptoms, which included the correspondent system with clinical parameters. As one of the most important qualities of NA is a high correlation between patients with a history characteristic of the presence of previous similar problems. For these reasons, as well as the results of conducted analysis

we included this feature in a history correspondent system with clinical parameters. The results of multivariate analysis conducted on clinical parameters, greatly contributing to the separation of character sets that are specific to each group.

Table 3. Potential diagnostic significance of the analyzed parameters.

Symptom	sensitivity	negative predictive value
antalgic position	0.880	0.550
coated tongue	0.930	0.591
muscle defance	0.945	0.647
ileocoecal pain	0.898	0.595

Patients with NA have the feature set: the antalgic position, ileocoecal pain, without coated tongue, low or normal values WBC, previous similar problems. NNA groups: without antalgic position, increased WBC, absence of ileocoecal pain. AA group is characterized by: the antalgic position-coated tongue-abdominal pain with percussion - moderately elevated WBC (class 3-5) - place the strongest pain periumbilical or ileocoecal,

**Results of ultrasound examination**

Ultrasound examination of the abdomen and the appendix has a high diagnostic value for diagnosis of appendiceal diseases in pediatric patients. The potential diagnostic significance of ultrasound signs is given in **Table 4**. Advanced ultrasound grade (III and IV) was absolutely dominant sign for the acute appendicitis diagnosis. Especially important factors are the diameter of the appendix > 7 mm and wall thickness > 2.2mm. The NA group is followed by: low US grade (I or II) - appendix wall thickness <2.2 mm - without hiperechogenic anechogenic content and appendix peristalses preserved. Characters related to the AA group: advanced US grade (III or IV) - appendix wall thickness > 2.2 mm, hiperechogenic and anechogenic content - appendiceal peristalses damaged and positive test of compressibility. NNA group: US grade I - appendix diameter <7 mm - wall thickness <2.2 mm – negative test compressibility.

**Histological examination results**

the results of histological examination in the whole sample are shown in **Table 5**.

In patients with negative appendectomy, histological examination was further performed of

Table 4. Results of US examination

US criteria	NA		NNA		AA	
	No	%	No	%	No	%
positive test compressible	12	63.16	13	41.94	153	98.08
outer diameter of appendix >7 mm	8	42.11	12	38.71	150	94.34
appendiceal wall thickness >2mm	6	31.58	9	29.03	123	77.36
hyperechogenic contents around the appendix	4	21.05	7	22.58	58	36.48
anechogenic contents around the appendix	4	21.05	6	19.35	56	35.22
appendicolith	2	10.53	3	9.68	25	15.72
aperistalts	6	31.58	6	19.35	32	20.13
fluid-filled abscess	0	0	0	0	19	11.95
free fluid in the RLQ of the abdomen	7	36.84	8	25.81	51	32.08
<b>US grade</b>						
grade I	4	21.05	19	61.29	12	7.55
grade II	11	57.89	11	35.48	43	27.04
grade III	4	21.05	1	3.23	50	31.45
grade IV	0	0.00	0	0.00	54	33.96

the direction of proving the presence of NA using S-100 protein immunohistochemistry.

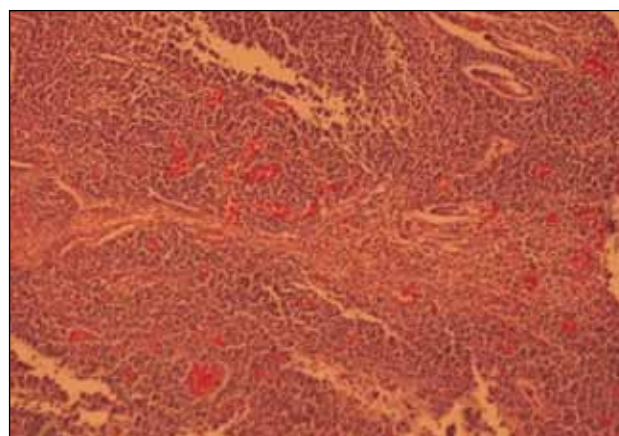
H-E staining confirmed the NA in 18 patients while the immunohistochemical staining to S-100 protein confirmed the NA in 19 patients. H-E staining emphasized rolled muscular wall with lymphocyte infiltrate. Hyperplastic lymph follicles are present in the lamina propria mucosae with increased germinative centers. Nerve fibers are damaged by the type of degenerative neurinoma. (Picture 1, 2)

Table 5. Histopathological results.

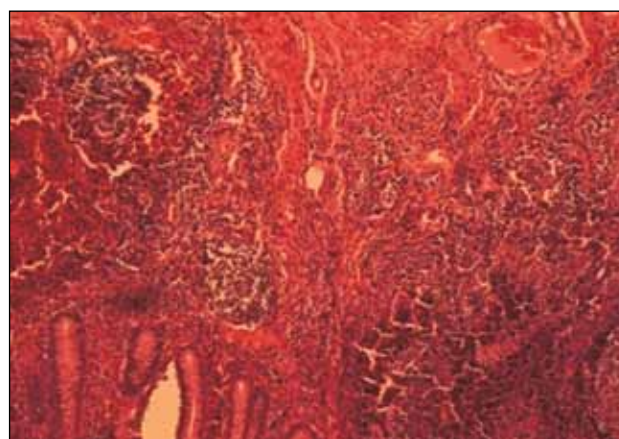
PH analysis	No	%
Negative appendectomy	50	23,92
Appendicitis catarrhalis	18	8,61
Appendicitis phlegmonosa	52	24,88
Appendicitis gangraenosa	43	20,57
Appendicitis perforativa	39	18,66
Abscessus periappendicularis	7	3,34
<b>Total</b>	<b>209</b>	<b>100</b>

S-100 protein immunohistochemistry Transverse section of appendix stained with antibodies to S-100 protein revealed that the nerve bundles and neurinomas are arranged between the circular and longitudinal muscle layers as well as within it. There is a clear layer of muscle interposition between some of the ganglia, which indicates that the ganglia are located at different levels of muscle layer. (Picture 3,4,5) Innervations of human appendicitis in longitudinal section. The tissue was

stained with antibody to S-100, which marks the ganglia and nerve fibers. Groups of neurons with distributed between and within the circular and longitudinal muscle layers.



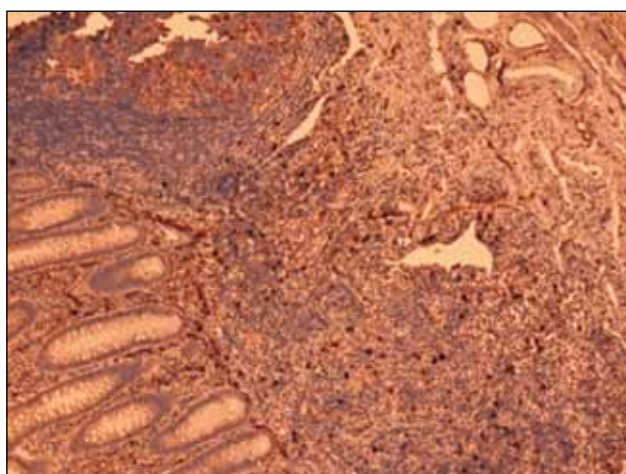
Picture 1. Hematoxylin-eosin staining



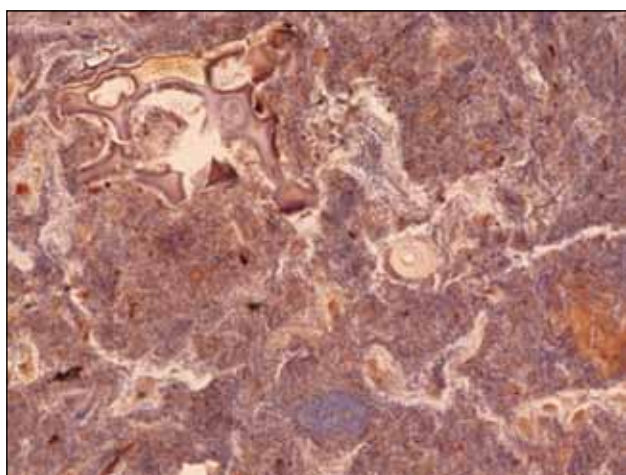
Picture 2. Hematoxylin-eosin staining



Picture 3. S-100 protein immunohistochemistry



Picture 4. S-100 protein immunohistochemistry



Picture 5. S-100 protein immunohistochemistry

Analysis of the spatial distribution of centroids in the space correspondent of the first and second axes shows that immunohistochemical techniques to the S-100 protein confirmed the existence of precise NA. **Figure 11**

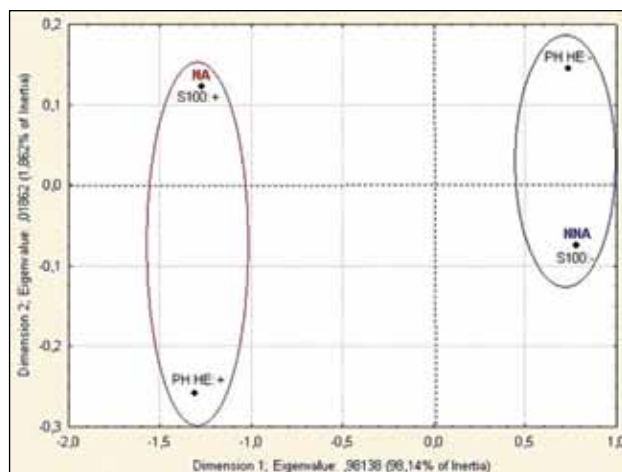


Figure 11. NA and NNA group in the space of the first two correspondence axes.

### **The clinical course results**

The operative wound healing, length of hospitalization and correlation with associated pathology were followed postoperatively. There is a predominance of primary healing in all tested groups (NA 94.7%, NNA 90.32%, AA 91.82%). Length of hospitalization was short. Girls are definitely the main carrier of the NA and NNA groups, followed by juvenile and adolescent ovarian pathology. Adhesions are more common in NA groups, while more common is mesenteric lymph node in NNA group. Body weight influences directly on the wound healing process, while the older girls with the elements directly linked ovarian pathology, most often in combination with the previous problems. This fact is supported by an increased incidence of ovarian juvenile physiological and pathological conditions in the study group.

Patients were followed up during the three months postoperatively. Particularly are noted the presence of pain in the right lower abdominal quadrant, pain in the scar, the presence of digestive disorders and reoperation. Summary of the above parameters is shown in **Table 6**. We analyzed postoperative parameters of patients' behavior in correlation with previous health problems and psychological assessment. Patients with neurogenic appendicopathy have a set of characteristics: psychologically unobtrusive, less conspicuous patient - female - present previous symptoms - without pain in the scar - no digestive disorders - age 16-19 years. Patients with negative appendectomy (NNA group): the patient psychologically striking

Table 6. Postoperative follow-up data

Symptom	NA		NNA		AA	
	No.	%	No.	%	No.	%
pain in the scar	2	10.52	5	16.12	18	11.32
RLQ pain	1	5.26	3	9.67	4	2.51
digestive disorders	1	5.26	4	12.9	9	5.66
reoperation	0	0.00	2	6.45	6	3.77

- half female, less male - present previous symptoms – with pain in the scar - present digestive disorders - age 12-15 years. Position AA group corresponds with a number of characters but not sexually classified - younger patients with no previous symptoms, psychological inconspicuous, rarely with postoperative problems.

### Discussion

Despite special investigations (ultrasound, laboratory, scores) the diagnosis of acute appendicitis in patients with equivocal signs of an acute inflammation is still a challenge, there is increasing evidence of involvement of the enteric nervous system in immune regulation and in inflammatory response. The potential role of local endocrine cells of appendix and neuroproliferation in the occurrence of repeated attacks of pain in RLQ is still a controversy.[27] The results of many studies indicated neurogenic appendicopathy as a possible cause of patient discomfort. [28] *Franke* performed multicenter clinical study to examine the differences between acute appendicitis, neurogenic appendicopathy and negative appendectomy. [20] In some aspects of medical history and clinical data were observed significant differences in these three groups, but none were strong enough to clearly distinguish these clinical conditions. Patients with NA had similar previous problems (38%) compared to patients with acute appendicitis (17%). Vomiting was more frequently present in patients with acute inflammation (41%), while in the NA group was present in 27% patients. There was no difference in the frequency of pain in the RLQ, abdominal pain migration, duration of pain, nausea, dizuric disturbance or gynecological conditions. Clinical parameters of inflammation were more often present in patients with AA compared to Na and NNA group: rebound tenderness 69% vs. 9% and 53%; muscle defance 26% vs. 2%

and 2%, median WBC higher than 10000 / ml: 78% vs. 53% and 45%. No differences were found in tenderness, rectal temperature or urine analysis. Multivariate analysis to differentiate the NA from the AA and NNA groups identified only sex as a significant predictor. This underlies the difficulty in identifying NA preoperatively. Many authors have not demonstrated a clear clinical differences and the conclusion that preoperative clinical differentiation between NA and AA is not yet possible. [4, 5, 6, 7] In our study six standard symptoms are analyzed and showed a different frequency and diagnostic value. There have been an increasing number of patients with distinct antalgic position in the NA and AA groups. This result is both a lower negative predictive value of this diagnostic parameter 0550, although it's high sensitivity of 0880. Multivariate canonical correspondent analysis has defined a set of clinical features that separates each group. NA group describes a set of clinical signs: antalgic position, ileocecal pain, without coated tongue, normal WBC with anamnestic data of previous similar problems. NNA group (negative appendectomy): antalgic position, elevated WBC, without ileocecal pain which indicate that no acute inflammation of the appendix. AA group is characterized by the set of characteristics: antalgic position, coated tongue, with abdominal pain at percussion, moderately elevated WBC (Class III-V), ileocecal or periumbilical pain.

Prospective studies confirmed that 25% of appendices who were intraoperatively seemed "normal" showed histopathological signs of inflammation. *Franke* in a prospective multicenter study compared the two methods of histopathological examination for the neurogenic appendicopathy diagnosis and found that NA is histopathological entity which can be detected by standard H-E staining with an accuracy of 93%. He found that staining with S-100 protein immunohistochemistry

increases the security of diagnosis. *Franke* found the incidence of NA in 46,9% patients without acute inflammation, whereas the incidence of NA in patients with acute appendicitis was much lower (3,8%). [20] Cross-section of the appendices stained with S-100 protein antibodies revealed that the nerve bundles and neurons are arranged between the circular and longitudinal muscle layers as well as within it. There is a clear layer of muscle interposition between some of the ganglia, which indicates that the ganglia are located at different levels of muscle layer. [21] *Wolf* on a sample of 127 appendices confirmed neurogenic appendicopathy in 44, 8% of patients who were without histological signs of acute inflammation, but at the same time the histological signs of NA were present in 14, and 5% of patients with acute appendicitis. [7] In our study, the degree of inflammation was determined macroscopically during the operation, and the diagnosis was confirmed by pathological examination of the appendix. In total sample, acute appendicitis was confirmed in 159 patients, while 50 appendices were without signs of inflammation (23.92%). This is the "negative appendectomy" rate which has been additionally histopathologically examined in the direction of proving the NA by H-E staining and S-100 protein immunohistochemistry. H-E staining confirmed NA in 94, 74%.

The diagnosis of acute appendicitis is still an open problem in pediatric surgical practice. Diagnosis of appendicitis remains a surgical challenge. Precise etiopathogenesis is unclear in the surgically treated patients with clinical signs of acute appendicitis and normal histological findings of standard H-E staining. Some findings indicate the presence of enlarged lymph follicles. The study derived nerve fibers positive for neuron specific enolase (NSE) were seen in the mucosa, especially around the base and around the crypt of appendix. [29] *Amber* studied the histopathological, immunohistochemical and quantitative imaging analysis in examining discrepancies between clinical and histopathological diagnosis of acute appendicitis. They found that about 25% appendices removed for a clinical presentation of acute appendicitis on standard H-E staining showed no signs of inflammation. [30] Since appendectomy relieves patient discomfort and pain, it is assumed that the cause lies in no inflammatory pathology. Inflammatory response involving local

endocrine cells and neuroproliferation caused of repeated attacks of pain which is proven by S-100 protein and NSE immunohistochemistry. Markers of inflammation such as cytokines can be detected immunohistochemically before the findings of inflammatory infiltrates in the histological analysis. Perhaps a normal appendices histological testing for the presence of inflammatory markers enable early detection of inflammation and potentially negative appendectomy declared justified. *Xiong* described fine, delicate nerve fibers near the epithelium and strong nerve fibers in the area between the crypts of appendix in 40% of histological negative appendices. [31] Neural components in all histological layers of the appendix are more prominent in histological negative appendix than in patients with histological positive appendicitis, indicating the possibility that the cause of acute pain in the RLQ is no inflammatory origin. *Franke* followed up in 85% of patients. More than 75% of patients with confirmed NA were completely without symptoms after appendectomy. The frequency and type of postoperative symptoms was similar in all three groups of subjects. Most frequently, patients suffered from symptoms related to their scar and increased sensitivity to meteorological changes. In our study on the evaluation of neurogenic appendicopathy the patients were followed up for three months. The presence of pain in the RLQ, pain in the scar, digestive disorders and re-operation were particularly noted. A comparative analysis showed the pain in the scar at 10, 52% patients with NA, 16.12% in NNA group and in 11.32% patients with acute appendicitis. Pain in RLQ was present postoperatively in 5, 26% patients with NA, 9.67% in NNA group, and 2.51% AA patients. Digestive disorders were present postoperatively in one (5.26%) patient with NA, 12.9% in the NNA group, and 5.66% in AA patients. There was no re-operation in the NA group, while in the NNA group was in two patients and in acute appendicitis group in six patients. The authors concluded that the NA can be diagnosed by H-E staining and confirmed as a pathological entity.

## Conclusion

The study confirmed the neurogenic appendicopathy as a clinical and histological entity. Clinical parameters in the diagnosis of NA are antal-

gic position of the patient with an ileocecal pain, coated tongue and muscle defance, normal WBC, and his previous similar symptoms especially in girls. Ultrasound criteria in the diagnosis of NA are low US grade (I or II), the wall thickness <2.2 mm, the absence of hiperechogenic and anechogenic content while appendiceal peristalses are preserved. NA is a histopathological entity that can be proved by H-E staining with an accuracy of 94.74%. S-100 protein immunohistochemistry increases the security of diagnosis. Confirming the presence of neurogenic appendicopathy in pediatric patient's part of negative appendectomy was therapeutically justified. Clinical and histological confirmation of the neurogenic appendicopathy, the phenomenon of negative appendectomy in pediatric patients is subject to revision.

### Abbreviations

NA - neurogenic appendicopathy  
 NNA - without neurogenic appendicopathy  
 AA - acute appendicitis  
 WBC - white blood cell  
 US – ultrasound  
 RLQ- right low quadrant  
 H-E- hematoxylin-eosin  
 VIP vasoactive-intestinal peptide  
 GAP-43 growth associated protein-43  
 NSE neuron-specific enolase  
 TNF-  $\alpha$  tumor necrosis factor-  $\alpha$   
 IL-2 interleukin-2

### References

1. Lintula H, Kokki H, Kettunen R, Eskelinen M. Appendicitis score for children with suspected appendicitis. A randomized clinical trial. *Langebecks Arch Surg*,2009;394 (6):999-1004.
2. Coursey CA, Nelson RC, Patel MB, Cochran C, Dodd LG, Delong DM, et al. Making the diagnosis of acute appendicitis: do more preoperative CT scans mean fewer negative appendectomies? A 10- years study. *Radiology*,2010;254(2):460-8.
3. Kosloske AM, Love CL, Rohrer JE, Goldthorn JF, Lacey SR. The diagnosis of appendicitis in children: outcomes of a strategy based on pediatric surgical evaluation. *Pediatrics*, 2004; 113: 29-34.
4. Doberaurer W. Neurogenic appendicopathy. *Journal of Gerontology*, 1957;12(4):398-400;
5. Quell M, Horvath W. Neurogenic appendicopathy-long term results following appendectomy. *Chirurg*,1997;58(9):597-600.
6. Höfler H. Neurogene Appendikopathie – eine häufige, aber selten diagnostizierte Krankheit. *Langenbecks Arch Chir*,1980;351:171–8
7. Wolf G, Stadler H. Das klinische Bild der “neurogenen Appendikopathie.” *Acta Chir Austriaca*,1981;25–9.
8. Naik R, Baliga P, Pai MR. Neurogenic appendicopathy- role of enterochromatoffin cells in its pathogenesis. *Indian J Pathol Microbiol*,1999;42(3):279-81.
9. Feyrter F. The theory of the peripheral endocrine (paracrine) glands. *Wien Med Wochenschr*,1956; 9;106(23):515-6.
10. Nemeth L, Rolle U, Reen D, Puri P. Nitrergic hyperinnervation in appendicitis and in appendicitis histologically classified as normal. *Archives of Pathology and Laboratory Medicine*,2002;127(5):573-8.
11. Di Sebastiano P, Fink T, Weihe E, Friess H, Beger H, Büchler M. Changes of protein gene product 9.5 (PGP 9.5) immunoreactive nerves in inflamed appendix. *Dig Dis Sci*,1995; 40:366–72.
12. Di Sebastiano, Fink T, di Mola F, Weihe E, Innocenti P, Friess H, Büchler M. Neuroimmune appendicitis. *The Lancet*,1999;354:461-6.
13. Coskun N, Indel M, Elpek G. Mast cell density and neuronal hypertrophy in patients with acute appendicitis. *The Turkish Journal of Gastroenterology*,2003;14(1):54-8.
14. Aubock L, Ratzenhofer M. Extraepihelial enterochromaffin cell- nerve-fibre complexes in the normal human appendix, and in neurogenic appendicopathy. *J Pathol*,1982;136(3):217-26.
15. Höfler H. Neurogene Appendikopathie – eine häufige, aber selten diagnostizierte Krankheit. *Langenbecks Arch Chir*,1980;351:171–8.
16. Höfler H, Kasper M, Heitz. The neuroendocrine system of normal human appendix, ileum and colon, and in neurogenic appendicopathy. *Virchows Arch Pathol Anat*,1983;399:127-40.
17. Laird W, Nolan L. Significance of the Schwannomas as a factor in obscure cases of appendicitis. *The Am J Surg*,1943;3:418-20.
18. Stanley MW,Cherwitz D,Hagen K, Snover DC. Neuromas of the appendix. A light-microscopic, immunohistochemical and electron-microscopic study of 20 cases. *Am J Surg Pathol*,1986;10(11):801-15.
19. Wang Y, Reen DJ, Puri P. Is a histologically normal appendix following emergency appendectomy always normal? *Lancet*, 1996; 347: 1076–9.



20. Franke C, Gerharz C, Bohner H, Ohmann C, Heydrich G, Krämling HJ, et al. Neurogenic appendicopathy: a clinical disease entity? *Int J Colorectal Dis*, 2002; 17:185-91.
21. Franke C, Gerharz C, Bohner H, Ohmann C, Heydrich G, Krämling HJ, et al. Neurogenic appendicopathy in children. *Eur J Pediatr Surg*, 2002; 12:28-31.
22. Khairy G. Acute appendicitis: Is removal of a normal appendix still existing and can we reduce its rate? *The Saudi Journal of Gastroenterology*, 2009; 3:167-70.
23. Landsdale N, Hill R, Hancock S, Thomson M, Marven S. Stress-related mucosal disease in childhood appendicitis. *Pediatr Surg Int*, 2008; 24:1219-22.
24. Van Voldrop V, Pattyn P, Ceelen W. Management of the „normal“ appendix during surgery for right fossa syndrome: proposed clinical algorithm. *Acta Chir Belg*, 2007; 107:8-11.
25. Grebeldinger S, Radojčić B, Meljnikov I, Drašković B, Uram-Benka A. The news in ultrasound diagnostic of acute appendicitis in pediatric patients. *HealthMED Journal*, 2010; 4(4) suppl. 1:964-72.
26. Stefansson K, Wollmann R, Jerkovic M. S-100 protein in soft-tissue tumors derived from Schwann cells and melanocytes. *Am J Pathol*, 1982; 106:261-8.
27. Bouchard S, Russo P, Radu A, Adzick N. Expression of neuropeptides in normal and abnormal appendices. *J Pediatr Surg*, 2001; 36 (8):1222-6.
28. Grunewald B, Keating J. Should the 'normal' appendix be removed at operation for appendicitis? *J R Coll Surg Edinb*, 1993; 38:158-60.
29. Guller U, Oertli D, Terracciano L, Harder F. Neurogenic appendicopathy: a frequent, almost unknown disease picture. Evaluation of 816 appendices and review of the literature. *Chirurg*, 2001; 72(12): 1508-9.
30. Amber S, Mathai AM, Naik R, Pai MR, Kumar S, Prasad K. Neuronal hypertrophy and mast cells in histologically negative, clinically diagnosed acute appendicitis: a quantitative immunophenotypical analysis. *Indian J Gastroenterol*, 2010; 29(2):69-73.
31. Xiong S, Puri P, Nemeth L, O'Briain DS, Reen DJ. Neuronal hypertrophy in acute appendicitis. *Arch Pathol Lab Med*, 2000; 124:1429-33.

Corresponding Author

Branka Radojčić

Clinic for Pediatric Surgery,

Institute of Child and Adolescent Health Care of Vojvodina,

Novi Sad,

Serbia,

E-mail: branka.radojčić@gmail.com

# Effects of education and exercise on pain, depression and quality of life in patients diagnosed with Fibromyalgia

Canan Demirbag<sup>1</sup>, Ferdane Oguzoncu<sup>2</sup>

<sup>1</sup> College of Health Services, School of Medicine, Karadeniz Technical University, Trabzon, Turkey,

<sup>2</sup> Department of Public Health, School of Medicine, Firat University, Elazig, Turkey.

## Abstract

**Objective:** Fibromyalgia syndrome is a very common rheumatological disorder and there are various treatment modalities. The aim of the present study was to investigate the effect of education and exercise programs in the treatment of patients with fibromyalgia syndrome.

**Materials and Methods:** One hundred-two patients who were diagnosed with fibromyalgia syndrome according to the American College of Rheumatology criteria were included in the study. Their ages ranged between 19 and 58 years. The patients were assigned into two groups: the intervention group (n=51) who received education and exercise programs at home and the control group (n=51) who did not receive these programs. All of the patients were asked to complete the Beck depression inventory to evaluate depression, visual analogue scale to evaluate the level of pain, and fibromyalgia impact questionnaire to assess the quality of life score.

**Results:** After the programs, there was a significant difference between the scores of Beck depression inventory, visual analogue scale, and fibromyalgia impact questionnaire in the intervention group ( $p < 0.05$ , for each). Furthermore, there was an improvement in between the scores of Beck depression inventory, visual analogue scale, and fibromyalgia impact questionnaire in the intervention group compared to the control group ( $p < 0.05$ , for each).

**Conclusion:** Patients with fibromyalgia syndrome mostly complained about the pain and the difficulty in the daily living activities. The present study showed that education and exercise programs at home had positive effect on pain, quality of life, and depression in patients with fibromyalgia syndrome.

**Key words:** Fibromyalgia, depression, education, exercise, quality of life

## Introduction

Fibromyalgia is a term used for the definition of medically unexplained and chronic widespread muscle pain of unknown etiology (Doksat MK, 2003). Fibromyalgia syndrome (FMS) is a clinical condition frequently encountered in middle-aged women accompanied by sleep disturbances or unrelaxing sleep, widespread pain, chronic fatigue, paresthesia and subjective swelling in the hands, migraine type headache, and psychosomatic complaints such as irritable bowel syndrome (Rummans TA et al, 2000; Thomas PK, 1993; Wolfe F, 1990). Patients with FMS have persistent complaint of pain in the neck, shoulders, arms, waist and knees. The term fibromyalgia has been begun to be used after acceptance of the outcomes of the study published by the American Collage of Multicenter Criteria Committee in 1990 (Wolfe F, 1990). The World Health Organization defined the disease as FMS in 1992 (Wolfe F, 1990; Müller W et al, 2007; Moldofsky H, 1986).

The exact prevalence of FMS is not known, it varies between 3.7% and 20% in the general population (3.4% in adult females and 0.5% in adult males). FMS is frequently encountered in middle-aged women between 30-50 years old (White KP et al, 1999; Yunus MB 2007). The prevalence of FMS was reported to be 3.5% in a family practice clinic, 6.5% in a primary health care center, 6%-8.5% in a hospital, and 14%-20% in a rheumatology clinic (White KP et al, 1999; Yunus MB, 2007). On the other hand, its prevalence varies between 7%-10.5% in European countries, and 1%-15% in USA. In a study performed in Canada and Lon-

don, the prevalence of FMS was found to be 4.9% in women and 1.6% in men (Yunus MB,2007). In another study conducted in Trabzon city of Turkey, the prevalence of FMS was reported to be 6.8% in women and 2.4% in men (Cebi A,2001).

Fibromyalgia syndrome is the third most common disease in USA following osteoarthritis and rheumatoid arthritis and constitutes 15%-20% of the patients in rheumatology practice (White KP et al,1999; Smith T,1994). Many studies have indicated that another rheumatic disease may develop in patients with FMS; particularly accompanying rheumatoid arthritis (RA) or systemic lupus erythematosus is frequently observed (Smith T,1994). Moreover, diseases such as depression, irritable bowel syndrome, migraine, and chronic fatigue syndrome may also be frequently seen in fibromyalgia patients. Thus, the differential diagnosis of FMS should be performed carefully. Moreover, the diagnosis of myofascial pain syndrome (MPS) is often confused with the diagnosis of FMS (Donmez A,2000). Fibromyalgia differs from the other dysfunctional syndromes by the presence of generalized musculoskeletal pain and multiple tender points. If fibromyalgia is diagnosed early, there will be no need for the many expensive, exhausting and invasive examinations (Bennet RM,1993).

Among the syndromes causing chronic pain, FMS is one of the leading causes of labor loss, and expenditures of medication and therapy, with an high incidence. FMS patients present to the hospital 3.5 times more frequently, and as well as, undergo various unnecessary operations 3-4 times more than the individuals within the same age group (Burckhardt CS et al,1993). Moreover, FMS patients cannot perform their daily activities because of their illness. Thus, it is considered that disability develops in FMS and one of the leading causes of the disability is exercise intolerance which is the most significant motor symptom of FMS. Moreover, these patients cannot perform repetitive dynamic work and prolonged static work (Burckhardt CS et al,1993). Although some factors have been described to coexist with a worse quality of life in patients with FMS, demographic and psychosocial factors are also play important roles. Burchardat et al. reported that income, anxiety, and depression affected the quality of life

(QoL) of the women with FMS. In that particular study, it was also indicated that different factors could affect the QoL in different patient groups (Burckhardt CS et al,1993).

There is no definite treatment in FMS because a single specific or pathophysiological factor cannot be determined, and thus, the treatment of FMS is generally empirical. The main steps in the treatment of FMS are patient education, medical therapy, aerobic, exercise and physical therapy, thermal spring therapy, and alternative therapies (Dursun H,1998). In the present study, we aimed to investigate the effects of education and exercise on pain, depression, and QoL in patients with FMS. and thus, to contribute to the treatment approach and further investigations (Kocanogullari H,1999).

### Materials and Methods

The present study was planned to determine the effects of education and exercise on depression and QoL in patients who were living in the city center and who were diagnosed as fibromyalgia in the outpatient Physical Therapy clinic of Trabzon Bone Diseases Hospital between 01 November 2004 and 31 December 2004. Because of patients arranged schule, this study finished 1 April 2009. The diagnosis of FMS was performed according to American College of Rheumatology criteria (1990) (Wolfe F,1990). Fifty-one patients who accepted to participate in education and exercise programs constituted the intervention group and 51 patients who did not accept to participate in programs constituted the control group. In order to provide homogeneity between the groups, age-, gender-, and marital status- matched patients who had similar pain complaints and medication usage were selected. The approval for the study was obtained from the Ethical Committee of the same hospital. Informed consents were obtained from all of the patients.

Medical histories of all patients were obtained and physical examinations were performed. All of the patients were asked to complete the sociodemographic data collection form, Visual Analogue Scale (VAS), Beck Depression Inventory (BDI) and Fibromyalgia Impact Questionnaire (FIQ).

*Sociodemographic Data Collection Form:* A questionnaire developed by the researcher based on the literature was given to the participants which

included questions regarding the age, education, marital status, number of children, monthly income, duration of illness, presence of other disease, people with whom they lived, psychiatric history of the family, used medications, previous operations, female health problems, location and severity of the pain and factors initiating the illness. Following the explanation of the content of the questionnaire and obtaining the patients' consents, the questionnaires were filled by the patients. However, if the patient had a difficulty to fill it, the researcher filled the questionnaire by face-to-face interview method.

*Visual Analogue Scale (VAS)*: It was developed by Price et al. (Price DD et al,1983), which measures the severity of pain. The validity and reliability of Turkish version of the scale was performed. The VAS is a horizontal or vertical line with 10 cm long, in which one end represents no pain (0 cm) and the other end represents the most severe pain (10 cm). The patients were asked to mark a point corresponding to the severity of pain that they felt.

*Beck Depression Inventory (BDI)*: It was developed by Beck et al. (Beck AT,1961) and it measures the physical, emotional, cognitive and motivational functions in depression. It is a self assessment scale including 21 items rated on a 4-point scale. The score of each item ranges between 0 to 3 points, in which 0 point represents the neutral condition and 3 points represent the most severe condition. The validity and reliability of Turkish version of BDI was performed by Hisli (Hisli N,1998).

*Fibromyalgia Impact Questionnaire (FIQ)*: It was developed by Burckhardt et al. (Burckhardt CS,1991) and it measures the state, course and outcomes in the patients with FMS. It is a self assessment scale consisting of Likert type 10 questions each scored between 0 and 3 points. The validity and reliability of Turkish version of FIQ was performed by Sarmer et al (Sarmer S et al,2000).

The education about FMS and exercise program developed by the physicians and physiotherapists were then given to 51 patients in the intervention group by the researcher. The education program included the information about the natural course of FMS, the relationship between personality traits and syndrome, and frequent recurrence of syndrome. The patients were told that they could diminish their complaints by controlling themselves. The patients were also briefly informed about the following is-

ues: what fibromyalgia was, how it was diagnosed, what the current treatment of fibromyalgia was, what the causes of fibromyalgia were, if the patients with fibromyalgia improved. They were also told that FMS was not a psychological disorder, but stress, depression, anxiety, sleep disturbances, trauma, hard working and bad posture accompanied it. Moreover, it was told that FMS was a benign illness, but did not cause tissue damage. The importance of sleep, stress, and medical treatment in FMS was explained to the patients. Time spending options and alternative hobby options were also recommended to the patients. The education program lasted approximately 20 minutes.

The exercise program was prepared by the hospital and one-to one basis included the practices of neck, hand, arm and foot exercises. The aerobics exercise instructor manuals developed according to the location of the pain were given to the patients. The exercise education program lasted about 15-20 minutes.

After the exercise education program, the researcher obtained permission from the patients in the intervention group for visiting them every week for one month to repeat the exercises, to control them that they did the exercises in a correct way, and to answer their questions. After one month, in the control follow-up visits, both the intervention and control groups were asked to re-complete the sociodemographic data collection form, VAS, BDI, and FIQ.

### **Statistical analysis**

The data of the study was analyzed using the statistical package for social sciences (SPSS Inc., Chicago, IL, US) version 11.0. In the evaluation of data, the chi-square test, the t-test for independent variables, and the McNemar chi-square test were used. Data were represented as mean±standard deviation, and percentages. The results were evaluated in a 95% confidence interval and a p value <0.05 was considered significant.

### **Results**

Of the patients in the intervention group, 45.1% were between the ages of 33 and 45, 92.2% were females, 94.1% were married, 49.0% were graduated from elementary school, and 80.4% were

housewives. Of the patients in the control group, 52.9% were between 33-45 years of age, 92.2% were females, 92.2% were married, 37.3% were graduated from elementary school, and 78.4% were housewives (Table 1).

The baseline distribution of the pain lasting for at least 1 week in the previous 3 months is represented in Table 2.

According to the localization of pain before the exercise program, 96.1% of the patients had muscle-bone-joint pain, 86.3% had shoulder-arm-hand pain, 88.2% had hip-knee-leg pain and 82.4% had

neck-chest-back pain in the intervention group. After the exercise program, muscle-bone-joint, shoulder-arm-hand, hip-knee-leg, and neck-chest-back pains were significantly decreased to 39.2%, 39.2%, 45.1%, and 47.1% in the intervention group ( $p < 0.05$  for each; Table 3).

When the patients in the intervention and control groups were evaluated according to the presence of symptoms related to FMS after the exercise program, the rates of morning stiffness, morning fatigue, weakness, restless sleep, and dizziness were 64.7%, 70.6%, 88.2%, 51.0%, and 72.5%,

Table 1. Demographic features of the patients at baseline

		Intervention Group n (%)	Control Group n (%)	
<b>Age</b>	<19 year	1 (20)	2 (3.9)	$X^2=14.370$ df=16 P=0.367
	20-32 years	11 (21.6)	11 (21.6)	
	33-45 years	23 (45.1)	27 (52.9)	
	46-57 years	15 (29.4)	8 (15.7)	
	59> years	1 (2.0)	3 (5.9)	
<b>Gender</b>	Female	47 (92.2)	47 (92.2)	$X^2=10.672$ df=1 P=0.027
	Male	4 (7.8)	4 (7.8)	
<b>Marital status</b>	Married	48 (94.1)	47 (92.2)	$X^2=0.271$ df=1 P=1.000
	Single	3 (5.9)	4 (7.8)	
<b>Education</b>	Illiterate	11 (21.6)	10 (19.6)	$X^2=24.773$ df=25 P=0.475
	Literate	6 (11.8)	2 (3.9)	
	Elementary school	25 (49.0)	19 (37.3)	
	Intermediate school	5 (9.8)	7 (13.7)	
	High school	2 (3.9)	10 (19.6)	
	University	2 (3.9)	3 (5.9)	
<b>Occupation</b>	House wife	41 (80.4)	40 (78.4)	$X^2=37.447$ df=20 P=0.010
	Worker	1 (2.0)	1 (2.0)	
	Officer	4 (7.8)	4 (7.8)	
	Retired	1 (2.0)	2 (3.9)	
	Self-employed	4 (7.8)	4 (7.8)	
<b>Number of children</b>	0-1	13 (25.5)	9 (17.6)	$X^2=11.918$ df=16 P=0.623
	2-3	26 (51.0)	30 (58.8)	
	More than 3	12 (23.5)	2 (23.5)	
<b>Living with</b>	Alone	1 (2.0)	2 (3.9)	$X^2=24.07$ df=18 P=0.750
	Spouse and children	42 (82.4)	39 (76.4)	
	Children	4 (7.8)	2 (3.9)	
	Other (relatives)	4 (7.8)	8 (15.7)	
<b>Average monthly income</b>	Low	9 (17.6)	5 (9.8)	$X^2=15.96$ df=16 P=0.406
	Moderate	16 (31.4)	17 (33.3)	
	Good	12 (23.5)	15 (29.4)	
	Better	14 (27.5)	14 (27.5)	

$X^2$ , Chi-square; df, degrees of freedom

Table 2. The distribution of the pain lasting at least 1 week in the previous 3 months before the exercise program in the intervention and control groups

		Intervention Group		Control Group		P Value
		n (%)		n (%)		
Muscle-bone-joint pain	Present	49 (96.1)		46 (90.2)		>0.05
	Absent	2 (3.9)		5 (9.8)		
Shoulder-arm-hand pain	Present	44 (86.3)		42 (82.3)		>0.05
	Absent	7 (13.7)		9 (17.6)		
Hip-knee-leg pain	Present	45 (88.2)		42 (82.4)		>0.05
	Absent	6 (11.8)		9 (17.6)		
Neck-chest-back pain	Present	42 (82.4)		47 (92.2)		>0.05
	Absent	9 (17.6)		4 (7.8)		

Table 3. The distribution of pain in the intervention group before and after the exercise program

		Before the Exercise Program		After the Exercise Program		P*
		n (%)		n (%)		
Muscle-bone-joint pain	Present	49 (96.1)		20 (39.2)		<0.05
	Absent	2 (3.9)		31 (60.8)		
Shoulder-arm-hand pain	Present	44 (86.3)		20 (39.2)		<0.05
	Absent	7 (13.7)		31 (60.8)		
Hip-knee-leg pain	Present	45 (88.2)		23 (45.1)		<0.05
	Absent	6 (11.8)		28 (54.9)		
Neck-chest-back pain	Present	42 (82.4)		24 (47.1)		<0.05
	Absent	9 (17.6)		27 (52.9)		

\*Mc-Nemar test was performed

Table 4. The distribution of the patients in the intervention and control groups according to the presence of symptoms related to FMS after the exercise program

	Intervention Group		Control Group		P value
	Present n (%)	Absent n (%)	Present n (%)	Absent n (%)	
Morning stiffness	33 (64.7)	18 (35.3)	45 (82.2)	6 (11.8)	<0.05
Morning fatigue	36 (70.6)	15 (29.4)	48 (94.1)	3 (5.9)	<0.05
Weakness	45 (88.2)	6 (11.8)	50 (98.0)	1 (2.0)	>0.05
Unrelaxing sleep	26 (51.0)	25 (49.0)	43 (84.3)	8 (15.7)	<0.05
Paresthesia in the hands and feet	26 (51.0)	25 (49.0)	39 (76.5)	12 (23.5)	<0.05
Headache	26 (51.0)	25 (49.0)	46 (90.2)	5 (9.8)	<0.05
Dizziness	37 (72.5)	14 (27.5)	44 (86.3)	7 (13.7)	<0.05
Weakness after working	29 (56.9)	22 (43.1)	37 (72.5)	14 (27.5)	<0.05
Burning, dryness and pain in eyes	32 (62.7)	19 (37.3)	41 (80.4)	10 (19.6)	<0.05
Cyanosis in cold	29 (56.9)	22 (43.1)	36 (70.6)	15 (29.4)	<0.05
Chest pain	8 (15.7)	43 (84.3)	19 (37.3)	32 (62.7)	<0.05
Palpitation	23 (45.1)	28 (54.9)	26 (51.0)	25 (49.0)	<0.05
Increase in the complaints in cold weather	27 (52.9)	24 (47.1)	29 (56.9)	22 (43.1)	<0.05
Dyspnea	31 (60.8)	20 (39.2)	41 (80.4)	10 (19.6)	<0.05
Nocturnal cramps	28 (54.9)	23 (45.1)	32 (62.7)	19 (37.3)	<0.05
Swelling in face, hands and feet	28 (54.9)	23 (45.1)	37 (72.5)	14 (27.5)	<0.05
Weight loss	29 (56.9)	22 (43.1)	16 (31.4)	35 (68.6)	>0.05
Fever	18 (35.3)	33 (64.7)	17 (33.3)	34 (66.7)	<0.05
Distraction during occupation	24 (47.1)	27 (52.9)	38 (74.5)	13 (25.5)	<0.05
Exaggerated reactions to events	30 (58.8)	21 (41.2)	45 (88.2)	6 (11.8)	<0.05

Table 5. Comparison of the Beck Depression Inventory, Fibromyalgia Impact Questionnaire and Visual Analogue Scale scores of the patients in the intervention and control groups at baseline and control follow-ups

	Intervention Group		P <sup>a</sup>	Control group		P <sup>b</sup>	P <sup>c</sup>
	Baseline	Follow-up		Baseline	Follow-Up		
<b>BDI</b>	20.33±7.4	14.20±4.5	<0.05	26.51±8.33	35.82±6.19	<0.05	<0.05
<b>FIQ</b>	67.19±13.9	47.58±11.82	<0.05	64.17±9.8	71.43±7.9	<0.05	<0.05
<b>VAS</b>	7.65±1.44	5.41±1.15	<0.05	6.98±1.34	8.59±0.94	<0.05	<0.05

BDI, Beck Depression Inventory; FIQ, Fibromyalgia Impact Questionnaire; VAS, Visual Analogue Scale

<sup>a</sup> p value for the comparison of the scores at baseline and follow-up in the intervention group

<sup>b</sup> p value for the comparison of the scores at baseline and follow-up in the control group

<sup>c</sup> p value for the comparison of the scores at baseline and follow-up between the intervention and control groups

respectively, in the intervention group; whereas 82.2%, 94.1%, 98.0%, 84.3%, and 86.3%, respectively, in the control group (Table 4).

The scores of BDI, FIQ, and VAS of the patients in the intervention and control group before and after the exercise program are presented in Table 5. There was a significant difference between the BDI, FIQ, and VAS scores of the patients before (20.33±7.4, 67.19±13.9, 7.65±1.44, respectively) and after the exercise program (14.20±4.5, 47.58±11.82, 5.41±1.15, respectively;  $p < 0.05$ ).

## Discussion

When the sociodemographic features of the patients were analyzed in order to investigate the characteristics of FMS, the mean age of the patients was between 33 and 45 and the mean educational level was elementary school both in the intervention and control groups. There was no difference between the intervention and control groups in terms of age and education status. The mean monthly income was moderate and the majority of the patients were married in both groups, with no significant differences ( $p = 0.406$ ,  $p = 1.000$ , respectively).

In the literature, the risk factors for FMS have been reported as female gender, middle age, low income, and low educational status (Yazıcı K et al, 2003; Makela M and Heliovaara M, 1991; Katz RS et al, 2006). In the study conducted by Yazıcı et al. (Yazıcı K et al, 2003) in 2006, they reported that 75%-95% of the FMS patients were female and the disease onset age of these patients was between 30 and 50 years. The prevalence of FMS differs according to the population and the method

used, and it varies between 3.2%-4.9% in the population studies (White KP et al, 1999).

Similar to the literature, the rate of female patients with FMS was higher, the majority of the patients were in middle age group, and the mean education level was low in the present study. Callahan (Callahan LF, 1989), as well, reported the education level of patients with FMS as low.

In contrast to the literature in which a low level of income has been indicated as a risk factor for FMS (Yazıcı K et al, 2003; Makela M and Heliovaara M, 1991; Katz RS et al, 2006; Callahan LF, 1989), we determined the level of income as moderate in patients with FMS. This can be attributed to the fact that we defined range of moderate income level as 150 TL-200 TL which could be accepted as low in recent conditions. Moreover, in the present study, there was no significant difference between the intervention and control groups in terms of age, marital status, education, number of children, monthly income, and the persons with whom they lived ( $p > 0.05$  for each). Furthermore, there was also no significant difference between the intervention and control groups in terms of number of stillbirth/abortion, age of first pregnancy, use of oral contraceptives, age of menopause, and age of marriage ( $p > 0.05$  for each). Some studies have shown that the age of menopause affects fibromyalgia (Yazıcı K et al, 2003; Makela M and Heliovaara M, 1991; Katz RS et al, 2006; Callahan LF, 1989). However, there was no effect of menopause on FMS in the present study as the number of patients in menopause was limited.

When the two groups were compared before and after the exercise program in terms of the localization of pain, no difference was obtained with regard to pain in the muscle-bone-joint, shoulder-

arm-hand, hip-knee-leg, and the neck-chest-back. However, there was a significant difference in the intervention group with respect to the localization of pain before and after the exercise program. Various studies have shown that regular exercise and education affect the pain (Goldenberg DL,1987; Yurtlu S,2007; Bircan C,1999). Evcik et al. (Evcik D, Aytac F,2001) reported that exercise therapy significantly decreased the pain in patients with the diagnosis of primary fibromyalgia. Our results were in consistent with the results in the literature.

In the intervention group, alterations in the duration of complaints before and after the exercise program were found to be significant ( $p<0.05$ ). Thus, education and exercise were effective in altering the duration of complaints in the intervention group. Studies have shown that disability may develop in FMS patients due to consistent pain which leads to social isolation (Evcik D, Aytac F,2001; Burckhardt CS et al,1991; Gülec H,2001). Yazıcı et al. (Yazıcı K et al,2003) and Bircan et al. (Bircan C,1999) reported that the consistent pain in FMS affected the QoL. In the present study, the alteration in the duration of pain after the exercise program had a positive effect on patients in the intervention group.

Before the exercise program, weakness, morning fatigue, dizziness, and morning stiffness were the most frequent complaints both in the intervention and control groups; however, a significant difference between the groups was observed only in unrelaxing sleep and distraction during occupation. After the exercise program, there were significant differences between the intervention and control groups in terms of morning stiffness, morning fatigue, unrelaxing sleep, paresthesia in the hands and feet, headache, dizziness, weakness after working, cyanosis in cold, chest pain, palpitation, increase in the complaints in cold weather, dyspnea, nocturnal cramps, swelling in face, hands and feet, fever, distraction during occupation, and exaggerated reactions to events ( $p<0.05$  for each). Moreover, before and after exercise program, there were also significant differences in the intervention group with respect to morning stiffness, morning fatigue, unrelaxing sleep, headache, dizziness, distraction during occupation, and exaggerated reactions to events ( $p<0.05$  for each). These results showed that education and exercise had an effect on the symptoms in FMS. In their

study conducted on FMS patients, Karakus et al. (Karakus I et al,2003) stated that the symptoms of the patients with FMS included pain, chronic fatigue, weakness, and other associated symptoms and that these symptoms were the mainstays in the differential diagnosis of FMS as they were more common symptoms encountered in fibromyalgia.

Fatigue is one of the most common symptoms of FMS and can be as severe as to affect the physical activities of the patients (Donmez A,2000). Many studies have revealed that exercise and education programs are very effective in reducing the symptoms (Smith T,1994; Taggart HM and al.,2003; Thomas PK,1993). There was a significant difference in the rates of symptoms in the intervention group before and after exercise and education program.

The BDI scores of the patients in the intervention group were found to be significantly different before and after the exercise program ( $p<0.05$ ). Thus, exercise and educational programs were effective on the depression of the patients in the intervention group. In their study conducted on 116 patients, Gulec et al. (Gulec H,2001) found that the rates of anger and depression were significantly higher in FMS patients compared to those with other diseases, and stated that depression had a negative impact on the treatment of the patients with FMS. Furthermore, Genc et al. (Genc A and Sagiroglu,2002) reported that different education and exercise programs had an effect on treatment of depression in FMS patients.

There was a significant difference between the VAS scores of the patients in the intervention group before and after the exercise program ( $p<0.05$ ). Thus, the exercise and educational programs affected the pain of the patients in the intervention group. Many studies have revealed that the frequency and continuity of the exercise programs, exercises on flexibility, stretching exercise or strengthening, aerobic, and condition exercises have an impact on pain, mood and disability of the patients (Maden E et al, 2007; Ataoglu S et al., 2002).

In the present study, the FIQ scores were  $67.19\pm 13.9$  in the intervention group and  $64.17\pm 9.8$  in the control group. The difference between FIQ scores of the patients in the intervention group before and after the exercise program were found to be significant ( $p<0.05$ ). Genc et al. (Thomas PK, 1993) applied stretching, strengthening and



posture exercises, post-isometric relaxation, and active mobilization exercises under certain temperature for 3 weeks on 150 computer users. They monitored the differences in the scores of FIQ and reported a significant improvement. Rolmann (Rolmann G, 1989) found that the severity of pain was high in the patients with FMS and affected the QoL in these patients (Rolmann G, 1989).

Yazici et al. (Yazici K et al, 2003) investigated the effects of FMS on QoL of 130 patients with FMS and 18 healthy controls by evaluating the effect of depression on QoL using short form-36 scale and concluded that as the severity of depression increased, the QoL decreased. Similarly, Bircan et al. (Bircan C, 1999) reported the QoL score of patients with FMS as lowest in their study conducted on 30 FMS patients, 20 healthy subjects, and 20 controls with a disease other than FMS (such as rheumatoid arthritis, chronic obstructive pulmonary disease, diabetes mellitus). The results of the present study were consistent with that of the literature.

There were significant differences between the intervention and control groups with respect to the scores of BDI, FIQ, and VAS at the follow-up visit ( $p < 0.05$  for each). Evcik et al. (Evcik D, Aytac F, 2001) applied three different exercise programs on 62 FMS patients who had never received exercise and therapy and obtained positive alterations in VAS and FIQ scores. Many studies have also emphasized the importance of regular exercise in the alleviation of pain and improvement of life standards (Bircan C, 1999; Bircan C, 1999; Evcik D, Aytac F, 2001). In the present study, we observed that regular exercise had a positive effect on pain and QoL when the scores of BDI, FIQ, and VAS were compared before and after exercise program.

In 2003, Yazıcı et al. (Yazıcı K et al, 2003) emphasized the importance of education for the determination of factors affecting the QoL of the patients and for the development of methods to cope with these factors. Akgöl stated that education was effective in the QoL and treatment of FMS patients in his study in 2005 (Akgöl I, 2005).

Guleç et al. (Gulec H, 2001) showed that the QoL of the patients with FMS was low. Informing the patients about their disease, and thus, education, is very important in the treatment of every disease. In accordance with the literature, we found that one-to-one education and exercise at

home had positive effects on the QoL, depression, and pain in patients with FMS.

In a study conducted by Sevimli (Sevimli D, 2007), the effects of swimming, gym, and aerobic exercises at home on physical and psychological parameters in patients with FMS were investigated. They found that each individual exercise program affected different physical and psychological parameters. Similarly, Taggart et al. (Taggart HM and al., 2003) investigated the effects of different types of exercise programs on fibromyalgia symptoms and obtained a positive correlation with the QoL.

In conclusion, one-to-one exercise at home and education programs played an important role in the treatment of patients with FMS. Moreover, their motivation to life was also higher. Thus, exercise and education programs have positive effects both on disease and patients. On the other hand, employment of trained medical professionals in primary healthcare and community health centers, and providing conscious and continuous care for patients with FMS would render healthy individuals, healthy families and a healthy population, and would decrease the disease burden for FMS.

## References

1. Akgöl I. *A multifaceted support and approach to patients with fibromyalgia*. [www.ptr-tr.com/tr/isikakgol](http://www.ptr-tr.com/tr/isikakgol) (06.2005)
2. Ataoglu S, Özçetin A, Ataoglu A, İcmeli C, Makarc S, Yaglı M. *The relationship pain intensity, anxiety, and depression in patients with fibromyalgia and rheumatoid arthritis*. *Anatolian Journal of Psychiatry* 2002; (3):223-226.
3. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. *An inventory for measuring depression*. *Arch Gen Psychiatry* 1961; (4): 561-71.
4. Bennet RM. *The Fibromyalgia Syndrome, Myofascial Pain and the Chronic Fatigue Syndrome*. In: Kelley WN, Harris ED Jr, Ruddy S, Sledge CB (eds). *Textbook of Rheumatology*. Philadelphia: WB Saunders Co, 1993; 471-9.
5. Bircan C, Akkos YS, Kirazlı Y. *The quality of life among patients with primary fibromyalgia syndrome*. *Aegean Journal of Physical Medicine and Rehabilitation*. 1999; (4):241-245.
6. Burckhardt CS, Clark SR, Bennett RM. *Fibromyalgia and quality of life: a comparative analysis*. *J Rheumatol* 1993; 20(3): 475-9.
7. Burckhardt CS, Clark SR, Bennett RM. *The fibromyalgia impact questionnaire: development and validation*. *J Rheumatol* 1991; 18(5): 728-33.

8. Burckhardt CS, Archenholtz B, Mannerkorpi K, Bjelle A. *Quality of life of Swedish women with fibromyalgia syndrome, rheumatoid arthritis and systemic lupus erythematosus. Studies Myofascial Pain Fibromyalgia* 1991;1:207
9. Callahan LF, Smith WJ, Pincus T. *Self-report questionnaires in five rheumatic diseases: comparisons of health status constructs and associations with formal education level. Arthritis Care Res* 1989; 2(4): 122-31.
10. Cebi A. *The prevalence and demographic characteristics of fibromyalgia in Trabzon, (Unpublished Dissertation) 2001, Trabzon.*
11. Doksat MK. *Pain and Psychiatry 2<sup>nd</sup> Edition. Bursa: Psychiatry and Art Publishing; 2003.*
12. Donmez A. *Fibromyalgia Syndrome. Oral ET, Yesilbursa D. (Editors). MSS and Common Chronic Pains. Okuyan Publishing, 2000, İstanbul.*
13. Dursun H. *Chronic pain and its treatment. Traditional Çubukçu Meetings, Pain Symposium, Aegean Journal of Physical Medicine and Rehabilitation (Special Issue). 1998; 4(3):3345*
14. Evcik D, Aytac F. *The effect of exercise treatment in patients with fibromyalgia. Rheumatism* 2001; 16:2.
15. Genc A, Sagioglu E. *A comparison of two exercise programs for fibromyalgia. Physiotherapy Rehabilitation* 2002; 13(2):90-95.
16. Gulec H, Sayar K, Topbas M ve ark. *Anger and Alexithymia in Female Patients with Fibromyalgia Syndrome. Turkish Journal of Psychiatry* 2004; 15:191-198.
17. Goldenberg DL. *Fibromyalgia syndrome. JAMA* 1987; 257:2782-2787.
18. Hisli N. *Beck The validity and reliability of the Depression Scale in a Turkish Sample. Journal of Psychology* 1998; (6):118-22.
19. Karakus İ, Topaloglu D et al. *Diagnosis and Treatment of Fibromyalgia and Myofascial Pain Syndrome. Turkish Journal of Physical Medicine and Rehabilitation* 2004; 42:367.
20. Katz RS, Wolfe F, Michaud K. *Fibromyalgia diagnosis. A comparison of clinical survey and ACD criteria. Arthritis Rheum* 2006; 54:169-76
21. Kocanogulları H. *Fibromyalji sendromu. Gumusdis G, Doganavsargil E: Klinik Romatoloji: Deniz matbaası, 1999: İstanbul, p:549-555.*
22. Koh KB. *Anger and somatization, Journal of Psychosomatic Research* 2004; 55:(2): 113.
23. Maden E, Herken H, Keven S. *Patients with Alexithymia at Clinics in Turkey. Journal Med. Science* 2007; 27:32-35
24. Makela M, Heliövaara M. (1991). *Prevalence of primary fibromyalgia in the Finnish population. BMJ* 1991; Jul 27;303(6796):216-9.
25. Moldofsky H. *Sleep and musculoskeletal pain. Am J Medical. Sep* 1986; 29:81(3A) 85-89.
26. Müller W, Schneider EM, Stratz T. *The classification of fibromyalgia syndrome. Rheumatol* 2007; 27:1005-10.
27. Price DD, McGrath PA, Rafii A, Buckingham B. *The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain* 1983; 17(1): 45-56.
28. Rolmann G. *Measurement of pain in fibromyalgia in clinic and laboratory. J Rheumatol* 1989; 16 (Suppl.16):113-9.
29. Rummans TA, Philbrick KL, O' Connor MK. *Psychological Factors Affecting Medical Conditions: Musculoskeletal Disorders. In: Kaplan HI, Sadock BJ, Sadock VA (eds). Comprehensive Textbook of Psychiatry. Philadelphia: Williams & Wilkins, 2000; 1832-4.*
30. Sarmer S, Ergin S, Yavuzer G. *The validity and reliability of the Turkish version of the Fibromyalgia Impact Questionnaire. Rheumatol Int* 2000; 20(1): 9-12.
31. Sevimli D. *The effect of various exercise practices on physical and psychological parameters in patients with fibromyalgia ( Unpublished Dissertation), 2007: Adana.*
32. Smith T. *Concepts and methods in the study of anger, hostility, and health. In: Siegman, A. and Smith, T., Editors. Anger, hostility, and the heart, Lawrence Earlbaum Associates, 1994: Hillsdale, NJ.*
33. Taggart HM, Arslanian CL, Bae S, Singh K. *Effects of T'ai Chi exercise on fibromyalgia symptoms and health-related quality of life. Orthop Nurs* 2003; Sep-Oct;22 (5):353-60.
34. Thomas PK. *The chronic fatigue syndrome: what do we know? BMJ* 1993; 306(6892): 1557-8.
35. Yazici K, Tot S, Biçer A, Yazici A, Buturak V. *Anxiety, depression and quality of life in patients with back and neck pain. Clinical Psychiatry* 2003; (6):95-101
36. Yunus MB. *Fibromyalgia Syndrome: Clinical Features and Spectrum. In: Pillemer SR (ed). The Fibromyalgia Syndrome: Current Research and Future Directions in Epidemiology, Pathogenesis, and Treatment. New York: Haworth Medical, 1994; 5-21.*
37. Yurtlu S. *Diagnosis and Treatment of Fibromyalgia Syndrome. Clinical Medicine* 2007, 1:39.
38. White KP, Speechley M, Harth M, Ostbye T. *The London Fibromyalgia Epidemiology Study: the prevalence of fibromyalgia syndrome in London, Ontario. J Rheumatol* 1999; 26(7): 1570-6.
39. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. *The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum* 1990; 33(2): 160-72.

Corresponding Author  
Ayse Ferdane Oguzoncul,  
Firat University Hospital,  
Department of Public Health,  
Elazig,  
Turkey,  
E-mail: aferdane@gmail.com

# Gingival enlargement induced by cyclosporine in nephrotic child

Zoran Bojanic<sup>1</sup>, Vladmila Bojanic<sup>3</sup>, Dragan Mladenovic<sup>3</sup>, Predrag Miljkovic<sup>2</sup>

<sup>1</sup> School of Medicine Nis, Institute for Pharmacology and Toxicology, Nis, Serbia,

<sup>2</sup> School of Medicine, Institute for Pathophysiology, Nis, Serbia,

<sup>3</sup> School of Medicine, Clinic for Stomatology, Nis, Serbia,

<sup>4</sup> Children's Internal Medicine Clinic, Clinical Center Nis, Nis, Serbia.

## Abstract

Cyclosporine is a potent immunosuppressant agent, that has significantly reduced the morbidity and mortality rates in patients with nephrotic edema. The major side effect of this drug in the oral cavity is gingival enlargement. Cyclosporine-induced gingival enlargement varying from 8% to 81%.

The case of gingival enlargement in a nine year old boy with nephrotic syndrome on cyclosporine therapy is reported. Different aspects of numerous factors which affect the gingival enlargement due to cyclosporine are discussed. In the case where a low drug concentration in serum and a relatively good oral hygiene are not sufficient measures for prevention of the gingival enlargement, it is necessary to suspend the use of cyclosporine and replace it with tacrolimus. However, if this is not possible, it is necessary to do surgery and good oral hygiene to prevent recurrence.

**Key words:** gingival enlargement, cyclosporine, nephrotic edema

## Introduction

Cyclosporine (Cs) is an immunosuppressive drug used to reduce the activity of the immune system of patients. Cyclosporine A (CsA) is the main form of medicine which is created by the fungus *Beauveria nivea* (*Tolyposcladium inflatum* Gams) and *Cylindrocarpon lucidum* Booth). Chemically it is a lipophilic cyclic nonribosomal enedekapeptid (consisting of 11 amino acids). CsA is used for treatment of diseases with an expressed autoimmune component: aplastic anemia, asthma, Behcet's syndrome, chronic active hepatitis, nephrotic syndrome, multiple sclerosis, myasthenia gravis, sarcoidosis, non-infective uveitis, scleritis, scleroderma, severe forms of psoriasis, atopic der-

matitis, pyoderma gangrenosum, rheumatoid arthritis, and similar diseases. Cyclosporine inhibits P-glycoprotein (efflux pump in the cell wall) and thus increases the intracellular concentration of other drugs, that is used during cytostatic therapy.

CsA is administered orally in the form of soft gelatin capsules and a solution for oral use, a solution for inhalation, and intravenously. CsA is incompletely, inadequately and unpredictably absorbed from the original formulation of the drug. For that reason, the microemulsion CsA formulation (Neoral) is used, which is characterized by better absorption. This enables a better long-term prognosis in patients treated with CsA<sup>1,2</sup>. Oral therapeutic doses needed for immunosuppression are 50-20 mg/kg/day, with obtained serum concentrations of 100-400 ng/ml<sup>3</sup>. Bioavailability after oral administration is low and ranges from 20-50%. It is extensively metabolized in the liver and excreted via bile or feces. Cyclosporine metabolism takes place in the liver under the action of cytochrome P450 3A4, while CsA metabolites exhibit weak immunosuppressive effects. About 6% of the administered dose is eliminated in the urine, while only about 0.1% of CsA is excreted unchanged. The half-life of CsA is 17-40 hours<sup>4,5</sup>, while for children it is significantly shorter.

*In vitro* and *in vivo* experiments revealed that CsA selectively weakened the function of T cells, specifically inhibiting T helper cells<sup>6-8</sup>.

The application of CsA often causes numerous adverse effects: gingival overgrowth, nephrotoxicity, hepatotoxicity, seizures, tremor, lingual fungiform papillae hypertrophy, vomiting, diarrhea, pruritus, hypertension, hypertrichosis, headache, myalgia, hyperlipidaemia, hyperkalaemia, hypomagnesaemia, hyperuricaemia, and so on. CsA induced gingival overgrowth is reported for the first time in 1980<sup>9</sup> or 1983<sup>10</sup>.

## Case report

Patient A.R., 9 years old, weighing 34 kg, was for the first time hospitalized at the Children's Internal Medicine Clinic in Nis in September 2004, due to the clinical signs of nephrotic syndrome (oedema, proteinuria over 4 g/L, hypoproteinemia, hypoalbuminaemia, hypercholesterolaemia with hypertriglyceridaemia). Steroid dependence is expressed in the third year of the treatment (the appearance of two consecutive relapses), thus it was necessary to apply an immunosuppressive therapy. The patient received cyclosporine (Sandimmun-Neoral, Novartis, Belgium) since September 2007. The level of cyclosporine in serum is determined regularly once a month, and serum concentration of the drug was 60.1 ng/L on April 28, 2010.

Biochemical analysis: glucose 4.86 mmol/L, urea 3.96 mmol/L, creatinine 50.2  $\mu$ mol/L, serum total proteins 63.8 g/L, serum albumin 42.0 g/L, uric acid 240  $\mu$ mol/L, cholesterol 4.24 mmol/L, triglycerides 1.11 mmol/L, CRP 0.830 mg/L.



Figure 1.

The clinical picture is dominated by a swelling and redness of the gums with a characteristic glow of its marginal segments, as well as an enlargement of the interdental papillae, which are mostly covering the labial surface of the anterior teeth.

On palpation gingiva is soft and flexible, bleeding due to minor irritations, caused by food or a toothbrush. The labial sides of the teeth are covered with heavy layers of dental plaque.



Figure 2.

On the left side of the gums around the anterior teeth, from incisors to canines, the clinical picture is the same as in the upper jaw. On the right side the gingiva around the frontal teeth is swollen, but normal (pale pink) colour. The consistency of gingiva is firm, inflexible on the pressure and does not bleed. The patient does not complain about discomfort, pain or similar symptoms.

## Discussion

Enlargement of the gingiva induced by cyclosporine is iatrogenic disease characterized by uncontrolled growth of periodontal tissue. It does not occur as a result of an increase in cell number, but as an increase in extracellular volume, i.e. matrix of gingival connective tissue. Therefore, it is wrong to use the term gingival hyperplasia, which is often used in contemporary literature. Gingival enlargement is manifested as a painless, beads similar interdental papillae enlargement, which exceeds the labial and lingual marginal gingival edge. The enlargement is usually generalized, but it is the most prominent in maxillary and in anterior mandibular region. Severe forms of gingival enlargement are not only an aesthetic problem, but also they interfere with speech, occlusion and mastication.

Epidemiological data about cyclosporine induced gingival enlargement are not consistent. It is difficult to determine its real incidence because of several reasons. First of all, there are different criteria for what is considered as the enlargement of the gums. It is connected with the fact that the epidemiological data in some studies are reported

by dentists and in the other studies by doctors of other specialties. According to the literature data, 8%-81% of patients treated with cyclosporine get enlarged gums<sup>11-15</sup>.

### **Etiopathogenesis**

The etiology of gingival enlargement caused by cyclosporine is not fully explained, and the main reason is that almost all clinical and epidemiological studies which have researched the issue were retrospective. There are two main theories about the possible cause of the drug induced gingival enlargement: non-inflammatory and inflammatory. According to the non-inflammation theory a particular subpopulation of gingival fibroblasts produces defective or inactive form of collagenase, which causes an increase in volume of the gingiva and in that way creates an imbalance in the formation and degradation of collagen. The inflammation theory says that inflammation is a result of direct toxic effects of the drug found in increased concentration in the gingival crevicular fluid and/or bacterial plaque<sup>16</sup> or bacterial toxins<sup>17,18</sup>. Some authors believe that enlargement of the gums occurs as delayed immune response to the bacterial plaque.

Gingival enlargement morphologically consists of two tissue components: fibrous, which is the drug taking result, and inflammatory, that is caused by the response to bacterial plaque. Increase in the volume of gingival tissue occurs primarily as a response of connective, but not of the epithelial tissue to the drug treatment that causes gingival hyperplasia<sup>19,20</sup>.

### **Risk factors**

A clinically detectable enlargement of gingiva caused by cyclosporine is a multifactorial disorder influenced by: plaque, pharmacokinetic characteristics of the drug, cyclosporine exposure duration, concomitant use with drugs that cause gingival enlargement, sex, age, genetic predisposition, diabetes, socioeconomic status and smoking.

During the therapy with some drugs that can cause gum enlargement, poor plaque control is the most important factor. For this reason, the hypertrophy of the gums is classified as the dental

plaque induced gingival diseases by The American Academy of Periodontology<sup>21</sup>. It is believed that the drug causes the impairment of the gingival connective tissue homeostasis and influences the growth factors and, in particular, the plaque induced inflammatory changes<sup>22</sup>.

Some authors believe that the intensity of the cyclosporine induced gingival enlargement is influenced by the high concentrations of CsA in the serum and/or saliva<sup>14,23-28</sup>. However, other researchers have reached a different conclusion, holding that gingival enlargement is unrelated to the levels of CsA<sup>29-31</sup>. In the patient described in this paper the concentration of CsA was significantly lower than that of the patients presented in the literature. There are great differences in reference values between laboratories, even when the same procedure is used<sup>32,33</sup>. Distribution of cyclosporine between blood cells and plasma depends on the temperature and can be twice higher at the 37°C than at 21°C<sup>34</sup>. This is the reason that the temperature at which the samples are stored and processed undoubtedly affect the results. It is recommended to determine the drug concentrations in whole blood. However, in many studies, especially in the earlier studies, are given plasma or serum concentrations, what complicates the comparison of the literature data. The presence of the circadian variations in the metabolism of cyclosporine contributes to this problem<sup>35</sup>, which means that samples should be taken at the same time. In the presented patient with nephrotic syndrome the degree of gums enlargement and a relatively slow progression is associated with a low concentration of the drug in the serum.

A cyclosporine induced gingival enlargement occurrence usually is manifested at least three months after the therapy<sup>36,37</sup>, as in the case of the patient described in this paper.

It was found that enlargement of the gums is more frequently induced by certain groups of drugs (immunosuppressants, anticonvulsants, slow calcium channel blockers). Some drugs within these groups are capable to induce this disorder significantly more frequently compared to other drugs of the same group. Thus, for example, differences in the incidence of gums enlargement were recorded during the application of immunosuppressants, because the gingival enlargement is more significantly manifested due to cyclosporine than due

treatment with tacrolimus<sup>38,39</sup>. The incidence of gingival enlargement occurrence is significantly increased during simultaneous application of the two drugs that cause it – eg. cyclosporine and nifedipine<sup>24,38,40-42</sup>. The incidence of gingival enlargement from 46% in cyclosporine treated renal recipients is rising to 86% during concomitant use with nifedipine<sup>38</sup>. However, during simultaneous application of cyclosporine and verapamil additive no effect on gingival enlargement is registered.

It is found that the age is inversely correlated with the appearance of the gingival enlargement due to use of drugs<sup>30,44,45</sup>, ie. It is manifested in more than 70% in children and in 25-30% of adult patients<sup>44</sup>. A possible explanation for more frequent and stronger expression of the gingival enlargement in children treated with cyclosporine is associated with the fact that high concentrations of sex hormones that are registered in that age enable creation of 5-alpha-dihydrotestosterone. Their effect on gingival fibroblasts subpopulation is to increase collagen synthesis and/or reduce the formation of collagenase<sup>46</sup>.

The fact that the gingival enlargement is not expressed in all patients, and that only certain parts of the gingiva are affected indicates that there is a genetic predisposition to its formation.

### Clinical features

The enlargement of the gingiva induced by CsA is manifested as an increase of interdental papilla and marginal gingiva. It occurs after at least three months after the start of therapy. A gingival growth was most pronounced in the first year of drug treatment. It was found that children and people younger than 30 years are prone to the occurrence of addictive disorders. Gingival enlargement is characteristically clinically manifested initially in the region of the interdental papilla, with a gradual increase in size and lateral spread to neighboring papilla to which it connects. Gingival enlargement can progress to the extent that the teeth are barely visible i.e. completely covered with gingival mass. Due to inconvenience caused by inflammation and enlargement of the gums oral hygiene is far more difficult to maintain. But doing so can result in caries, periodontal diseases, and immunosuppression (due to malnutrition)<sup>44</sup>. The incidence and/or the extent of the expressi-

on of gingival enlargement are directly correlated with the accumulation of plaque and tartar<sup>47</sup>.

### Prevention and treatment

Outstanding and ongoing oral hygiene, removal of local irritative factors, and plaque control by the dentist to prevent or reduce the magnitude of the changes in the gums of patients treated with cyclosporine. Local application of antifungals, antiseptics rinse (chlorhexidine) and application of antibiotics can give good results. If the increase in gingival express these measures are insufficient in the treatment of changes<sup>48</sup>, and in some cases it is necessary to stop the use of drugs that caused the enlargement of gingiva. Patients using CsA often not possible to stop treatment, but it is possible to replace cyclosporine with tacrolimus as the immunosuppressive will not cause increased gum.

In any case, the replacement or the eventual cessation of cyclosporine use, which caused the gingival enlargement is a good choice in attempt to regulate a functional and aesthetic medical disorder. However, in cases were that is not possible, or if iatrogenic changes do not retreat, it is necessary to do surgery. Such cases are solved by periodontal surgical interventions: gingivectomy or periodontal flap surgery. After a gingivectomy or periodontal flap surgery it is necessary to maintain periodontal health by frequent monitoring of dental plaque and by removing supragingival deposits, in order to prevent recurrence.

### Conclusion

A case of gingival enlargement occurrence due to the influence of cyclosporine in nine years old boy with nephrotic syndrome is reported. In this paper are discussed aspects of the numerous factors that affect the gums caused by cyclosporine, which is crucial for treatment. In the case when low drug concentration in serum of the patient and the relatively good oral hygiene are not sufficient measures to prevent the formation of gingival enlargement, it is necessary to suspend the use of cyclosporine and replace it with tacrolimus. However, if this is not possible, it is necessary to do surgery and to maintain a good oral hygiene to prevent recurrence.

## References

1. Mueller EA, Kovarik JM. Improved dose linearity of cyclosporine pharmacokinetics from a microemulsion formulation. *Pharm Res* 1994; 11: 301-4.
2. Grant D, Kneteman N. Peak cyclosporine levels ( $C_{max}$ ) correlate with freedom from liver graft rejection: results of a prospective, randomized comparison of neoral and sandimmune for liver transplantation (NOF-8). *Transplantation* 1999; 67: 1133-7.
3. Yatscoff RW, Rush DN, Jeffery JR. Effects of sample preparation on concentrations of cyclosporin A measured in plasma. *Clin Chem* 1984; 30: 1812-4.
4. Schultz KR, Nevil TJ, Toze CL, Corr T, Currie C, Strong DK, et al. The pharmacokinetics of oral cyclosporin A (Neoral) during the first month after bone marrow transplantation. *Transplant Proc* 1998; 30: 1668-70.
5. Grevel J, Nuesch E, Abisch E, Kutz K. Pharmacokinetics of oral cyclosporin A (Sandimmun) in healthy subjects. *Eur J Clin Pharmacol* 1986; 31: 211-6.
6. Gao EK, Lo D. Abnormal differentiation of thymocytes in mice treated with cyclosporin A. *Nature* 1988; 336: 176-9.
7. Jenkins MK, Schwartz RH. (1988). Effects of cyclosporine A on T cell development and clonal deletion. *Science* 1988; 241: 1655-8.
8. Thomson AW, Webster LM. The influence of cyclosporin A on cell-mediated immunity. *Clin Exp Immunol* 1988; 71: 369-76.
9. Starzl T, Weil R, Iwatsuki S, Klintmalm G, Schröter GP, Koep LJ, et al. The use of cyclosporin A and prednisone in cadaver kidney transplantation. *Surg Gynecol Obstet* 1980; 151: 17-26.
10. Rateitschak-Pluss EM, Hefti A, Lortscher R, Thiel G. Initial observation that cyclosporin-A induces gingival enlargement in man. *J Clin Periodontol* 1983; 10: 237-46.
11. Tyldesley WR, Rotter E. Gingival hyperplasia induced by cyclosporine-A. *Br Dent J* 1984; 157: 205-9.
12. Friskopp J, Klintmalm G. Gingival enlargement. *Swed Dent J* 1986; 10: 85-96.
13. Daley TD, Wysocki GP, Day C. Clinical and pharmacologic correlations in cyclosporine-induced gingival hyperplasia. *Oral Surg Oral Med Oral Pathol.* 1986; 62: 417-21.
14. McGaw T, Lam S, Coates J. Cyclosporin-induced gingival overgrowth: correlation with dental plaque scores, gingivitis scores, and cyclosporin levels in serum and saliva. *Oral Surg Oral Med Oral Pathol* 1987; 64: 293-7.
15. Seymour RA, Smith DG, Rogers SR. The comparative effects of azathioprine and cyclosporine on some gingival health parameters of renal transplant patients. *J Clin Periodontol* 1987; 14: 610-3.
16. van der Vleuten CJ, Trijbels-Smeulders MA, van de Kerkhof PC. Telangiectasia and gingival hyperplasia as side-effects of amlodipine (Norvasc) in a 3-year-old girl. *Acta Derm Venereol* 1999; 79: 323-4.
17. Penarrocha-Diago M, Bagan-Sebastian JV. Diphenylhydantoin-induced gingival overgrowth in man: a clinico-pathological study. *J Periodontol* 1990; 61: 571-4.
18. Hancock RH, Swan RH. Nifedipine-induced gingival overgrowth. Report of a case treated by controlling plaque. *J Clin Periodontol* 1992; 19: 12-4.
19. Mariani G, Calastrini C, Carinci F, Marzola R, Calura G. Ultrastructural features of cyclosporine A-induced gingival hyperplasia. *J Periodontol* 1993; 64: 1092-7.
20. Mariani G, Calastrini C, Carinci F, Bergamini L, Calastrini F, Stabellini G. Ultrastructural and histochemical features of the ground substance in cyclosporin A-induced gingival overgrowth. *J Periodontol* 1996; 67: 21-7.
21. Armitage GC. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999; 4: 1-6.
22. Seymour RA, Thomason JM, Ellis JS. The pathogenesis of drug induced gingival overgrowth. *J Clin Periodontol* 1996; 23: 165-75.
23. Somacarrera ML, Hernández G, Acero J, Moskow BS. Localization of gingival overgrowth in heart transplant patients undergoing cyclosporin therapy. *J Periodontol* 1994; 65: 666-70.
24. Rostock MH, Fry HR, Turner JE. Severe gingival overgrowth associated with cyclosporin therapy. *J Periodontol* 1986; 57: 294-9.
25. Pisanty S, Shoshan S, Chajek T, Maftsir G, Sacks B, BenEzra D. The effect of cyclosporin A (CsA) treatment on gingival tissue of patients with Behcet's disease. *J Periodontol* 1988; 59: 599-603.

26. *Fuiano G, Pacchiano G, Lotito MA, Vaia E, Matara-ssio S, Andreucci VE. Relations of gingival hypertrophy and blood levels of cyclosporin A in patients with renal transplants. Ann Ital Med Int 1989; 4: 161-6.*
27. *Thomas DW, Baboolal K, Subramanian N, Newcombe RG. Cyclosporin A-induced gingival overgrowth is unrelated to allograft function in renal transplant recipients. J Clin Periodontol 2001; 28: 706-9.*
28. *Vlckova-Laskoska MT. Cyclosporin A-induced gingival hyperplasia in psoriasis: review of the literature and case reports. Acta Dermatovenerol Croat 2005; 13: 108-13.*
29. *Hassell TM, Hefti AF. Drug-induced gingival overgrowth: old problem, new problem. Crit Rev Oral Biol Med 1991; 2: 103-37.*
30. *Seymour RA, Jacobs DJ. Cyclosporin and the gingival tissues. J Clin Periodontol 1992; 19: 1-11.*
31. *Lowry LY, Welbury RR. Gingival overgrowth in paediatric cardiac transplant patients: a study of 19 patients aged between 2 and 16 years. Int J Paediatr Dent 1995; 54: 217-22.*
32. *Moyer TP. Measurement of cyclosporine: a challenge to the professional laboratory organizations. Ther Drug Monit 1985; 7: 123-4.*
33. *Johnston A, Marsden JT, Holt DW. The United Kingdom Cyclosporin Quality Assessment Scheme. Ther Drug Monit 1986; 8: 200-4.*
34. *Dieperink H. Temperature dependency of cyclosporin plasma levels. Lancet 1983; 1: 416.*
35. *Venkataramanan R, Yang S, Burckart GJ, Ptachcinski RJ, Van Thiel DH, Starzl TE. Diurnal variation in cyclosporine kinetics. Ther Drug Monit 1986; 8: 380-1.*
36. *Wysocki GP, Gretzinger HA. Fibrous hyperplasia of the gingiva: a side effect of cyclosporin A therapy. Oral Surg Oral Med Oral Pathol 1983; 55: 274-8.*
37. *Karpinia KA, Matt M. Factors affecting cyclosporine-induced gingival overgrowth in pediatric renal transplant recipients. Pediatr Dent 1996; 18: 450-5.*
38. *Radwan-Oczko M, Boratyńska M, Klinger M, Zietek M. Risk factors of gingival overgrowth in kidney transplant recipients treated with cyclosporine A. Ann Transplant 2003; 8: 57-62.*
39. *Ellis JS, Seymour RA, Taylor JJ, Thomason JM. Prevalence of gingival overgrowth in transplant patients immunosuppressed with tacrolimus. J Clin Periodontol 2004; 31: 126-31.*
40. *Slavin J, Taylor J Cyclosporin, nifedipine and gingival hyperplasia. Lancet 1987; 2: 739.*
41. *Nishikawa S, Nagata T, Morisaki I, Oka T, Ishida H. Pathogenesis of drug-induced gingival overgrowth. J Periodontol 1996; 67: 463-71.*
42. *López-Pintor RM, Hernández G, de Arriba L, Morales JM, Jiménez C, de Andrés A. Amlodipine and nifedipine used with cyclosporine induce different effects on gingival enlargement. Transplant Proc 2009;41:2351-3.*
43. *Cebeci I, Kantarci A, Firatli E, Carin M, Tuncer O. The effect of verapamil on the prevalence and severity of cyclosporine-induced gingival overgrowth in renal allograft recipients. J Periodontol 1996; 67: 1201-5.*
44. *Dongari-Bagtzoglou A. Drug-associated gingival enlargement. J Periodontol 2004; 75: 1424-31.*
45. *Hassell TM. Evidence for production of an inactive collagenase by fibroblasts from phenytoin-enlarged human gingivae. J Oral Pathol 1982; 11: 310-7.*
46. *Sooriyamoorthy M, Gower DB. Androgen metabolism in gingival hyperplasia induced by nifedipine and cyclosporin. J Periodontol Res 1990; 25: 25-30.*
47. *Silverstein LH, Garnick JJ, Szikman M, Singh B. Medication-induced gingival enlargement: a clinical review. Gen Dent 1997; 45: 371-6.*
48. *Marshall RI, Bartold PM. A clinical review of drug-induced gingival overgrowths. Aust Dent J 1999; 44: 219-32.*

## Corresponding Author

Zoran Bojanic,  
School of Medicine Nis,  
Institute for Pharmacology and Toxicology,  
Nis,  
Serbia,  
E-mail: vladmilab@gmail.com



# Sport-Related Injuries in the Emergency Department: An analysis of 1636 cases

Semih Akkaya<sup>1</sup>, Mustafa Serinken<sup>2</sup>, Nuray Akkaya<sup>3</sup>, Özgür Karcioğlu<sup>4</sup>

<sup>1</sup> University of Pamukkale, Faculty of Medicine, Department of Orthopedics and Traumatology, Denizli, Turkey,

<sup>2</sup> University of Pamukkale, Faculty of Medicine, Department of Emergency Medicine, Denizli, Turkey,

<sup>3</sup> University of Pamukkale, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Denizli, Turkey,

<sup>4</sup> Emergency Physician, Department of Emergency Medicine, Acibadem University, School of Medicine, Istanbul, Turkey.

## Abstract

**Objective:** To investigate the characteristics of patients with sport injuries and to compare the injury rates in different kinds of sports with regard to age groups.

**Method:** Emergency department (ED) records of patients with sport injuries between 2006 and 2010 were retrospectively searched, and analyzed with regard to demographics, injured body parts, type and nature of injury.

**Results:** Among 1636 consecutive eligible patients admitted to the ED with any kinds of sport injuries, 1317 (80.5%) patients were men, and mean age was 25,7±5,1 years. There were football injuries in 1196 (73.1%) cases, basketball injuries in 229 (14.0%) cases, and running or walking injuries in 167 (10.2%) cases. While football was the most common cause of injury identified in all age groups, basketball was the second cause of injury for age under 35 years. Running and walking was the second cause of injury in those over 35 years. The most commonly injured body part was the lower extremities (62.7%), followed by the upper extremities (23.3%) and the head and neck, (6.9%) respectively. While strains and sprains were more frequent in basketball, fractures-dislocations and other superficial injuries were more common in artificial surface football games.

**Conclusion:** Sport-related injuries remains to be an important health problem for the community, men and football players being the main target population. Preventive measures including usage of protective equipment, arrangement of specially designed sports facilities with necessary conditions for the activities and proper supervision for children may prove useful in alleviating the toll.

**Keywords:** emergency department; sport-related injuries; football; basketball

## Introduction

Regular physical exercise is a prerequisite for children to achieve normal growth and physical development. Sportive activities are sine qua non for prevention of cardiovascular diseases and obesity in adults, as well as healthy living in the long term (1). However, the risk of sport-related injuries are inherent in these healthy activities (2).

Emergency department records of patients with sport-related injuries are invaluable data sources for these entities as Most sport-related injuries are minor, non-fatal injuries treated in Emergency department which do not warrant admission (3).

In a study comparing sport-related injuries and non- sport-related injuries in the Emergency department, fractures, sprains and strains constituted the majority in sport-related injuries, 50.5% underwent extremity X-rays and 43.3% warranted consultation with orthopedics (3).

Many studies were conducted to investigate the characteristics of sport-related injuries in children and young individuals, since the injuries mostly inflict the young age groups (4-8). However, since sportive activities are encouraged as an integral part of healthy lifestyle, these injuries became a significant lifelong health hazard (9). Increasing awareness on risk stratification and distribution of sport-related injuries respecting age groups and types of sports will render measures to prevent these injuries be established on more scientific and concrete basis (2).

The objective of this study is to investigate the characteristics of patients with sport injuries and to compare the injury rates in different kinds of sports according to age groups.

## Materials and methods

This is a cross-sectional study which was designed to investigate records of all consecutive patients with sport-related injuries in all age groups between 2006 and 2010 in the University-based Emergency department. The hospital registry system and Emergency department charts were retrospectively searched respecting injury-related data and analyzed with regard to demographics, body parts injured, type, mechanism and nature of injury as well as clinical course.

Injuries occurred in activities other than sports, those with incomplete registration data, patients who left the hospital against medical advice and those injured while on any form of vehicles (bicycle or motor vehicles) were excluded from the analysis (10). Injuries noted to have happened in houses, fitness centers etc. while in sportive activities were included.

## Statistical Analysis

All statistical analyses were performed using "Statistical Package for Social Sciences for Windows" 19.0 program (SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as numbers and percentages, while numerical variables were defined as mean  $\pm$  standard deviations. Categorical variables (i.e., sex, age groups, sports types and body parts injured) were analyzed using Chi-square test. Post-hoc analysis were done with chi-square test and Bonferroni correction was performed. A p value  $<0.05$  was considered to be statistically significant.

## Results

A total of 1636 patients admitted to the Emergency department meeting the inclusion criteria constituted the study sample. Male patients comprised the majority (n=1317, 80.5%) and mean age was  $25,7 \pm 5,1$  years (range: 5 and 68). Nearly half of the patients in the sample (n=815, 49.8%) were between 15 and 35 years of age. There were football injuries in 1196 (73.1%) cases, basketball injuries in 229 (14.0%) cases, and running or walking injuries in 167 (10.2%) cases (Table 1). Football injuries were found to have occurred mostly during artificial surface football games (n=1023, 85.5%).

The patients were assigned to either of three age groups: younger than 15 years of age, between 15 and 35, and older than 35 years of age. While football was the most common cause of injury identified in all age groups (51.0%, 84.2%, 70.7%, respectively). Basketball was the second cause of injury for age under 35 years. Running and walking was the second cause of injury in those over 35 years (n=109, 23.5%).

The lower extremities was the body part which was found to be injured most commonly in the sample (n=1026, 62.7%), followed by the upper extremities (n=381, 23.3%) and the head and neck, (n=114, 6.9%) respectively (Table 2).

While strains and sprains were more frequent in basketball, fractures-dislocations and other superficial injuries were more common in artificial surface football games. The majority of patients with football injuries were between 15 and 35 years of age while basketball injuries were mostly seen in those younger than 15 years of age (Table 1).

Table 1. Distribution of sport-related injuries with respect to age groups and type of activity

	Age groups		
	<15 years of age n / %	Between 15 and 35 years of age n / %	>35 years of age n / %
<b>Football</b> n=1196	182 / 51.0	686 / 84.2	328 / 70.7
<b>Basketball</b> n=229	114 / 31.9	97 / 11.9	18 / 3.9
<b>Running and walking</b> n=167	37 / 10.4	21 / 2.6	109 / 23.5
<b>Others</b> n=44	24 / 6.7	11 / 1.3	9 / 1.9

Types of injuries were classified as fracture-dislocations, strain-sprain and others (contusion, abrasion, laceration, hematoma). Head injuries were a distinct classification among the sport-related injuries including all types; i.e., superficial injuries, fractures and intracranial injuries. Head injuries were found to be the main finding in 107 (6.5%) (Table 2). There were no patients with intracranial injury, while linear skull fractures were identified in 11 patients (10.3%), nasal fractures in seven (6.5%) and depressed skull fractures in two (1.9%). Blunt head injuries were noted in 68 (63.6%) and the remaining 19 (17.7%) had lacerations and abrasions in scalp and/or facial area.

*Table 2. Injured Body sites and types of Sports Related Injuries*

Injured body region	n	%
Head and neck	114	6.9
Torso	76	4.7
Upper extremities	381	23.3
Lower extremities	1026	62.7
More than one region	39	2.4
Type of injury		
Head injury	107	6.5
Fractures and/or dislocations	249	15.2
Strain/sprain	616	37.7
Contusion, abrasion, laceration, hematoma and miscellaneous	664	40.6
<b>Total</b>	<b>1636</b>	<b>100.0</b>

Contusions, lacerations, abrasions and hematoma accounted for the most common type of injuries in the whole sample (n=664, 40.6%) followed by strain-sprain type injuries (n=616, 37.7%) (Table 2).

Different types of injuries were compared with each other with respect to demographics (Table 3). Head injuries, fracture-dislocations, strain-sprain type injuries are significantly more common in men compared to women (p=0.03). strain-sprain type injuries occurred more frequently in those older than 35 years of age when compared to those younger than 15. These type of injuries were more common in basketball compared to football. Artificial surface football games accounted for 85.5% of football injuries. When compared to other surfaces (field, park, saloon, house etc) these games had a significant propensity for fracture-dislocations, and other superficial injuries (contusions and lacerations, etc.) (p=0.001, p=0.01, respectively) (Table 3).

A total of 221 (13.5%) patients were admitted to the hospital (212 patients to the wards and nine to the intensive care unit) in the study sample. All of the patients admitted to the intensive care unit were those suffered from head injuries, who were discharged from the hospital with full recovery. In brief, no patient with sport-related injuries turned out to have life-threatening serious injuries.

The majority of patients (n=1354, 82.7%) were treated in and discharged from the ED, while 61 (3.7%) patients left the hospital against medical advice. Of these latter group, 19 (1.1%) were transferred to another institution and 42 refused to be admitted into the hospital.

## Discussion

This cross-sectional study demonstrated that sport-related injuries occurred predominantly in males (80.5%) and in lower extremities (62.7%). Football ranked the highest among sport types in all age groups as a cause of sport-related injuries, whereas the second most common cause of injury for age under 35 years was found to be basketball and over 35 years the second cause was running and walking. Playing football was associated with fractures-dislocations, contusion and lacerations, while strains and sprains were more prevalent in basketball.

Conn et al. published a study which pointed out that sport-related injuries were more common in those younger than 24 years of age, men were twice more likely than women to be injured, basketball was the type of sport most commonly associated with sport-related injuries and that strains and sprains were the most common type of injury (31.5%) followed by fractures-dislocations (22%) (9). On the contrary, the present study demonstrated football was the most common cause for the all age groups and that basketball ranked the second in those younger than 35, and that strains and sprains were the most common types of injuries in basketball. The difference between studies regarding sport types may stem from popularity of football in our country, rather than being more likely to cause injuries. Accordingly, the same rationale may also result in the higher percentage of sport-related injuries among men, a feature more prominent than the study by Conn et al., because of male predominance in football players.

Table 3. Analysis of relationships of injury types with demographic and other variables

	Head injuries n / %	Fracture- dislocations n / %	Sprain/ Strain n / %	Contusions, lacerations, other superficial n / %
<b>Sex</b>				
Male	96 / 7.28	220 / 16.70	478 / 36.29	523 / 39.71
Female	11 / 3.44	29 / 9.09	138 / 43.26	141 / 44.20
<i>P</i>	<b>0.02</b>	<b>0.001</b>	<b>0.03</b>	<i>0.16</i>
<b>Age groups</b>				
<15 years of age	32 / 8.96	49 / 13.72	114 / 31.93	162 / 45.37
15-35 years of age	52 / 6.38	122 / 14.96	311 / 38.15	330 / 40.49
>35 years of age	23 / 4.95	78 / 16.81	191 / 41.16	172 / 37.06
<i>P</i>	<i>0.09</i>	<i>0.51</i>	<b>0.02*</b>	<i>0.06</i>
<b>Sport types</b>				
Football	83 / 6.93	191 / 15.96	426 / 35.61	496 / 41.47
Basketball	14 / 6.11	33 / 14.41	105 / 45.85	77 / 33.62
Other	10 / 4.73	25 / 11.84	85 / 40.28	91 / 43.12
<i>P</i>	<i>0.57</i>	<i>0.34</i>	<b>0.01**</b>	<i>0.07</i>
<b>Surface type***</b>				
Artificial surface (football)	64 / 6.25	184 / 17.98	364 / 35.58	411 / 40.17
Other fields	34 / 6.82	49 / 9.83	170 / 34.13	245 / 49.19
<i>P</i>	<i>0.67</i>	<b>0.001</b>	<i>0.57</i>	<b>0.01</b>

\*The difference between the groups younger than 15 years of age and older than 35 was found significant.

\*\* The difference between football and basketball groups was found significant.

\*\*\*Patients with unknown or unregistered regions of injury (n=115) were excluded from analysis.

The present study showed a male predominance with regard to sport-related injuries in patients younger than 15 years of age, a finding compatible with the literature. This is thought to be resulting from greater activity of boys in most types of sports (11).

Conn et al. wrote that 42% of patients with sport-related injuries between 5 and 24 years of age never present to the Emergency department to seek medical care, therefore the prevalence of sport-related injuries is underestimated, necessitating more strict preventive measures (9). Simon et al. analyzed 2990 cases with sport-related injuries younger than 19 years of age between 1997 and 2001 and cited that sport-related injuries constituted 23% of all trauma-related admissions in the Emergency department (12). They showed that fractures-dislocations, strain-sprains, open wounds, and contusions were the most common types of injuries and sport-related injuries were most commonly encountered in basketball followed by football among team sports (12). However, in the present study football ranked the highest among sport types in those younger than 15 years of age as a cause of sport-related injuries, followed by basketball.

In a research study carried out on epidemiological and clinical features of 3115 sport-related and recreational injuries presenting into the Emergency department, authors pointed out that three-fourths of sufferers were male, 46.5% had injuries in upper extremities, 35% in lower extremities 18.5% in head-neck and torso. Football was the most common type of sport associated with sport-related injuries (1). This study also showed that 34% of the patients necessitated orthopedic follow up, while 7% underwent physical therapy; 1029 (33.0%) patients were diagnosed with fractures (69.8% upper extremities, 22.3% lower extremities, and 8% axial fractures) and finally, field sports such as football had a greater tendency for fractures (1). These findings are in unison with the present study in that the victims are mostly males and football players, and that fractures-dislocations are encountered predominantly in football. Some different results were also elicited: In the present study nearly two-thirds of all injuries were identified in lower extremities, while Conn et al. noted the corresponding figure as 38.9%, while the order of frequency regarding injured regions remained unchanged (9).

Team sports performed in fields notoriously cause sport-related injuries in lower extremities since they inherently include close contact and strenuous activity (2). The greater percentage of lower extremity injuries compared to literature data can be attributed to overrepresentation of team sports- i.e., football and basketball- in the present study as the cause of sport-related injuries.

Sytema et al. reported that 53% of all sport-related injuries was noted in the lower extremities, while upper limbs comprised 35%, most of which were recorded in football players. Falls and hits by balls constituted most of upper extremity injuries and fractures were more common in this part of the body (2). Interestingly, they noted female basketball players were more likely to injure their upper limbs when compared to men and those in other sports activities (2). A number of previous studies greater likelihood of women to have upper extremity injuries in basketball were postulated to be linked to poorer ability of women in sports (13-15). Another study indicated a higher rate of falls in women in sports (16). In the present study, however, men were represented four times women in terms of sport-related injuries in the Emergency department, which can be attributed to greater prevalence of sports activities in men.

Elderly people tend to exercise recreational sports more than challenging team sports, resulting in a greater tendency to minor injuries rather than fractures (1). This is compatible with the results in the present study that sprain/strain-type injuries are more frequent in those older than 35 years of age with walking and running as a second most common type of sport following football.

Sport-related injuries were reported to comprise 10% to 19% of all acute injuries treated in Emergency department, highlighting the importance of increased awareness of this target population on modifiable risk factors in prevention of injuries (17,18).

The mechanisms of injury most commonly noted during sports activities are hits (34%) and falls (28%), as reported by Conn in 2003 (9). One of the limitations of the present study is failure to identify patients' injury mechanisms. Another issue to raise is inability to extrapolate the results to all sport-related injuries, since the injuries admitted to the Emergency department were analyzed exclusively. Fi-

nally, regional and seasonal variations have a strong influence on preferences of sports types, which inhibits generalizability to general population.

Despite all these limitations, this study provided important information on the characteristics of sport-related injuries admitted to the Emergency department with respect to age groups, types of sports and properties of injuries. Need for radiological investigations, orthopedic follow-up and physical therapy in most cases with sport-related injuries indicates magnitude of financial burden inflicted by the injuries in this context. Preventive measures including usage of protective equipment, arrangement of specially designed sports facilities with necessary conditions for the activities and supervision for children provided by legitimate bodies may prove useful in alleviating the toll for the community.

## References

1. Falvey EC, Eustace J, Whelan B, et al. Sport and recreation-related injuries and fracture occurrence among emergency department attendees: implications for exercise prescription and injury prevention. *Emerg Med J* 2009; 26: 590-5
2. Sytema R, Dekker R, Dijkstra PU, ten Duis HJ, van der Sluis CK. Upper extremity sports injury: risk factors in comparison to lower extremity injury in more than 25 000 cases. *Clin J Sport Med* 2010; 20: 256-63
3. Burt CW, Overpeck MD. Emergency visits for sports-related injuries. *Ann Emerg Med* 2001; 37: 301-8
4. Adirim TA, Cheng TL. Overview of injuries in the young athlete. *Sports Med* 2003; 33: 75-81. Review.
5. Monroe KW, Thrash C, Sorrentino A, King WD. Most common sports-related injuries in a pediatric emergency department. *Clin Pediatr (Phila)* 2011; 50: 17-20.
6. Ergen E. Sports injuries in children and adolescents: etiology, epidemiology, and risk factors. *Acta Orthop Traumatol Turc.* 2004; 38 :1:27-31. Review.
7. Fernandez WG, Yard EE, Comstock RD. Epidemiology of lower extremity injuries among U.S. high school athletes. *Acad Emerg Med* 2007; 14: 641-5.
8. Babul S, Nolan S, Nolan M, Rajabali F. An analysis of sport-related injuries: British Columbia children's hospital Emergency Department 1999 - 2003. *Int J Inj Contr Saf Promot* 2007; 14: 192-5.

9. Conn JM, Annest JL, Gilchrist J. Sports and recreation related injury episodes in the US population, 1997-99. *Inj Prev* 2003; 9: 117-23.
10. Gurses D, Sarioglu Buke A, Baskan M, Herek O, Kilic I. Epidemiologic evaluation of trauma cases admitted to a pediatric emergency service. *Ulus Travma Acil Cer* 2002; 8: 156-9. Turkish.
11. Güzel A, Karasalihoğlu S, Küçükkuşurhluoğlu Y. Evaluation of the fall-related trauma cases applied to our pediatric emergency department. *Ulus Travma Acil Cer* 2007; 13: 211-6. Turkish.
12. Simon TD, Bublitz C, Hambidge SJ. Emergency department visits among pediatric patients for sports-related injury: basic epidemiology and impact of race/ethnicity and insurance status. *Pediatr Emerg Care* 2006; 22: 309-15
13. Kelm J, Ahlhelm F, Anagnostakos K, et al. Gender-specific differences in school sports injuries. *Sportverletz Sportschaden* 2004; 18: 179-184
14. Fischman MG, Moore JB, Steele KH. Childrens' one-hand catching as a function of age, gender, and ball location. *Res Q Exerc Sport* 1992; 63: 349-355
15. McConnell A, Wade G. Effects of lateral ball location, grade, and sex on catching. *Percept Mot Skills* 1990; 70: 59-66
16. McGuine T. Sports injuries in high school athletes: a review of injury-risk and injury-prevention research. *Clin J Sport Med* 2006; 16: 488-499
17. Gür S. Principles and Prevention of Sports Injuries. *Türkiye Klinikleri J Orthop & Traumatol-Special Topics* 2010; 3: 11-3. Turkish.
18. Verhagen EA, van Stralen MM, van Mechelen W. Behaviour; the key factor for sports injury prevention. *Sports Med.* 2010; 40: 899-906

*Corresponding Author*

Semih Akkaya,

University of Pamukkale,

Medicine Faculty,

Department of Orthopedics and Traumatology,

Turkey,

E-mail: semihakkaya@yahoo.com

# Our experience in treatment of thoracic aortic intramural hematoma

Aleksandar Mikic<sup>1,2</sup>, Petar Djukic<sup>1,2</sup>, Krstina Doklestic<sup>3</sup>, Slobodan Cvetkovic<sup>1,2</sup>

<sup>1</sup> Clinic for Cardiac Surgery, Clinical Center of Serbia, Belgrade, Serbia,

<sup>2</sup> Faculty of Medicine, University of Belgrade, Serbia,

<sup>3</sup> Clinic for Emergency Surgery, Emergency Center, Clinical Center of Serbia, Belgrade, Serbia.

## Abstract

**Aim:** The purpose of this study was to explain our strategy in treatment patients with intramural hematoma (IMH) and to establish the optimal mode of management patients with type A IMH.

**Methods:** This study retrograde analyzes the treatment strategies for acute IMH managed by our program. We have evaluated 32 patients with IMH, who were admitted at hospital from January 2001 to December 2010. On arrival urgent operation was performed for the patients of IMH with cardiac tamponade and persistent pain. Uncomplicated patients with IMH were treated medically. During the early and late follow-up medically treated patients, IMH showed signs of progression to type A dissection, ruptured aneurysm or aneurismal enlargement (>55 mm). Long term survival was evaluated statistically.

**Results:** Three urgent operations were performed with patients type A IMH, successfully. The rest 29 patients were treated medically (11 type A and 18 type B IMH). Among them, 6 patients with type A and 1 type B were converted to early surgical intervention (one patient died). During a late follow-up 2 patients type A were converted to late surgical intervention (none of them died). During that period 5 of medically treated patients died (1 type A and 4 type B). The 10-years survival rate was 81% for patients with IMH.

**Conclusion:** According to results of our study, we still prefer medical treatment for type B IMH patients. But, we believe that early surgical treatment of acute type A IMH have a better results than medical treatment.

**Key words:** aorta, intramural hematoma, prognosis

## Introduction

Acute aortic syndrome (AAS) describes the acute presentation of patients with characteristic

“aortic pain”<sup>1</sup>. It is a serious disease with high early mortality and describes with one of several life threatening thoracic aortic pathologies<sup>1</sup>. These include: aortic dissection (AD), intramural hematoma (IMH), aneurismal leak, penetrating atherosclerotic ulcer (PAU) and iatrogenic or traumatic dissection<sup>2</sup>. In 2001 European Society of Cardiology proposed a new classification of aortic dissection into 5 classes derived from the initial description by Svensson et al.<sup>3</sup> IMH is a variant or precursor of AD without intimal flap, intimal tear and direct flow communication<sup>4</sup>. With the use of new noninvasive imaging techniques IMH has been reported with increasing frequency and accounts for roughly 10% to 30% of AAS cases<sup>5</sup>. Based on the concept of the Stanford classification, IMH can be classified as type A or type B<sup>5</sup>. It is generally accepted that patients with type B IMH can be managed conservatively with hypotensive drugs, in the absence of disease progression<sup>4</sup>. Treatment of patients with type A IMH is still controversial. Some reports have recommended early surgery for all patients with type A IMH, because of their poor prognosis with medical treatment and high risk for early progression to classic aortic dissection, aneurysm, pseudoaneurysm, or aortic rupture<sup>6</sup>. However, others have suggested medical therapy with timed surgical repair for cases with progression<sup>7</sup>. The purpose of this study was to explain our strategy in treatment patients with IMH and to establish the optimal mode of management patients with type A IMH.

## Patients and methods

### Patients

Between January 2001 and December 2010, 312 patients were admitted at our hospital with symptoms of AAS. Among them 32 patients (14 male and 18 female: mean age 67 years, range 43-

80 years) were suffered from IMH [10%]. Seventeen patients (53%) were admitted within 6 hours after onset of symptoms, others (47%) were admitted within 48 hours. The diagnosis was confirmed by clinical and diagnostic evaluations. All patients underwent computed tomography (CT) and transesophageal echocardiography (TEE) after admission. IMH was diagnosed in absence of a dissecting membrane, intimal disruption, or false lumen flow but in presence of regional aortic wall thickness  $\geq 7$  mm in circular or crescent shape caused by intramural accumulation of blood<sup>8</sup>.

Table 1. Characteristics of patients with intramural hematoma

Variable	Value	%
Age (years)	67; (43-80)	
Type A/B	14 / 18	44 / 56%
Sex (male/female)	14 / 18	44 / 56%
Admission with 6 hours	17	53%
Hypertension	27	84%
Chest or back pain	28	87%
Previous neurologic deficit	4	12%
Shock	3	9%
Pericardial effusion	2	6%
Pleural effusion	2	6%

## Methods

On arrival at hospital initial management of patients with IMH was based on hemodynamic stability and clinical signs and symptoms. Patients with persistent pain or hemodynamic instability (cardiac tamponade, coronary malperfusion, marked dilatation of the aorta  $> 55$  mm - impending rupture, or rupture) underwent early surgery on an emergency basis. Other patients were treated medically with intensive antihypertensive therapy in the intensive care unit, during the acute phase (2 weeks). Invasive blood pressure monitoring was performed during administration of intravenous  $\beta$ -adrenergic receptor blockers, calcium channel antagonists and nitrates to maintain systolic blood pressure between 100 and 120 mm Hg. After that treatment, oral antihypertensive drugs, including calcium channel antagonists, angiotensin-converting enzyme inhibitors, and  $\alpha$ - or  $\beta$ -adrenergic receptor blockers were administered orally to maintain blood pressure between 100 and 120 mm Hg. These patients remained in our clinic another

2 weeks. During their medical treatment they followed up. Clinical follow-up based on using transthoracic echocardiography (TTE), TEE and CT to minimize the risk of fatal complications. During the acute phase TTE was performed daily to detect pericardial effusion and aortic regurgitation or to measure aortic wall thickness and aortic dilatation. TEE was performed every third day and CT examination was generally repeated at the first and third week after the admission. Patients who demonstrated regression or completely disappearance of hematoma were discharged with oral therapy (regression was considered to have occurred if aortic diameter or aortic wall thickness decreased)<sup>9</sup>. If the size of hematoma was not change, TEE or CT was performed once a month, in the next period. Patients with recurrent pain, progression to overt dissection, ruptured aneurysm or progressive aortic dilatation of more than 55mm had their therapy converted to surgery.

In this study all patients with type B IMH were treated conservatively, except one who had early surgical conversion with successful endovascular treatment. After admission, patients with type A IMH were divided into two groups. One group was included severe cases that were complicated by persistent pain and hemodynamic instability and they were underwent early surgery. Another group was comprised cases who were not complicated and they were treated medically.

Our surgical technique in patients with type A included femoral or right subclavian artery and right atrium venous cannulation and perfusion of cardiopulmonary bypass (CPB) through a median sternotomy. In the most of cases ascending aortic replacement with an open distal anastomosis was performed, using hypothermic circulatory arrest (16-18C<sup>0</sup>) and ante-grade cerebral perfusion. During the CPB reinstated and rewarming started proximal anastomosis was performed. Coexisting mild aortic insufficiency was treated conservatively with resuspension of the aortic cusps.

Follow-up in this study was obtained from clinic visits or telephone interviews with the patients or the patient's family. Follow-up was included outpatient visit with clinical control and CT imaging 1, 3 and 6 months after discharge and then in yearly intervals. Mean follow-up was (58  $\pm$  31) years.



All statistical analyses were performed using a statistical software program. The Kaplan-Meier method was used to calculate the cumulative survival rate.

## Results

IMH was diagnosed in 32 patients. Table 1. summarizes demographic and clinical features in these patients. IMH were located in the descending aorta in 56% (type B). Ascending aorta was involved in 44% (type A). There were 14 men and 18 women, ranging in age from 43 to 80 years (mean age, 67 years). Severe chest or back pain was the most common presenting symptom. Hypertension had 27 patients (84%), which was severe in three patients. Three of them had syncope and another three had been in shock on admission. CT was used for diagnosis in all patients, but the diagnosis of IMH was definitively made after TEE was performed. In two patients conventional contrast angiography was performed.

Among the 32 IMH patients, 29 (91%) were preferred for medical treatment on admission. Three patients type A IMH (9%) underwent early surgery intervention with a diagnosis of cardiac tamponade ( $n = 2$ ) or coronary malperfusion ( $n = 1$ ). Ascending aortic replacement was performed and none of them died. During the subsequent course of the 29 medically treated patients, IMH showed signs of early progression in 7 patients within 30 days. They were converted to surgical intervention. Six were type A IMH (4 classic aortic dissections, 2 aortic ruptured). Ascending aortic replacement was performed (early surgical conversion). One patient died five days after operation AD. One patient with type B IMH who developed progressive aneurysm (aortic diameter  $> 55$  mm) received endovascular procedure before complications.

Late surgical conversion was performed in 2 patients with type A IMH who had late progression to overt type A dissection (1) and ruptured aneurysm (1). Replacement of ascending aorta was performed and both survival. During late follow-up 20 patients were treated medically and they were divided into 2 groups. In the first group we had 3 type A IMH patients. One of them died (sudden death) after 3 years. In other 2 patients we diagnosed resolution of the IMH (1 complete

within 6 months, another partial). In second group we had 17 type B IMH patients. During follow-up 4 of them died (brain hemorrhage-2 and sudden death-2) and in 9 of 17 patients we diagnosed completely disappearance of IMH within 2 years.

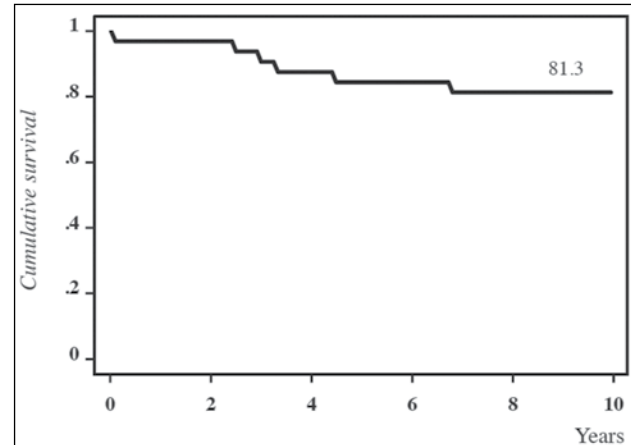


Figure 1. Long-term survival in patients with IMH

In our study there was 1 early death (in-hospital) and there were 5 late deaths during follow-up. Survival was evaluated with Kaplan-Meier analysis, Figure 1. The 10-year survival rate was 81% for patients with IMH. Finally, we examined the mural changes of IMH during follow-up. CT or TEE was used as an imaging modality. During a follow-up changes in IMH were studied in 29 patients. Analysis was complete for all patients to an endpoint of either death or completion of the study (December 2010). Progression to typical dissection was detected in 5 patients and to aortic rupture in 3 patients. One patient had developed aneurysm with aortic diameter  $> 55$  mm. Completely resolution was detected in 10 (1 type A, 9 type B), partial disappearance in 7 (2 type A, 5 type B) and no significant change in 3 patients (type B).

## Discussion

A large variety of acute, threatening disease can affect the thoracic aorta<sup>10</sup>. While typical aortic dissection with primary intimal disruption has been extensively described, other diseases with similar clinical presentation, including IMH and PAU, have been recognized later<sup>10</sup>. In the early 1900s several authors independently described the existence of IMH as a hemorrhagic dissection of the media without intimal tear<sup>11</sup>. Of these authors, Krukenberg in

1920 first described IMH of the aorta as “dissection without intimal tear”<sup>11</sup>. Two different pathophysiologic processes are currently believed to lead to the occurrence of IMH. One is IMH without intimal disruption and develops as a result of spontaneous rupture of the vasa vasorum of the aorta<sup>12</sup>. The other type of IMH is associated with an atherosclerotic ulcer that penetrates into the internal elastic lamina and allows hematoma formation within the media of the aortic wall<sup>13</sup>. However, these subtypes have similar clinical and radiologic findings.

IMH has been reported with increasing frequency with the development of modern diagnostic imaging techniques<sup>14,15</sup>. In our study about 10% of patients with AAS were suffered from IMH and it is according with studies from Europe and North America. IMH is diagnosed much more frequently among patients with AAS in Japan and Korea<sup>16</sup>. Kang et al. reported a diagnosis of IMH in 27 of 100 (27%) cases of AAS among Korean patients<sup>17</sup>. Yamada et al. reported 41% and Shimizu et al. reported 53% of IMH among the Japanese patients with AAS. This discrepancy may indicate that imaging diagnostic criteria for IMH or application of diagnostic technologies may be different between the two regions. Another possibility is that the cause of AAS is distinct between these regions based on genetic or environmental influences<sup>18</sup>.

IMH is difficult to distinguish from typical dissection on purely clinical grounds. The most common initial presentation of IMH is chest or back pain (50 to 84%)<sup>5</sup>. In our study this presentation occurred in 87% of patients. Patients with IMH are typically elderly (mean age 66 years) with a history of hypertension<sup>19</sup>. In our study mean age was 67 years and 84% of patients had a hypertension, which was severe in three patients.

It is clear that IMH has a high rate of mortality and morbidity, and most investigators have focused on the initial presenting episode and its management. Type B IMH is currently considered to be less severe and medical treatment is considered appropriate, in absence of disease progression<sup>17</sup>. Clinical treatment for type B IMH has been well discussed. Robbins et al. first reported that patients with type B IMH could probably be treated conservatively but require antihypertensive therapy<sup>20</sup>. Song et al. reported excellent results in medical treatment with these patients<sup>19</sup>. Considering both low in-hospital

mortality and good long-term prognosis, it seems that supportive medical therapy with frequent follow-up imaging studies and timed surgical repair may be a reasonable option as an optimal treatment in patients with type B IMH<sup>16</sup>. In our study, on arrival at hospital all type B IMH patients were treated medically. During a follow-up we had (1 early successful surgical conversion, 9 patients with completely and 5 with partial resolution of IMH, 3 without change and 4 deaths).

Some different opinions exist about the treatment of patients with type A IMH. Nienaber et al. reported statistically worse results with medically treated cases of type A IMH than with surgical repaired<sup>5</sup>. Maraj et al.<sup>21</sup>, and Mohr-Kahaly et al.<sup>20</sup> reported similar results. After recommendation of Robbins and associates<sup>6</sup>, early surgery intervention for type A IMH was widely adopted in the West. It is well known that IMH type A evolves towards true dissection with its complications. Moreover, early surgical intervention appears to be easier to perform because aortic wall yet non-dissected results stronger offering a better tissue for the suture. However, in Asia exists different approach to treatment the patients with type A IMH<sup>16</sup>. For them is important pathophysiologic process in IMH. The absence of flow and pressure communication with aortic lumen might produce good results. IMH is a disease of media and spontaneous regression is able. Kang et al.<sup>14</sup> suggested medical management. Song et al.<sup>19</sup> suggested the medical treatment because of absence of continuous flow communication. In our study, on arrival at hospital, acute type A IMH patients were subdivided onto two groups. First group included 3 patients with severe complications. They underwent early emergency surgery. Another group were treated medically, but they had 6 early and 2 late surgical conversion. In our study only 2 type A IMH patients had successful medical treatment.

## Conclusion

IMH of the aorta is a potentially lethal disorder with frequent progression to aortic rupture, dissection, or aneurysm. According to results of our study, we still prefer medical treatment for type B IMH patients. But, we believe that early surgical treatment of acute type A IMH with open distal

replacement of ascending aorta results in lower mortality rates and acceptable survival. Patients with complications we have to operate early emergency. Other patients type A IMH without complications; we have to prepare for early surgery.

## References

1. Ince H, Nienbar CA. *The concept of interventional therapy in acute aortic syndrome. J Card Surg* 2002; 17:135-42.
2. Macura JK, Corl FM, Fishman EK, et al. *Pathogenesis in acute aortic syndromes: aortic dissection, intramural haematoma and penetrating atherosclerotic aortic ulcer. A J R Am J Roetgenol* 2003; 181:309-16.
3. Erbel R, Alfonso F, Boileau C, Dirsch O, Eber B, Haverich A, Rakowski H, Struyven J, Radegran K, Sechtem U, et al. *Diagnosis and management of aortic dissection. Recommendations of the Task Force on Aortic Dissection, European Society of Cardiology. Eur Heart J* 2001; 22:1642-1681.
4. Von Kodolitsch Y, Csoz SK, Koschyk DH, Schalwat I, Loose R, Karck M, et al. *Intramural hematoma of the aorta: predictors of progression to dissection and rupture. Circulation* 2003; 107:1158-63.
5. Vilacosta I, San Roman JA, Ferreiros J, et al. *Natural history and serial morphology of aortic intramural hematoma : a novel variant of aortic dissection. Am Heart J* 1997; 134:495-507.
6. Robbins RC, MacManus RP, Mitchell RS, et al. *Management of patients with intramural hematoma of the thoracic aorta. Circulation* 1993; 88(5 pt2):III-10.
7. Kazui T, Washiyama N, Bashar AHM et al. *Surgical outcome of acute type A aortic dissection: analysis of risk factors. Ann Thorac Surg* 2002; 74:75-82.
8. von Kodolitsch Y, Schwartz AG, Nienaber CA. *Clinical prediction of acute aortic dissection. Arch Intern Med.* 2000; 160:2977-2982.
9. Naotaka M, Yoshimasa M, Tsunehiro K, Koichi T. *Intramural hematoma and dissection involving ascending aorta: the clinical features and prognosis. Eur J Cardiothorac Surg.* 2003; 24:237-242.
10. Dake MD. *Aortic intramural haematoma: current therapeutic strategy. Heart* 2004; 90:375-8.
11. Keren A, Kim CB, Hu BS, et al. *Accuracy of biplane and multiplane transesophageal echocardiography in diagnosis of typical aortic dissection and intramural hematoma. J Am Coll Cardiol* 1996; 28:627-36.
12. Moizumi Y, Komatsu T, Motoyoshi N, Tabayashi K. *Management of patients with intramural hematoma involving the ascending aorta. J Thorac Cardiovasc Surg.* 2002; 124:918-24.
13. Kaji S, Nishigami K, Akasaka T, Hozumi T, Tagaki T, Kawamoto T, et al. *Prediction of progression or regression of type A aortic intramural hematoma by computed tomography. Circulation.* 1999; 100(suppl II):II281-6.
14. Kang DH, Song JK, Song MG, et al. *Clinical and echocardiographic outcomes of aortic intramural hemorrhage compared with acute aortic dissection. Am J Cardiol* 1998;81:202-6.
15. Bolognesi R, Manca C, Tsialtas D, et al. *Aortic intramural hematoma: an increasingly recognized aortic disease. Cardiology* 1998; 89:178-83.
16. Uchida K, Imoto K, Takahashi M, Suzuki S, Isoda S, Sugiyama M, et al. *Pathologic characteristics and surgical indications of super acute type A intramural hematoma. Ann Thorac Surg* 2005; 79:1518-21.
17. Moriyama Y, Yotsumoto G, Kuriwaki K, et al. *Intramural hematoma of the thoracic aorta. Eur J Cardiothorac Surg* 1998; 13:230-9.
18. Isselbacher EM. *Intramural hematoma of the aorta: should we let down our guard? Am J Med* 2002; 11:244-6.
19. Song JK, Kim HS, Kang DH, et al. *Different clinical features of aortic intramural hematoma versus dissection involving the ascending aorta. J Am Coll Cardiol* 2001; 37:1604-10.
20. Mohr-Kahaly S, Erbel R, Kearney P, et al. *Aortic intramural hemorrhage visualized by transesophageal echocardiography: findings and prognostic implications. J Am Coll Cardiol.* 1994; 23:658-664.
21. Maraj R, Rerkpattanapipat P, Jacobs LE, Makornwattana P, Kotler MN. *Meta-analysis of 143 reported cases of aortic intramural hematoma. Am J Cardiol* 2000; 86:664-8.

Corresponding Author  
Aleksandar Mikic,  
Clinic for Cardiac Surgery,  
Clinical Center of Serbia,  
Serbia,  
E mail: mickation@yahoo.com

# Laparoscopic management of tubal pregnancy misdiagnosed and missed by Laparotomy 35 days ago

*Hakan Nazik, Murat Api, Orçun Özdemir, Emre Destegül, Hasan Can Toyganözü*

Departments of Obstetrics and Gynecology, Adana Numune Research and Education Hospital

## Abstract

The difficulties in the diagnosis of early ectopic pregnancy still remains. We report a case of tubal ectopic pregnancy misdiagnosed as an ovarian ectopic pregnancy 35 days ago. The patient had been operated on suspicion of ectopic pregnancy by laparotomy at a private hospital. A woman, suffering from lower abdominal pain was performed transvaginal ultrasonography (TVS) and revealed a hematoma on the right adnexial side. Laparoscopy was performed and a moderate amount of intra-abdominal hemorrhagic fluid was evident. Hematoma was observed in the ruptured right tube. Right salpingectomy was performed. Histopathologic examination of the specimen was reported to be tubal ectopic pregnancy. We conclude that misdiagnosis of ectopic pregnancy may be associated with early operative approach. The factors contributing to misdiagnosis of ectopic pregnancy are discussed and compared with those reported in other studies.

**Key words:** Pregnancy, Ectopi; Laparoscopy

## Introduction

Ectopic pregnancies are common, increasing in incidence, and preventable causes of reproductive morbidity and death. They are also frequently misdiagnosed, and one of the most common causes of malpractice claims made against physicians. Despite remarkable advances in diagnosis and treatment, ectopic pregnancies account for 9% of all maternal deaths.<sup>1</sup> To decrease the complications and preserve fertility, ectopic pregnancies must be detected before they cause tubal rupture. A retrospective clinical study, 'missed diagnosis' at initial presentation had reported incidence of 12% and had been discharged with an incorrect diagnosis, then subsequently readmitted for definite

treatment of a tubal ectopic pregnancy.<sup>2</sup> Furthermore, if the intervention takes place in very early stages and there was no abnormal appearance on the evaluation of pelvic organs during laparoscopy, the ectopic pregnancy could easily be missed. The difficulties in the diagnosis of early ectopic pregnancy still remains. We report a case of tubal ectopic pregnancy misdiagnosed as an ovarian ectopic pregnancy 35 days ago during laparotomy.

## Case Presentation

A 32-year-old woman, gravida 1, para 1, suffering from lower abdominal pain and slight vaginal bleeding was referred to our hospital. The patient was operated on suspicion of ectopic pregnancy 35 days ago by laparotomy at a private hospital. At her operation, ovarian wedge resection was performed due to the normal appearance of Fallopian tubes and hemorrhagic lesion on the right ovary. Histopathologic examination of the pathologic specimen was reported to be normal ovarian tissue. On admission, she had a history of a cesarean section 3 years ago and she did not remember when her last menstrual period was, because of her irregular periods. Blood pressure and pulse rate were normal. Laboratory parameters were revealed that a hemoglobin concentration of 8.2 g/dL. and the serum beta-human chorionic gonadotrophin ( $\beta$ -hCG) level was 1073 IU/mL. Transvaginal ultrasonography revealed a mass with heterogeneous echogenicity with a 5 cm in diameter on the right adnexial side.

Under general anesthesia, laparoscopy was performed and a moderate amount of intra-abdominal hemorrhagic fluid was evident. Hematoma were observed in the right tube 5-6 cm in diameter (Figure 1). Right salpingectomy was performed and pathology of ectopic pregnancy were reported as a result.



Figure 1. Primary tubal pregnancy.

### Discussion

Ectopic pregnancy prevalence continues to rise because of increases in the incidence of the risk factors predisposing to ectopic pregnancy. The diagnosis is often not that simple, especially when the patient presents early, has minimal pain, is haemodynamically stable, and transvaginal sonography shows an empty uterus but no obvious adnexal mass. This could then be an early intrauterine pregnancy, or would indeed be an ectopic pregnancy of unknown location.<sup>3</sup> In the present case, we were able to demonstrate tubal ectopic pregnancy misdiagnosed missed by laparotomy 35 day ago. A retrospective clinical study of 255 surgically proven cases of ectopic pregnancy, thirty-one patients (12%) had presented and been discharged with an incorrect diagnosis, then subsequently readmitted for definite treatment of a tubal ectopic pregnancy. In this group, the mean time from initial presentation to definitive surgery was 8 days.<sup>2</sup>

The recent use of progesterone-only pills and intrauterine devices with a history of surgery, pelvic inflammatory disease, sexually transmitted disease, and allergy increases the risk of ectopic pregnancy. Our patient had not been using any contraception, and did not report a history of the other risk factors.<sup>4</sup>

Salpingo(s)tomy has become an option in patients desiring future fertility. Compared to salpingectomy, salpingo(s)tomy aims to save tubal integrity to maintain reproductive capacity.<sup>5</sup> In this case right salpingectomy was performed.

If pregnancy is diagnosed, its location needs to be ascertained by ultrasound examination. A

physician needs to insist on pathologic examination of all abortions. The authors concluded that TVS should be the first diagnostic test to be used when ectopic pregnancy is suspected.<sup>6</sup> A gestational sac, either intra-uterine or extrauterine, is typically visible if the beta human chorionic gonadotrophin (beta-hCG) is more than 1,500 IU.<sup>7-9</sup>

We conclude that misdiagnosis of ectopic pregnancy may be associated with early operative approach.

### References

1. Ehrenberg-Buchner S, Sandadi S, Moawad NS, Pinkerton JS, Hurd WW. Ectopic pregnancy: role of laparoscopic treatment. *Clin Obstet Gynecol.* 2009;52(3):372-9.
2. Robson SJ, O'Shea RT. Undiagnosed ectopic pregnancy: a retrospective analysis of 31 'missed' ectopic pregnancies at a teaching hospital. 1996 May;36(2):182-5.
3. Coşar E, Nadirgil Köken G, Aral İ, Kır Şahin F, Ariöz DT, Yılmaz M. Ovaryan Ektopik Gebelik. *Türkiye Klinikleri J Gynecol Obst* 2008;18(2):134-137.
4. Özyapı Alper AG, Büyükbayrak EE, Bayramoğlu MB, Karşıdağ YK, Kars B, Pirimoğlu ZM, Ünal O, Turan MC. Treatment Approaches in Ectopic Pregnancy: A Four Year Retrospective Analysis of a Tertiary Referral Center. *Türkiye Klinikleri J Gynecol Obst.* 2010;20(6):362-6.
5. Van Mello NM, Mol F, Opmeer BC, de Bekker-Grob EW, Essink-Bot ML, Ankum WM, Mol BW, van der Veen F, Hajenius PJ. Salpingotomy or salpingectomy in tubal ectopic pregnancy: what do women prefer? *Reprod Biomed Online.* 2010;21(5):687-93.
6. Erdem A, Erdem M, Yıldız A, Yıldırım M, Transvaginal Ultrasonography in the Diagnosis of Ectopic Pregnancy. *Türkiye Klinikleri J Gynecol Obst.* 1992;2(1):32-38.
7. Gracia CR, Barnhart KT Diagnosing ectopic pregnancy: decision analysis comparing six strategies. *Obstet Gynecol* 2001 Mar;97(3):464-70.
8. Evaluation of the Laparoscopically Treated Ectopic Pregnancies. Balcı O, Mahmoud CS, Çapar M. *Selçuk Tıp Derg* 2010;26(3):76-8
9. Ercan CM, Keskin U, Çoksuer H, Karaşah KE, Alambay İ, Dede M, Başer İ. Ektopik gebeliklerin laparoskopik yaklaşımla tedavilerinin retrospektif incelemesi. *Gülhane Tıp Derg* 2011;53(2):99-103

Corresponding Author

Hakan Nazik,

Department of Obstetrics and Gynecology,

Adana Numune Education and Research Hospital,

Adana,

Turkey,

E-mail: drhakannazik@gmail.com

# Health related quality of life during pregnancy

Jelena Dotlic<sup>1,2</sup>, Milan Terzic<sup>1,2</sup>, Slobodanka Janosevic<sup>3</sup>, Dragan Babic<sup>3</sup>, Momcilo Ristanovic<sup>4</sup>, Tatjana Pekmezovic<sup>5</sup>

<sup>1</sup> Faculty of Medicine, University of Belgrade, Serbia,

<sup>2</sup> Clinic of Obstetrics and Gynecology, Clinical Centre of Serbia,

<sup>3</sup> Institute of Medical Statistics and Informatics, Faculty of Medicine, University of Belgrade, Serbia,

<sup>4</sup> Institute of Human Genetics, Faculty of Medicine, University of Belgrade, Serbia,

<sup>5</sup> Institute of Epidemiology, Faculty of Medicine, University of Belgrade, Serbia.

## Abstract

**Introduction:** Numerous parameters can affect the quality of life (QL) during pregnancy.

**Goal:** The aim of the study was to evaluate QL in healthy pregnant women.

**Methods:** Study involved every sixth woman who gave birth in Clinic of Gynecology and Obstetrics Clinical Center of Serbia, Belgrade, during the year 2010. They filled in the SF-36 questionnaire, Beck's Depression Inventory (BDI), Fatigue Severity Scale (FSS), Pregnancy Symptom Scale (PSS), Multidimensional Personal Support Scale (MSPSS) and Acceptance of Illness Scale (AIS).

**Results:** There were 604 women included in the study. Mean scores of the scales were: total SF-36-70.7, BDI-3.8, FSS-3.5, PSS-2.1, MSPSS-70.3, AIS-14.0. The values of total QL, PSS and MSPSS scores were highly significantly correlated with all other examined scale scores. BDI and FSS were not correlated only with MSPSS. Significant models of correlation were obtained for SF-36 scores: total QL ( $R=0.597$ ;  $\text{adj}R^2=0.351$ ;  $F=66.281$ ;  $p=0.000$ ).

**Conclusion:** The QL during pregnancy was good. Examined women did not have significant levels of depression, fatigue and symptoms during pregnancy. Women had good social support and tolerated pregnancy well. However, depression, fatigue, pregnancy tolerance and social support can all significantly affect the quality of life during pregnancy. Most attention should be directed to pregnancy-related depression and fatigue.

**Key words:** quality of life, pregnancy

## Introduction

The population of pregnant women represents an important part of any society. Although pregnancy

lasts only 10 lunar months, it changes the life of women as well as their whole families and surroundings for the rest of their lives. Even though medically classified as a physiological condition, pregnancy is normally associated with numerous changes in organ functions. Some women accept and tolerate these changes better and some are severely symptomatic. Furthermore, various pathological conditions, preexisting or pregnancy-related, can affect the course and outcome of pregnancy (1-3). All these factors may play a role in women's health-related quality of life (HRQoL) during pregnancy.

## Goal

The aim of the study was to evaluate the HRQoL in healthy pregnant women.

## Methods

The study involved all women who gave birth in the Clinic for Gynecology and Obstetrics, Clinical Centre of Serbia, Belgrade, during the year 2010. Inclusion criteria were: term singleton pregnancy, vaginal birth within last 12-24h, newborn's Apgar score  $>8$ ,  $\geq 18$  years of age, resident of Belgrade, speaking Serbian and signed informed consent. Exclusion criteria were: failure to meet the inclusion criteria, decline participation in the study and verified psychiatric disorders. Women were randomized by a simple manual randomization process which led to administration of questionnaires to every sixth woman. Moreover, adequate sample size was calculated. Information for sample size calculation was obtained from annual health statistics of the Belgrade Institute for Public Health and birth statistics of Clinic for Gynecology and Obstetrics Clinical Center of Serbia. Data for past

5 years were taken into consideration. Consequently, the minimal sample of 193 women was determined as appropriate for the study.

Study was designed as cross-sectional. On the first postpartal day, respondents filled in SF-36 (Short Form – 36) questionnaire (Serbian translation) (4), Beck's Depression Inventory (BDI) (5), Fatigue Severity Scale (FSS) (6), Pregnancy Symptom Scale (PSS) (7), Multidimensional Personal Support Scale (MSPSS) (8), and Acceptance of Illness Scale (AIS) (9). All questionnaires were self-administered; yet, the examiner was available to answer all possible questions.

The SF-36 is a generic HRQoL instrument that measures eight different dimensions of life which are calculated as 8 domains: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and emotional well-being (EW). Scoring and calculation of scales were performed by using the Ware's survey manual (14). Based on these eight domains, two summary composite scores were constructed: the Physical Health Composite score (PHC) and the Mental Health Composite score (MHC). Finally, the Total quality of life score (TQL) is calculated. PHC, MHC and TQL were used for further analyses in this study. Higher values of all SF-36 scores mean better functioning and well-being (4).

BDI is 21-question scale that enables assessment of psychological state and depression level of respondents. It explores feelings and attitudes towards general depressive state. Answers are graded from 0 to 3. The BDI score higher than 21 is considered as presence of depression (5).

Krupp's FSS is consisted of 9 statements. Responders grade them from 1 (completely disagree) to 7 (completely agree). Therefore, the total score can range from 9 to 63. This total score is then divided by 9 in order to obtain the average value. This score can range from 1 (no fatigue) to 7 (severe fatigue). FSS score above 4.8 is considered to be pathological (6).

PSS, developed and validated by authors of this paper, is used to evaluate which symptoms and to what extent had the most impact on HRQoL during pregnancy. It consists of 42 symptoms both physiological pregnancy and the most usual pathological conditions during pregnancy. PSS in-

vestigates period before pregnancy, first, second and third trimester as well as the entire antepartum course. Respondents grade each symptom from 1 (not present) to 10 (severe) (7). The simple score is a sum of all grades. Mean score is made by dividing the simple score by 42. It has a range from 0 (no symptoms) to 10 (severe symptoms). The mean score of entire antepartum course was regarded as PSS score and used for further analyses.

Zimet's MSPSS enables quantitative and qualitative assessment of the support that respondent is receiving from people close and important to him/her. Scale comprises of 12 statements regarding partners support (4 items), family support (4 items) and friends support (4 items). Respondents grade them from 1 (completely disagree) to 7 (completely agree). Maximal score of 84 stand for maximal social support (8).

Felton's AIS has 8 statements with 5 grades of response and maximum score of 40. Higher score means worse acceptance of one's illness or condition. This scale shows the level of adaptation on new condition and the ability of the respondent to make him/her happy (9).

Statistical analysis: Methods of descriptive statistics were employed for general impression of the examined scores as well as depiction of the examined population. Kolmogorov-Smirnov test was used for assessing distribution of score values. Spearman's correlations were used to test the influence of scale scores one on another. Furthermore, multiple linear regression was applied for assessing the effects of all examined scale scores together on SF-36 scores. The level of statistical significance was 0.05 and of high significance 0.01. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software (Advanced Statistics, version 17.0, SPSS Inc. - Chicago, IL, USA).

## Results

There were 4572 women who delivered vaginally during the year 2010 in our Clinic. After randomization 762 pregnant women were involved in the study. Out of that number, 158 women had to be excluded, due to unfulfilling the inclusion criteria. There were 54 women who declined to participate in the study, 33 women were not from Belgrade, 4

women did not speak Serbian, 12 women were younger than 18 years of age, 10 women delivered before term, while 18 women had twin pregnancies. The newborns of 27 respondents had Apgar score  $\leq 8$ . There were no patients with mental disorders. Consequently, the responses of 604 pregnant women underwent the final statistical analysis.

The age of examined women ranged from 18 to 49 years (mean  $\pm$  SD = 29.43  $\pm$  5.14).

The values of all scores were not normally distributed ( $KSZ_{PHC}=2.114$ ;  $p=0.000$ ;  $KSZ_{MHC}=2.531$ ;  $p=0.000$ ;  $KSZ_{TQL}=1.849$ ;  $p=0.002$ ;  $KSZ_{BDI}=5.654$ ;  $p=0.000$ ;  $KSZ_{FSS}=1.802$ ;  $p=0.003$ ;  $KSZ_{AIS}=3.675$ ;

$p=0.000$ ;  $KSZ_{MSPSS}=4.073$ ;  $p=0.000$ ;  $KSZ_{PSS}=1.781$ ;  $p=0.004$ ). Therefore, non-parametrical methods were used for analyzes.

Tables 1, 2 and 3 show descriptive parameters for examined scale scores. As it can be seen, women have scored their HRQoL during pregnancy in average with 73.6 (out of maximal 100). Pregnancy symptoms were enhancing trough pregnancy and, so, they were the most dominant in the third trimester. Women mostly did not have significant psychological problems during pregnancy. Fatigue was present in all examined women at least in a low level, but the overall grade for

Table 1. Descriptive parameters for SF-36 scores

Scores	Min	Max	Range	IR	Mean	Median	SE	SD
PF	0.00	100.00	100.00	40.00	<b>78.63</b>	90.00	0.96	23.59
RP	0.00	100.00	100.00	100.00	<b>52.81</b>	50.00	1.70	41.88
BP	0.00	100.00	100.00	42.50	<b>75.26</b>	77.50	0.99	24.36
GH	20.00	100.00	80.00	30.00	<b>69.53</b>	70.00	0.67	16.42
VT	0.00	100.00	100.00	30.00	<b>65.27</b>	65.00	0.72	17.78
SF	12.50	100.00	87.50	37.50	<b>77.41</b>	75.00	0.87	21.41
RE	0.00	100.00	100.00	67.00	<b>72.58</b>	100.00	1.62	39.88
EW	8.00	100.00	92.00	24.00	<b>73.96</b>	76.00	0.69	16.96
PHC	18.13	100.00	81.88	33.75	<b>69.06</b>	71.56	0.77	18.95
MHC	13.75	100.00	86.25	28.29	<b>72.30</b>	76.21	0.76	18.59
TQL	22.19	99.38	77.19	28.33	<b>70.68</b>	73.61	0.71	17.35

IR - Interquartile Range; SE - Standard Error; SD - Standard Deviation

Table 2. Descriptive parameters for PSS

Scores	Min	Max	Range	IR	Mean	Median	SE	SD	
Before pregnancy	simple	0.00	102.00	102.00	12.00	<b>8.99</b>	0.00	0.62	15.18
	mean	0.00	2.43	2.43	0.29	<b>0.21</b>	0.00	1.80	0.35
First trimester	simple	0.00	198.00	198.00	55.00	<b>35.04</b>	27.00	1.87	36.62
	mean	0.00	4.71	4.71	1.31	<b>0.83</b>	0.64	4.44	0.87
Second trimester	simple	0.00	234.00	234.00	53.75	<b>32.72</b>	23.00	1.87	36.95
	mean	0.00	5.57	5.57	1.28	<b>0.78</b>	0.55	4.45	0.87
Third trimester	simple	0.00	251.00	251.00	92.00	<b>57.36</b>	52.5	2.66	52.21
	mean	0.00	5.98	5.98	2.19	<b>1.37</b>	1.25	6.34	1.24
Entire antepartum course	simple	0.00	420.00	420.00	60.75	<b>89.27</b>	83.00	2.63	51.59
	mean	0.00	10.00	10.00	1.45	<b>2.13</b>	1.98	6.27	1.23

IR - Interquartile Range; SE - Standard Error; SD - Standard Deviation

Table 3. Descriptive parameters for scores of BDI, FSS, AIS and MPSS scores

Scales	Min	Max	Range	IR	Mean	Median	SE	SD
BDI score	0.00	41.00	41.00	6.00	<b>3.83</b>	2.00	0.21	5.18
FSS score	1.00	7.00	6.00	2.64	<b>3.53</b>	3.48	6.72	1.66
AIS score	8.00	40.00	32.00	8.00	<b>13.99</b>	12.00	0.22	5.44
MSPSS score	12.00	84.00	72.00	19.00	<b>70.31</b>	73.00	0.55	13.47

IR - Interquartile Range; SE - Standard Error; SD - Standard Deviation



fatigue was average. According to the MPSS, pregnancy is, in majority of cases, well accepted and tolerated by the mothers. Examined women, also, thought that their family and friends were supporting them well during pregnancy.

Table 4 presents results of Spearman's correlation between examined scale scores. The values of all three assessed SF-36 (PHC, MHC and total QL) scores were significantly correlated with all other examined scale scores. BDI, FSS and PSS were not significantly correlated only with AIS. MSPSS was significantly correlated with all other examined scale scores.

After having confirmed numerous significant relationships between single scale scores, multiple associations of composite and total SF-36 scores with all other examined scale scores together were tested using Enter and Stepwise methods of multiple linear regression. Statistically significant linear regression equations were obtained for all assessed SF-36 scores: MHC ( $R=0.581$ ;  $adjR^2=0.332$ ;  $F=60.953$ ;  $p=0.000$ ), PHC ( $R=0.531$ ;  $adjR^2=0.276$ ;  $F=47.036$ ;  $p=0.000$ ) and total QL ( $R=0.597$ ;  $adjR^2=0.351$ ;  $F=66.281$ ;  $p=0.000$ ). According to the results of Stepwise method BDI has the most and AIS the least importance for determining

Table 4. Spearman's correlation ( $\rho$ ) between examined scale scores

Scale scores		PHC	MHC	TQL	BDI	FSS	MSPSS	AIS	PSS
PHC	$\rho$	1.000	0.705	0.930	-0.200	-0.355	0.266	-0.160	-0.312
	p	-	0.000	0.000	0.000	0.000	0.000	0.000	0.000
MHC	$\rho$	0.705	1.000	0.911	-0.326	-0.404	0.250	-0.149	-0.276
	p	0.000	-	0.000	0.000	0.000	0.000	0.000	0.000
TQL	$\rho$	0.930	0.911	1.000	-0.289	-0.404	0.269	-0.168	-0.313
	p	0.000	0.000	-	0.000	0.000	0.000	0.000	0.000
BDI	$\rho$	-0.200	-0.326	-0.289	1.000	0.193	0.145	0.003	0.111
	p	0.000	0.000	0.000	-	0.000	0.000	0.944	0.006
FSS	$\rho$	-0.355	-0.404	-0.404	0.193	1.000	-0.131	0.053	0.212
	p	0.000	0.000	0.000	0.000	-	0.001	0.195	0.000
MSPSS	$\rho$	0.266	0.250	0.269	0.145	-0.131	1.000	-0.133	-0.084
	p	0.000	0.000	0.000	0.000	0.001	-	0.001	0.039
AIS	$\rho$	-0.160	-0.149	-0.168	0.003	0.053	-0.133	1.000	0.076
	p	0.000	0.000	0.000	0.944	0.195	0.001	-	0.061
PSS	$\rho$	-0.312	-0.276	-0.313	0.111	0.212	-0.084	0.076	1.000
	p	0.000	0.000	0.000	0.006	0.000	0.039	0.061	-

Table 5. Models of relations between SF-36 scores and all other examined scale scores

Linear regression equations
MHC = 78.083 – 31.706xBDI
MHC = 89.309 – 25.607xBDI – 3.491xFSS
MHC = 68.070 – 26.509xBDI – 3.165xFSS + 3.456xMSPSS
MHC = 72.652 – 25.295xBDI – 2.918xFSS + 3.262xMSPSS – 2.107xPSS
MHC = 78.556 – 25.699xBDI – 2.882xFSS + 3.036xMSPSS – 2.765xAIS – 2.012xPSS
PHC = 83.938 – 4.211xFSS
PHC = 90.092 – 3.656xFSS – 3.764xPSS
PHC = 68.122 – 3.401xFSS – 3.496xPSS + 3.497xMSPSS
PHC = 66.866 – 2.824xFSS – 3.121xPSS + 3.718xMSPSS – 15.836xBDI
PHC = 73.261 – 16.273xBDI – 2.785xFSS + 3.473xMSPSS – 2.995xAIS – 3.018xPSS
TQL = 86.043 – 4.347xFSS
TQL = 87.000 – 3.530xFSS – 21.097xBDI
TQL = 64.075 – 3.177xFSS – 22.069xBDI + 3.730xMSPSS
TQL = 69.759 – 2.871xFSS – 20.565xBDI + 3.490xMPSS – 2.614xPSS
TQL = 75.909 – 20.986xBDI – 2.834xFSS + 3.255xMSPSS – 2.880xAIS – 2.515xPSS

MHC. For PHC and total QL calculations FSS was of most and AIS of least significance. Nevertheless, all scores had statistically significant place in the achieved models (Table 5).

## Discussion

Numerous factors that can affect HRQoL during pregnancy demand for a multidisciplinary approach to this issue and the use of various questionnaires that can estimate HRQoL from different aspects. However, not enough attention has been paid to HRQoL of pregnant women. Up to now, there are few studies that give the overall picture of HRQoL during pregnancy (10-12). Most studies regarding HRQoL during pregnancy deal with the influence of different pregnancy complications on HRQoL (11-14) or investigate the attitude of future mothers concerning pregnancy or delivery course and outcome (10). Moreover, there are almost no studies dealing with the HRQoL of healthy pregnant women.

The total quality of life during pregnancy, as well as physical and mental functioning, of healthy women who gave birth per vies naturals to a vigorous child was, as expected, quite high. Furthermore, examined women did not have significant levels of depression or fatigue during pregnancy. Pregnancy-related symptoms were not pointed out as a factor of great importance, although there were a variety of attitudes regarding pregnancy-related symptoms. Women thought that they were well supported during pregnancy by family and friends. Therefore, the majority of women accepted and tolerated pregnancy well. Having a baby proved once again to be one of the most joyful moments of woman's life. Thus, it can be concluded that these are content women with few problems.

The HRQoL during pregnancy is far better than of women who are suffering from illnesses (15). Further studies should compare in more details the population of healthy pregnant and non-pregnant women. Unfortunately, the standards for the SF-36 questionnaire in the Serbian general population do not exist so far, thus there was no possibility to compare the HRQoL of pregnant women to our age-matched general population. Nevertheless, when compared to the HRQoL of female Belgrade university students, that are considered to be one of the most healthy populations, total QL was

somewhat (approximately 5 points) lower in pregnant women. Physical functioning and especially role were also worse in pregnant women. On the other hand pregnant women had higher scores of all other SF-36 domains. Therefore, PHC was lower and MHC higher in pregnant women compared to students population (16). These findings are easily understandable, as pregnancy-related bodily changes and symptoms deteriorate physical performance. On the other hand, becoming a mother, of a healthy child, makes women happier than ever and few things can affect that feeling.

However, according to our results pregnancy-related symptoms, depression and fatigue as well as pregnancy tolerance and social support to pregnant women can all significantly affect the quality of life during pregnancy even if mother and child are healthy. Therefore, the role of obstetrician/gynecologist is to remove pregnancy-related symptoms and prevent complications not only in order to ensure the good course and outcome of pregnancy but also the HRQoL during pregnancy.

According to available data the proportion of women with depressive symptoms is 15%, 14%, and 30% in the first, second and third trimesters, respectively, and 9% after delivery. Women who became depressed had scores in the social domains that were 10-23 points and 19-31 points lower in the second and third trimesters, respectively, compared to women with no depressive symptoms. So it can be noted that alterations in depressive symptoms have a substantial effect on functioning during pregnancy and after delivery (17). Our study confirmed the influence of pregnancy-related depression on HRQoL during pregnancy. To decrease the depression level removing or at least reducing the pregnancy symptoms and complications should be done. Detailed explanations of physiological and expected conditions during pregnancy should be provided to future mothers. In that way, they can accept and tolerate their pregnancy better.

Studies show that women in the first trimester of pregnancy experience significantly greater fatigue compared to a similar group of non-pregnant women (18). Pregnant women reported greater number of hours spent sleeping each day. There was no significant difference in BDI, State Trait Anxiety Inventory scores, but pregnant women had significantly higher scores on the Numerical

Rating Scale for Fatigue (18). Moreover, fatigue is a significant consequence of anemia in pregnancy and during delivery (10). Our results show that fatigue during pregnancy can deteriorate the HRQoL. Therefore, regular daily periods of rest as well as limiting physically demanding activities and work will ensure reduction of fatigue that is usual problem. Better mental and physical functioning improves subjective feeling of overall HRQoL during pregnancy. Furthermore, anemia during pregnancy must be properly treated.

The inverse relationship between social support and anxiety in pregnancy and the postpartum was found in some investigations (19). The support score of husbands increased gradually over the period of pregnancy, while parents were found to be most supportive one month after birth. Additionally, husbands and parents were found to compensate for each other in their support (19). The more support the pregnant women received in a given period, the higher the mean scores for child care, health conditions and HRQoL were. "Positive feeling" was influenced by the husband's support during the whole study period. "Daily life" correlated with the support most strongly after birth. Therefore, family support was shown to be a strong correlate for the HRQoL of pregnant women. Providing family support could improve mothers' child care, health conditions and HRQoL (20). We also found that, in order to improve mental and physical functioning during pregnancy, appropriate social support needs to be provided to pregnant women from not only partner, family and friends but also from the whole society.

Frequency, discomfort, and the effect of physical symptoms all consistently correlated with higher scores for depressive symptoms, but less consistently with lower self-esteem (19). Discomfort and the effect of symptoms predicted variance in depressive symptoms after accounting for symptom frequency. Relationships between pregnancy-related physical symptoms, depressive symptoms, and low self-esteem suggest that when women report any of these constellations of factors, further screening is indicated (21). Moreover, two-thirds of women reported three or more health issues, the most common being exhaustion (87%), nausea (64%), back pain (46%), constipation (44%) and severe headaches/migraines (30%). Younger women had significantly lower SF-36 scores (po-

orer self perceived health). So, it can be seen that common pregnancy symptoms have a marked impact on women's physical and mental health in early pregnancy, with the greatest impact apparent for younger women (22). Our research also proves the existence of positive correlation with depression and fatigue. The correlation between PSS and total QL was negative, meaning that more severe symptoms influenced deterioration of HRQoL. Women receiving less social support complained more on pregnancy symptoms. This correlation is well-established for hyperemesis gravidarum (23).

Multiple correlations performed in our study confirm strong relationships of all examined parameters and HRQoL. As it could be predicted, pregnancy-related depression had the most influence on mental functioning while fatigue had the most deteriorating affect on both physical functioning and total QL during pregnancy. Therefore, the most attention while treating pregnant women should be paid on these two parameters.

The cross-sectional design and the fact that the answers were based on recollection might be considered as methodological limitations of this study. However, other studies have been similarly designed as cross sectional, based on various self-reported questionnaires and were performed either during the last trimester just before birth (10, 24) or during first postpartal days (12-48h) (11). Moreover, we considered that pregnancy is such an important time in a woman's life that she remembers it clearly for a long time. Additionally, we would like to notice that, in the delivery department of our clinic which is the largest in Belgrade, women of all different backgrounds give birth, thus providing a representative sample. Moreover, avoiding selection bias, concerning that we were conducting a clinical study, was also accomplished by randomization of respondents.

## Conclusion

The total quality of life during pregnancy, as well as physical and mental functioning, of healthy women who gave birth per vies naturals to a child with Appgar score higher than 8 was, as expected, good. Furthermore, examined women did not have significant levels of depression or fatigue as well as symptoms during pregnancy. Women had good social support during pregnancy and, there-

fore, the majority of women accepted and tolerated pregnancy well. However, according to our results pregnancy-related symptoms, depression and fatigue as well as pregnancy tolerance and social support to pregnant women can all significantly affect the quality of life during pregnancy even if mother and child are healthy. Multiple correlations confirm strong relationships of all examined parameters and HRQoL and point out that the most attention while treating pregnant women should be directed to depression and fatigue during pregnancy.

### Acknowledgements

This work was supported by a grant of the Ministry of Science and Technological Development of the Republic of Serbia (grant No. 175087).

### References

- Kontic-Vucinic O, Terzic M, Radunovic N. The role of antioxidant vitamins in hypertensive disorders of pregnancy. *J Perinat Med* 2008; 36: 282-290.
- Lee KA, Gay CL. Sleep in late pregnancy predicts length of labour and type of delivery. *Am J Obstet Gynecol* 2004; 191:2041-2046.
- Terzic M. HELLP syndrome – Therapeutic dilemma. *Arch Gastroenterohepatol* 1998; 17: 32-36.
- Ware JE, Snow KK, Kosinski M, Gandek B. *The SF-36 Health Survey Manual and interpretation guide*. Boston: Nimrod Press 1993.
- Beck AT, Beck RW. Screening depressed patients in family practice: a rapid technique. *Postgrad Med* 1972; 52: 81-85.
- Krupp LB, Larocca NG, Nash JM, Steinberg AD. The Fatigue Severity Scale. Application to patients with multiple sclerosis and systematic lupus erythematosus. *Arch Neurol* 1989; 46:1121-1123.
- Wewers ME, Lowe NK. A critical review of visual analogue scales in the measurement of clinical phenomena. *Res Nurs Health* 1990; 13:227-236.
- Zimet GD, Powell SS, Farley GK, Werkman S, Berkoff KA. Psychometric characteristics of the MSPSS. *J Pers Assess* 1990; 23:56-62.
- Felton BJ, Revenson TA. Coping with chronic illness: a study of illness controllability and influence of coping strategies on psychological adjustment. *J Consult Clin Psychology* 1984; 2:343-353.
- Jansen AJ, Duvekot JJ, Hop WC, et al. New insights into fatigue and health-related quality of life after delivery. *Acta Obstet Gynecol Scand* 2007; 86:579-584.
- Rojas G, Fritsch R, Solis J, Gonzalez M, Guajardo V, Araya R. Quality of life of women depressed in the postpartum period. *Rev Med Chil* 2006; 134:7134-7120.
- Symon AG, Dobb BR. An exploratory study to assess the acceptability of an antenatal quality-of-life instrument (the Mother-generated Index). *Midwifery* 2008; 24:442-450.
- Amador N, Juarez JM, Guizar JM, Linares B. Quality of life in obese pregnant women: a longitudinal study. *Am J Obstet Gynecol* 2008;198:203.e1-5.
- Heimstard R, Romundstard PR, Hyett J, Mattsson LA, Salvesen KA. Women's experiences and attitudes towards expectant management and induction of Labour for post-term pregnancy. *Acta Obstet Gynecol Scand* 2007; 86:950-956
- Husic S, Ljuca F, Hasukic S, Mesic D. Quality of life after mastectomy of the breast cancer. *HealthMED* 2009; 3: 254-261
- Pekmezovic T, Popovic A, Kistic Tepavcevic D, Gazibara T, Paunic M. Factors associated with health-related quality of life among Belgrade University students. *Qual Life Res* 2011; 20:391-397
- Setse R, Grogan R, Pham L, et al. Longitudinal study of depressive symptoms and health-related quality of life during pregnancy and after delivery: the Health Status in Pregnancy (HIP) study. *Matern Child Health J* 2009; 13:577-587.
- Behrenz KM, Monga M. Fatigue in pregnancy: a comparative study. *Am J Perinatol* 1999; 16:185-188.
- Aktan NM. Social Support and Anxiety in Pregnant and Postpartum Women: A Secondary Analysis. *Clin Nurs Res*. 2011; doi: 10.1177/1054773811426350.
- Nohara M, Miyagi S. Family support and quality of life of pregnant women during pregnancy and after birth. *Nihon Koshu Eisei Zasshi* 2009; 56:849-862.
- Kamysheva E, Wertheim EH, Skouteris H, Paxton SJ, Milgrom J. Frequency, severity, and effect on life of physical symptoms experienced during pregnancy. *J Midwifery Womens Health* 2009; 54:43-49
- Gartland D, Brown S, Donath S, Perlen S. Women's health in early pregnancy: findings from an Australian nulliparous cohort study. *Aust N Z J Obstet Gynaecol* 2010; 50:413-418.
- Munch S, Korst LM, Hernandez GD, Romero R, Goodwin TM. Health-related quality of life in women with nausea and vomiting of pregnancy: the importance of psychosocial context. *J Perinatol* 2011; 31:10-20.
- Jansen AJ, Essink-Bot ML, Duvekot JJ, van Rhenen DJ. Psychometric evaluation of health-related quality of life measures in women after different types of delivery. *J Psych Res* 2007; 63:275-281.

Corresponding Author

Jelena Dotlic,  
Clinic for Gynecology and Obstetrics,  
Clinical Center of Serbia,  
Belgrade,  
Serbia,  
E-mail: enadot@yubc.net

# Consumers' Kefir consumption: A pilot study in Turkey

Saniye Bilici<sup>1</sup>, Eda Köksal<sup>1</sup>, Özge Küçükerdönmez<sup>2</sup>, Nevin Şanlıer<sup>1</sup>

<sup>1</sup> Department of Nutrition and Dietetics, Faculty of Health Sciences, Gazi University, Besevler, Ankara, Turkey,

<sup>2</sup> Department of Endocrinology and Metabolism, Gülhane Military Medical Academy Hospital, Etlik, Ankara, Turkey.

## Abstract

This study was carried out to determine the attitudes and consumption levels of kefir and factors effecting the kefir consumption among 400 volunteer Turkish adults between 19-65 years age. A questionnaire was administered to determine the study data. The mean age of the subjects was ( $\pm$  SD)  $34.2 \pm 12.1$  years. Only 15.8% of subjects were consumed kefir and the consumption ratio is 20.2% in females, 9.5% in males. In logistic regression analysis; kefir consumption had significantly positive associations with gender [OR: 0.413 (0.232–0.736),  $p < .01$ ], age [OR: 1.05(1.022-1.078),  $p < .001$ ] and education [OR: 2.217(1.505-3.266),  $p < .001$ ]. The mean kefir consumption period and a daily mean intake was found  $3.6 \pm 3.11$  year and  $62 \pm 61.7$  ml, respectively. Majority of the participants stated that they consume kefir because of positive health effects (95.2%) while the most reason for not consuming kefir was lack of knowledge (71.0%). The 96.8% of participants who consume kefir make their own kefir drinks in the home. The use of health claims, advertising and educational campaigns might be necessary in order to make awareness of the health benefits of the product and therefore consider substituting conventional foods by their functional alternatives.

**Key words:** kefir, fermented milk, dairy products, consumption, consumers' attitudes

## Introduction

Kefir is a cultured dairy product due to combined lactic acid and alcoholic fermentation of lactose in milk that originated in the Caucasus mountains.<sup>1,2</sup> The word *kefir* originates from the Turkish word "*keyif*" which means "good feeling."<sup>3,4</sup> The Caucasian people discovered that the fresh milk

carried in leather pouches would occasionally ferment to produce an effervescent beverage.<sup>5</sup>

Kefir is a distinctive fermented dairy product due to the unique, multi-species natural kefir grains used as the starter culture during the product manufacture. In many countries kefir-related products are also produced manufactured using blends of microorganisms which results in a varying range of sensory properties, but lacking the typical characteristics of traditional kefir. Products within these categories are known as Omaere (in South-West Africa), Rob or Roba (in some Arab countries), KjaKlder Mjoklk (in Norway), Kellermilch (in Germany), Tarag (in Mongolia) and Kefir (in Turkey).<sup>6</sup>

Kefir grains have a structure similar to tiny florets of cauliflower which vary in size from 0.3 to 3.5 cm diameter. They are composed mostly of proteins and polysaccharides in which the complex microflora is enclosed. The chemical composition of kefir grains is 890–900 g/kg water, 2 g/kg lipid, 30 g/kg protein, 60 g/kg sugars and 7 g/kg ash.<sup>7</sup> Although less well known than yoghurt, nonetheless the compositional analysis of *kefir* indicates that it may contain bioactive ingredients and the microbiological and chemical composition of kefir provide a complex probiotic effect. Kefir is accepted as a potentially important probiotic product results from the symbiotic metabolic activity of a number of bacterial and yeast species.<sup>8-10</sup>

Kefir has been traditionally consumed for potential health benefits. It has been widely recommended for consumption by healthy individuals as well as by patients with gastrointestinal and metabolic disease, hypertension, ischemic heart disease and allergy. It was begun to be consumed in Russia, then was spread to some areas of the world, southwestern Asia, eastern and northern Europe, North America and Japan for its nutritional and therapeutic aspects.<sup>3,9</sup> In the former Soviet Union, *kefir*

has traditionally been used in hospitals and sanatoria for the treatment of a wide variety of conditions such as metabolic disorders, atherosclerosis, allergic disease, peptic ulcers biliary tract diseases, chronic enteritis, bronchitis, and pneumonia even for tuberculosis and cancer.<sup>3,6</sup> Due to the claimed health benefits of kefir it has become an important functional dairy food and consequently, research on kefir has increased in the past decade.<sup>1,4,8,10</sup>

In Turkey there are both industrially made and home-made kefir products and recent years kefir industry were gradually developing.<sup>11</sup> While it is known that the consumption of milk per capita in Turkey is lower than many European countries<sup>12</sup>, to the best of our knowledge limited studies focusing on the consumption of fermented dairy products have been found in the literature and there is no study concerning data on kefir consumption in Turkey and the World. Therefore, this study aimed to determine the attitudes and consumption levels of kefir and factors effecting the kefir consumption among Turkish adults.

### Methods and materials

A cross-sectional study was conducted and the questionnaire was administered between December - March 2009 to determine the knowledge about kefir and consumption levels of 400 consumers who were randomly recruited at shopping

areas, universities and public places in Ankara, the capital of Turkey. The sample included 232 females (58%) and 168 males (42%), ranging in age from 19 to 65 years. A structured questionnaire was designed to collect the research data. The questionnaire was pilot tested by 25 participants from October to November 2009, resulting in minor modifications made to the wording of the questionnaire. The revised questionnaire contained 25 questions in 2 sections, was administered by intern dieticians as a face to face method. Section A of the questionnaire contained open-ended and closed questions dealing with demographic characteristics (age, education, marital status etc.). Section B contained questions concerning with the consumption and attitudes about kefir. The questionnaire took approximately 10 minutes to be completed. Consumers' consent was required prior to commencement of the study. Each participant signed a voluntary participation form and filled the questionnaires adhered to the Declaration of Helsinki (World Medical Association). The participants were informed about the subject and the purpose of the research.

### Statistical Analysis

The SPSS program 15.0 was used for data entry and statistical analysis. Numeric values are reported as the mean  $\pm$  standard deviation (SD).

Table 1. General characteristics of participants according to consumption status of kefir

General characteristics	Consumption Status		Total n(%)	$\chi^2(p)$
	Consume n(%)	Not consume n(%)		
<b>Gender</b>				
Men	16(9.5)	152(90.5)	168(42.0)	8.462(0.003)*
Women	47(20.2)	185(79.8)	232(58.0)	
<b>Age (years)</b>				
19–29	17(13.1)	113(86.9)	130(32.5)	1.93(0.381)
30–49	28(15.6)	152(84.4)	180(45.0)	
$\geq 50$	18(20.0)	72(80.0)	90(22.5)	
<b>Education period</b>				
< 11 years	20(8.6)	212(91.4)	232(58.0)	21.158(0.000)*
$\geq 11$ years	43(25.6)	125(74.4)	168(42.0)	
<b>Marital status</b>				
Single	27(13.6)	171(86.4)	198(49.5)	1.32(0.251)
Married	36(17.8)	166(82.2)	202(50.5)	
<b>Total</b>	63(15.8)	337(84.2)	400(100.0)	

\* $p < 0.05$

Table 2. Binary logistic regression for kefir consumption status according to general characteristics

General characteristics	B	SE	Odds ratio (95% CI)	p
Gender	-0.885	0.295	0.413(0.232-0.736)	0.003*
Age	0.048	0.014	1.050(1.022-1.078)	0.000*
Education	0.796	0.198	2.217(1.505-3.266)	0.000*
Marital Status	-0.106	0.290	0.900(0.510-1.587)	0.715
*p<0.05				

The chi-square test was used to compare frequencies between the independent variables and “kefir consumption status”. Odds ratios (OR) were calculated in the binary logistic modeling to identify influencing factors on kefir consumption (gender, age, education and marital status). ORs were reported with a 95% confidence interval. The Mann Whitney-U and Kruskal Wallis tests were used to compare mean rank between the independent variables and “amount and duration of kefir consumption”. In all analyses, a  $p < 0.05$  was considered significant.

## Results

General characteristics of participants by gender, age group, education and marital status according to consumption status of kefir were described in Table 1. Only 15.8 % of participants were consumed kefir and the consumption ratio is 20.2% in females, 9.5% in males. Above 50 years old, having more than 11 years education period and married participants have higher consumption ratio. But significant differences were found only for gender and education period ( $p < 0.05$ ).

Table 2 showed that binary logistic regression and odds ratio (OR) for kefir consumption status and general characteristics. Results indicated that alone or with age, gender was effective in kefir consumption. In logistic regression analysis; kefir consumption had significantly positive associations with gender [OR: 0.413 (0.232–0.736),  $p < .01$ ], age [OR: 1.05(1.022-1.078),  $p < .001$ ] and education [OR: 2.217(1.505-3.266),  $p < .001$ ].

The only 29.0 % of students have knowledge about kefir and the sources of obtained information were especially from radio/television (42.2%), internet (18.1%), neighbors (15.5) and health workers (13.8%). The participants stated that kefir especially protect intestinal system (77.6%) and have anticarcinogenic effect (61.2%). Majority of

the participants stated that they consume kefir because of positive health effects (95.2%). It was found that reasons for not consuming kefir was lack of knowledge (71.0%), difficult to supply or produced (19.0%). The most of participants (96.5%) who consume kefir make their own kefir drinks in the home and only 3.5% of them buy commercial kefir (Table 3).

Table 3. Knowledge and Attitudes about kefir

Knowledge about kefir	n (%)
Yes, I know	116 (29)
No, I don't know	284 (71)
<b>Source of knowledge (n:116)</b>	<b>n (%)</b>
Neighbors	18 (15.5)
Health workers	16 (13.8)
Internet	21 (18.1)
Radio/television	49 (42.2)
Newspaper	9 (7.8)
Scientific publications	3 (2.6)
<b>Health impacts of kefir (n:116)</b>	<b>n (%)</b>
Protect intestinal system	90 (77.6)
Improve immune system	28 (24.1)
Reduce kolesterol	11 (9.5)
Anticarcinogenic effect	71 (61.2)
Have no idea	8 (6.9)
<b>Reasons for consume kefir (n:63)</b>	<b>n (%)</b>
Good for health	60 (95.2)
Taste is good	19 (30.2)
It is good for my disease	13 (20.6)
<b>Reasons for not consume kefir (n: 337)</b>	
I don't know what it is.	239 (71.0)
Taste is bad	31 (9.2)
Produce and/or supply is difficult	64 (19.0)
<b>Obtaining sources of kefir (n:63)</b>	
Home made	61 (96.8)
Commercial production	2 (3.2)

Table 4 shows the amount and duration of kefir consumption according to gender, age, educational and marital status of participants. The mean kefir consumption period and a daily mean intake was found  $3.6 \pm 3.11$  year and  $62 \pm 61.7$  mL, respective-

Table 4. Amount and duration of kefir consumption according to gender, age, educational and marital status

General characteristics	Consumption Status			
	Amount (mL)	p	Duration (day)	p
<b>Gender</b>				
Men	56.6±37.1	0.561	2.9±1.0	0.438
Women	65.1±69.5		4.2±3.7	
<b>Age (years)</b>				
19–29	63.5±65.11	0.435	2.8±1.0 <sup>a</sup>	0.007*
30–49	46.4±41.41		2.8±2.2 <sup>a</sup>	
≥50	75.7±56.93		5.9±4.4 <sup>b</sup>	
<b>Education period</b>				
< 11 years	62.7±16.28	0.199	3.3±1.55	0.899
≥ 11 years	61.0±60.47		3.6±3.05	
<b>Marital status</b>				
Single	57.7±52.56	0.436	4.2±3.78	0.536
Married	64.9±61.62		2.9±1.11	
<b>Total</b>	62.0±61.7		3.6±3.11	

\* $p < 0.05$ ,<sup>a,b</sup> Values with different superscripts mean  $p < 0.05$ , with same superscripts mean  $p > 0.05$ .

ly. The consumption amount and duration of kefir consumption did not differ significantly according to gender, age, educational or marital status ( $p > 0.05$ ) while duration of kefir consumption differed significantly according to age classification ( $p < 0.05$ ). Participants in the  $\geq 50$  years age group had a higher duration of kefir consumption ( $p < 0.05$ ).

## Discussion

In recent years, there has been an increased interest in the consumption of traditional fermented products both nationally and internationally. It is estimated that today, more than 3,500 different fermented foods and drink products, either milk based, vegetable, or fruit based are being produced all over the world.<sup>3</sup> Research on fermented milks that are accepted as functional foods which exert health benefits beyond basic nutrition has grown dramatically in the past 20 years.<sup>13</sup> There are many different types of fermented foods and beverages produced at a household level in Anatolia. The most common traditional fermented milk products consumed in Turkey include *yoghurt*, *ayran* and *kefir*.

Limited studies focusing on the consumption of fermented milk products have been found in the literature. The data of World and Turkey on consumption of yoghurt, cheese and milk is available but data concerning about kefir consumption is

not available. Therefore, this study aimed to determine the attitudes and consumption levels of kefir and factors effecting the kefir consumption among Turkish adults.

Some demographic background variables, such as gender, age and education could have some influence on food choice behavior and functional foods acceptance.<sup>12,14</sup> In the study only 15.8 % of participants were consumed kefir and the consumption ratio is significantly high in females (20.2%) than in males (9.5%). Our results showed that age, gender and education period effects the consumption of kefir ( $p < 0.05$ ). According to binary logistic regression alone or with age, gender was effective in kefir consumption. Participants who were male [OR: 0.413 (0.232–0.736),  $p < .01$ ] were significantly less consume kefir. But participants who were high age and education (OR: 1.05(1.022-1.078),  $p < .001$ ; OR: 2.217(1.505-3.266),  $p < .001$ , respectively) were significantly high consume kefir. According to some authors, the most positive group towards functional foods is women and middle-aged or elderly consumers.<sup>15</sup> It is considered that due to health concerns, aging of the population, increased education of consumers could be the biggest factors influencing consumption of kefir.

Nutritional knowledge could also have a significant impact on consumers' perception and acceptance of functional foods. Lack of knowledge



about the benefits related to the consumption of functional foods could discourage the consumption of them.<sup>16</sup> It is important to remark that knowledge is not the only determinant of consumers' interest in functional foods.<sup>17,18</sup> and therefore several factors probably being interest in health and nutrition may outweigh the influence of nutritional knowledge. In the study the participants stated that they consumed kefir because of positive health impacts (96.5%). Majority of participants who do not consume kefir stated that they do not know what kefir is (71.0%) and difficult to reach or produced (19.0%). The use of health claims might be necessary in order to ensure that consumers are aware of the health benefits of the product and therefore consider substituting conventional foods by their functional alternatives like kefir.

In 2009, the annual per-capita consumption of dairy products in Turkey was found to be 173 kg and 24 kg of this amount was milk.<sup>19</sup> unfortunately there is no data about kefir consumption in the World and Turkey. In our study daily mean intake of kefir was found  $62 \pm 61.7$  ml. Consumption of dairy products in Turkey is low compared to most of European countries. The prospects for globally and for Turkey consumption of milk and other liquid dairy products tend towards an increase during the next few years. These patterns suggest great potential for increasing consumption of dairy products in Turkey relative to the potential in many other developed countries.<sup>20</sup>

In Turkey, kefir grains are available only from Faculty of Agriculture and also kefir beverage is made commercially. Because a few company produce kefir beverage and maybe the composition and sensory profiles are different from homemade kefir consumers tend to produce their own kefir traditionally (96.5%).

## Conclusion

The possible protective role of fermented dairy products such as kefir, is accepted as a potentially important probiotic product and has regained attention in the past decade. Increasing consumers' interest on healthy and safety food items for their health concern should be of growing importance to fermented food industrial processors and firms. In addition to positive health effects medi-

ated by microorganisms, kefir also can contribute substantially to individuals' daily calcium intake. As the milk consumption levels are low in Turkey compared with some European countries kefir consumption in the regular diet can be promoted. Because it is considered that the lack of knowledge about kefir may limit the consumption levels, to make awareness and to raise the intake of kefir marketing, advertising and educational campaigns involving public information provision and related activities would be useful. The use of health claims might be necessary in order to ensure that consumers are aware of the health benefits of the product and therefore consider substituting conventional foods by their functional alternatives.

## References

1. Guzel-Seydim ZB, Kök-Tas T, Greene AK, Seydim AC. Review: Functional properties of kefir. *Critical Reviews in Food Science and Nutrition* 2011; 51:261–8.
2. Liu JR, Lin CW. Production of kefir from soymilk with or without added glucose, lactose or sucrose. *J. Food Sci.* 2000; 65: 716–9.
3. Kabak B, Dobson ADW. An Introduction to the Traditional Fermented Foods and Beverages of Turkey. *Critical Reviews in Food Science and Nutrition* 2011; 51:248–260.
4. Lopitz-Otsoa F, Rementeria A, Elguezabal N, Garaizar J. Kefir: A symbiotic yeasts-bacteria community with alleged healthy capabilities. *Rev Iberoam Micol.* 2006; 23:67-74.
5. Irigoyen A, Arana I, Castiella M, Torre P, Ibáñez FC. Microbiological, physicochemical, and sensory characteristics of kefir during storage. *Food Chem.* 2005; 90: 613–620.
6. Otles S, Cagindi Ö. Kefir: A Probiotic Dairy-Composition, Nutritional and Therapeutic Aspects. *Pakistan Journal of Nutrition* 2003; 2 (2): 54-59.
7. Garrote GL, Abraham AG, De Antoni GL. Preservation of Kefir Grains, a Comparative Study. *Lebensm. Wiss.u.Technol.* 1997; 30, 77–84.
8. Kampman E, Goldbohm RA, van den Brandt PA, van 't Veer P. Fermented dairy products, calcium, and colorectal cancer in the Netherlands cohort study. *Cancer Research* 1999; 54: 3186-3190.
9. Terzi G. Kefirin bileşimi ve beslenme açısından önemi. *Veteriner Hekimler Derneği Dergisi* 2007; 78(1): 23-30. (article in Turkish)

10. Vinderola G, Perdigon G, Duarte J, Thangavel D, Farnworth E, Matar C. Effects of kefir fractions on innate immunity. *Immunobiol.* 2006; 211: 149–156.
11. Özden A. Diğer fermente süt ürünleri. *Güncel Gastroloji* 2008; 12(3): 169-181.
12. Tiryaki GY, Akbay C. Consumers' fluid milk consumption behaviours in Turkey: an application of multinomial logit model. *Oual Ouant.* 2010; 44: 87-98.
13. Generoso M, Wolf M, Dondi CA, Vecchio C, De Rosa M. Kefir: a border line probiotic between innovation and tradition, 3rd Probiotics and Prebiotics New Foods, 2005, Rome, Italy.
14. Ares G, Gambaro A. Influence of gender, age and motives underlying food choice on perceived healthiness and willingness to try functional foods. *Appetite* 2007; 49:148–158.
15. van Kleef E, van Trijp HCM, Luning P. Functional foods: Health claim-food product compatibility and the impact of health claim framing on consumer evaluation. *Appetite* 2005; 44, 299–308.
16. Gaston A, Gimenez A, Gambaro A. Influence of nutritional knowledge on perceived healthiness and willingness to try functional foods. *Appetite* 2008; 51: 663–668.
17. Rasanen M, Niinikoski H, Keskinen S, Helenius H, Talvia S, Ronnema T. Parental nutrition knowledge and nutrient intake in an atherosclerosis prevention project: the impact of child-targeted nutrition counselling. *Appetite* 2003; 41: 69–77.
18. Wardle J, Parmenter K, Waller J. Nutrition knowledge and food intake. *Appetite* 2000; 34:269–275.
19. [http://www.asuder.org.tr/sut\\_envanteri/sut\\_envanteri.pdf](http://www.asuder.org.tr/sut_envanteri/sut_envanteri.pdf)
20. [http://www.tetrapak.com/TR/about\\_tetra\\_pak/press\\_room/Haberler/Pages/10yildakureselsuttuketimi.aspx](http://www.tetrapak.com/TR/about_tetra_pak/press_room/Haberler/Pages/10yildakureselsuttuketimi.aspx) (accessed Sep 2011)

*Corresponding Author*

Saniye Bilici,  
Gazi University,  
Faculty of Health Sciences,  
Department of Nutrition and Dietetics,  
Besevler,  
Ankara,  
Turkey,  
E-mail: [sgbilici@gmail.com](mailto:sgbilici@gmail.com)

# Influence of inhaled Corticosteroids on growth in asthmatic children

Gordana Kostic<sup>1,7</sup>, Vesna Skodric-Trifunovic<sup>2,6</sup>, Branislav S. Gvozdenovic<sup>3</sup>, Marina Petrovic<sup>4,7</sup>, Nevenka Ilic<sup>5</sup>, Mihailo I. Stjepanovic<sup>2</sup>

<sup>1</sup> Clinic for Pediatrics, Clinical Hospital Center "Kragujevac", Serbia,

<sup>2</sup> Clinic for Pulmonology, Clinical Center of Serbia, Belgrade, Serbia,

<sup>3</sup> AbC.R.O Inc. Serbia, Belgrade, Serbia,

<sup>4</sup> Center for Pulmonary Diseases, Clinical Hospital Center „Kragujevac“, Kragujevac, Serbia,

<sup>5</sup> Institute for Public Health, Kragujevac, Serbia,

<sup>6</sup> Faculty of Medicine, University of Belgrade, Serbia,

<sup>7</sup> Faculty of Medicine, University of Kragujevac, Serbia.

## Abstract

Numerous studies evaluated the influence of inhaled corticosteroids (ICS) on growth and development of asthmatic children. The aim of this study was to estimate the growth in asthmatic children and to examine the influence of continuous administration of ICS within a period of one year on their growth and development in relation to age, gender and the level of asthma control. The study group consisted of 60 boys and 40 girls, aged 7 to 18 years, diagnosed with partly controlled (76 children) and uncontrolled allergic asthma (24 children). Most of children received a moderate ICS doses. Body height increased during the analyzed period, and the increase rate was different depending on the age group. The largest height increase in both genders was seen in patients 7-14 years old and it was statistically significant ( $p < 0.001$ ). In the age over 15 years, in both genders, there were no statistically significant differences in height after three months. Statistical significance existed between start point and the 12th month as well as between 3-12 months ( $p = 0.041$  and  $p = 0.031$ , respectively). Slower growth is explained with a short time difference, having in mind that children of that age are usually growing slower. There was no statistically significant difference in the increase of body height in relation to the level of asthma control. We concluded that prolonged use of the ICS in asthmatic children has a favorable effect on clinical course of disease, while at the same time does not have an adverse effect on children's growth.

**Key words:** children, inhaled corticosteroids, asthma

## Introduction

Asthma is the most frequent chronic disease in childhood with a tendency of further growth. Having in mind the possibility of developing the disease at an early age and its long-term course, a question arose if asthma as a chronic disease influences the growth and development of asthmatic children. Numerous studies evaluated this problem and found that asthmatic children do not experience a slowdown in growth in comparison to healthy children. However, it has been determined that many asthmatic children experience delayed puberty, especially children with uncontrolled asthma, which may lead to a slowdown in growth at a certain age, but not due to the disease itself (<sup>1</sup>).

Modern therapeutic concept requires constant treatment of the chronic persistent inflammation and prevention of acute exacerbations of asthma. Inhaled corticosteroids (ICS) are anti-inflammatory drugs that reduce the symptoms in both adults and children by calming the inflammation in respiratory tract, reducing secretion of mucus and bronchial hyperreactivity, at the same time renewing the integrity of respiratory tract. That is why in the past few these medicines have been considered the first-line therapy for controlling this frequent disease (<sup>2,3,4</sup>).

The aim of this study was to estimate the growth in asthmatic children and to examine the influence of continuous administration of ICS within a period of one year, on their further growth and development in relation to age, gender and the level of asthma control.

## Methods

The study included 100 patients aged 7 to 18 years, diagnosed with partly controlled and uncontrolled allergic asthma, who were treated in Pulmonary Ambulance in Pediatric Clinic of the Clinical Center in Kragujevac between September 2007 and May 2009. All patients received a continual therapy of ICS with the purpose of prevention of asthmatic attacks within one year, during which time certain parameters were monitored. Prevention was undertaken with the following ICS: Beclomethason-dipropionate (BDP), Fluticason propionate (FP) and Budesonide (BUD) in low (equivalent 100-200 mcg-FP), moderate (equivalent 250-500 mcg-FP) and high therapeutic doses (equivalent >500 mcg-FP), <sup>(2)</sup> depending on the level of asthma control. All subjects have taken ICS using a metered-dose inhaler through a spacer. They were adequately trained to use it and proper medicine administration was checked during each visit. The patients' body height was measured with an anthropometer with gun (Harpenden type), and body mass was measured with a digital decimal scale. The research was conducted at the beginning of the therapy, after three months and after 12 months of continuous ICS therapy. Body height of asthmatic children was compared to body height of healthy children using the charts of the National Center for Health Statistics (NCHS) <sup>(3)</sup>.

Medical history includes information about the beginning and the course of disease, therapy and place of residence (village or city). All subjects were classified according to gender: male (60 boys

and female (40 girls); according to age into groups: group I – 7-10 years, group II – 11-14 years, group III – 15-18 years; according to the level of asthma control: group A – patients with partially controlled asthma, group B – patients with uncontrolled asthma. All subjects underwent the estimation of the level of control according to GINA parameters <sup>(1)</sup>, and they received ICS therapy. Type of ICS was delivered according to means available at that moment and the dosage was determined according to the level of asthma control <sup>(1)</sup>.

Statistical analysis has been performed with standard computer statistical software package *SPSS 8.0 for Windows*. Quantitative variables were expressed as mean with a standard deviation (SD). The comparison between groups was performed with Student's *t* test and  $\chi^2$  test, while one or two factors analysis of variance was used for comparison of repeated measurements. A degree of correlation between certain parameters of groups was determined by means of Cramer's V test. Probability value  $p < 0.05$  was considered to be statistically significant and the value  $p < 0.01$  statistically highly significant.

## Results

The study group consisted of 60 (60%) boys and 40 (40%) girls (Table 1). At the beginning of the study uncontrolled asthma was diagnosed in 24 children and partly controlled asthma in 76 of them. There were no significant statistical differences in the number of children in relation to age ( $\chi^2=1.43$ ,  $p=0.489$ ), gender ( $\chi^2=0.04$ ,  $p=0.848$ ) and place of residence ( $\chi^2=2.69$ ,  $p=0.101$ ) between the

Table 1. Distribution of patients by age, gender and place of residence in regards to the level of asthma control

	Partly controlled asthma		Uncontrolled asthma		Total		$\chi^2$	df	p
	N	(%)	N	(%)	N	(%)			
Age									
I: 7-10	29	78,4	8	21,6	37	100,0	1.43	2	0.489
II: 11-14	36	78,3	10	21,7	46	100,0			
III: 15-18	11	64,7	6	35,3	17	100,0			
Gender									
Boys	46	76,7	14	23,3	60	100,0	0.04	1	0.848
Girls	30	75,0	10	25,0	40	100,0			
Place									
City	58	72,5	22	27,5	80	100,0	2.69	1	0.101
Village	18	90,0	2	10,0	20	100,0			

groups of asthmatic patients with partly controlled and uncontrolled asthma (Table 1).

Patients that have previously used ICS had a statistically significant lower probability to have an uncontrolled asthma (Cramer  $V=0.28$ ,  $p=0.006$ ). The vast majority of patients (74%) have already started ICS therapy before the study and those were usually the children with a more severe uncontrolled asthma (95.8%).

There was a difference in the time when disease was diagnosed ( $t=2.316$ ,  $p=0.023$ ) and the duration of the disease ( $t=-2.321$ ,  $p=0.022$ ) between children with uncontrolled and partly controlled

asthma. In children with uncontrolled asthma, the diseases started before (at the age of 21.96 months on average) and lasted longer (9.96 years) in comparison with children with partly controlled asthma (31.82 months and 8.26 years, respectively).

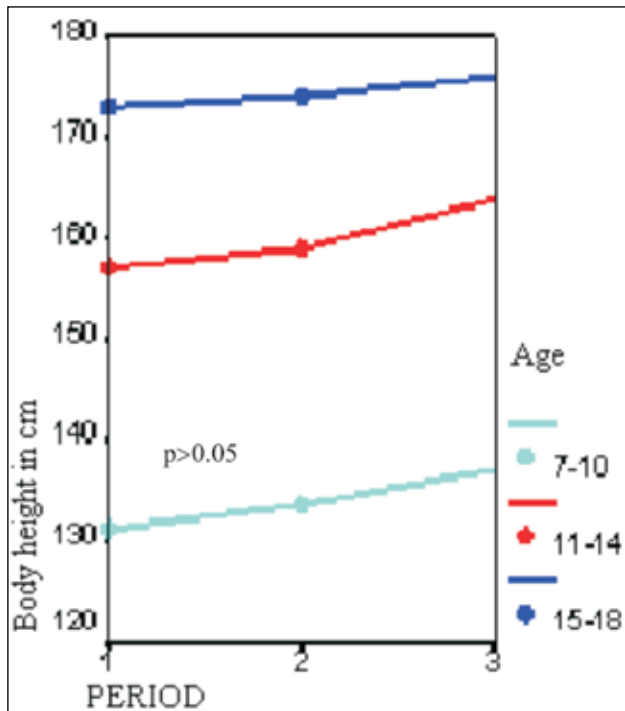
Body height and mass of asthmatic children by gender and age before therapy, after 3 months and after a year of continuous treatment with ICS are shown in Table 2.

We found that body height of asthmatic boys over time marks a statistically significant increase during the observed period, and the increase trend of body height is different in distinct age groups (Graph 1).

Table 2. Body height and mass by age and gender in asthmatic children within one year after the study start

Age	Gender		At the beginning of prevention		After 3 months		After 12 months	
			Height (cm)	Mass (kg)	Height (cm)	Mass (kg)	Height (cm)	Mass (kg)
Group I 7-10	M	N	22	22	22	22	22	22
		Mean	131.1	28.9	133.8	30.0	137.2	32.0
		SD	6.69	5.18	6.76	4.87	6.64	5.19
		minimum	121	20	123	23	125	24
		maximum	145	39	147	40	149	41
	F	N	15	15	15	15	15	15
		Mean	135.3	31.3	137.0	32.4	141.7	35.4
		SD	8.04	6.42	8.42	6.99	8.71	7.94
		minimum	118.0	22	119.0	24	122	25
		maximum	148	45	152	48	157	51
Group II 11-14	M	N	29	29	29	29	29	29
		Mean	157.2	44.5	159.0	46.3	163.9	50.1
		SD	8.60	10.09	8.97	10.39	9.11	10.15
		minimum	140	29	141	30	144	33
		maximum	175	70	177	72	180	76
	F	N	17	17	17	17	17	17
		Mean	151.7	41.8	152.6	42.6	158.2	45.6
		SD	9.33	10.12	9.01	10.54	8.15	10.24
		minimum	131	28	131	28	140	33
		maximum	168	66	168	70	171	63
Group III 15-18	M	N	9	9	9	9	9	9
		Mean	173.1	62.0	174.1	62.0	175.9	63.2
		SD	7.22	9.73	6.43	9.50	5.90	8.32
		minimum	164	48	164	48	164	53
		maximum	183	81	183	81	183	81
	F	N	8	8	8	8	8	8
		Mean	166.8	63.0	167.0	63.1	167.5	63.9
		SD	3.81	10.61	3.70	11.49	3.66	9.89
		minimum	164	48	164	48	164	51
		maximum	174	79	174	79	174	79

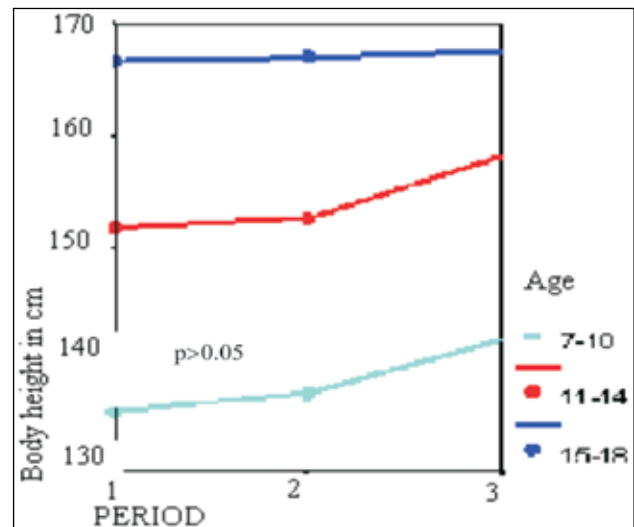
In age groups I and II the difference in height was statistically significant ( $p < 0.001$ ) between all periods, while group III (age 15 to 18) marked no statistically significant difference ( $t = -1.66, p = 0.135$ ) in height between the study start and after three months. Statistical significance existed in other measurement periods – between first and third measurement ( $t = -2.44, p = 0.041$ ) and between second and third measurement ( $t = -2.604, p = 0.031$ ).



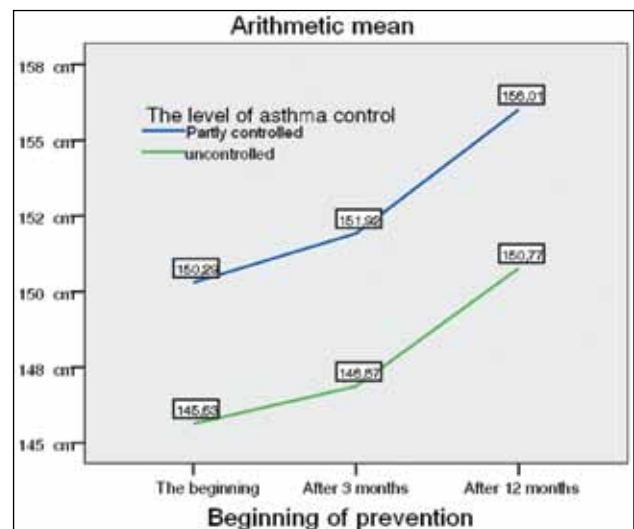
Graph 1. Body height of boys according to the age at the beginning, after three months and at the end of the study  
 Legend: PERIOD 1 = Beginning of the study, PERIOD 2 = After 3 months, PERIOD 3 = After 12 months

Body height in asthmatic girls demonstrated a statistically significant increase during the analyzed period, and the increase of body height is different in regards to the age groups which is shown in Graph 2. The difference in age groups I and II was statistically significant ( $p < 0.001$ ) in all measurement periods, while in group III there was no statistical statistically significant difference ( $t = -1.53, p = 0.170$ ) between height at the beginning and 3 months after the continuous ICS treatment. Statistically significant difference existed in other measurements – between the first and the third measurement ( $t = -3.00, p = 0.020$ ) and between the second and the third measurement ( $t = -2.65, p = 0.033$ ).

Graph 3 shows the average values of body height depending on the level of asthma control. The increasing lines on the graph are parallel due to the lack of interaction effect (time-level of asthma control), which means that the children have made equal progress in height. The distance between the lines is related with the mentioned difference in average height. Children with uncontrolled asthma were 4.98 centimeters shorter on average than children with partly controlled asthma. During the analyzed period there was no statistically significant difference in the increase of body height in relation to the level of asthma control.



Graph 2. Body height of girls according to the age at the beginning, after three months and at the end of the study  
 Legend: PERIOD 1 = Beginning of the study, PERIOD 2 = After 3 months, PERIOD 3 = After 12 months



Graph 3. Arithmetic mean of body height by the level of asthma control

## Discussion

Numerous studies have dealt with the influence of inhaled corticosteroids (ICS) on growth and development of asthmatic children (4,5). Conducted research confirms that a 4-year long continuous administration of ICS has proved safe for children aged over 5 years and diagnosed with persistent asthma (6). Several studies showed that application of ICS in small doses at the beginning of the treatment in the first few months can affect child's growth (7). There is also an explanation that with some asthmatic children reduced growth can be caused by delayed puberty. New studies that deal with ICS and growth of asthmatic children concluded that after the therapy is completed there is no difference in finally attained height between asthmatic patients that received ICS therapy and the ones that did not (8,9,10).

Before participating in the study, the largest percentage of patients (74%) that had already started ICS therapy were mostly children with a more severe case of uncontrolled asthma (95,8%) and a smaller percentage of children with partly controlled asthma. Clinically significant result of our study was the earlier development of uncontrolled asthma in children (aged 21.96 months on average) in comparison to a less severe, partly controlled asthma (31.82 months, in average) which is also found in the literature (11,12,13,14). In addition, children with more severe uncontrolled asthma had significantly longer course of disease (age of 9.96 vs. 8.26 years).

At the beginning of the study boys' body height in all age groups (7-18) was in accordance with the height of healthy children according to the NCSH (National Center for Health Statistics) charts. These results were in accordance with the results of population study that included 4.131 school children on the same territory (15).

During our study, all asthmatic children received ICS therapy in the period of one year and mostly in moderate doses, while in some cases high doses were prescribed for a certain period of time, and the results showed that body height of boys and girls increased during the analyzed period, while the increase of body height was different depending on the age group. The largest height velocity was marked in boys and girls in groups I and II (age 7-14) which is logical since the biggest

linear increase of the same group was also recorded in healthy population (13,15,16).

In the age over 15 years, in both genders, in the first three months of the ICS therapy, slower growth is explained with a short time difference, having in mind that children of that age are usually growing slower, especially girls, so this phenomenon can not be considered a side effect of ICS. Our results show that we haven't found a slowdown in growth in the first three months of the therapy, even though some studies describe the side effect of ICS in the first months of the therapy (7). Other studies have also come to the conclusion that these medications do not affect the finally attained adult height, although they may lead to a temporary slowdown in growth of children (7,8,17,18,19).

Our results showed that continuous application of ICS within one year did not lead to a slowdown in growth of asthmatic children of both genders and all ages, having in mind that the children marked a linear growth of 4.6 cm on average, which is also confirmed by other studies (19). In view of the level of asthma control, the results of this study show that the children with uncontrolled asthma have a significantly lower height on the beginning of the study than the children with partly controlled asthma. During the study in the period of one year with continuous application of ICS, the results show that the children grew equally fast (growth lines were completely parallel). Other studies also found the correlation between the level of asthma control and the height of the children (6), but they have also found that reduced growth and body mass was recorded with asthmatic children living in poor socio-economic conditions (20).

During a year-long monitoring of continuous application of ICS with children with partly controlled asthma and uncontrolled asthma, there was no significant difference in the growth velocity in relation to gender or level of asthma control. Application of ICS in asthmatic children has a favorable effect on clinical course of disease, while at the same time does not have an adverse effect on children's growth.

## Acknowledgment

This work was supported by the Ministry of Education and Science of Serbia, contact No.175046, 2011-2014

## References

1. *Global strategy for asthma management and prevention. National Institutes of Health: National Heart, Lung, and Blood Institute. Bethesda, MD: National Institutes of Health; 2002. Publication No. NIH-NHLI 02-3659 (updated 2009).*
2. Maksic H, Heljic S, Dizdarevic J, Misanovic V, Catibusic F, Dzinovic A. *The effects of antenatal corticosteroids on neonatal morbidity and mortality. HealthMed 2010; Vol. 4 (No. 3): 684-688*
3. Behmanesh F, Alamdaram A, Gangi Kheibari F. *Chest radiograph abnormalities in childhood asthma. HealthMed 2010; Vol.4 /No.4 (Suppl.1): 1100-1102*
4. Minic P, Sovtic A. *Endoscopic findings and flow-volume patterns in children with vocal cord dysfunction mimicking "Difficult to treat asthma". [Abstract P64] Abstracts from the 12th European Respiratory Society (ERS) Annual Congress, Stockholm, Sep 14-18 2002. Eur Respir J 2002; 20(38 Suppl):149S.*
5. De Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. *Development of a WHO growth reference for school-aged children and adolescents. Bull World Health Organ 2007; 85:660-667*
6. Balfour-Lynn L. *Effect of asthma on growth and puberty. Pediatrician 1987; 24:237-41.*
7. Moudiou T, Theophilatou D, Priftis K, Papadimitrou A. *Growth of asthmatic children before long-term treatment with inhaled corticosteroids. J Asthma 2003; 40(6): 667-71.*
8. Sheffer AL, Silverman M, Woolcock AJ, Diaz PV, Lindberg B, Lindmark M. *Long-term safety of once-daily budesonide in patients with early-onset mild persistent asthma: results of the Inhaled Steroid Treatment as Regular Therapy in Early Asthma (START) study. Ann Allergy Asthma Immunol 2005; 94:48-54.*
9. Wolthers OD, Heuck C. *Assessment of the relation between short and intermediate term growth in children with asthma treated with inhaled glucocorticoids. Allergy 2004; 59:1193-7.*
10. Pedersen S. *Clinical safety of inhaled corticosteroids for asthma in children: an update of long-term trials. Drug Saf 2006; 29 (7):599-612.*
11. Osman M, Tagiyeva N, Wassall HJ, Ninan TK, Devenny AM, McNeill G et al. *Changing trends in sex specific prevalence rates for childhood asthma, eczema, and hay fever. Pediatr Pulmonol 2007; 42: 60-65.*
12. Leone FT, Fish JE, Szeffler SJ, West SL. *Corticosteroid Use. Systematic review of the evidence regarding potential complications of inhaled corticosteroid use in asthma. Chest 2003; 124:2329-40.*
13. Grinfeld A, Just J. *Clinical characteristics of childhood asthma. Clin Exp Allergy 1998; 28(Suppl 5):67-70.*
14. Holt PG. *Key factors in Development of Asthma: Atopy. Am J Respir Crit Care Med 2000; 161:172-5.*
15. Zivanovic S. *Characteristics of child asthma. In: Bronchial asthma. Stankovic I, ed. Nis: School of Medicine, University of Nis, 2005:71-96.*
16. Cock C, Rofit DW, Swystun VA. *Asthma control versus asthma severity. J Allergy Clin Immunol 1996; 98:1016-8.*
17. Markovic S. *Clinical assessment of growth and development of the school children. Master thesis. School of Medicine, University of Belgrade, 2000.*
18. Tanner JM, Whittehouse RH. *Atlas of Childrens Growth Normal Variation and Growth Disorders. London: Academic Press, 1992.*
19. Allen DB, Bielory L, Derendorf H, Dluhy R, Colice GL. *Inhaled corticosteroids: Past lessons and future tissues. J Allergy Clin Immunol 2003; 112:51-40.*
20. Leone FT, Fish JE, Szeffler SJ, West SL. *Corticosteroid Use. Systematic review of the evidence regarding potential complications of inhaled corticosteroid use in asthma. Chest 2003; 124:2329-40.*
21. Arend E, Fischer G, Debiassi M, Schmid H. *Inhaled corticosteroid treatment and growth of asthmatic children seen at outpatient clinics. J Pediatr (Rio J) 2006; 82(3):197-203.*
22. McCowan C, Neville RG, Thomas GE, et al. *Effect of asthma and its treatment on growth: four year follow up of cohort of children from general practices in Tayside, Scotland. Br Med J 1998; 316(7132):668-72.*

Corresponding Author  
 Vesna Skodric Trifunovic,  
 Clinic for Pulmonology,  
 Clinical Center of Serbia,  
 Faculty of Medicine,  
 University of Belgrade,  
 Belgrade,  
 Serbia,  
 E-mail: vesna.skodric@kcs.ac.rs



# The influence of very low calorie diet on parameters of metabolic activity of bone

Olivera Rankov<sup>1</sup>, Branka Kovacev-Zavistic<sup>2</sup>, Edita Stokic<sup>2</sup>, Jovanka Novakovic Paro<sup>2</sup>, Tijana Icin<sup>2</sup>, Nemanja Kovacev<sup>3</sup>

<sup>1</sup> Clinic of gynecology and obstetrics, Clinical center of Vojvodina Novi Sad, Serbia,

<sup>2</sup> Clinic of endocrinology, diabetes and metabolic disease, Clinical center of Vojvodina Novi Sad, Serbia,

<sup>3</sup> Clinic of orthopedics and traumatology, Clinical center of Vojvodina Novi Sad, Serbia.

## Abstract

**Introduction:** Osteoporosis is a systemic skeletal disease characterized by low bone density and changes in microarchitecture of bone, that have resulted in an increased tendency to fractures. On the metabolic activity of bone affect the following factors related to nutritional status: increased body mass, gravity, and the fact that adipose tissue is "metabolic and endocrine organ," which secretes its hormones, mainly estrogen, leptin and adiponectin, that can affect bone metabolic activity.

**Objective:** was to show whether, and how, rapid weight loss influence on bone metabolism.

**Method:** The prospective study included 30 women in the generative period hospitalized for obesity treatment with very low calorie diet, which means taking 800 mg of calcium and 500 ij vitamin D daily. Influence of therapy on metabolic bone activity is estimated by analyzing the parameters of bone metabolic activity: osteocalcin, beta cross laps and PTH in serum was measured by "Elecsys" methodology, based on the sandwich immunometric reaction, at the beginning and end of therapy. In the same time, we determined levels of ionized calcium by measuring the potential difference (potentiometry) on an automated analyzer AVL. Nutritional status at the beginning and end of therapy was evaluated based on TM (kg) and BMI (kg / m<sup>2</sup>), waist circumference and BIA used to evaluate parameters: FAT% (percentage of body fat), FATM (amount of body fat mass in kg) and FFM (percentage of lean body weight in kg).

**Results:** After treatment there were reduction in body weight (p<0.0063), BMI (p<0.0082), waist circumference (p<0.274), percentage of fat mass (p<0.051), amount of fat mass (p<0.077), and amounts of fat free mass (p<0.075). There was a statistically significant difference in parameters of bone resorption at the end of treatment compared

to initial values - CrossLaps (p<0.005) and ionized calcium (p <0.009). Serum osteocalcin (p<0.667) and PTH (p<0.430) were not significantly changed during treatment.

**Conclusion:** The regime of very low calorie diet leads to increased bone resorption, with unchanged bone formation, resulting in increased serum calcium from bone tissue, probably caused short and reversible engagement of PTH.

**Key words:** bone metabolism, bone remodeling, very low calorie diet

## Introduction

Osteoporosis is a systemic skeletal disease characterized by reduction in bone density and changes in bone microarchitecture, that results in increased propensity to fractures. [1,2,3] According to the National Osteoporosis Foundation in 2004 in the United States has 10 million people with from osteoporosis and 34 million people who are predisposed to get osteoporosis. [4] The consequences of untreated osteoporosis are different location of fractures, usually distal radius, spine and hip, which can occur with a small trauma, pain, inability to perform common daily physical activities, dependence on others, depression, anxiety, isolation, and even increased mortality compared with persons of the same age. [3]

The main pathogenetic factors for osteoporosis are menopause in women and the aging process, but many other factors have influence on its contribute to its occurrence. According to the Grujic et al, 63,2% people older than 20 years wrongly assess their nutritional status [4]. One factor is certainly underweight, a BMI below 21kg/m<sup>2</sup> [6], till the obesity is a protective factor for osteoporosis [7] At the same time, obesity is a significant independent risk factor for cardiovascular disease,

diabetes and breast cancer, that it must be treated. The question is whether weight reduction causes changes in bone remodeling with domination bone resorption over formation, that lead an increased risk of osteoporosis. Some results show that 5-10% weight loss leads to a significant reduction in bone mass (8,9).

Several factors related to nutritional status may influence bone remodeling. First, it is gravity which influence on osteocyte's mechanoreceptors, the main stimulator of bone formation (7,8). On the other hand, fat as, "metabolic and endocrine organ," which secretes its hormones, mainly estrogen, leptin and adiponectin may affect the metabolic activity of bone.

### Objective

The aim of study is to investigate whether changes in body weight, BMI, percentage fat body mass, body fat mass and quantity of fat free mass achieved during low-calorie diet regime impact on bone metabolic activity and on bone formation and resorption parameters.

### Method

The a prospective study was done at the Clinic for Endocrinology, Diabetes and Metabolic Diseases at the Clinical Center of Vojvodina in the group of 30 patients in the generative period of life, aged 20-50 years hospitalized for treatment of obesity with BMI over 30 kg/m<sup>2</sup> during 30 days.

Very low calorie diet during which patients took dietary purchasable product four times a day instead of meal. The total daily intake of nutrients was: 22.4 g protein, 7.8 g. fat, linoleic acid 2.56 g, 60 g carbohydrates, 10.4 g lactose, 8 g dietary fiber, Vitamin A 1.12 mg, vitamin E 34.9 mg, 8.36 mg vitamin B1, vitamin B2 7.24 mg, Vitamin B6 6.98 mg, 6.9 mg vitamin B12, vitamin D3 500 IU, 0.5 mg of fluoride, 8.96 mg of pantothenic acid, folic acid 0.44 mg, 63.44 mg of nicotinamide, biotin 0.336 mg, Vitamin C 189.6 mg, Calcium 802 mg, Phosphorus 480 mg, Magnesium 315 mg, 1002.5 mg of potassium, sodium 592mg, chloride 848mg, iron 21.2 mg, Copper 1.62 mg, Manganese 2.74 mg, 0.05 mg of cobalt, molybdenum 0.1 mg, 96 mg Iodine, zinc 96 mg, 0.12 mg, 1232 mg

isoleucine, leucine 1904 mg, 1512 mg of lysine, tyrosine fenilalnina + 2128 mg + metinina 1400 mg cystine, threonine 940 mg, 300 mg of tryptophan, valine 1360 mg. Patients consumed every day and three to four liters of mineral water and a multivitamin.

Inclusion criteria was:

- females
- The age of 20-50 years
- Have regular menstrual cycles, there are no signs of cardiovascular disease, liver, kidney, CNS, or other endocrine or metabolic disorders (except for hyperlipoproteinemia)
- Have no medication therapy which can have influence on the metabolism of carbohydrates and fats (oral contraceptives, hormone replacement therapy, antihypertensive drugs and other medications)

Non-inclusion cruteria:

- Women with any of the above diseases
- Women who are on medical therapy that can have influence on the metabolism of carbohydrates and fats

Exclusion criteria:

- Fealure to cooperate (non-compliance with prescribed therapy)
- The development of the disease or condition during the tests that could affect the health of patients

In the study were included women who were agree to engage in research with the prior introduction to the work plan, methods and research goals.

Before initiation of therapy and after therapy were measured anthropometric parameters: body mass (TM), body mass index (BMI) and body composition parameters: the percentage of fat body mass (fat%), the amount of fat body mass (FATM) and the amount of lean body mass (FFM). Body composition was determined using BIA (bioelectrical impedance) device Tanita.

First and 30 days of treatment were measured biochemical bone metabolic parameters: osteocalcin (OCL), Cross-Laps (CL) and parathormone (PTH) in serum using "Elecsys" methodology, based on the sandwich imunometric reaction in the ionized calcium (Ca) measured on the basis of potential

difference (potentiometry) on an automated analyzer laboratory equipment manufacturers of AVL.

Data are presented in tables and graphs, and statistical analysis was performed using ANOVA methods, discrimination method, which assessed the statistical significance of observed changes in the numerical characteristics after treatment compared to the values before treatment patients. The significance of differences between measurements subjects before and after treatment was measured by Mannova's method.

**Results**

The study involved 30 women generative period of life between the ages of 20 and 50 years who were treated with very low calorie diet during 30 days.

The results of anthropometric parameters before and after treatment are shown in Table 1

*Table 1. Changes in anthropometric parameters Thought investigation*

Parameters	Therapy	x	SD	p
TM (kg)	Before	111.54	18.99	-
	After	102.17	19.38	0.063
BMI (kg/m <sup>2</sup> )	Before	40.45	7.74	-
	After	36.93	7.63	0.082

Body weight decreased after treatment for an average of 9.37 kg (8.4%) compared to values before treatment.

The average value of the average reduction in BMI of 3.52 kg / m<sup>2</sup> (8.7%), which is border of significance.

After statistical processing of data can be seen that the reduction in body weight and BMI at the end of treatment was statistically significantly increased risk compared with the initial values.

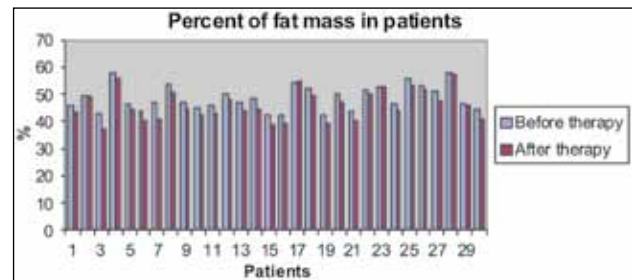
*Table 2. Changes in body composition parameters of thought investigation*

Parameters	Therapy	x	SD	p
FATM % (%)	Before	48.48	4.61	-
	After	45.86	5.54	0.051
FAT (kg)	Before	54.63	14.26	-
	After	47.88	14.77	0.077
FFM (kg)	Before	57.28	5.72	-
	After	54.64	5.54	0.075

Of the total 30 patients, in 29 (97%) was observed FATM% reduction. The average value FATM% statistically significant decrease, in the 2.62 kg (5.4%) compared to initial values.

Also, it was statistically insignificant reduction FATM average of 6.75 kg (12.36%)

The average value of the FFM statistically insignificant decrease of 2.64 (4.75%) compared with initial values.



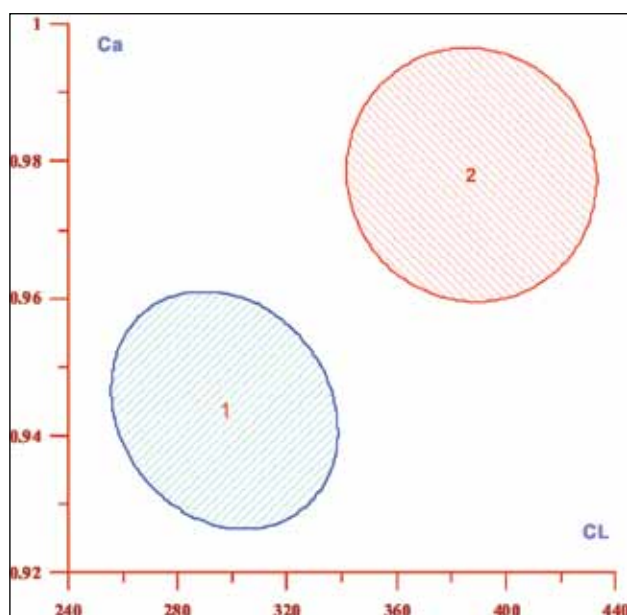
*Graph 1. Percentage fat body mass in women*

Of the 30 respondents in 29 (97%) there was a decrease in the percentage of fat body mass

*Table 3. Changes in parameters of bone metabolism thought investigation*

Parameters	Therapy	x	SD	p
OCL (ng/ml)	Before	17.85	6.50	-
	After	17.14	6.21	0.667
CL (pg/ml)	Before	297.11	112.58	-
	After	387.29	124.31	0.005
PTH (pg/ml)	Before	46.28	17.21	-
	After	49.86	17.64	0.430
Ionized Ca (mmol/l)	Before	0.94	0.05	-
	After	0.98	0.05	0.009

During the research it has been found insignificant reduction in OCL (p < 0.667) and PTH nonsignificant increase (p < 0.430). Values of Cross-laps and ionized calcium were statistically significantly increased (p less than 0.005 and p less than 0.009)



Graph 2. Confidence interval for Cross-Laps and ionized calcium

Legend: before treatment (1), after treatment (2), Cross-Laps (CL), ionized calcium (Ca)

## Discussion

Obesity is an independent risk factor for mass non-communicable diseases such as cardiovascular disease, diabetes and breast cancer. Therefore, the treatment of obesity is considered prevention of these diseases. On the other hand, obesity is considered a protective factor for osteoporosis in postmenopausal women, so the question is whether the treatment of obesity increases the risk of osteoporosis through the imbalance in remodeling of bone, with predominant bone resorption.

It is known that the key risk factor for osteoporosis in menopause. Estrogen deficit accelerated bone resorption, influence on the proinflammatory cytokines TNF-alpha family including RANKL responsible for osteoclastogenesis [10,11] In order to avoid the impact of estrogen deficiency on bone metabolism during treatment of obesity, the examination included a group of 30 women in generative period of life.

The authors in their papers show that during the reduction of body weight by 5-10% there is a significant decrease in bone mass [12] and acceleration of bone resorption. [9,13,14] The risk of bone loss during a diet depends on the initial weight loss, weight loss, age, gender, physical activity and intake of calcium and vitamin D during low-calorie

diet [15] In our study has shown that low-calorie diet with a calcium intake of 800 mg and vitamin D 500 IU leads to a statistically significantly elevated values of Cross Laps-bone resorption parameters, and the initial increase low ionized calcium values, until the value of a parameter of bone formation, osteocalcin, did not change. This finding suggests that the changes in the remodeling of our patients more responsible than applied dietetic regimen reduce the force of gravity and weight. In fact, no one knows the precise mechanism of action of mechanical loads on the bone, but it is assumed that the mechanical stimulus acts on a data network osteocytes, which registers changes in the level of mechanical force and converts them into appropriate signals, which then regulate the metabolic activity of bone. [16,17] There are assumptions that create osteocyt's signal proportional to the mechanical load. It supports premise that women with higher levels of physical and nutritional status have a greater amount of bone mass. Through weight loss women will reduce mechanical stress, and consequently reduce stimulation of bone formation which lead losses of bone mass. Some authors assume that the rate of bone loss after weight loss result of stress on the bones was due to reduced loads on the bone. [18] The absence of reduction in bone formation in our work can be attributed: 1) insufficient degree of reduction of body weight achieved a treatment, 2) the follow-up period of 30 days is too short for a definitive assessment of effects on osteoblasts and whose life and the ultimate effect on bone formation takes several months.

That a daily intake of calcium and vitamin D probably as well as their intestinal absorption is important for the effect of weight loss on bone metabolism and bone mass showed numerous authors. Parameters of bone metabolism during weight reduction are significantly greater in women who did not receive therapy during Ca supplementation, compared with the group that received 1.7 g Ca daily. [19,20] Ricci et al noted that during starvation there was a statistically significant increase of bone resorption parameters (deoxypyridinolin and piridinolin) and increasing the value of statistical nonsignificant PTH and osteocalcin, as shown in our work. [14] The initial low values of ionized with insufficient calcium intake of 800 mg daily intake during the regime of low-calorie

diet, may lead to short-term engagement PTH in terms of increased tubular reabsorption of calcium and/or to increased mobilization of calcium from bone by stimulating osteoclasts and depots as evidenced by statistically significant increase in Cross Laps. Otherwise, the low level of calcium is not surprising. In the NHANES III study was observed that as much as 50% of female generative period in the United States takes less than 600 mg of calcium per day and has low levels of calcium in the blood. [21]

However, it is known that fat is "metabolic and endocrine" organ in which, among other things, produce or secrete hormones such as estrogen, leptin, and adiponectin. It is known that obese people have a much greater amount and percentage of body fat mass. Adipocytes secrete leptin, a hormone which are currently not well understood mechanism is operating in the center of hunger and satiety in the hypothalamus and is one of the key regulators of nutritional status. The concentration of leptin is significantly different among individuals and correlates with the degree of nutritional status. It is known that leptin levels positively correlated with fat% [22,23,24]. It is possible that the anabolic effect of leptin on bone influences the positive correlation between bone mass and FATM. Obese people have significantly higher concentrations of leptin than normal weight individuals. [22,23,24] By reducing the level of nutrition and reduces the concentration of leptin in the blood. In the literature it has been observed statistically significant decrease in leptin concentrations during the weight reduction. [22] Although not yet know the exact mechanism of action of leptin on bone, previous research suggests that leptin affects the differentiation of osteoblasts, and that there is no direct effect on osteoclasts. [25] It is thought that leptin has a dual role in bone metabolism: central, it inhibits bone formation through effects on the hypothalamus, while its peripheral role increases the creation of OPG (Osteoprotegerin) in osteoblasts. OPG secreted by osteoblasts can bind to RANKL and inhibit action RANK-a, and thus inhibit the osteoclasts differentiation. Peripheral role of Leptin si to increases the level of OPG, a higher concentration of leptin and higher mean concentrations of OPG, which significantly reduces the degree of bone resorption. In our work,

as in the literature [25,26] observed a statistically significant decrease in FFM than FATM modified through starvation which would reduce the level of leptin was partly responsible for the decreased levels of inhibition of bone resorption parameters contributing to the growth of absorption Cross Laps at the end of treatment.

Regardless of the apparently "communication" between the metabolism of fat and bone tissue, one of the offered solutions for the prevention of increased bone resorption that occurs during the implementation low calorie diet in our patients is an additional supplementation of calcium and possibly vitamin D. For this intervention is advocated by other authors. Riedt et al. in their work recognized that in patients taking 1.7 g of calcium per day has been reduced or trochanter BMD or BMC, and spine, as opposed to women who consumed 1 g per day of Ca, where the observed significant reduction in BMD (4%) and BMC (5%) from baseline values. [20] It is also the patients who did not receive further observed a significant increase in Ca parameters of bone resorption, and PTH than in the group that received supplementation of Ca. It was observed that the women that are in addition to 800 mg Ca (who consumed diet) consumed 1 g Ca even further, there were no changes in the amount of bone mass, in contrast to other groups of women who did not receive supplementation of Ca where there has been a significant decrease of bone mass. [27] The group to which Ca was added and reduction was observed during PTH treatment, which explains the fact that a sufficient quantity of either entering Ca prevented increase PTH and consequently prevented bone resorption. Several authors suggest that the Ca intake of 1.6 grams per day for the restrictive child stabilized PTH levels and prevent bone resorption. Moreover, it appears that increased Ca intake may increase bone mass by 1.7% despite the reduction of weight. [27].

### Conclusion

During 30 days of low calorie diet treatment there was reduction in body weight, BMI, percent body fat mass, fat body mass quantities and amounts of lean mass. Differences in body mass, fat percentage and amount of body mass and BMI are borderline statistical significance.

Low calorie diet regimen administered in the manner as shown in our trial, leading to increased bone resorption, with unchanged bone formation, resulting in an increase initially low ionized calcium, possibly caused transient and reversible engagement at the level of PTH renal tubule and osteoclast activity.

Since there is a negative correlation between the decrease in body weight and bone resorption, and given the absence of changes in bone formation, the obtained results it follows that the dominant influence bone metabolism of calcium and possibly vitamin D during the regime of low calorie diet, rather than changes in the state nutritional status.

Additional supplementation of calcium and possibly vitamin D during the low calorie diet, it is possible to order to prevent stimulation of bone resorption and restore balance with bone formation.

In further studies would be necessary for more monitoring of parameters of bone remodeling during and after low calorie diet regime as well as after completion of treatment of obesity. We should take into account changes in other parameters such as leptin, adiponectin and vitamin D as well as changes in bone mass.

## References

1. Kasper D.L, Fauci A.S, Longo D.L, et al Harrison's Principles of Internal Medicine 16 th Edition, McGraw-Hill, Inc 2005, 2268-2278
2. C.Christiansen. Skeletal osteoporosis, J Bone Miner Res, 1993; 8 (S2): 475-80
3. National Foundation of osteoporosis, 2004
4. Grujic V, Dragnic N, Ukropina S, Niciforovic Surkovic O, Cankovic D: Self perception of being overweight in Serbia adults. 2011 Health MED 5(2): 372-382
5. Kanis JA, McCloskey EV, Johansson H: Development and use of FRAX in osteoporosis. Osteoporos Int 2010, 21Suppl.2: S407-S413
6. Kovacev B. Prepoznavanje faktora od znacaja za prevenciju i lecenje osteoporozе. Doktorska disertacija, Medicinski fakultet Novi Sad, odbranjena 1992
7. L.J. Zhao, H. Jiang, C.J. Pappasial et al. Correlation of obesity and osteoporosis: Effects of fat mass on the determination of osteoporosis, J Bone Miner Res 2008; 23(1): 17-29
8. J.J.W.A.Van Loon, D.J. Bervoets, E.H. Burger et al. Decreased mineralization and increased calcium release in isolated fetal mouse long bones under near weightlessness. J Bone Miner Res 1995; 10(4): 550-7
9. Ofeilschifter J.,Koditz R.,Pfol M.,Schatz H.: Changes in proinflammatory cytokine activity after menopause. Endocrine Reviews 2002, 23(1):90-119
10. Nordin BEC,Wishart JM,Clifton PM: A longitudinal study of bone-related biochemical changes at the menopause. Clin Endocrinol 2004;61:123-130
11. Kovacev B., Ivkovic Lazar T.,Babic Lj., Todorovic-Dilas Lj-, Lepšanovic L.: Bone changes in extremely obese patients in the course of body weight reduction. International Symposium on Osteoporosis,Kuopio,Finland,1988: Abstract book, 24
12. E.H. Burger, J Klein-Nulend and J.P. Veldhuijzen: Mechanical stress and osteogenesis in vitro. J Bone Miner Res 1992; 7 (S 2): S397- 401
13. Ricci T.A, Heymsfield S.B, Pierson JR R.N,et al. Moderate energy restriction increases bone resorption in obese postmenopausal women. J Clin Clin Nutr 2001;73: 347-52
14. S.Shapses, C.S.Riedt: Bone, body weight, and weight reduction: What are the concerns?. The J of Nutrition 2006; 136: 1453-6
15. Nguyen DN, Center JR, Eisman JA et al: Bone loss, weight loss and weight fluctuation predict mortality risk in elderly men and women. J Bone Miner Res 2007; 22(8): 1147-54
16. Reid IR, Comish J. Direct action of leptin on bone remodeling. Calcif Tissue Int 2004; 74(4): 313-6
17. Shu T, Gerard K. Central control of bone formation. J Bone Miner Metabol 2001; 19(3): 195-8
18. Tim L, Radak RD. Caloric restriction and calcium's effect on bone metabolism and body composition in overweight and obese premenopausal women 2004; 62(12):468-81
19. C.S. Riedt, M. Cifuentes, T.Stahl et al: Overweight postmenopausal women lose bone with moderate weight reduction and 1 gr/day calcium intake. J Bone Miner Res 2005; 20 (3):
20. A.C.Looker, E.S.Orwoll, C.C.Johnson JR et al. Prevalence of low femoral bone density in older US adults from NHANES III. J Bone Miner Res 1997; 12(11):1761-8

21. *Mecevska-Jovcevska J, Subeska-Stratrova S, Gjorgovski I et al. Bone turnover markers relations to postmenopausal osteoporosis J Med Biochem 2009; 28(3): 161-5*
22. *Samra R.A, Baba N.H, Torbay N, et al. High plasma leptin is not associated with higher bone mineral density in insulin-resistant premenopausal obese women. J Clin Endocrinol and Metabolism 2005; 90(5):2588-2594*
23. *Sato M, Takeda N, Sarui H, Takami R, et al. Association between serum leptin concentrations and bone mineral densita, and biochemical markers of bone turnover in adult men. J Clin Endocrinol and Metabolism, 2001; 86(11): 5273-5276*
24. *Ducy P, Amling M, Takeda S et al. Leptin inhibits bone forming through a hypothalamic relay: a central control of bone mass. Cell 2000; 100 (2):197-207*
25. *L.B.Jensen, F.Quaade and O.H.Sorensen. Bone loss accompanying voluntary weight loss in obese humans. J Bone Miner Res 1994; 9(4):459-63*
26. *Dawson-Hughes B,Harris SS,Krall EA et al. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. NEJM 1997; 337(10): 670-6*

*Corresponding Author*

*Olivera Rankov,*

*Clinic of gynecology and obstetrics,*

*Clinical center of Vojvodina Novi Sad,*

*Serbia,*

*E-mail: O\_rankov@yahoo.com*

# Postural status and self-perception profile of children

*Suncica Pocek, Visnja Djordjic, Tatjana Tubic*

Faculty of Sport and Physical Education, Novi Sad, Serbia

## Abstract

Proper postural status includes proper functioning, growth and development of a child's organism and it is most evident in physical appearance. At the same time, physical appearance affects self-perception of children and adolescents to a great extent. Given that the results of previous researches are inconsistent, the purpose of this study was to examine the self-perception profiles of children with and without postural deviations. The sample of subjects consisted of 111 pupils who attended the first grade of a primary school and were divided in two groups: children with certain deviations in postural status and children with normal postural status. A clinical method was applied for the assessment of postural status, while for the assessment of children's domain-specific perceptions and global self-worth the Self-Perception Profile for Children (Harter, 1985) was used. The obtained results show that the children with and without postural deviations are not significantly different, neither in domain-specific self-perceptions, nor in global self-worth. Besides, self-perceptions in specific domains represent a significant set of predictors of global self-worth of children with and without postural deviations. Physical appearance and athletic competence have the highest effect on global self-worth of children with postural deviations, while physical appearance and behaviour conduct represent the strongest predictors of global self-worth of children with normal posture.

**Key words:** postural status, children, global-self worth, domain-specific self-perception

## Introduction

Proper postural status includes proper alignment of all body segments, which is a precondition of their proper functioning. The most significant role in establishing and maintaining of proper postu-

ral status belongs to muscles, as an active part of a locomotor system. Muscular effort is smaller if a vertical line drawn from the mutual centre of all segments loading the particular joint, goes near the centre of that joint [1]. The weakness of certain groups of muscles and their asymmetric overloading can cause different deviations of the spine, thorax, upper or lower limbs and feet. Deviations in the ideal postural status cause an increased pressure on tissues, muscles and joints, causing headache, pain in the neck and back. If the first symptoms are neglected functional changes can progress to the structural level of deformity. The period of starting school and a few years after that are very sensitive regarding the increase of postural deviations. Growth spurt, hypokinesia, asymmetric and static load, carrying school bag, etc., can add to the occurrence of a poor posture [2]. Maturing of sensory and motor systems in function of postural stability usually ends between the age of 7 and 10 [3]. Changes and deviations which occur in this period have negative implications in adolescence and adulthood, not only in terms of physical appearance and health, but also the whole personality [4,5,6].

The quality of life of individuals with postural deviations can be observed through three main domains: physical, psychological and social functioning. Besides negative influence on health, spine deviations are also reported to have negative influence on psychosocial functioning of adolescents, varying from the development of anxiety and depression, suicidal thoughts and negative self-perception of physical appearance, to poor communication with peers [6, 7]. The results of epidemiological studies suggest that the young with a physical disability have a greater risk of maladaptation to psychosocial difficulties. The phase of initial diagnosis represents a traumatic experience, not only for adolescents, but also for their families; it is usually accompanied by the feelings of anxiety, fear, retreating, isolation and denying [8, 9, 10].



Owing to cognitive maturing and social experiences, the number and contents of the self-perception domains increase from the early childhood till adolescence and adulthood [11]. All individuals have their own hierarchy of self-worth, based on discrepancies and congruities in the self-perception of their own competences in a specific domain and importance which an individual attributes to being successful in that domain. Children develop their self-worth according to different sources of information. Generally, children greatly rely on the outside sources of information about their competence (predominantly parents, coaches, teachers), while in the early adolescence there is a shift towards the preference of inner sources of information, such as accomplishment of inner goals and standards of achievement [11, 12, 13].

Besides the perceived competence in significant domains, another significant determinant of global self-worth is social support. Similarly to the self-perception of competence, where special attention is paid to the domains which are important for particular person, there are also proofs that a support from the sources which are considered to be important has a greater importance in the prediction of self-worth [14, 15]. Examinations of the connection of specific domains and global self-worth of children consistently show that the physical appearance is the most reliable predictor of global self-worth, not only in relation to the age [16, 17], but also the sex [17, 18, 19, 20, 21]. Besides physical appearance, boys find athletic competence equally important [22, 23, 24, 25] to scholastic competence, while the girls pay special importance to the behavioral conduct [17].

Previous researches indicate several factors important for understanding the relations between self-worth and postural deviations of children and adolescents. Thus, the later the diagnosis is determined, the stronger negative influence on self-concept and quality of life is [26, 27, 28, 29, 30]. DeLoach & Greer [31] point out that the children born with disability (spina bifida) have a greater possibility of developing a positive self-image, in comparison to their peers who acquired a disability later in their lives (spinal cord injury), because the children with congenital deformities find physical differences normal. Taking into account that physical appearance is a strong predictor of self-worth, the higher the level of disability is, the lower self-

worth is [32, 33]. When it comes to differences between two sexes, the results are rather inconsistent. Negative body image is typical for all adolescents with scoliosis, but girls show more concern about their altered postural status and physical appearance [34], while the research done by Payne et al. [7] shows that the boys with scoliosis express greater concern about their physical appearance and development in comparison to girls. Besides the above mentioned factors, the support of close friends and family strongly influences self-worth as well [31]. Kahanovitz and Weiser [35] pointed out that the attitude of a mother towards the diagnosis of their children has implications on the attitude of the children themselves, a higher level of children's self-esteem and a lower level of the symptoms of anger, depression, tiredness and confusion is related to the mother's positive perceptions. Long-term effects of adolescent idiopathic scoliosis on psychosocial functioning manifest in the initial phase through anxiety, fear and timidity, while the presence of these symptoms later depends on the therapy applied, with permanently affected self-perception of physical appearance, lower self-confidence, life dissatisfaction, weaker self-concept and global self-worth [5, 33, 34, 36, 37, 38].

### **The aim of the study**

Proper postural status implies proper functioning, growth and development of a child's organism and it is most evident in physical appearance. Taking into account that physical appearance greatly affects global self-worth of children to a great extent, there is a question whether there are differences in domain-specific and global self-worth between the children with and without postural deviations, and which domain-specific perceptions significantly add to global self-worth of both groups of children. In this respect, the aim of this study was to analyze the self-perception profiles of children with and without postural deviations.

### **Method**

#### **Subjects**

The sample consisted of 111 pupils who attended the first grade of primary school and lived in urban surroundings (63 boys and 48 girls). Within

the total sample, 28 subjects (14 boys and 14 girls) had certain deviations of postural status, while 83 of them (49 boys and 34 girls) had no deviations of postural status.

### ***Measuring instruments***

*Postural status.* The group of subjects with certain postural deviations consisted of the children with postural deviations of functional stadium, noticed by a pediatrician during a medical check-up. The other group consisted of the children who had no diagnosis of deviations in postural status.

*Self-perception profile.* The chosen measuring instrument supports a multidimensional approach to self-concept [39]. Unlike one-dimensional and hierarchical models, it takes into account judgments in a number of specific domains and it treats global self-worth as a separate dimension. The applied measuring instrument, Self-Perception Profile for Children [39], contains 36 items, divided into six subscales:

*Scholastic Competence* – refers to children's perceptions of their competence or ability in school surroundings;

*Social Acceptance* – refers to the degree to which children have friends, feel they are popular and feel that most kids like them;

*Athletic Competence* – refers to the degree to which children are satisfied with their motor abilities and competence in sports;

*Physical Appearance* – refers to the degree to which the children are happy with the way they look;

*Behavioral Conduct* - refers to the degree to which children like the way they behave;

*Global Self-Worth* – refers to the extent to which the children like themselves as persons and their lives as a whole.

Each subscale consists of six statements (items) and they are formulated as complex, bipolar sentences; one part of a sentence describes a competent behaviour of a child, and the other one describes less competent (e.g. *Some kids find it hard to make friends*, but *Other kids find it pretty easy to make friends*). Children should determine whether the first or the second part of the sentence describes them better; then they should decide whether that description refers to them completely or just

partially. The answer which fits is marked by X. The score on every subscale represents the arithmetic mean of the responses given to each item scored on a four-level scale, where 1 means the lowest competence in the observed domain, and 4 is the highest. The instrument shows satisfactory metric characteristics, with the Cronbach's Alpha Reliability Coefficients ranging from 0.74 to 0.83 for certain subscales.

### ***Procedure***

The data was collected in June 2011. The testing was done during the classroom lessons and it takes 40 minutes on average. After explaining the way how to fill in the scale, the examiner reads out every item loud, which made the testing easier for children. The children were allowed to ask the examiner if they found any sentence unclear. Out of 115 examined children, four of them filled in the scale incorrectly and those scales were excluded from further data processing.

### ***Data processing***

The statistical package SPSS 15 was used after the data entry to calculate basic parameters of descriptive statistics. The analysis of differences in self-worth of children, depending on their postural status, was done by applying the t-test. Multiple Regression Analysis was used to determine which specific domains influence global self-worth of the children with and without postural deviations.

### ***Results***

The results of testing the differences in self-perceptions between the children with and without postural deviations are shown in the Table 1.

According to the results shown in the Table 1, it can be stated that there are no statistically significant differences in any of the variables of self-worth between the children with and without postural deviations.

The Table 2 shows the results obtained by using the Multiple Regression Analysis.

According to the results shown in the Table 2, it can be concluded that in both groups of children there is a statistically significant influence of domain-specific perceptions on Global Self-Worth. The

Table 1. The differences in domain-specific self-perceptions and global worth between children with and without postural deviations

Variables	Children with postural deviations		Children without postural deviations		t	p
	Mean	SD	Mean	SD		
Scholastic Competence	2.95	0.43	3.00	0.42	-0.62	0.54
Social Competence	3.24	0.58	3.22	0.51	0.14	0.89
Athletic Competence	2.99	0.54	2.94	0.48	0.43	0.67
Physical Appearance	3.41	0.69	3.44	0.60	-0.25	0.81
Behavioral Conduct	3.38	0.62	3.34	0.66	0.25	0.80
Global Self-Worth	3.38	0.59	3.56	0.44	-1.53	0.13

Table 2. The influence of domain-specific perceptions on Global Self-Worth of children with and without postural deviations

Variables	Children with postural deviations		Children without postural deviations	
	Beta	p	Beta	p
Scholastic Competence	0.08	0.70	0.06	0.52
Social Competence	-0.19	0.39	0.06	0.55
Athletic Competence	0.43	<b>0.02</b>	0.06	0.57
Physical Appearance	0.62	<b>0.00</b>	0.38	<b>0.00</b>
Behavioral Conduct	0.11	0.57	0.34	<b>0.00</b>
	R = 0.79 R <sup>2</sup> = 0.63 P = 0.00		R = 0.70 R <sup>2</sup> = 0.49 P = 0.00	

observed predictors explain 63% of total variance for the children with postural deviations, while the percentage of the explained variance for the children with normal posture is somewhat lower (49%). Physical Appearance and Athletic Competence strongly influence Global Self-Worth of the children with postural deviations, while in the case of the children without deviations a significant influence on Global Self-Worth have Physical Appearance and Behavioral Conduct variables.

## Discussion

Bearing in mind the importance of physical appearance self-perception in global self-worth of children and adolescents, this paper analyses the relations of postural status and self-worth of the first-grade pupils. Having the obtained results in mind (Table 1), it has been concluded that the differences in the domain-specific and global self-worth between the children with and without postural deviations, are not statistically significant. The results of previous researches are inconsistent; our results are in accordance with the recent

researches which have offered no proofs for the existence of differences in global self-worth of children and adolescents in relation to their postural status [31, 36, 39]. However, there is a high number of researches which show the differences in global self-worth of children and adolescents with and without postural deviations [5, 7, 33, 37, 38]. The obtained differences in global self-worth between these two groups of children can be explained by the fact that the Physical appearance is consistently the strongest predictor of global self-worth, not only for the children with normal postural status [16, 17, 18, 19, 21, 41, 42] but also for the children with postural deviations [5, 6, 7, 32, 33]. Depending on the therapy applied, the accompanying psychosocial difficulties can be alleviated, but long-term consequences of affected physical appearance remain, especially when it comes to the self-concept [5, 6, 7, 36].

Absence of differences in global and specific self-worth of children with and without postural deviations in our study can be explained, first of all, by the age of the subjects. Namely, deviations in postural status in the sample we examined belong

to a functional type. They are not marked enough to endanger physical appearance to a great extent, and consequently affect self-worth in specific domains and global self-worth. If postural deviations, which occur in this period, progress to a structural level, which most often co-occurs with the period of adolescence, that can cause the decrease of self-concept and loss of self-confidence, which is directly proportional to the level of postural deformity [38].

The analysis of the influence of domain-specific perceptions on global self-worth showed that the observed system of predictors is statistically significant at the level of 0.01, with Physical Appearance being consistently the strongest predictor of Global Self-Worth (Table 2). These results are consistent with the previous researches [5, 6, 7, 16, 17, 18, 19, 20, 21, 32, 33, 40, 41]. The Athletic Competence is a significant predictor of Global Self-Worth in the children with postural deviations ( $\beta=0.43$ ,  $p=0.02$ ). It is possible that due to weaker or disproportionally (non-symmetrically) developed musculature, which is typical of the functional stadium of postural status deformity, these children have weaker motor control and notice that their functioning in this domain differs from the one of their peers. The children who have postural deviations may have a lower level of physical activity in comparison to their peers, which affects on their athletic competence and self-perceptions in this domain. Besides Physical Appearance, the Behavioral Conduct ( $\beta=0.34$ ,  $p=0.00$ ) has a significant influence on Global Self-Worth of the children with normal posture, too.

When discussing the results obtained, it is necessary to take into account a certain limitations originating from the criterion for dividing the children in groups, the size of the sample, as well as the instrument used for assessment of children self-perception profile. The assessment of postural status is made by a common clinical method, so the implementation of an objective and stricter criterion of selection might give somewhat different picture. Even though the number of children in the observed groups reflects the ratio between the number of children with and without postural deviations in general population, a larger number of subjects would increase the possibility of generalizing the results. When it comes to self-worth, the measuring instrument used in this research, SPPC [18], is

developed for children aged 8 and older. Although this scale is most often applied in the analysis of children's self-worth [42], and acceptable psychometric characteristics are found in different populations, it should be born in mind that the subjects are closer to the lower recommended age limit. Piek et al. [43] claim that the children aged 5 are capable of assessing their own competence in relation to their peers, which can justify the reason why this scale is used on eight-year-old children.

## Conclusions

Posture reflects functioning, growth and development of a child, including mental health. The posture is most noticeable in physical appearance, which represents the strongest predictor of global self-worth of children and adolescents. Taking into account that the results of previous researches are inconsistent, this research was conducted on the pupils of the first grade, with the aim of analyzing possible differences in the self-perception profile of children with and without postural deviations. The obtained results show that the children with and without postural deviations are not significantly different, neither in the domain-specific self-perceptions, nor in global self-worth. Besides that, self-perceptions in specific domains represent a significant set of predictors of global self-worth of children with and without postural deviations. Physical appearance and athletic competence largely affect global self-worth of children with postural deviations, while physical appearance and behavioral conduct represent the significant predictors of global self-worth of children with normal posture.

## References

1. Đorđić V. *Posturalni status predškolske dece. U G. Bala (Ur.) Antropološke karakteristike i sposobnosti predškolske dece (str. 154-202). Novi Sad: Fakultet sporta i fizickog vaspitanja; 2007.*
2. Negrini S, Negrini A. *Postural effects of symmetrical and asymmetrical loads on the spines of schoolchildren. Scoliosis 2007;2(8):1748-1761.*
3. Pausić J, Pedisić Ž, Dizdār D. *Reliability of a Photographic Method for Assessing Standing Posture of Elementary School Students. J Manip Physiol Ther 2010;33(6):425-431.*

4. Harreby M, Kjer J, Hesselsoe G, Neergaard K. *Epidemiological aspects and risk factors for low back pain in 38-year-old men and women: a 25-year prospective cohort study of 640 school children.* *Eur Spine J* 1996;5(5):312-318.
5. Noonan KJ, Dolan LA, Jacobson WC, Weinstein SL. *Long-term Psychosocial Characteristics of Patients Treated for Idiopathic Scoliosis.* *J Pediatr Orthop* 1997;17(6):712-717.
6. Tones M, Moss N, Polly DW. *A Review of Quality of Life and Psychosocial Issues in Scoliosis.* *Spine* 2006;31(26):3027-3038.
7. Payne WK, Ogilvie JW, Resnick M, Kane RL, Transfeldt EE, Blum RW. *Does Scoliosis Have a Psychological Impact and Does Gender Make a Difference?* *Spine* 1997;22 (12):1380-1384.
8. Breslau N. *Psychiatric disorders in children with physical disabilities.* *J Am Acad Child Psy* 1985; 24:87-94.
9. Cadman D, Boyle M, Szatmari P, Offord DR. *Chronic illness, disability and mental and social well-being: Findings of the Ontario child health study.* *Pediatrics* 1987;79:805-813.
10. Pless IB, Roghmann KJ. *Chronic illness and its consequences: Some observations based on three epidemiological surveys.* *J Pediatr* 1971;79:351-359.
11. Đorđić V, Tubić T. *Fizicko vaspitanje i fizicki self-koncept adolescenata.* *Pedagogija* 2009;3:415-426.
12. Fenzel ML. *Prospective Study of Changes in Global Self-Worth and Strain During the Transition to Middle School.* *J Early Adol* 2000;20(1):93-116.
13. Cantin S, Boivin M. *Change and stability in childrens social network and self-perceptions during transition from elementary to junior high school.* *Int J Behav Dev* 2004;28(6):561-570.
14. Bois JE, Sarrazin PG, Brustad RJ, Trouilloud DO, Cury F. *Mothers Expectancies and Young Adolescents Perceived Physical Competence: A Yearlong Study.* *J Early Adol* 2002;22(4):384-406.
15. Harter S. *The development of self-representations during childhood and adolescence.* In M.R. Leary & J.P. Tangney (Eds.), *Handbook of self and identity* (pp. 610-642). New York: Guilford Publications; 2005.
16. Boivin M, Vitaro F, Gagnon C. *A reassessment of the Self-perception Profile for Children: Factor structure, reliability, and convergent validity of a french version among second through sixth grade children.* *Int J Behav Dev* 1992;15:275-290.
17. Van Den Bergh BR, Marcoen A. *Harterts Self-Perception Profile for Children: Factor structure, reliability, and convergent validity in a Dutch speaking Belgian sample of fourth, fifth and sixth graders.* *Psych Belgica* 1999;39(1),29-47.
18. Harter S. *Manuel for the Self-perception Profile for Children.* Denver CO: University of Denver; 1985.
19. Granleese J, Trew K, Turner I. *Sex differences in perceived competence.* *B J Soc Psych* 1988;27:181-184.
20. Straathof MA, Treffers D, Siebelink B, Goedhart AW. *Self-esteem and self-perception: A study of 8-12 year old children at a child psychiatric clinic.* *Tijdschrift voor Psychiatrie* 1991;33:375-390.
21. Van Dongen-Melman JE, Koot HM, Verhulst FC. *Cross-cultural validation of Harterts Self-Perception Profile for Children in a Dutch sample.* *Educ Psych Measurement* 1993;53:739-753.
22. Janjetovic D. *Polne razlike u osloncima generalnog koncepta o sebi adolescenata.* *Psihologija* 1996;4:487-498.
23. Chasse MA, Dummer GM. *The role of sports as a social status determinant for children.* *Res Q Exerc Sport* 1992;63(4):418-424.
24. Skinner RA, Piek JP. *Psychosocial implications of poor motor coordination in children and adolescents.* *Hum Mov Sci* 2001;20:73-94.
25. Lazarevic D, Radisavljevic S, Milanovic, S. *Relacije fizickog self-koncepta i fizickog vežbanja učenika osnovne škole.* *Zbornik Instituta za pedagoška istraživanja* 2008;40 (2):306-326.
26. Antonak RF, Livneh H. *Psychosocial adaptation to disability and its investigation among persons with multiple sclerosis.* *Soc Sci Med* 1995; 40: 1099-1108.
27. Dewis ME. *Spinal cord injured adolescents and young adults: The meaning of body changes.* *J Adv Nurs* 1989;14:389-396.
28. Clayton KS, Chubon RA. *Factors associated with the quality of life of long-term spinal cord injured persons.* *Arch Phys Med Rehabil* 1994;75:633-638.
29. Stiens SA, Bergman SB, Formal CS. *Spinal cord injury rehabilitation: 4. Individual experience, personal adaptation, and social perspectives.* *Arch Phys Med Rehabil* 1997;78:65-72.
30. Timberlake EM. *Coping and adaptation by children with mild physical differences.* *Child Adol Soc Work* 1990;7:199-216.

31. Anile BJ. *Factors Associated with Self-Worth in Young People with Physical Disabilities.* *Health Soc Work* 2004;29(3):167-175.
32. Appleton PL, Minchom PE, Ellis NC, Elliott CE, Boll V, Jones P. *The self-concept of young people with spina bifida: A population based study.* *Dev Med Child Neurol* 1994;36:198-215.
33. Appleton PL, Ellis NC, Minchom PE, Lawson V, Boll V, Jones P. *Depressive Symptoms and Self-Concept in Young People with Spina Bifida.* *J Ped Psych* 1997;22(5):707-722.
34. Sapountzi-Krepia DS, Valvanis J, Panteleakis, GP, Zangana DT, Vlachojiannis PC, Sappas GS. *Perceptions of body image, happiness and satisfaction in adolescents wearing a Boston brace for scoliosis treatment.* *J Adv Nurs* 2001;35(5):683-690.
35. Kahanovitz N, Weiser S. *The psychological impact of idiopathic scoliosis on the adolescent female. A preliminary multy-center study.* *Spine* 1989;14:483-485.
36. Danielsson AJ, Wiklund I, Pehrsson K, Nachemso AL. *Health-related quality of life in patients with adolescent idiopathic scoliosis: a matched follow-up at least 20 years after treatment with brace or surgery.* *Eur Spine J* 2001;10:278-288.
37. Zhang J, He D, Gao J, Yu X, Sun H, Chen Z, Li M. *Changes in Life Satisfaction and Self-esteem in Patients with Adolescent Idiopathic Scoliosis With and Without Surgical Intervention.* *Spine* 2011;36(9):741-745.
38. Zhang J, Wang D, Chen Z, Gao J, Yu X, Sun H, Li M. *Decrease of Self-concept in Adolescent Patients With Mild to Moderate Scoliosis After Conservative Treatment.* *Spine* 2011;36(15):1004-1008.
39. Wai EK, Young NL, Feldman BM, Badley EM, Wright JG. *The Relationship Between Function, Self-perception and Spinal Deformity Implications for Treatment of Scoliosis in Children With Spina Bifida.* *J Pediatr Orthop* 2005;25:64-69.
40. Granleese J, Joseph S. *Factor analysis of the Self-Perception Profile for Children.* *Pers Ind diff* 1993;15:343-345.
41. Granleese J, Joseph S. *Reliability of the Harter Self-perception Profile for Children and predictors of global self-worth.* *J Genet Psychol* 1994;155:487-492.
42. Muris P, Meesters C, Fijen P. *The self-perception profile for children: Further evidence for its factor structure, reliability, and validity.* *Pers Ind Diff* 2003;35:1791-1802.
43. Piek JP, Baynam GB, Barrett NC. *The relationship between fine and gross motor ability, self-perceptions and self-worth in children and adolescents.* *Hum Mov Sci* 2006;25:65-75.

Corresponding Author  
 Visnja Djordjic,  
 Faculty of Sport and Physical Education,  
 Novi Sad,  
 Serbia,  
 E-mail: visnja@uns.ac.rs

# Early detection of postoperative deep vein thrombosis after general surgical procedures

Milan M. Jovanovic<sup>1,2</sup>, Aleksandra Z. Krstic<sup>3</sup>, Goran Stanojevic<sup>1,4</sup>, Miroslav Stojanovic<sup>1,4</sup>, Igor D. Smiljkovic<sup>2</sup>, Zoran Damnjanovic<sup>2</sup>

<sup>1</sup> Medical Faculty of Nis, Serbia,

<sup>2</sup> Vascular Surgery Clinic, Clinical Centre of Nis, Serbia,

<sup>3</sup> Clinic for gastroenterology, Clinical Centre Serbia, Belgrade, Serbia,

<sup>4</sup> General Surgery Clinic, Clinical Centre of Nis, Serbia.

## Abstract

**Background:** Diagnostic algorithm in patients with suspected deep vein thrombosis (DVT) is well established: repeated ultrasound examinations, ultrasound examination combined with determination of D-dimer (DD) serum level, and evaluation of clinical probability of DVT combined with ultrasound examination and/or D-dimer serum level estimation.

**Methods:** We have performed a prospective, randomized clinical study, evaluating 4802 operated patients with suspected DVT at University Surgical Clinic Nis, during the period from 01.01.2003 to 31.12.2004. Patients were randomized into two groups: DD and control group. Stratification of clinical probability for DVT ("unlikely" and "likely") was performed using Wells's clinical model.

**Results:** Normal serum levels of DD excluded the presence of DVT in 1156 (68.9%) patients with «unlikely» DVT and in 53.4% (1679) of all patients in DD group regardless of the clinical probability. Negative values of DD also excluded DVT in 47.3% (193/408) of patients with «likely» DVT, who had the negative first US examination. DVT was definitely ruled out in 1990 patients in DD group and in 1943 patients in control group. During the three months follow up period venous thromboembolism (VTE) was registered in 10 patients (0.51%; 95%CI=0.19-0.83%) in the control group and in 3 patients (0.15%; 95%CI= 0.0-0.4%) in the DD group ( $\chi^2=3.95$ ;  $p=0.047$ ;  $p<0.05$ , 95% CI=0.01-0.7%). The DD diagnostic strategy reduced the need for US examination by 68%.

**Conclusion:** Proposed strategy significantly raises accuracy and reliability of early detection of postoperative DVT in patients undergoing general surgical procedures.

**Key words:** detection, deep vein thrombosis, surgical procedures

## Introduction

The incidence of deep vein thrombosis (DVT) in the USA is approximately 159 cases per 100,000 persons annually<sup>1,2,3</sup>. In hospitalized patients, the incidence of venous thrombosis is considerably higher and varies from 20-70%. Death from DVT is attributed to massive pulmonary embolism, which causes 200,000 deaths annually in the United States<sup>1,3</sup>. Pulmonary embolism is the leading cause of preventable in-hospital mortality.

Furthermore, DVT is affecting postoperative course of operated patients. Scintigraphy and contrast venography detected DVT in 20-30% of patients after general surgical operations, 10-35% after gynecological, and 50-75% after orthopedic procedures (higher incidence after pelvic and knee injuries).

Venous ulceration and venous insufficiency of the lower leg, which are long-term complications of DVT, affect 0.5% of the entire population. Extrapolation of this data reveals that as many as 5 million people only in the USA have venous stasis and varying degrees of venous insufficiency.

Prevention of DVT complications (pulmonary embolism and venous hypertension with skin changes, including lipodermatosclerosis and ulceration) emphasize the necessity of early detection of DVT, especially in asymptomatic patients.

Diagnostic algorithm in patients with suspected DVT is established: repeated ultrasound examinations, ultrasound examination combined with estimation of D-dimer serum level, and evaluation of clinical probability combined with ultrasound examination and/or D-dimer serum level estimation<sup>3,4</sup>.

High sensitivity and sensibility of ultrasound examination in detecting and confirming vein thrombosis of the lower extremities in patients with suspected DVT is well known. On the other hand, repeated ultrasound examinations are too expensive, time consuming, and examiner depending. Furthermore, in 17-24% of patients with suspected DVT, vein thrombosis was actually present<sup>5-12</sup>. Taking these figures into account, the simpler, less expensive, faster, more available tools, as the initial screening test in detecting DVT in suspected patients was introduced<sup>4,6,11</sup>.

D-dimer test was established as useful, inexpensive noninvasive tool in initial screening of patients with suspected DVT with moderate specificity, high sensitivity and high negative predictive value (NPV)<sup>4,13-15</sup>.

Since 1995, *Well's* clinical model for estimation and grading clinical probability of DVT is in use. However, in initial version a lot of required data needed for the questionnaires limited their clinical application. The additional two revisions resulted in present model, in which 10 clinical characteristics form grading score with two alternatives: probable and less probable DVT<sup>4</sup>.

## Material and Methods

We have performed a prospective, randomized clinical study, evaluating all patients who underwent general surgical procedures at University Surgical Clinic, Clinical Center Nis, during the period from 01.01.2003 to 31.12.2004 (table 1).

Patients with one or more excluding characteristics were not included in the study (table 2). All other patients were randomized into two groups: D-dimer group and control group. In all patients PTP (pretest probability) score was calculated using *Wells* clinical model<sup>4</sup>. Patients with score  $< 2$  were classified in the subgroup of unlikely DVT, and patients with score  $\geq 2$  in the subgroup of likely DVT.

All patients in the control group underwent deep vein ultrasound examination of the lower extremities. In patients with unlikely DVT, DVT was excluded in case of negative ultrasound. In patients with likely DVT, control ultrasound was performed within 3-5 days of initial ultrasound examination.

Within the D-dimer group, in patients with unlikely DVT: D-dimer positive test proceeded with

ultrasound examination. In patients with D-dimer negative test, DVT was excluded. In the group of patients with likely DVT, ultrasound examination was performed first. If patients had negative ultrasound examination, D-dimer test was performed. If D-dimer test was negative, DVT was excluded. If D-dimer was positive control ultrasound re-examination was performed.

Patients with excluded DVT were followed up for 3 months in order to register venous thromboembolic event (VTE).

D-dimer values were evaluated from venous blood obtained by vein puncture, (vacutaner system with 3.8% sodium citrate) and centrifuged at 2000G during the 15 minutes. D-dimer level was assessed on coagulation IL ACL<sup>TM</sup> 6000 analyzer. IL – test was negative if D-dimer values were less than 200  $\mu\text{g/l}$ , and positive if D-dimer values were equal or greater than 200  $\mu\text{g/l}$ .

Only patients with unlikely DVT, and negative D-dimer test, were not assessed by ultrasound examination while all others underwent ultrasound examination. Ultrasound re-examinations were performed in all patients with likely DVT, with negative initial ultrasound examination, and positive D-dimer test. In the group of patients with unlikely DVT ultrasound re-examinations were performed in cases where initial ultrasound was uncertain. Color Doppler duplex ultrasound examination assessed compressibility of the deep veins from the common femoral to the proximal popliteal vein. In patients with no history of DVT, incompressible vein was referred as sign of DVT. In patients with previous DVT, diagnosis of new DVT was established if new areas of incompressible vein were detected, or if the increase of more than 4 mm in thrombus diameter comparing to initial ultrasound examination was detected<sup>16</sup>. Increase in thrombus diameter for  $\leq 1$  mm excluded new DVT. If increase in thrombus diameter was within the range from 1.1 to 3.9 mm, ultrasound re-examination was performed after seven days.

The patients with diagnosed DVT were treated with conventional anticoagulant therapy. All other patients, or their relatives, were informed (orally, and in written) how to detect any symptoms or signs of VTE. The patients check up was performed on 7<sup>th</sup> and 30<sup>th</sup> day after discharge, and immediately if VTE was suspected.



## Results

The study included 4802 patients operated at University Surgical Clinic Clinical Center of Nis, during the period of two years (01.01.2003 to 31.12.2004). The type of surgical procedure and estimated clinical probability (pre-test probability -PTP) for DVT are presented in table 1.

Among 4802 surgically treated patients, 471 patients were excluded from the study because they didn't fulfill the criteria. Therefore, the study included a total of 4331 patients. The reasons for exclusion of these 471 patients from the study are presented in table 2.

Overall 4331 patients were randomized into two groups: control group with 2148 patients and D-dimer group with 2183 patients. Twenty-five patients in the control group, and 19 in D-dimer group were not available for surveillance (refused

further evaluation), meaning that final statistical analysis included 4287 patients.

Normal values of D-dimer test definitely excluded diagnosis of DVT in 1156 patients in D-dimer group (68.9%) with unlikely DVT (1679 patients), and in 53.4% of all patients in D-dimer group (2164 patients), unrelated to pretest probability score. Negative D-dimer test was the reason for ending the further evaluation and surveillance in 47.3% (193/408) patients with likely DVT, with previous initial negative ultrasound examination. In that case the necessity for ultrasound re-examination was limited.

Among 4287 completely evaluated patients, venous thrombo-embolism was detected postoperatively or during the follow up period in 177 patients (8.18%) in the D-dimer group, and in 190 patients (8.95%) in the control group. Total prevalence of VTE was 8.56% (graph 1).

Table 1. Distribution of patients according to type of surgery and pre-test probability for DVT

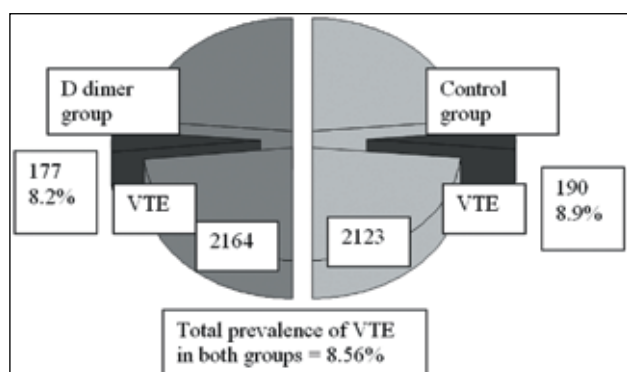
Type of surgery	No of operated patients	No of excluded patients	No of study patients	«PTP score»	
				< 2	≥ 2
Gastrointestinal surgery	1371	332	1039	732	307
Colorectal surgery	494	20	474	180	294
Hepatobiliar/pancreatic surgery	1175	57	1118	991	127
Thoracic surgery	407	20	387	344	43
Extraabdominal surgery	1355	42	1313	1083	230
Total	4802	471	4331	3330	1001

Table 2. Exclusion criteria from the study for 471 operated patients

Reason for exclusion	Number
-Sudden death in the immediate postoperative period	15
-Postoperative neurologic event	20
-Postsplenectomy sepsis	1
-Postoperative acute myocardial infarct	27
-Postoperative MOSF	41
-Life expectancy less than 3 months	75
-Younger than 18 years of age	39
-Pregnancy	7
-Unilateral lower limb amputation	6
-Refused/ not capable to give written consent**	73
-Unavailable for control (geographical)	89
-More than 72 h of symptoms subsiding	14
-Previous PE/DVT*	9
-Symptoms suspected on PE	22
-Patients on anticoagulant therapy	24
-Contrast allergy	9
-TOTAL	471

\* Previous detected PE and/or DVT of ipsilateral leg, without documented recanalisation

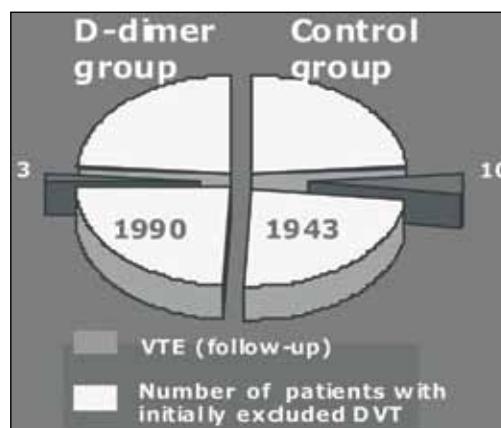
\*\*Refused or mentally incapable for written consent



Graph 1. Distribution of VTE in D-dimer and control group

Deep vein thrombosis was definitely excluded in 1990 patients in the D-dimer group, and in 1943 patients in the control group. During the follow up period of 3 months in the control group, VTE was detected in 10 patients with no previous history of DVT (0.51%; 95%CI=0.19-0.83%). During the follow up period of 3 months in 1990 patients in D-dimer group, when DVT was excluded in immediate postoperative period, DVT was detected

only in three patients (0.15%; 95%CI=0.0-0.4%). Comparing D-dimer and control group regarding frequency of VTE during the follow up period statistically significant difference was detected (chi square test = 3.95; p = 0.047; p < 0.05), as shown on graph 2, with 95% CI for difference of 0.36% is 0.01-0.7%.



Graph 2. The incidence of VTE in the follow up period in patients with initially excluded DVT

Table 3. Results of D-dimer testing in patients in the D-dimer group

D-dimer test	«PTP score»		Total
	← unlikely TDV	likely DVT n (%; 95% CI)	
True positive (TP)	74 (4.44; 3.45-5.43)	4 (0.99; 0.5-4.9)	78 (3.77; 2.95-4.59)
False positive (FP)	437 (26.21; 24.1-28.32)	204 (50.88; 45.98-55.78)	641 (30.99; 37.89-42.11)
True negative (TN)	1153 (69.17; 66.95-71.39)	193 (48.13; 43.23-53.03)	1346 (65.09; 63.03-67.14)
False negative (FN)	3 (0.18; 0.09-0.8)	0 (0.0-0.9)	3 (0.15*; 0.0-0.6)
<b>Total</b>	<b>1667 (100.0)</b>	<b>401 (100.0)</b>	<b>2068 (100.0)</b>

Table 4. Diagnostic characteristics of D-dimer test

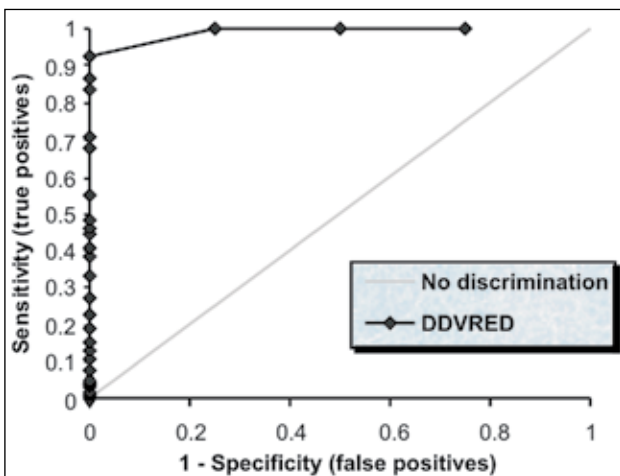
D-dimer test	«PTP score»		
	< 2 (unlikely DVT)		≥ 2 (likely DVT)
	← %; 95%CI →		
<b>Sensitivity</b>	96.1 (89.0-99.2)	100 (96.3-100)	96.30 (89.6-99.2)
<b>Specifity</b>	72.51 (70.2-74.7)	48.61 (43.6-53.7)	67.74 (65.6-69.8)
<b>NPV</b>	99.74 (99.2-99.9)	100 (99.0-100)	99.77 (99.4-100.0)
<b>PPV</b>	14.48 (11.5-17.8)	1.92 (0.5-4.9)	10.85 (8.7-13.4)
<b>Diagnostic efficacy</b>	73.61	49.10	68.86

In table 3 are given different forms of results of D-dimer testing in the above mentioned group of patients, in order to perform exact quantitative evaluation of different diagnostic characteristics of method, presented in table 4. Sensitivity, specificity, diagnostic efficacy as well as predictive values of D-dimer test in the D-dimer group are shown in table 4.

Patients that had negative D-dimer didn't undergo US examination (1349 patients -65.23% of patients in D-dimer group). In these patients we excluded any possibility of developing DVT. However, during a three month follow-up period in these patients we registered 3 cases of DVT (false negative test, FN – 0.15%; 95% CI 0.0-0.6%). We may conclude the data that 65.09% then had a true negative test. In the D-dimer group we had 719 patients, (34.77%) who had positive D-dimer test. These patients underwent US examination to confirm the presence of DVT. Ultrasound was negative in 641 patients and none developed DVT. Negative predictive value of D-dimer test for the entire D-dimer group was 99.77% (95% CI 99.4-100%) while positive predictive value was 10.85% (95% CI 8.7-13.4%). (table 4)

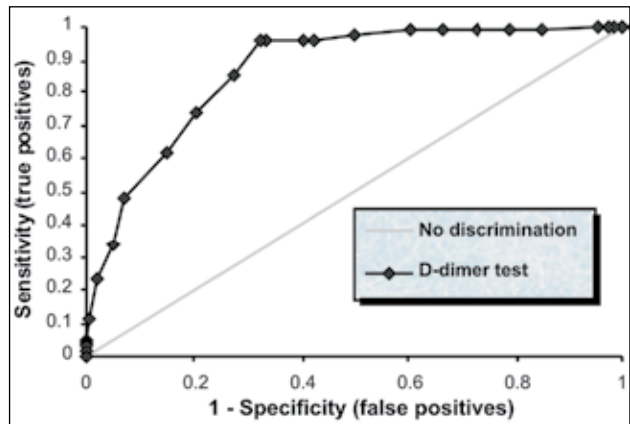
Relation between sensitivity and specificity of D-dimer test in order to evaluate diagnostic characteristics of this test in the D-dimer group and its subgroups is shown in graphs 3 and 4.

AUC	0,991
95%CI	0,972-1,000
SE	0,0097
P	< 0,0001



Graph 3. ROC curve for D-dimer test in patients with unlikely DVT

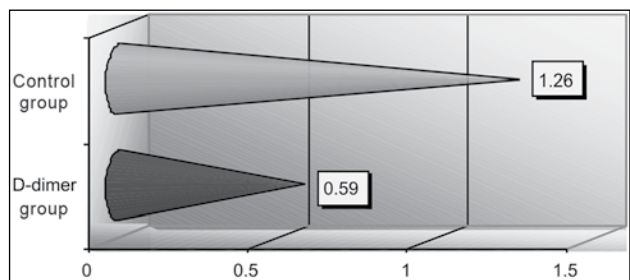
AUC	0,868
95%CI	0,835-0,901
SE	0,0169
P	< 0,0001



Graph 4. ROC curve for D-dimer test in patients with likely DVT

Clinical examination (estimation of clinical probability) and D-dimer testing were sufficient for establishing correct and prompt definitive diagnosis. Exclusion of DVT was made in 53% of patients in D-dimer group who had low PTP score ("unlikely" DVT) and negative D-dimer test (1156 out of 2164 patients). These patients also had insignificant incidence of DVT in the follow-up period (3/1156). We have also excluded DVT in 47.3% of patients with clinically "probable" DVT that had negative initial US and negative D-dimer (193/408). In this way, we have limited the need for repeated US examination without a single DVT case registered in the follow-up period.

Comparing the two study groups, we have noticed statistically significantly higher average number of ultrasounds examinations performed per patient in the control group in comparison to the D-dimer group. (Graph 5)



Graph 5. Mean number of US examinations per patient (Mann-Whitney=-33.6; p<0.0001)

D-dimer testing reduced the need for US examinations for establishing diagnosis of DVT by 68%.

Analysis of US diagnostics among the two groups (table 5) showed a low false negative rate of 0.25%, proving the high sensitivity of this diagnostic tool for establishing DVT (table 6).

Ultrasound is much more sensitive as a diagnostic tool for establishing DVT in the D-dimer group than in the control group (Fisher's exact test = 0.002;  $p < 0.01$ ). Difference in negative predictive value of US between patients with "less probable" and "probable" DVT is not statistically significant (Fisher's exact test= 0.750;  $p > 0.05$ ). In the D-dimer group, negative predictive value of US is 100% while in the control group is lower

(99.6%). This difference shows statistical significance (Fisher's exact test=0.0397;  $p < 0.05$ ) (table 6). Comparing sensitivity and negative predictive value of D-dimer test and US we have registered insignificant difference (table 7).

Comparison of the results of D-dimer and ultrasound (control) strategy are shown in table 8, while their diagnostic characteristics are evaluated in table 9. Negative predictive value and diagnostic efficacy are statistically significantly higher in the D-dimer group compared to control group. D-dimer strategy is also more sensitive than US with statistically significant difference for  $p < 0.1$  (table 9).

Table 5. Results of ultrasound (US) examination in the study group

US	Unlikely TDV			Likely TDV	
	D-dimer group	Control group	n	D-dimer group	Control group
	←			→	
Positive	74	60	100	120	354
Negative	484	1754	612	743	3593
False negative	0	7	0	3	10
Total	558	1821	712	866	3957

Table 6. Sensitivity and negative predictive value (NPV) of ultrasound examination in examined groups

US	«PTP score» D-dimer group Control group			
	< 2 (unlikely DVT)		≥ 2 (likely DVT)	
	← %; 95% CI →			
<b>Sensitivity*</b>	95.04 (90.0-98.0)	98.65 (96.1-99.7)	100 (97.9-100.0)	94.74 (90.5-97.4)
<b>NPV**</b>	99.69 (99.4-99.9)	99.78 (99.4-100.0)	100 (99.7-100.0)	99.6 (99.3-99.8)

\*Sensitivity (D-dimer/ control group) Fisher=0.002;  $p < 0.01$

\*\*NPV (unlikely/likely)  $p > 0,05$

(D-dimer/ control group) Fisher=0.0397;  $p < 0.05$

Table 7. Relation between sensitivity and NPV of D-dimer and ultrasound examination

	D-dimer test	Ultrasound (95%CI)	Fisher's exact test (p)
<b>Sensitivity</b>	96.3 (89,6-99,2)	97.25 (95.0-98.7)	0.713 ( $p > 0.05$ ; NS)
<b>NPV</b>	99.8 (99,4-100,0)	99.72 (99.5-99.9)	1.000 ( $p > 0.05$ ; NS)

Table 8. Results of different diagnostic methods implemented in the study

Result	D-dimer strategy/ Control strategy (n/n)
POSITIVE	174/180
FALSE POSITIVE	0/0
NEGATIVE	1987/1933
FALSE NEGATIVE	3/10

## Discussion

Diagnostic possibilities of ultrasound and the experience of the echosonographers have made it feasible for the DVT to be easily confirmed or excluded either with a single or with several subsequent ultrasound examinations of deep veins. Reliability of this noninvasive diagnostic method is validated by the fact that the false negative rate for diagnosis of DVT by ultrasound is only 0.9%<sup>10</sup>. In addition, results of two recent studies with a follow-up period of 3-6 months, demonstrate an even lower rate of thrombo-embolic complications (0.6%) in patients with suspected DVT, in whom the results of repeated DV ultrasounds had been negative<sup>9,10</sup>. In order to reduce the need for performing DV ultrasound exams, other diagnostic tools have been implemented, such as estimation of PTP score and D-dimer<sup>7,17,18</sup> serum levels testings<sup>6,17,19,20,21,22</sup>. Numerous studies confirm the safety of omitting anticoagulant treatment in patients with low PTP score and normal initial ultrasound<sup>7</sup>, as well as in patients with normal D-dimer levels and normal DV ultrasound<sup>11,19,22</sup>.

Clinical evaluation of DVT today encompasses stratification of patients with suspected disease into categories with low, intermediate and high risk for developing clinically evident symptoms and signs. Official scoring system of vein thrombo-embolism (VTE) was instituted by Wells et al.<sup>23,24</sup> and has so far proven its' validity. This system runs respectively with the clinical characteristics and presence or absence of alternate diagnosis, with the final score which estimates clinical (pre test) probability (PTP).

Published studies have demonstrated reliability of the restricted diagnostic and treatment algorithm in patients with suspected VTE, low clinical probability and negative D-dimer test (Simpli RED<sup>25,26</sup>, AGEN Biomedical, Brisbane, Australia; or VI-DAS<sup>27</sup>, BioMerieux, Marcy l'Etoile, France). Diagnostic approach has been reduced according to proposed guidelines in all 773 patients in these studies, with only 2 confirmed episodes of VTE (0.3%) in the 3 month follow up period. In one of the studies<sup>25</sup>, the same approach has initially excluded pulmonary embolism (PE) in 47% of the patients.

Three recent studies have confirmed safety of the restricted diagnostic and treatment regimen in patients with suspected VTE, belonging to a low or intermediate risk group for clinical probability, using two highly sensitive latex agglutination immunoturbidimetric tests- Tinaquant assay<sup>17,28</sup> (Roche; Frankfurt am Main, Germany) and MDA D-dimer assay<sup>29</sup> (BioMerieux). VTE was excluded in 553 patients on the basis of the mentioned criteria. In these patients over the 3 month follow-up

Table 9. Comparative evaluation of diagnostic characteristics of implemented strategies

Diagnostic characteristics	D-dimer strategy	Control strategy	$\chi^2$ test	p
	←———— % (95%CI) —————→			
Sensitivity	98.31 (95.1-99.6)	94.74 (90.5-97.4)	3.41	0.06; p>0.05 (<0.1)
Specificity	100.0 (99.8-100.0)	100.0 (99.8-100.0)	-	-
PPV	100.0 (97.9-100.0)	100.0 (98.0-100.0)	-	-
NPV	99.85 (99.6-100.0)	99.49 (99.1-99.8)	3.95	0.047; p<0.05
<b>Diagnostic Efficacy</b>	99.86	99.53	3.92	0.048; p<0.05

period, only 2 cases (0.4%) of VTE occurred. In one of these studies, same approach enabled exclusion of DVT in 51% of the patients<sup>29</sup>. D-dimer estimation as a single implemented diagnostic tool for exclusion of DVT was implemented in only one of the mentioned studies. Restricted diagnostics and treatment was used in 159 out of 444 patients (36%) with suspected PE and negative VIDAS D-dimer assay, regardless of the clinical probability, without a single VTE case registered over 3 months follow-up<sup>19</sup>. The study doesn't note the exact percentage of patients that belonged in a high clinical probability group and had negative D-dimer assay. However it does state that the probability of having a negative D-dimer test is in direct correlation with the clinical probability of developing VTE<sup>13,24</sup>. This fact is also repeated in other studies where patients in a high risk group of VTE had a negative D-dimer test in only 2%<sup>13,24</sup>.

High negative predictive value of D-dimer test is confirmed in studies evaluating reliability of this diagnostic tool in ambulatory patients with suspected DVT<sup>19, 22, 30</sup>.

Unfortunately, there are no data in modern literature estimating reliability of the DVT early detection model in patients previously subjected to general surgical procedures, a group of patients with high risk for DVT as a postoperative complication.

Implementation of Wells Clinical Model in this research demonstrated that the combination of low probability for DVT and normal D-dimer levels (negative D-dimer test), excludes DVT as well as the need for further diagnostic testing, in 68.9% of patients, whose PTP score is less than 2, and in 53.4% of all patients regardless of the probability level. Conveniently, results of the utilized turbodimetric IL D-dimer test are acquired in a only few minutes, representing a fast and efficient method for exclusion of DVT and reaching definitive diagnosis in more than half of the patients subjected to D-dimer diagnostic strategy.

Research also verifies low incidence of DVT (0.51%) during follow-up period in the control group. Registered tromboembolic complications were 0.6% in the control group. This indicates high reliability and verifies quality of the implemented ultrasound diagnostic model in the control group. However, incidence of DVT in the follow-up period was even lower in the D-dimer group (0.15%)

in patients where DVT was initially disregarded as a probability. The difference in DVT incidence between the control and the D-dimer group is statistically significant ( $\chi^2=3.95$ ;  $p=0.047$ ;  $p<0.05$ ; 95% CI=0.01-0.7%).

Tendency to maintain the sensitivity of ELISA tests, while simplifying the procedure and raising specificity and speed, created new, quantitative, turbodimetric immuno-assays that may be equally sensitive and show even greater specificity than ELISA<sup>31</sup>.

In this study we used turbodimetric D-dimer IL (Instrumentation Laboratory) Test<sup>TM</sup>. It is a fully automatic quantitative latex immunoassay, designed to work on coagulation IL analyzers, like ACL<sup>TM</sup> 6000, ACL<sup>TM</sup> 7000 and ACL Futura<sup>TM</sup>. This test demonstrated superb technical characteristics enabling us to obtain precise numerical D-dimer values in less than 7 minutes<sup>32</sup>.

The results of this study confirm high sensitivity (96.3%) and negative predictive value of the D-dimer test (99.77%), while its specificity remains lower, however still significant (67.74%) in comparison to other D-dimer tests.

Our study has showed statistically significant specificity and diagnostic efficacy in the subgroup of patients with low clinical probability for DVT in comparison to the patients from the higher clinical probability for DVT. These results correspond with the ROC curve, indicating extremely good diagnostic potential of implemented D-dimer IL test in the low probability subgroup. ROC curve is almost entirely placed in the upper left quadrant (ROC curve for the ideal method, if there were such, would cut through the upper left angle and the area under curve AUC would equal 1.00). AUC in our case is 0.991, meaning that the candidate from the diseased group has a higher D-dimer value that the candidate from the disease absent group in 99.1% of the cases. Also, CI of 95% which estimates the distribution of the AUC in general population is 0.972-1.000.

In the subgroup with "probable" DVT, D-dimer test has somewhat lower diagnostic value, however still most convincing. ROC curve is near the upper left angle, AUC=0.868 (95% CI=0.835-0.901), and the AUC for the D-dimer test shows statistically significant difference ( $p<0.0001$ ) in comparison to the theoretical curve where we see

no separation, (null hypothesis = there is no difference between the diseased and disease-free patients) where AUC=0.

Comparing the two examined subgroups, we observed statistically significant difference ( $Z=33.657$ ;  $p<0.0001$ ) in the average number of performed US exams per patient between the control group and D-dimer group. Implementation of D-dimer diagnostic strategy has significantly (by 68%) reduced the need for the initial and repeated US exams, thereby simplifying and making diagnostic procedure more efficient and less time consuming. Furthermore, this method is cost-effective, reduces unnecessary inconvenience for the patient, the staff and echosonographers, while at the same time providing timely treatment of the selected patients.

The role of PTP score and/or D-dimer levels in DVT diagnosis was examined in numerous studies <sup>6,7,13,17,18,19,20,21,22,33</sup>. All proposed diagnostic models did not manage to correct the failure rate (percentage of estimated DVTs) of 0.6% and 0.7%, that was documented in two large studies examining safety of repeated US exams <sup>9,10</sup>. Failure rate of 0.15% (95% CI, 0.0-0.4%), in our patients, where D-dimer model was implemented is significantly lower ( $\chi^2=3.95$ ;  $p=0.047$ ;  $p<0.05$ ) than the failure rate of 0.51% in the group of patients where repeated US diagnostic regimen was utilized. This rate of 0.15% is also lower than in the other published studies.

## Conclusion

D-dimer diagnostic strategy, based on turbidimetric IL immunoassay and vein ultrasonography, implemented according to the protocol of estimated level of clinical probability for developing DVT, significantly raises efficacy, accuracy, and reliability, augments cost-effectiveness of early detection of postoperative deep vein thrombosis in patients subjected to general surgical procedures. A strategy such as this one reduces the need for more expensive ultrasound examinations, at the same time making easier exclusion of DVT in difficult clinical cases, while not jeopardizing patient safety.

## References

1. Bulger CM, Jacobs C, Patel NH. *Epidemiology of acute deep vein thrombosis. Tech Vasc Interv Radiol* 2004; 7: 50-54.
2. Tovey C, Wyatt S. *Diagnosis, investigation, and management of deep vein thrombosis. BMJ* 2003; 326: 1180-1184.
3. Coiteux I, Mazzolai L. *Deep vein thrombosis: epidemiology, risk factors and natural history. Praxis (Bern 1994)* 2006; 95: 455-459.
4. Vanfleteren L, Wesseling G. *Evaluation of the diagnostic yield of D-dimer testing in suspected venous thromboembolism in primary care: a 2-year retrospective analysis. Prim Care Respir J* 2011; 20: 102-103.
5. Miron MJ, Perrier A, Bounameaux H. *Clinical assessment of suspected deep vein thrombosis: comparison between a score and empirical assessment. J Intern Med* 2000; 247: 249-254.
6. Cosmi B, Legnani C, Cini M, Guazzaloca G, Palareti G. *D-dimer and residual vein obstruction as risk factors for recurrence during and after anticoagulation withdrawal in patients with a first episode of provoked deep-vein thrombosis. Thromb Haemost* 2011; 105: 837-845.
7. Vinson DR, Patel JP, Irving CS. *Pretest probability estimation in the evaluation of patients with possible deep vein thrombosis. Am J Emerg Med* 2011; 29: 594-600.
8. Bucek RA, Koca N, Reiter M. *Algorithms for the diagnosis of deep-vein thrombosis in patients with low clinical pretest probability. Thromb Res* 2002; 105: 43-47.
9. Righini M, Le Gal G, Aujesky D, et al. *Complete venous ultrasound in outpatients with suspected pulmonary embolism. J Thromb Haemost* 2009; 7: 406-412.
10. Bounameaux H, Perrier A, Righini M. *Diagnosis of venous thromboembolism: an update. Vasc Med* 2010; 15: 399-406.
11. Bernardi E, Prandoni P, Lensing AW, et al. *D-dimer testing as an adjunct to ultrasonography in patients with clinically suspected deep vein thrombosis: prospective cohort study: the Multicentre Italian D-dimer Ultrasound Study Investigators Group. BMJ* 1998; 317: 1037-1040.
12. Perrier A, Buswell L, Bounameaux H. *Non-invasive diagnostic aids are cost-effective in suspected pulmonary embolism. Arch Intern Med* 1997; 157: 2309-2316.
13. Kearon C, Ginsberg JS, Douketis J. *Management of suspected deep venous thrombosis in outpatients by using clinical assessment and D-dimer testing. Ann Intern Med* 2001; 135: 108-111.

14. Nazarenko GI, Kungurtsev VV, Anokhin NV, Iugova TM, Kungurtsev EV, Repnikova TR. D-dimer in diagnosis of acute thromboses of lower-limb deep veins]. *Angiol Sosud Khir* 2009; 15: 15-18.
15. Goldin Y, Pasvolsky O, Rogowski O, et al. The diagnostic yield of D-Dimer in relation to time from symptom onset in patients evaluated for venous thromboembolism in the emergency medicine department. *J Thromb Thrombolysis* 2011; 31: 1-5.
16. Kearon C, Julian JA, Newman TE, et al. Noninvasive diagnosis of deep venous thrombosis. *Ann Intern Med* 1998; 128: 663-677.
17. Perrier A, Bounameaux H. Cost-effective diagnosis of deep vein thrombosis and pulmonary embolism. *Thromb Haemost* 2001; 86: 475-487.
18. Penalzoza A, Laureys M, Wautrecht JC, Lxeureux P, Motte S. Accuracy and safety of pretest probability assessment of deep vein thrombosis by physicians in training using the explicit Wells clinical model. *J tromb haemost* 2006; 4: 278-281.
19. Perrier A, Desmarais S, Miron M, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet* 1999; 353: 190-195.
20. Bates SM, Grand'Maison A, Johnston M. A latex D-dimer reliably excludes venous thromboembolism. *Arch Intern Med* 2001; 161: 447-453.
21. Van der Graaf F, van den Borne H, van der Kolk M, et al. Exclusion of deep venous thrombosis with d-dimer testing—comparison of 13 d-dimer methods in 99 outpatients suspected of deep venous thrombosis using venography as reference standard. *Thromb Haemost* 2000; 83: 191-198.
22. Kraaijenhagen RA, Piovella F, Bernardi E. Simplification of the diagnostic management of suspected deep vein thrombosis. *Arch Intern Med* 2002; 162: 907-911.
23. Wells PS, Hirsh J, Anderson DR. A simple clinical model for the diagnosis of deep vein thrombosis combined with impedance plethysmography: potential for an improvement in the diagnostic process. *J Intern Med* 1998; 243: 15-23.
24. Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorise patients probability of pulmonary embolism: increasing the model's utility with the SimpliRED D-dimer. *Thromb Haemost* 2000; 83: 416-420.
25. Michiels JJ, Gadisseur A, van der Planken M, et al. Screening for deep vein thrombosis and pulmonary embolism in outpatients with suspected DVT or PE by the sequential use of clinical score: a sensitive quantitative D-dimer test and noninvasive diagnostic tools. *Semin Vasc Med* 2005; 5: 351-364.
26. Kelly J, Hunt BJ. The utility of pretest probability assessment in patients with clinically suspected venous thromboembolism. *Thromb Haemostas* 2003; 1: 1888-1896.
27. Schutgens RE, Ackermark P, Haas FJ, et al. Combination of a normal d-dimer concentration and a non-high pretest clinical probability score is a safe strategy to exclude deep vein thrombosis. *Circulation* 2003; 107: 593-597.
28. Leclercq MG, Lutisan JG, van Marwijk, et al. Ruling out clinically suspected pulmonary embolism by assessment of clinical probability and d-dimer levels: a management study. *Thromb Haemost* 2003; 89: 97-103.
29. Bates SM, Kearon C, Crowther M, et al. A diagnostic strategy involving a quantitative latex d-dimer assay reliably excludes deep venous thrombosis. *Ann Intern Med* 2003; 138: 787-794.
30. Michiels JJ, Gadisseur A, van der Planken M, et al. Screening for deep vein thrombosis and pulmonary embolism in outpatients with suspected DVT or PE by the sequential use of clinical score: a sensitive quantitative D-dimer test and noninvasive diagnostic tools. *Semin Vasc Med* 2005; 5: 351-364.
31. Shitrit D, Heyd J, Raveh D. Diagnostic value of the d-dimer test in deep vein thrombosis: improved results by a new assay method and by using discriminate levels. *Thromb Res* 2001; 102: 125-131.
32. Dryjski M, O'Brien-Irr MS, Harris LM. Evaluation of screening protocol to exclude the diagnosis of deep venous thrombosis among emergency department patients. *J Vasc Surg* 2001; 34: 1010-1015.
33. Janes S, Ashford N. Use of a simplified clinical scoring system and d-dimer testing can reduce the requirement for radiology in the exclusion of deep vein thrombosis by over 20%. *Br J Haematol* 2001; 112: 1079-1082.

Corresponding Author  
 Milan M. Jovanovic,  
 Clinical Center of Nis,  
 Vascular Surgery Clinic,  
 Nis,  
 Serbia,  
 E-mail: milan.m.jovanovic@gmail.com



# Lymphangioma of the spermatic cord in an elderly man: A case report

Shi Deng, Shangqing Ren, Lin Hou, Qiang Dong

Department of Urology, West China Hospital of Sichuan University, Chengdu, Sichuan Province, China,

## Abstract

Lymphangioma is a rare congenital malformation of the lymphatic system. It is frequently documented in the pediatric age group, and rarely presents in older people, especially its location in the spermatic cord. Thus far, only one case has been reported in the spermatic cord of an elderly Chinese male. Here we report a case of spermatic cord lymphangioma in a 79-year-old male with the aim of raising awareness regarding this rare disease.

**Key words:** lymphangioma, spermatic cord, ultrasound

## Introduction

Lymphangioma is an uncommon benign malformation of the lymphatic system.<sup>1</sup> According to the cases reported in the literature, lymphangioma occurs most commonly in infants and children.<sup>2</sup> A study comprising 45 cases of cystic lymphangioma in children found that the neck, face, and axilla are the most common sites of the malformation, while the inguinal region is a rare site.<sup>3</sup> In clinical reports regarding the urinary system, lymphangioma in adults is rare, especially when occurring in the spermatic cord. To the best of our knowledge, only one case of lymphangioma of the spermatic cord in an elderly male has been reported in Chinese, and there has been no in English-language report showing images of a specimen. In this study, we present a case of cystic lymphangioma of the spermatic cord in a 79-year-old male patient.

## Case Presentation

A 79-year-old male patient suffering from diabetes and hypertension found a lump similar to a soybean in appearance inside his right scrotum. The lump remained there for four years and without apparent change. Last year, the bump started

to increase, and gradually enlarged to the size of a pigeon egg. The patient did not feel any discomfort such as aches, heavy feelings and so on. In addition, the patient denied having suffered from trauma or prior infection.

Physical examination revealed an oval, non-tender, firm swelling, 3 × 4 cm in size, and located in the right spermatic cord. The transillumination test was negative. The routine laboratory results, including blood routine, serum electrolyte, etc., as well as tests for related serum tumor markers such as carcino-embryonic antigen (CEA), alpha fetoprotein (AFP), lactate dehydrogenase (LDH), and β-human chorionic gonadotropin (β-HCG) were all within the normal range. Color Doppler ultrasonography (US) showed a 29×24×40 mm multiseptated, irregularly sized, and well-circumscribed mass in the right spermatic cord (Figure 1). No additional enlarged lymph node in region of retroperitoneal was discovered by ultrasound.

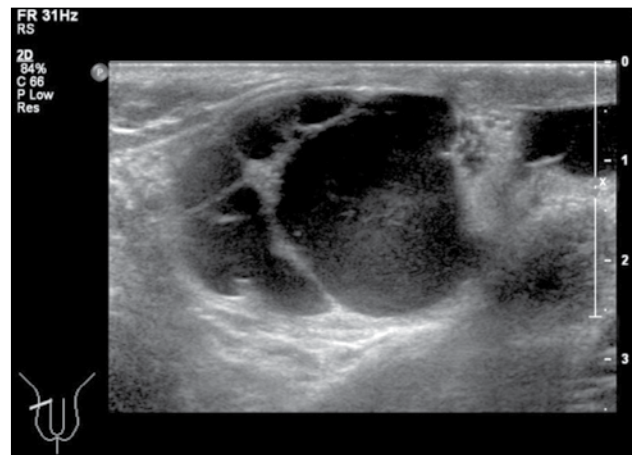


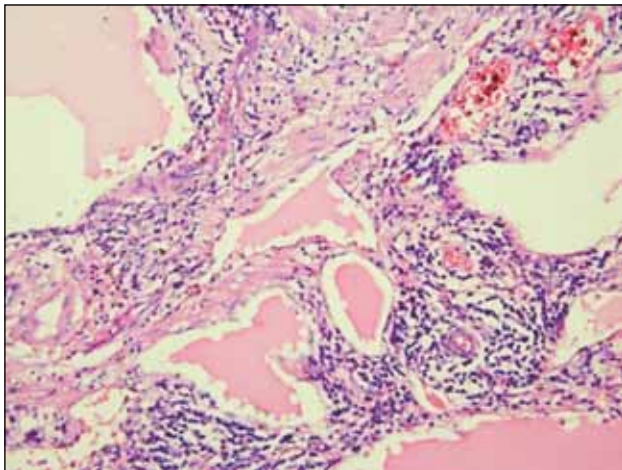
Figure 1. US shows an approximately 29×24×40 mm multiseptated, irregularly sized, and well-circumscribed mass

Exploratory operation through the right groin area indicated a multiseptated cystic mass with hemorrhagic and serous fluid contents clinging the right spermatic cord and abutting the upper pole of the right testis. The mass was multiloculated, thin-

walled, and was chocolate-colored (Figure 2). The adhesion between spermatic cord and mass was not very tight. A complete surgical excision was performed, and the microscopic sections were postoperatively demonstrated as cystic lymphangioma (Figure 3). The patient was discharged and stayed at home after an uneventful convalescence. During 20 months of follow-up, no local recurrence was noted.



*Figure 2. The mass was oval , multiloculated, thin-walled, and contained chocolate-like contents*



*Figure 3. Hematoxylin-eosin stain of the lymphangioma showed the lymphatic vessels was cystic expansion, and contained lymph in it. The inner cystic wall lined with simple squamous endothelium and the outer cystic wall covered with smooth muscle, blood vessels, adipose and lymphatic tissues. (hematoxylin-eosin staining  $\times 200$ )*

## Discussion

Lymphangioma is a benign malformation of the lymphatic system.<sup>1</sup> At present, the exact mechanisms of lymphangioma development remains poorly defined. Possible pathogenic causes include congenital factors such as sequestration of lymph tissue, abnormal budding of lymph vessels, and lack of fusion with the venous systems. In addition, trauma, infections, and chronic inflammations may contribute to this disease.<sup>4</sup> However, no evidence of these causes was considered in our case.

Clinically, the rare benign tumor is most commonly seen in the pediatric age group.<sup>5</sup> So far, only 100 cases have been reported in adults worldwide.<sup>6</sup> Lymphangioma may arise in any part of the body. In contrast to its location in other sites, lymphangioma of the spermatic cord is rare. Actually, according to the published literatures, only one article was available addressing adult-related lymphangioma of the spermatic cord. Thus, the disease is very easy to misdiagnose. From our clinical experience, if the cyst occurs in the spermatic cord, we generally consider this as the funicular hydrocele first because tumors arising in the spermatic cord are usually very rare.<sup>7</sup> In addition, the clinical features between lymphangioma and the funicular hydrocele are very similar, so obtaining a definite diagnosis preoperatively is difficult. US plays an important role in differentiating cystic from a solid lesion.<sup>8</sup> Sonography usually shows circular or elliptic photic zones in funicular hydrocele, while displaying a cystoid mass behind the testis in lymphangioma.

As the tumor size increases rapidly in a relatively short period of time in our case, we also consider the possibility of malignancy. Leiomyosarcoma is a malignant neoplasm which frequently occurs on sixth and seventh decade. Although leiomyosarcoma of the spermatic cord is rare, it has been reported up to 110 times.<sup>9</sup> Clinically, it usually presents as a painless, firm mass, and has not any unique clinical features. In this regard, it is difficult to get a precise pre-operative diagnosis. CT or MRI also can be used for effective imaging examination, and the latter has greater advantage in determining the scope of lesions. In our case, due to economic conditions, the patient declined to have a CT or MRI. Pathological diagnosis is the

gold standard for this disease. According to the histological appearance, lymphangioma can be classified into different types: capillary, cavernous, and cystic.<sup>4</sup> Our case belongs to the third type, which is also the most common one.<sup>2</sup>

At present, although surgical excision is the best choice for therapeutic treatment with lymphangioma to prevent the recurrence, however, surgical management of lymphangioma at head and neck region, which are the most commonly involved sites, is associated with possible complications. Some non-surgical methods of management have been used as alternative therapeutic tools, such as simple drainage, aspiration, radiation and so on. Among these approaches, topical injection of OK432 or bleomycin displayed very promising therapeutic effect.<sup>10-11</sup> However, spermatic cord injection of sclerosing agents may cause fibrogenesis. Are there any adverse influences that fibrosis deal with testis's function in adult patients? And the frequency and right doses of injection is still open to question. Until now, we have not seen any reports regarding alternative management for lymphangioma in the spermatic cord. For surgical operation, in our experience, the cystic lesion should not be decompressed during the separation so that the lump can be removed entirely.

In conclusion, an adult presented with a lump in the spermatic cord, and sonography revealed a neoplasm of multiseptated cysts, lymphangioma should be a differential diagnosis in our consideration.

## References

1. Wiegand S, Eivazi B, Barth PJ, von Rautenfeld DB, Folz BJ, Mandic R, et al. Pathogenesis of lymphangiomas. *Virchows Arch.*2008; 453:1–8.
2. Loberant N, Chernihovski A, Goldfeld M, Sweed Y, Vais M, Tzilman B, et al. Role of Doppler sonography in the diagnosis of cystic lymphangioma of the scrotum. *J Clin Ultrasound.*2002; 30:384-387.
3. Pandit SK, Rattan KN, Budhiraja S, Solanki RS. Cystic lymphangioma with special reference to rare sites. *Indian Journal of Pediatrics.*2000; 67:339-341.
4. Bloom DC, Perkins JA, Manning SC. Management of lymphatic malformations. *Curr Opin Otolaryngol Head Neck Surg.* 2004; 12:500–504.
5. Grossgold ET, Kusuda L. Scrotal lymphangioma in an adult. *Urology.*2007;70:590.
6. Sherman BE, Kendall K. Unique case of the rapid onset of a large cystic hygroma in the adult. *Am J Otolaryngol.* 2001.22 (3):206–210
7. Schwartz SL, Swierzewski SJ 3rd, Sondak VK, Grossman HB. Liposarcoma of the spermatic cord: Report of 6 cases and review of literature. *J Urol.* 1995; 153(1): 154.
8. Weidman ER, Cendron M, Schned AR, Harris RD. Scrotal lymphangioma: an uncommon cause for a scrotal mass. *J Ultrasound Med.*2002; 21:669-672.
9. Weiss SW, Goldblum JR. *Leiomyosarcoma*, In: *Enzinger and Weiss's Soft tissue Tumors 4th ed.* St.Louis (MI): Mosby Inc; 2001. p. 727-48.
10. Woolley SL, Smith DR, Quine S. Adult cystic hygroma: successful use of OK-432 (Picibanil). *J Laryngol Otol.* 2008 ;122(11):1260-1264.
11. Sanlialp I, Karnak I, Tanyel FC, Senocak ME. Sclerotherapy for lymphangioma in children. *J Pediatr Otorhinolaryngol.* 2003 Jul;67(7):795-800

Corresponding Author  
Qiang Dong,  
Department of Urology,  
West China Hospital of Sichuan University,  
Chengdu,  
Sichuan Province,  
China,  
E-mail: dongqianghxi@163.com

# Postpericardiotomy syndrome as a complication of nuss procedure - Case report

*Radoica Jokic, Jelena Antic, Smiljana Marinkovic, Svetlana Bukarica*

Institute for Children and Youth Health Care, Pediatric Surgery Clinic, Novi Sad, Serbia

## Abstract

**Introduction:** Pectus excavatum or funnel chest is a congenital deformity, with a wide range of physical disorders and psychological disturbances that are treated operatively. The Nuss procedure is a minimal invasive technique for the funnel chest correction with minimal surgical trauma, small scars, quicker postoperative recovery, and acceptable results. Many major and minor complications were recorded. In the group of minor complications, pleural and pericardial effusions are explained as an isolated incident or as a part of postpericardiotomy syndrome (PPS). Postpericardiotomy syndrome occurs after any chest surgery where the pericardium was opened. Conservative treatment, using anti-inflammatory drugs is usually adequate. But pericardiocentesis and drainage must be applied if there is no response to administered therapy.

**Case report:** This is a case report of a 17 year old patient who underwent Nuss operation for the funnel chest. In the postoperative course he developed a clinical picture of postpericardiotomy syndrome. He responded well to the medical treatment but needed to be reoperated for pectus bar displacement. Reoperation was performed with an uneventful postoperative recovery.

**Conclusion:** Postpericardiotomy syndrome is a serious complication that can occur following any surgical procedure due to the opening of the pericardium. Success in treatment depends on prompt diagnosis and appropriate therapy.

**Key words:** Pectus excavatum, Minimal invasive repair, children

## Introduction

Pectus excavatum or funnel chest is a congenital deformity with posterior intrusion of the sternum and costal cartilages, which may present at birth, or during the teenage growth spurt. There is

a wide range of physical disorders and psychological disturbances in these patients. The first attempt of surgical treatment was noted at the beginning of the twentieth century.<sup>1</sup> Ravitch contributed greatly in the surgical treatment of deformities during the 1950's. His surgical approach was implemented worldwide.<sup>1</sup> Afterwards a wide variety of techniques such as use of substernal meshes, silicone bags etc were utilized.

After tests in clinical practice numerous reports highlighted the difficulties with the Ravitch procedure. In 1998 Nuss presented in his historical article a 10-year experience with 42 patients using a minimal invasive repair of pectus excavatum (MIRPE). Soon after, his new technique became accepted by many surgeons around the world.<sup>1,2</sup> In the next period, there have been numerous modifications of this method such as the introduction of thoracoscopy, stabilization of the bar, using wire or absorbable sutures, and use of innovative instruments to facilitate the operation.<sup>1</sup>

Minimal surgical trauma with tiny scarring, quicker postoperative recovery, earlier return to daily activities, and overall gratifying results are perceived as clear advantages of this method.

Although the Nuss procedure belongs to a group of minimal invasive procedures, many major and minor complications were recorded. Major complications involved organ injury or a need for secondary surgical intervention. Minor complications could be resolved by endoscopy, puncture or drainage, without the necessity for extensive additional therapy. In the group of minor complications, pleural and pericardial effusions are explained as an isolated incident or as a part of postpericardiotomy syndrome (PPS).<sup>3</sup> Postpericardiotomy syndrome is a phenomenon that occurs after thoracic surgery due to the opening of the pericardium. Furthermore there is an accumulation of fluid in the pericardial space.<sup>4,5</sup> Clinical features of PPS include fever, chest pain, irritability, and

malaise. In the initial stage, the treatment consists of conservative medical therapy usually using anti-inflammatory drugs. If the response to conservative therapy is inadequate pericardiocentesis, drainage, and other surgical procedures should be considered,

### Case report

A 17 years old boy was hospitalized at the Clinic of Pediatric Surgery for surgical treatment of funnel chest. Antibiotic prophylaxis (Amoxicillin) was given due to the existence of mitral valve prolapse. We performed a Nuss operation in a balanced general anesthesia with epidural analgesia. Operative course was without complications, although we verified a small pericardium lesion during the placement of the introducer. Postoperatively, the patient was admitted to the surgical intensive care unit as standard. Antibiotic therapy (Ceftriaxon) was continued. Analgesia was performed using Metamisol parenteral, and a combination of Marcain and Morphine through the epidural catheter. Immediately following the operation, mild hypertension was recorded (154/89) but was normalized within a short period. During the first days postoperatively, the patient had mild chest pains. Auscultation showed diminished vesicular murmur in the basal part of the lung. Carbon dioxide retention was found in the gas analysis. A controlled chest X-ray showed a reduction of basal pulmonary transparency of the right side due to mild pleural effusion (Figure1). On the same side, a small apical pneumothorax was seen as well. The left costophrenic sinus was without fluid. The cardiac silhouette was in the physiological range. Physical respiratory management was performed according to the standards of postoperative treatment. On the fourth postoperative day the epidural catheter was removed. Pain was control was continued with combination of Trodon and Paracetamol. The patient was transferred to the ward and discharged home on the 7th postoperative day. Subsequently, postoperative period was uneventful.

After few days at home, the patient arrived at our clinic with pain on the left side of the chest. The non-steroidal anti-inflammatory steroid (Ketorolac) was prescribed immediately. On the echocardiograph (ECHO) findings, up-to 10ml of fluid

showed in the pericardial space. Obviously there were no signs of impending tamponade. Chest radiograph and ultrasound showed persistent pleural effusions in the right costophrenic sinus. The cardiac shadow was not enlarged (Figure 2). Pectus bar was in the correct position. Non-steroidal anti-inflammatory drugs were changed to ibuprofen. The applied therapy led to a complete reduction of fluid in the pericardial space. On the 7<sup>th</sup> day the child was discharged. Because of another recurrence of symptoms on the seventeenth postoperative day, the child's parents took the child to the Adult Cardiology Clinic. The patient was admitted as an emergency case for an appearance of a vast pericardial effusion. Nevertheless, the patient was transferred to our clinic again when the colleagues confirmed the rotation of the pectus bar of up to 30 degrees (Figure3). Therapy consisted of dual antibiotic therapy (Cefotaxim and Metronidazole), non-steroidal anti-inflammatory drug (Indomethacin), and analgetic (Trodon). Following the applied therapy, the patient gradually improved. On the follow-up of ECHO, a reduction of pericardial fluid was noted. However, there were fibrin adhesions and thickening of the tissue.

The child was once again discharged home with a plan for a reoperation (revision of the pectus bar position). Finally, we lost the confidence of parents and they had taken their own initiative. The child was reoperated at another institution where a recorection of the deformity was performed with satisfactory outcome.

### Discussion

Correction of funnel chest by Ravitch procedure consists of serial transections of the rib cartilages and horizontal mobilization of the sternum. Even though the results of the operation were satisfactory, the procedure was very demanding with a respectable number of complications. Since Donald Nuss introduced minimal invasive repair for pectus excavatum, surgeons around the world have begun to accept it with great enthusiasm.<sup>1</sup> The operation was successfully performed of all ages but the ideal time is just before puberty. Children who undergo this operation before the age of 8 have excellent results, but there is a great possibility of recurrence in their subsequent years. In

these situations changing the pectus bar needs to be considered. On the other hand it necessary to place more than one bar in over 50 percent of the adult cases. However, good cosmetic results, less surgical trauma, quicker postoperative recovery are invaluable in this technique. There are a great number of complications from minor complications to those that threaten life. The last European multicenter study showed a 9 percent of complications.<sup>3</sup> One of the most serious complications is the perforation of the heart. So far, six cases with perforation were recorded without any deaths.<sup>4</sup> Mechanism of this injury is the puncture of the right atrium and/or ventricle of the heart during the placement of introducer. Therefore, in the pre-operative program it is necessary to perform CT scan or MRI to assess the heart position and its relations to the sternum and chest wall.<sup>5</sup> Infections are mentioned in almost all clinical series. Therapy consists of appropriate systematic use of antibiotics without the removal of the pectus bar. Antibiotic prophylaxis is also advised together with use of all principles of asepsis during surgery.<sup>6</sup> Bar dislocation is one of the most common complications of the Nuss procedure that commonly occur during the first few weeks after the operation.<sup>3,5,7</sup>

It depends on the specific characteristics of the patient, muscular development, and also the learning curve of the operating team. In this case pectus bar was dislocated in the second week following the operation. Pectus bar stabilizer was used and fixed to the appropriate rib by PDS sutures except that we placed the bar above the muscular layer which may have been the reason for its shift. Further attention should be directed to the appropriate size of the bar, its modeling, accurate projection of entering and exiting points, fixation of the bar, and etc.

A question concerning the position of the bar placed either above or below the muscle layer is still expressed in literature. In our experience, there is less movement of the bar if set up under muscular layer. Pleural effusions after the Nuss procedure occur very often. Croitoru and associates described pleural effusions in 16.7% of patients.<sup>8</sup> Other authors reported these types of complications at a similar level but with only 1-3% of cases required thoracic drainage. Accumulation of pleural effusion is explained by the process of filling the empty space generated by raising the sternum

or as a nonspecific inflammatory response of the pleura. Some authors speculate that this is the immuno-allergic reaction to the pectus bar material.<sup>5</sup> In most cases, pleural effusion is resolved spontaneously after several days.

In the presented case pleural effusions were reported on the right side, but the fluid did not require surgical evacuation. Postpericardiotomy syndrome or by the author name Dressler syndrome is a complication of the Nuss-operation. It is a very rare but a potentially dangerous complication.<sup>4</sup> Even though the exact etiology is unknown one of the current hypotheses explains that the damage of the pericardial mesothelium is the trigger for antigen release. This stimulates the autoimmune response and results in the production of immune complexes.

During their attachment to the pericardial or pleural surface, the inflammatory reaction leads to the exudation and fluid accumulation. This process can occur in cases of minimal pericardial injury. Nomura and colleagues have shown that there is no correlation between the extensiveness of pericardial injury and development of pericardiotomy syndrome.<sup>9</sup> This syndrome is characterized by chest pain, fever, and leukocytosis. Relevant differential diagnoses of postpericardiotomy syndrome include pneumonia, pleuritis, atelectasis, viral or bacterial endocarditis, and wound infection. In therapy a 14-day course of nonsteroidal antiinflammatory medication is usually recommended. Ibuprofen and indomethacin have been successful in more than 90 percent of cases.<sup>2</sup> Recently, an increasing number of studies showed that the treatment of Colchicine (anti-rheumatic) as a monotherapy or together with non-steroidal anti-inflammatory drugs is very efficient for the pericardial effusion and especially for the prevention of relapse. Sometimes the use of steroids may be necessary and can speed up the recovery significantly. However, prophylactic use of systemic steroids neither prevents postpericardiotomy syndrome, nor reduces its intensity. In case of recurring symptoms, medical treatment should be extended up till 4-6 weeks. Surgical procedures such as Pericardiocentesis and drainage are applied only in situations of failure in medical therapy with a clear progression of hemodynamic disorders. In the presented case, conservative medical treatments were not completely successful. Despite the gradual improvement of the general condition, clinical and

echocardiography findings several relapses with pericardial effusion had occurred. In addition, the displacement of the pectus bar added troubles and complicated the clinical picture. Due to pectus bar displacement more than 30 degrees, a reoperation was necessary. After the stabilization of the patient's condition, all prerequisites for an uneventful operative and postoperative period were achieved. As a personal statement, it is very important to highlight that the operating team must include a psychologist. In making decisions for the operation, it is necessary to determine the psychological profile of the patient and parents. Confidence of the operating team greatly influences postoperative outcome.

### Conclusion

Nuss procedure is very practical and promising technique for the funnel chest treatment. Although there are a wide range of possible complications, most of these complications can be prevented and reduced by improving operative techniques, adequate preoperative preparations, and postoperative follow-ups. Postpericardiotomy syndrome is a serious complication that can occur after any surgical procedure with lesions of the pericardium. Success of the treatment depends on prompt diagnosis, appropriate and extended therapy.

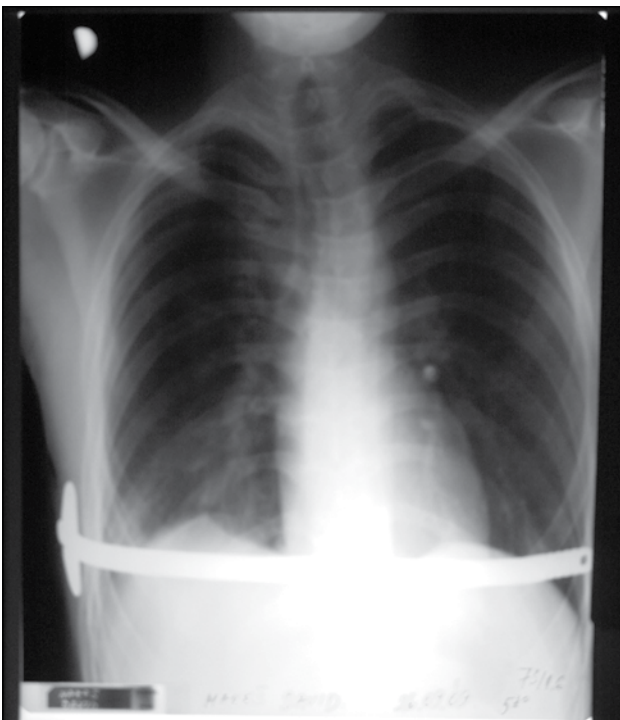


Figure 1. Postoperative chest radiography

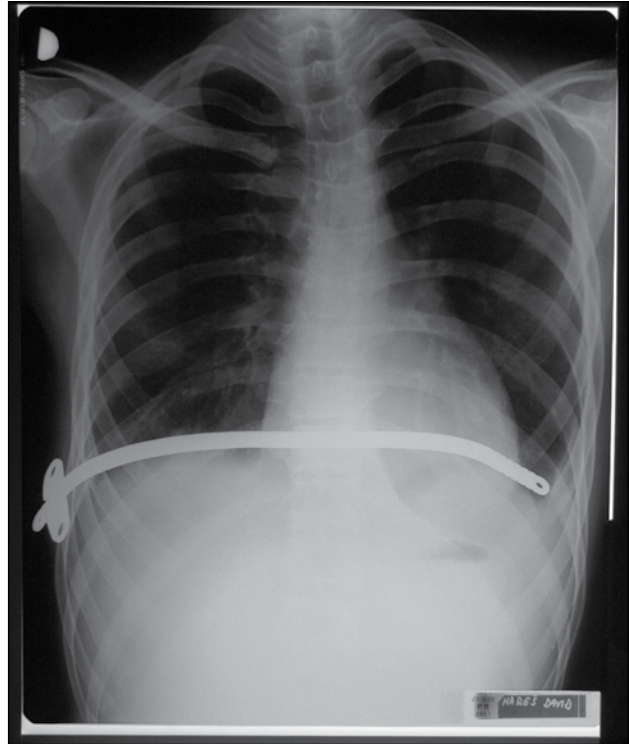


Figure 2. Chest radiography that showed pleural effusions in the right phrenicocostal sinus. The cardiac shadow was not enlarged

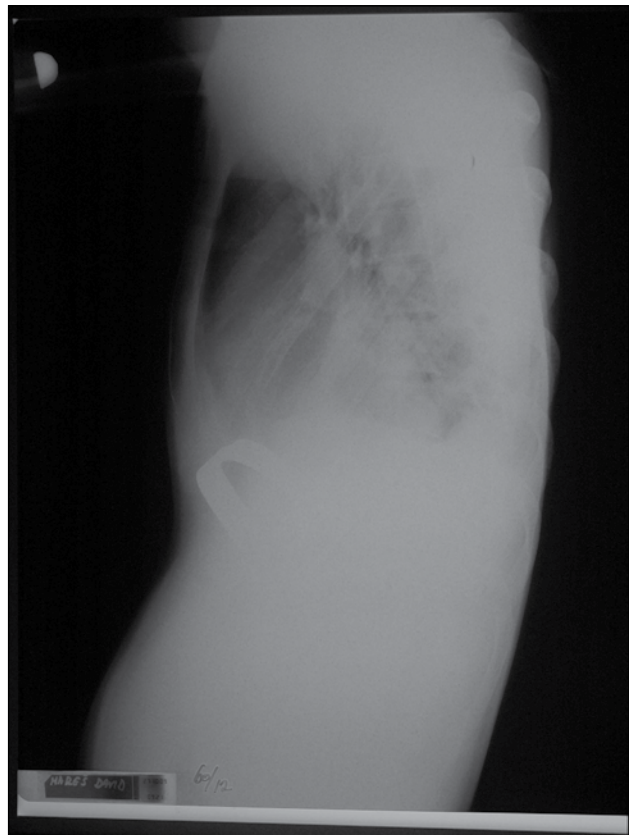


Figure 3. Chest radiography that showed the rotation of pectus bar by 30 degrees

## References

1. Nuss D, MB. *Minimally Invasive Surgical Repair of Pectus Excavatum. Seminars in Pediatric Surgery, 2008; Vol 17, No 3.*
2. Nuss D, Kuhn A, Obermeyer R. *Our Approach to MIS Repair of the Pectus Excavatum. Contemp Surg, 2007; 63(9):444-53.*
3. Park HJ, Lee SY, Lee CS. *Complications Associated With the Nuss Procedure: Analysis of Risk Factors and Suggested Measures for Prevention of Complications. J Pediatr Surg, 2004; 39:391-395.*
4. Berberich T, Haecker FM, Kehrer B, Thomas OE. *Postpericardiotomy Syndrome After Minimally Invasive Repair of Pectus Excavatum. Journal of Pediatric Surgery, 2004; Vol 39, No 11; E43.*
5. Castellani C, Schalamon J, Saxena A, Höellwarth M. *Early Complications of the Nuss Procedure for Pectus Excavatum: A Prospective Study. Pediatr Surg Int, 2008; 24:659-666.*
6. Calkins CM, Shew SB, Sharp RJ, Ostlie DJ, Yoder SM, Gittes GK, Snyder CL, Guevel W, Holcomb GW 3<sup>rd</sup>. *Management of Postoperative Infections After the Minimally Invasive Pectus Excavatum Repair. J Pediatr Surg, 2005; 40:1004-1007.*
7. Ong CC, Choo K, Morreau P, Auld A. *The Learning Curve in Learning the Curve: A Review of Nuss Procedure in Teenagers. ANZ J Surg, 2005; 75:421-424.*
8. Croitoru DP, Kelly RE Jr, Goretsky MJ, Lawson ML, Swoveland B, Nuss D. *Experience and Modification Update for the Minimally Invasive Nuss Technique for Pectus Excavatum Repair in 303 Patients. J Pediatr Surg, 2002; 37:437-445.*
9. Nomura Y, Yoshinaga M, Haraguchi T, et al: *Relationship Between the Degree of Injury at Operation and the Change in Antimyosin Antibody Titer in the Postpericardiotomy Syndrome. Pediatr Cardiol, 1994; 15:116-120.*
10. Sakac D, Kovacevic DV, Koracevic G: *Pericarditis and Cardiac Tamponade: Urgent Condition Not Only in Cardiology. Med Pregl, 2011; LXIV (3-4): 194-197.*

*Corresponding Author*

*Radoica Jokic,*

*Institute for Children and Youth Health Care,*

*Pediatric Surgery Clinic,*

*Novi Sad,*

*Serbia,*

*E-mail: jokicrs@gmail.com*



# Complicated peritonitis in patient on Chronical Peritoneal Dialysis – Case report

Tatjana Djurdjevic-Mirkovic<sup>1</sup>, Mladjan Protic<sup>2</sup>, Lada Petrovic<sup>1</sup>, Sinisa Mirkovic<sup>3</sup>, Slavenka Vodopivec<sup>1</sup>

<sup>1</sup> Clinical center of Vojvodina, Clinic for Nephrology and Clinical Immunology, Serbia,

<sup>2</sup> Clinical center of Vojvodina, Clinic for Abdominal, Endocrine and Transplant Surgery, Serbia,

<sup>3</sup> Faculty of Medicine Novi Sad, Clinic for Dentistry of Vojvodina, Department of Oral Surgery, Serbia.

## Abstract

**Introduction:** Peritonitis is the most common complication of peritoneal dialysis. Inflammatory bowel disease is the most common factor associated with peritonitis development.

**Case report:** A 62-year old patient has been undergoing the peritoneal dialysis program for six years. The patient had a long-term history of cardiopathy. In November 2008, the patient was treated for peritonitis. One month later he suffered acute myocardial infarction, thus surgical treatment was recommended. The patient was admitted at the Clinical Center of Vojvodina for preoperative preparation for cardiac surgery and creation of AV fistula. After 14 days the diarrheal syndrome occurred. The coproculture revealed *Clostridium difficile* toxin A, and the appropriate therapy was applied. Three days after termination of therapy the diarrheic syndrome recurred, and the infectologist confirmed relapse of *Clostridium difficile* enterocolitis. At the same time, dialysate turbidity and clinical picture of acute abdomen was evident. Radiography and computed tomography revealed ascendant colon perforation. Subtotal colectomy with terminal ileostomy was performed, and the patient was transferred to hemodialysis program.

**Conclusion:** The described peritonitis case is a rare and severe complication of peritoneal dialysis.

**Key words:** enterocolitis, peritonitis, colectomy

## Introduction

Peritoneal dialysis is one of the modalities used for treatment of end-stage chronic kidney failure. There are numerous advantages of peritoneal dialysis over hemodialysis: it is simpler to perform and safer for the patient, the patient is independent of the hospital, i.e. treatment can be done at home, it is suitable for school-age children, students,

working patients, and it provides a better quality of life. Major disadvantages of peritoneal dialysis are infections – peritonitis, exit site infection and tunnel infection. Nowadays, PD-related complications show a decreasing incidence compared to previous period. Application of Tehckhoff catheter, PVC dialysate bags, technological advances in the field of dialysis systems and solutions as well as introduction of automated peritoneal dialysis have reduced the rate of aforementioned infection complications to a minimum (averagely one peritonitis episode in 24-36 months of treatment) (1). Bacteria that normally colonize the skin of hands and nasal mucosa (Staphylococci) are the *most common* etiologic agents of peritonitis. Episodes of peritonitis can be caused by bacteria normally present in the intestinal flora in consequence of intestinal permeability or intestinal diseases such as inflammation, diverticulosis, and/or *gastrointestinal tract perforation*. Such peritonitis complications are less frequent, yet clinically severe and more difficult to treat. This pertains particularly to peritonitis caused by Gram negative bacteria (*Escherichia coli*) that are highly resistant to therapy. This type of peritonitis is mostly associated with loss of peritoneal catheter and may in some cases result even in fatal disease outcome (2,3,4,5,6,7,8). In very rare cases, peritonitis can be associated with enterocolitis caused by *Clostridium difficile*, an anaerobic Gram positive, spore-forming bacterial species (9). The organism is widely distributed in the nature and can be found in the soil, lower intestinal tract of animals, healthy children and adults. It is shed in the feces of the host, and the infection can be acquired from the spores germinating in the digestive system or spores and vegetative forms of the organism transmitted via contaminated food, water or through the unwashed hands (10). *C.difficile* has been recogni-

zed as the leading nosocomial pathogen, frequently causing infection in hospitalized patients and the transmission occurs mostly via the contaminated environment and inadequate hand hygiene of medical staff. Pathogenic strains of *C. difficile* produce two distinct exotoxins, A and B; however, some strains produce only B toxin. *C. difficile* infection results from an *impairment* of the normal intestinal flora or gastrointestinal *motility disorders*. Clinical manifestation can range from asymptomatic colonization to different grades of diarrhea, and even life-threatening pseudomembranous colitis. The main symptoms include pain and cramps in the abdomen, profuse, slimy, greenish, liquid and stinky stools accompanied with high body temperature. Laboratory findings commonly reveal elevated levels of acute inflammation reactant (11). The infection generally occurs after exposure to antibiotics (lincomycin, clindamycin, ampicillin, cephalosporins, etc.) (12). Major predisposing factors for development of *C. difficile* enterocolitis, besides the antimicrobial therapy, are: cytostatic, radio- and immunosuppressive therapy, prolonged hospital stay for more than 10 days, application of invasive gastrointestinal procedures, administration of enema as well as advanced age of the patient (more than 65 years) (11).

In this paper, we presented our experience with *C. difficile* enterocolitis in a patient on peritoneal dialysis and peritonitis occurring as a complication of inflammation process in the colon.

### Case report

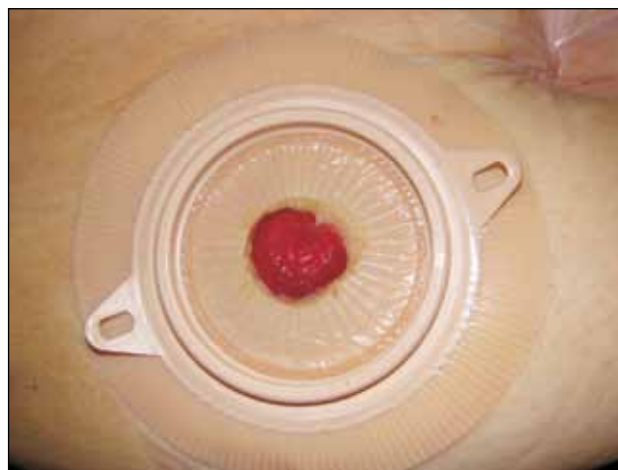
A 62-year old patient has been undergoing *chronic peritoneal dialysis, using the CAPD method*, over the past 6 years. The patient had a long-term history of cardiovascular disease, and was treated for dilatation cardiomyopathy and mitral and tricuspid valve insufficiency. In November 2008, peritonitis was diagnosed (dialysate culture negative, dialysate WBC count 285/m<sup>3</sup>, exit site smear revealed coagulase negative *Staphylococcus spp*). One month earlier, patient had dental intervention ( noncomplicated tooth extraction ) with appropriated antibiotics prevent. Intraperitoneal (cephalosporins) and local (aminoglycoside solution) antimicrobial therapy was administered resulting in negative finding of the exit site smear,

without complications. One month after peritonitis was cured, the patient suffered acute lateral wall infarction and was hospitalized at the Institute for Cardiovascular Diseases Sremska Kamenica for further treatment. During the hospitalization period, the patient continually administered CAPD. Coronarographic examination revealed three-vessel coronary disease and IV stage mitral insufficiency, thus surgical treatment was recommended. Once the coronary status was stabilized, on December 17, 2008, the patient was transferred to our Clinic for pre-operative *preparation for cardiac surgery and creation of arterio-venous (AV) fistula for potential hemodialysis procedure*. Two weeks later, *diarrheal syndrome developed (watery stools, 5-6 times a day) accompanied with febrile state and abdominal cramping*. Laboratory examination confirmed elevated level of acute inflammation reactants (SE 66/ mm/h, Le 10.1 x 10<sup>9</sup>/l, CRP 28.2 mg/l, fibrinogen 5.05 g/l, albumins 37.7 g/l). Bacteriological examination of the feces revealed *Clostridium difficile* toxin A. After consulting with infectologist, peroral antimicrobial therapy was applied (orvagil, vancomycin) along with a strict dietary regimen (tee, toast) resulting in gradual improvement of general health status of the patient and normalization of stool number and consistency. Laboratory findings revealed decrease in level of acute inflammation reactants. In the same period, *Clostridium difficile* toxin A positive enterocolitis was detected in another two patients at the Clinic. During hospitalization, the patient continued with regular peritoneal dialysis. Bacterial cultures of the dialysate, catheter exit site and nose and throat were negative, whereas dialysate WBC and RBC counts were within the reference range. On January 29, 2009 the relapse of diarrheal syndrome occurred, accompanied with pronounced abdominal cramps, worsening of general health status, fever and hypotension. The infectologist diagnosed a relapsing *C. difficile* enterocolitis and ordered an appropriate antimicrobial therapy and strict dietary regimen. Laboratory findings confirmed increased values of inflammation parameters (SE 96/ mm/h, Le 12.7 x 10<sup>9</sup>/l, CRP 32.5 g/l, fibrinogen 6.34 g/l, albumins 30.3 g/l). Within 24 hours, worsening of local abdominal finding was observed, manifested by pronounced meteorism, muscular defense in the ileocecal region

and gurgling phenomenon on auscultation. At the same time, dialysate turbidity and reduced ultrafiltration were observed during peritoneal exchange. Examination of the dialysate confirmed elevated WBC and RBC counts (Le 2980/m<sup>3</sup>, Er 70/m<sup>3</sup>), thus intraperitoneal administration of aminoglycosides and vancomycin was started. *Dialysis fluid culture revealed the presence of Escherichia coli as a causative agent of peritonitis. Control stool cultures were positive for C.difficile. Considering the clinical course of the disease colonoscopy has not been performed, thus native x-ray examination of the abdomen followed by computed tomography (CT) was performed, revealing ascending colonic perforation. Abdominal surgeon recommended urgent surgical treatment due to suspicion of acute abdomen. Surgical procedure confirmed occurrence of the toxic megacolon, gangrene of the ascending colon and peritonitis, thus subtotal colectomy with formation of terminal ileostomy at anterior abdominal wall was performed (Figures 1, 2). Postoperative course was regular resulting in full recovery of the patient, who was then transferred to chronic hemodialysis program.*



*Figure 1. Toxic megacolon with gangrenous changes and microperforation*



*Figure 2. Ileostomy with the ring seal of anus bag*

### Discussion

Peritonitis, along with catheter exit site infections are the most common complications occurring in patients on peritoneal dialysis. Unlike surgical peritonitis, PD peritonitis is less severe and more likely to have mild disease course and mostly results in complete recovery after appropriate antimicrobial therapy (mainly intraperitoneal). In rare cases, inadequate response to therapy results in the removal of PD catheter and transfer of the patient to HD. Only exceptionally, highly severe complicated peritonitis may develop, which is associated with high mortality rate. Such peritonitis forms are mostly due to Gram negative bacteria (2). Inflammatory bowel disease plays a role in the etiology of these peritonitis types in PD patients, and *C.difficile* is frequent causative agent of enterocolitis. It is mostly associated with preceding antimicrobial therapy (3). Treatment of *C.difficile* enterocolitis according to adopted guidelines (metronidazole, vancomycin) mostly results in suppression of the inflammatory process in the intestines; however, in some cases relapse may occur. Pronounced inflammatory changes in the intestines may result in intestinal perforation and development of severe peritonitis associated with high mortality rates.

Clinical experiences confirmed that increased mortality rate in patients with CRF as well as high relapse incidence can be attributed to *C.difficile* enterocolitis (13,14,15). In this study, we presented a case of patient on chronic PD (CAPD) in whom antimicrobial treatment of peritonitis

resulted in development of *C.difficile* enterocolitis and subsequent recurrence of underlying disease. Further course of the disease revealed development of toxic megacolon and intestinal perforation. Timely diagnosis and surgical treatment resulted in effective sanitation of this severe complication and patient was transferred to a chronic HD program. Complicated peritonitis is highly uncommon in patients on PD. According to most authors, *mortality rate attributed to these peritonitis types is very high within general patient population, particularly in patients on dialysis (associated comorbidity)* (13, 15, 17). Medical literature contains reports on individual peritonitis cases with lethal outcome, in which *C.difficile* was isolated from peritoneal dialysate fluid (10). Some recent research has confirmed positive effects of immunoglobulins in cases of refractory *C.difficile* enterocolitis in patients with CRF or patients on dialysis (16). Considering high morbidity and mortality rates in these patients, an early diagnosis of inflammatory intestinal changes, peritonitis and severe complications (intestinal perforation) is of paramount importance. Surgical treatment is the method of choice for successful curing and reducing mortality rate, which has also been demonstrated in this report.

### Conclusion

The reported case of severe peritonitis in patients on peritoneal dialysis, in whom relapsing *C.difficile* enterocolitis and development of toxic megacolon and gangrene of the ascending colon was diagnosed, strongly indicates that inflammatory intestinal diseases can induce life-threatening complications. Antibiotic therapy, transmission of pathogens from the environment, prolonged hospitalization and advanced age of the patient have most likely contributed to development of such severe complication. Only timely diagnosis and surgical treatment of the complication (intestinal perforation) can ensure successful outcomes and decrease in dialysis mortality rate.

### References

1. Radojević M, Maksić Dj, Kovačević Z, Hrvačević R, Veljančić Lj. Mesto i uloga peritoneumske dijalize u modelu integrisanog lečenja terminalne bubrežne insuficijencije. In: Maksić Dj, editor. Peritoneumska dijaliza. Beograd 2006: 35-46.
2. Maksić Dj, Hrvačević R, Stanković-Popović V, Mirović V. Peritonitis. In: Maksić Dj, editor. Peritoneumska dijaliza. Beograd 2006: 273-300.
3. Gokal R, Ramos JM, Francis DM, Ferner RE, Godship TH, Proud G, Bint AJ, Ward MK, Kerr DN. Peritonitis in continuous ambulatory peritoneal dialysis. Laboratory and clinical studies. Lancet 1982; 2 (8312): 1388-91.
4. Keane WF et al. Adult peritoneal dialysis-related peritonitis treatment recommendations: 2000 Update. Perit Dial Int 2000; 20: 396-411.
5. Laroche MC, Alfa MJ, Harding KM. Isolation of toxigenic *Clostridium difficile* from dialysate fluid in a fatal case of chronic ambulatory peritoneal dialysis-related peritonitis. Clinical Infectious Disease 1997; 25: 1248-48.
6. Barany P, Stenvinkel P, Nord CE, Bergstrom J. *Clostridium difficile* infection- a poor prognostic sign in uremic patients? Clin Nephrol 1992; 38 (1): 53-7.
7. Zehia M, de Zoysa JR, Collins JF. Is computerized tomography useful in identifying abdominal catastrophes in patients presenting with peritonitis? Perit Dial Int 2008; 28 (4): 385-390.
8. Zang ChY, Chen TW, Lin ZP, Lin ChCh, Ng ZZ, Zang WCh, Chen JY. Determinants of catheter loss following continuous ambulatory peritoneal dialysis peritonitis. Perit Dial Int 2008; 28 (4): 361-370.
9. Borriello SP. Pathogenesis of *clostridium difficile* infection. J Antimicrob Chemother 1998; 41( SupplC): 13-9.
10. Kuijper EJ, Coignard B. Emergence of *Clostridium difficile*-associated disease in North America and Europe. Clin Microbiol Infect Dis 2006; 12: 2-18.
11. Guerrant RL et al. Practice guidelines for the management of infectious diarrhea. Clin Inf Dis 2001; 62: 331-350.
12. Bartlett JG. Antibiotics-associated diarrhea. N Eng J Med 2002; 346: 334-9.
13. Kovithavong Th. *Clostridium difficile* colitis associated with chronic renal failure. Nephrol Dial Transplant 1999; 14: 2256-7.

14. Cunney RJ, Magee C, McNamara E, Smyth EG, Walshe J. *Clostridium difficile* colitis associated with chronic renal failure. *Nephrol Dial Transplant* 1998; 13: 2842-6.
15. Popoola J, Swann A, Warwick G. *Clostridium difficile* in patients with renal failure-management of an outbreak using biotherapy. *Nephrol Dial Transplant* 2000; 15: 571-4.
16. Chandrasekar T, Naqvi N, Waddington A, Cooke RPD, Anijeet H, Gradden CW, Abraham KA, Wong CF. Intravenous immunoglobulin therapy for refractory *Clostridium difficile* toxin colitis in chronic kidney disease: case reports and literature review. *Nephrol Dial Transplant Plus* 2008 1 (1): 20-2.
17. Ostrvica E, Ostrvica Dz, Vahidin K. Dosage of erythropoetin and iron replacement therapy in patients on chronic hemodialysis. *HealthMed* 2011; 4 (1): 138-142.

*Corresponding Author*

Tatjana Djurdjevic Mirkovic,  
Clinical Center of Vojvodina,  
Clinic for Nephrology and Clinical Immunology,  
Novi Sad,  
Serbia,  
E-mail: sinisa.mirkovic021@gmail.com

# New Ruthenium Complexes with Schiff Bases as Mediators for the Low Potential Amperometric Determination of Ascorbic Acid, Part II: Voltametric and Amperometric evidence of mediation with Bromo-derivative of Tetraethylammonium dichloro-bis[N-phenyl-5-halogeno -salicylideniminato-N,O]ruthenat (III)

Emira Kahrovic, Emir Turkusic

Department of Chemistry, Faculty of Science, University of Sarajevo, Sarajevo, Bosnia and Herzegovina

## Abstract

A bulk modified screen printed electrode was prepared with *Tetraethylammonium dichloro-bis[N-phenyl-5-bromo -salicylideniminato-N,O]ruthenat (III)* using carbon ink. The cyclovoltamograms scanned between -0.4 V to + 0.4 V vs. Ag/AgCl exhibited apparent increase of current responses in phosphate buffered ascorbic acid solution due to modification of SPE. The amperometric measurements in hydrodynamic and flow injection mode, performed at applied potential of 0.22 V vs. Ag/AgCl, showed fast current responses with increasing ascorbic acid concentration.

**Key words:** Ru (III) complexes, Schiff Bases, Amperometry, Ascorbic acid, Carbon modified screen printed electrode.

## Introduction

Electrochemical characterization of complex compounds is of great importance due to their use in many fields especially in catalysis, electron transfer mediation and anticancer therapy. Therefore the relationship between redox potentials and other chemical and physical properties of metal complexes has steadily the subject of numerous investigations. The inductive effects of ligands and substituents on the ligands, as well as stereochemistry of the complex, have a particularly important role in the electrochemical behavior of metal complexes. From this standpoint the ruthenium complexes like chloride-bridged triruthenium complexes with linear Ru(III)-Ru(II)-Ru(III) array were investigated (1-2) demonstrating how electrode potentials reflect the changes in ligands and substituents on ligands.

Apart from the structure-electrode potential relationship, ruthenium complexes were subject of investigation in electrode modification for determining various analytes like ascorbic acid (3-5). In continuation of our earlier work (Part I) we report here the first results of the investigation of bromo-derivative of *Tetraethylammoniumdichloro-bis[N-phenyl-5-halogeno -salicylideniminato-N,O]ruthenat (III)* for determination of ascorbic acid. The complex is hereafter referred to as  $Et_4N[Ru(SB^II)_2Cl_2]$ , where  $SB^II$  denotes an anionic form of 5-bromosalicylideneaniline Schiff base ( $HSB^II$ ). *Chloro-derivative of titled compound, reported in Part I, has evidently demonstrated the properties of electron-transfer mediation on carbon SPE for ascorbic acid determination. Here we briefly argued voltametric and amperometric evidence that bromo- derivative of titled compound also can serve as a mediator in new sensor for ascorbic acid determination.*

## Experimental

*Synthesis of  $Et_4N[Ru(SB^II)_2Cl_2]$ . 5-bromosalicylideneaniline ( $HSB^II$ ) and  $Et_4N[Ru(SB^II)_2Cl_2]$  were prepared according to published procedures (6-7). The solution of Schiff base (2 mmol ; 0.56 g  $HSB^II$ ) in 30 mL ethanol absolute was added to the solution of  $RuCl_3 \cdot x 3H_2O$  (1 mmol, 0.26 g) in absolute alcohol (10 mL). The mixture was refluxed for 3 hours at 65-70 ° C after which the volume was reduced in rotary evaporator to the half of the initial volume. The precipitation was performed by adding of tetraethylammonium bromide (2 mmol, 0.32 g) dissolved in water (10 mL). The dark green solid was washed with diethyl ether and dried over  $P_2O_5$ .*

**Apparatus.** Cyclovoltametry (CV), Hydrodynamic amperometry (HA) and Flow injection analysis (FIA) were performed with an electrochemical workstation Autolab potentiostat/galvanostat (PGSTAT 12).

**Reagents and solutions.** All chemical of analytical grade were purchased from commercial sources and used without further purification. L-ascorbic acid was obtained from Fluka, other compounds were obtained from Merck. A buffer stock standard solution containing 10 g /L ascorbic acid and working standard solutions were prepared before use.

**Fabrication of the electrodes.** A bulk modified carbon SPE were prepared by mixing of carbon ink (C50905DI, Gwent, Pontypol, UK) and  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$ . For amperometric measurements in HA mode SPE was protected by an insulating layer on the electrode surface leaving an area of 10 mm<sup>2</sup> electrically non-insulated.

**Procedures.** Cyclic voltammetry, Hydrodynamic amperometry and Flow injection analysis procedures were performed as we reported in Part I.

## Results and discussion

The complexes of general formula  $\text{Et}_4\text{N}[\text{Ru}(\text{SB})_2\text{Cl}_2]$ , where SB represents anionic form of 5-halogeno-salicylideneaniline Schiff bases ( $\text{SB}^{\text{I}}$ = chloro and  $\text{SB}^{\text{II}}$ =bromo-derivative) were prepared for the first time in our laboratory. Ru (III) is tightly coordinated with two monobasic (NO) Schiff bases derived from 5-x-salicylaldehydes and aniline (Figure 1.) through deprotonated phenolic oxygen and azometine nitrogen (Figure 2.) in an octahedral environment.

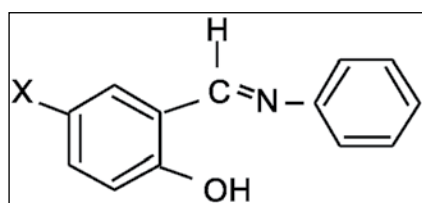


Figure 1. Schiff base; 5-x -Salicylideneaniline ( $x = \text{Cl}$ ,  $\text{HSB}^{\text{I}}$ ;  $x = \text{Br}$ ,  $\text{HSB}^{\text{II}}$ )

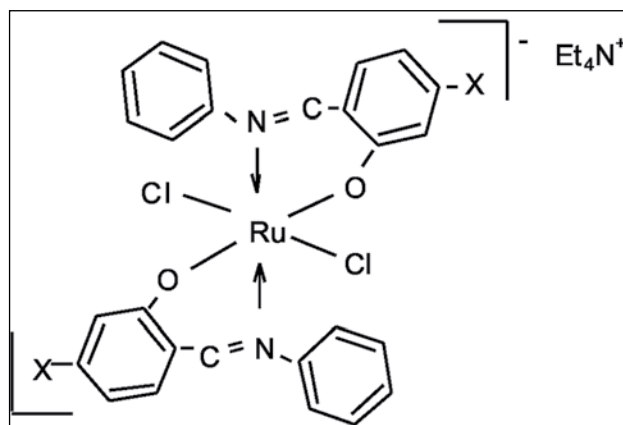


Figure 2. Tetraethylammonium dichloro-bis[N-phenyl-5-halogeno-salicylideneiminato-N,O]ruthenate (III)

**Electrochemical examination of  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{I}})_2\text{Cl}_2]$**  ( $\text{SB}^{\text{I}}$  -represents chloro-derivative described in Part I) has shown clear evidence for electron transfer mediation of carbon screen printed electrode for determination of ascorbic acid, therefore bromo-derivative is also investigated.

**Voltammetric behavior of  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$ -modified carbon ink electrodes.**

Cyclic voltammograms of  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$  carbon bulk modified SPE in ascorbic acid solution and carbon bare electrode in the same buffered solution (pH= 7.4) notably differ (Figure 3. ) showing an apparent increase of current responses more than three times what has already been found in chloro-derivative of titled compound (Part I).

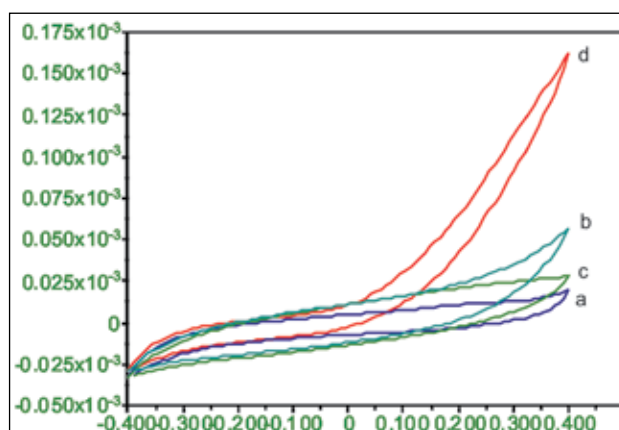


Figure 3. Cyclic voltammograms: a- bulk modified electrode by  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$ ; b-bare SPE electrode with ascorbic acid; c- bare electrode; d- ascorbic acid at  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$  modified electrode

**Hydrodynamic amperometry.**  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$  modified carbon SPE was used as an amperometric detector for ascorbic acid. The current responses to dynamic changes of ascorbic acid concentration in phosphate buffer were fast and electrochemical equilibrium were observed in few seconds (Figure 4.). The addition of each new quantities of ascorbic acid (1 mL equal 1000 ppm) in 50 mL measurement cell corresponds to the increasing concentration of 20 ppm of ascorbic acid and produces current response of about  $1.8 \mu\text{A}$ , as a proof that  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$  carbon SPE modified electrode can be used as an amperometric sensor for ascorbic acid.

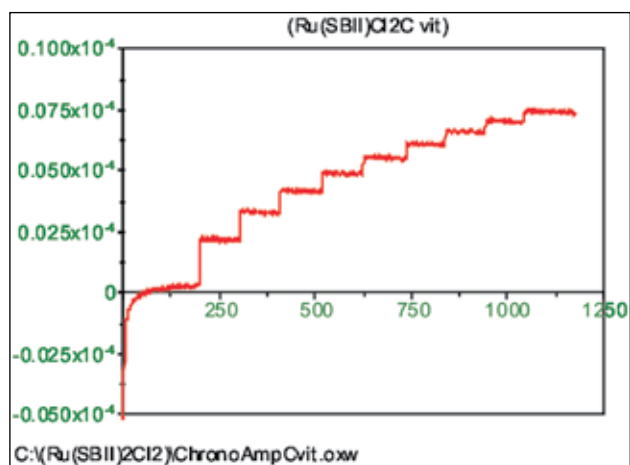


Figure 4. Hydrodynamic amperogram of ascorbic acid with  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$  carbon bulk modified SPE under bath conditions; operating potential 0.22 V vs Ag/AgCl electrode in phosphate buffer, pH 7.4. Steps correspond to the addition of 1 mL ascorbic acid concentration of 1000 ppm.

**Flow injection analysis with an amperometric detection.** Flow injection analysis (FIA) for  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$  modified carbon SPE was performed at applied potential of 0.22 V vs. Ag/AgCl reference electrode. Current peak heights, as a result of the injections of different ascorbic acid concentrations, evidently exhibited fast response and reproducibility of new sensor for ascorbic acid (Figure 5.)

In accordance with Hammett equation in its electrochemical form and parameter  $\sigma$ , which refers to the influence of substituents on the aromatic ring to the value of electrode potentials (8), a significant difference in the electrochemical behavior of complex formulated by  $\text{Et}_4\text{N}[\text{Ru}(\text{SB})_2\text{Cl}_2]$  where SB represent 5-x -Salicylideneaniline

( $x = \text{Cl}, \text{HSB}^{\text{I}}; x = \text{Br}, \text{HSB}^{\text{II}}$ ) is not expected. The first results presented here, for both compounds, are in good accordance with this presumption. On the ground of first evidences Ru (III) compounds of general formula  $\text{Et}_4\text{N}[\text{Ru}(\text{SB})_2\text{Cl}_2]$  showed the properties of the promising electron transfer mediators for the determination of ascorbic acid.

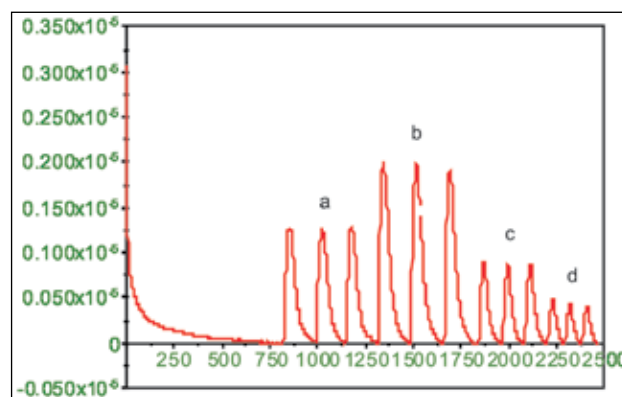


Figure 5. FIA current responses  $\text{Et}_4\text{N}[\text{Ru}(\text{SB}^{\text{II}})_2\text{Cl}_2]$  carbon modified SPE; a-250, b-500, c-125, d-50 (ppm); flow rate 0.4 mL/min; injection volume 100  $\mu\text{L}$ ; applied potential  $E = 0.22 \text{ V}$

## Conclusion

The first inspection of possible electrochemical uses of Ru(III) complexes with 5-x -Salicylideneaniline ( $x = \text{Cl}, \text{Br}$ ) Schiff bases showed that  $\text{Et}_4\text{N}[\text{Ru}(\text{SB})_2\text{Cl}_2]$  compounds are good electron transfer mediators and that they could be used for developing of new amperometric sensors for the determination of ascorbic acid. In future, we will focus our attention to optimize measurement parameters, linear range and detection limit in order to develop a new sensor for ascorbic acid determination in real samples.

## Acknowledgements

This work was supported by Ministry of Education and Science of Sarajevo Canton, Bosnia and Herzegovina (project 02-05-16280-9.18/07). The authors are also grateful to Bosnalijek Pharmaceutical and Chemistry Industry, Sarajevo, Bosnia and Herzegovina.



## References

1. A. Bino and F.A. Cotton, *J. Am. Chem. Soc.*, 102 (1980) 608.
2. F.A. Cotton and R.C. Torralba, *Onotg. Chem.*, 30 (1991) 3293.
3. B. Nalini, S. S. Narayanan, *Analitica Chimica Acta*, 405 (2000) 93.
4. RLC Thiago Paixao, M. Bertotti, *J. of Pharmaceutical and Biomedical analysis*, 46 (2008) 528.
5. P. M. Santos, B. Sandrino, T. F. Moreira, K. Wohnrath, N. Nagata and C. A. Pessoa, *J. Braz. Chem. Soc.*, 18 (2007) 93.
6. P.P. Dholakiya and M.N. Patel, *Synth. React. Inorg. Met.-org.Chem.* 32 (2002) 753.
7. E. Kahrovic, S. Dehari, D. Dehari, H. Reci, S. Begic, N. Ljubijankic. *Technics Technologies Education Management-TTEM.* 5 (2010) 799.
8. P. Zanello, *Inorganic Electrochemistry, Theory Practice and Application*, Royal Chemical Society, 2003. p 580-581.

### *Corresponding Author*

*Emira Kahrovic,  
Department of Chemistry,  
Faculty of Science,  
University of Sarajevo,  
Sarajevo,  
Bosnia and Herzegovina,  
E-mail: emira\_kahrovic@yahoo.com*

# 24 h Holter-monitoring of heart in diagnostics of cardiac rhythm disorders in University of Sarajevo students

Zana Pozderac<sup>1</sup>, Nehru Mackic<sup>2</sup>, Zumreta Kusljagic<sup>3</sup>

<sup>1</sup> J.U.K.S. Institute for Health Protection of Students University of Sarajevo, Bosnia and Herzegovina,

<sup>2</sup> Privatna internistička ordinacija, Sarajevo, Bosnia and Herzegovina,

<sup>3</sup> UKC –Tuzla, Klinika za kardiologiju, Bosnia and Herzegovina.

## Abstract

**Introduction:** Heart rhythm disorders affect the contractility of myofibrils, reducing it mostly indirectly. In cases where an abnormal heart rhythm disturbs the coronary circulation and cause ischemia of myofibrils, it influences the contractility in a depressive manner. It is believed that changing the rhythm can directly affect the contractile force, increasing it what is happening when accelerating cardiac action or after extrasystole.

**Objective:** To determine the frequency, type and complexity of heart rhythm disorders via 24-h Holter heart monitoring in University of Sarajevo students.

**Materials and methods:** The study was prospective, retrospective, clinical, descriptive and analytical. The sample consisted of the University of Sarajevo students. The sample survey included students in regular and systematic examinations at Public Institute for Health Protection of University of Sarajevo Students in the period 2006 - 2009.

**Results of investigation:** Based on this study, the following disorders of cardiac rhythm were recorded: bradycardia in 78 patients or 71.56%, tachycardia in 100 patients or 91.74%; pauses in 48 patients or 44.03%, ventricular extrasystole in 98 patients or 89.08%; couplet in 79 patients or 89.08%; triplet in 43 patients or 39.44%; bigeminy in 62 patients or 56.88%; trigeminy in 48 patients or 44.03%; discontinued ventricular rhythm in 26 patients or 23.85%; ventricular uninterrupted rhythm in 7 patients, or 6.42%, ventricular tachycardia interrupted in 3 patients, or 2.75%; continuous ventricular tachycardia in 5 patients, or 4.58%, supraventricular extrasystole in 98 patients or 89.90%, supraventricular tachycardia in 82 patients or 75.22%; Atrial atrium in 76 patients or 82.84%, ri-

ght bundle branch block in 17 patients or 15.59%; left branch block 2 or 1.83%, nodal rhythm in 8 patient or 7.34%, Torsade de pointes in 5 patients, or 4.59%, and AV block in 35 patients or 32.11%.

**Key words:** cardiac rhythm disorders, 24-h Holter monitoring in the heart of the University of Sarajevo students.

## Introduction

Heart rhythm disorders affect the contractility of myofibrils, mostly by reducing it indirectly. In cases where an abnormal heart rhythm disturbs the coronary circulation it causes ischemia of fibers, which influences depressively the contractility. It is believed that changing the rhythm can also directly affect the contractile force by increasing it, what is happening when accelerating or after cardiac extrasystole. Main mechanisms in which arrhythmias disturb hemodynamic relationships are:

- a) Change in the duration of diastole;
- b) disorders of atrial contraction;
- c) changing the sequence of contractions of ventricle.

Rhythm disorders are reflected in the coronary flow by aggravating it. Tests have shown that early atrial attack decreases coronary flow by 5%, while early ventricular attack reduces it by 25%. During continuous ventricular tachycardia coronary flow can be reduced by 30%, and in untreated fibrillation by 40%. During ventricular tachycardia coronary flow is reduced by 60%, and in ventricular fibrillation cannot be measured. The consequences of reduced coronary flow may be seen so that during tachycardia may exist distinctly pathological ST-segment depression, and after extra systo-

le could exist post-extra systolic phenomenon of inverse-T-wave, in the first QRST-complex that follows the extra systole. Consequences of arrhythmia may have an impact on cerebral circulation. Frequent ventricular extra systole can reduce flow for 8%, and frequent ventricular extrasystole for 12%. During tachyarrhythmia coronary flow may drop to 14-25%, with tachycardia it declines by 40%, and ventricular tachycardia for 40-75%.

Each arrhythmia if a person feels it, is harassing and intimidating sensation in the chest.

Doctor is obliged to assess the significance of arrhythmias, or to assess:

- whether the arrhythmia can not be ignored, and in this case, the patient should be convinced of her innocence and released him fear;
- are check-ups needed to monitor the arrhythmia;
- whether it should be treated;
- whether to treat it urgently?

To estimate the significance of arrhythmia an important factor is whether at the same time there is a cardiac disease or arrhythmias occur in people without signs of heart disease.

A person without heart disease is considered:

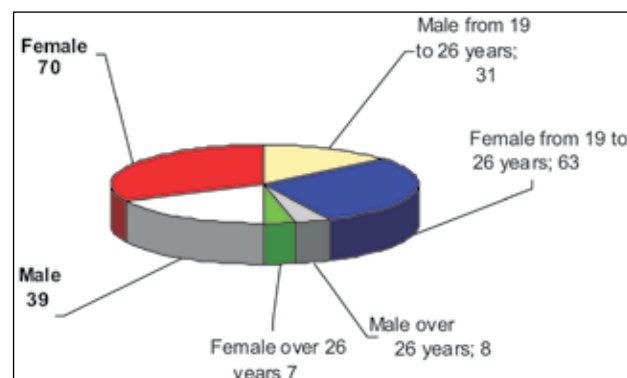
- A person who does not give anamnesis data of functional heart disturbances, dyspnea, palpitations, fatigue, pre-syncope, syncope;
- The person who have a normal ECG findings;
- Persons who have a normal physical finding on the heart and normal arterial tension.

The significance of arrhythmias in patients with heart disease is far more important. In what portion arrhythmia will disturb the functional ability of the heart depends on the hemodynamic disturbances that it causes. The severity of hemodynamic disturbance will depend on the type of arrhythmia and the type of heart rhythm disorders. The significance in people with heart disease is reflected in the fact that the initial disturbance of rhythm as extrasystole, can initiate the formation of severe and very severe rhythm disorders.

### Material (Respondents)

The study was prospective, retrospective, clinical, descriptive and analytical. The sample consisted

of students at the University of Sarajevo. The sample survey included students in regular and systematic examinations at the Public Institute for Health Protection of University of Sarajevo students in the period 2006 - 2009 years. The first comprehensive analysis was performed on 109 students. Our intention is to continue to study and include as many students of all ages and to make a comparative study with similar studies from the region.



The largest number of patients belonged to age group: 19-26 years with 63 female patients or 90% and 31 male patients or 79.49% over 26 years, 7 female patients or 10% 8 or 20.51% male patients or a total of 94 (86.24%) of all examined. The difference is highly significant at  $p < 0.0005$  for the male population at  $t = 3.68$ , and for the female population at the level of  $p < 0.0000$  with  $t = 6.69$ , and for the total sample at  $p < 0.0000$  with  $t = 7.57$ . Total 70 females or 64.22% and 39 men or 35.78%

### Research methods

Prolonged and continuous recording of ECG was introduced by Holter in 1961. Introducing Holter-monitors in clinical practice started in the era of dynamic or outpatient electrocardiography. To record the electrocardiogram bipolar leads are used with the electrodes placed on the arms and legs, as well as unipolar wires with electrodes placed on precordium.

Bipolar leads with electrodes placed on precordium to monitor the ECG on a monitor or record with Holter monitor are used. This removes the restriction of movement of patients. Unlike conventional bipolar leads, these leads are commonly referred to as continuous monitor-leads. The existence of the electric field of the heart that creates the electrical activity of myocardial cells may electrocardiographic device sense and registers

across the electrode pair wherever they are placed on the body surface. Such a nonstandard bipolar lead shows all the characteristics of the electrocardiogram, all waves and segments with characteristic duration and appropriate time relation. Therefore, such an electrocardiogram can fully be used in the diagnosis of rhythm disorders.

However, the line of waves and their amplitudes in electrocardiogram recorded in such a manner change depending on the location of the body where the electrodes are fitted and depending on the sequence as they are placed. To capture electrocardiogram, Holter monitor typically uses two bipolar leads. Two leads enable to see electric field of the heart from this projection, and provides a record if one lead accidentally is not technically correctly recorded.

Conventional long-term recording with Holter-monitors that continuously record during a specific time period each heart's electrical activity and lets you see everything that happens in the period. Recording is performed with light weight machine (recorder), equipped with batteries and a magnetic stripe, and analysis of recorded data is done later on a special apparatus (scanner).

The advantage of long-term continuous recording with Holter monitor is in the fact that number paroxysmal arrhythmias are recorded this way, while they are rarely caught during the recording of the standard electrocardiogram. The disadvantage of a classical recording with Holter monitor is that the difficulties to which the patient complains, and why it is performed made, do not have to occur within 24 h of recorded electrocardiogram. If the arrhythmia does not arise, it certainly can not be excluded as a cause of problems.



Figure 1. Card X plore 24 h Holter-monitoring of heart and blood pressure

On a Holter-report the doctor should present the following information:

- Start time of recording, and the duration and completion of recording of the heart and blood pressure;
- The technical accuracy of the recording, and the number of recorded cardiac cycle;
- Average values of blood pressure, and separately the average daily value and average evening value;
- Average values of heart frequency, with a special display of the average daily value and average evening value;
- Maximum and minimum values of heart frequency, with an accurate display of the day, hour and minute when they were recorded, and the circumstances, adjusted to the patient's diary, in which they occurred;
- The dominant rhythm and intermittent changes of rhythm, with an accurate display of the length of their duration expressed in hours, minutes and seconds;
- verification of heart blocks, complete or intermittent and AV dissociation, according to:
  - a) their number;
  - b) the time of their appearance;
  - c) objectifying, i.e. display of mentioned with ECG findings.
- Equally important segment of Holter-report is the expression of ventricular rhythm disorders in many manners:

Equally important segment of Holter report is presentation of supraventricular disorders of heart rhythm in many manners (figure 2)

Ultimate part of the Holter report is recording pauses in heart action and their display:

- According to the number of pauses and duration expressed in seconds of duration;
- Exact time of their recording expressed in date, hour and minute;
- Documentation of listed pauses in heart action with ECG display.

Important segment in performing each single Holter report is comparing the result of Holter monitoring with patient diary with all daily activities including stressful situations, physical efforts or

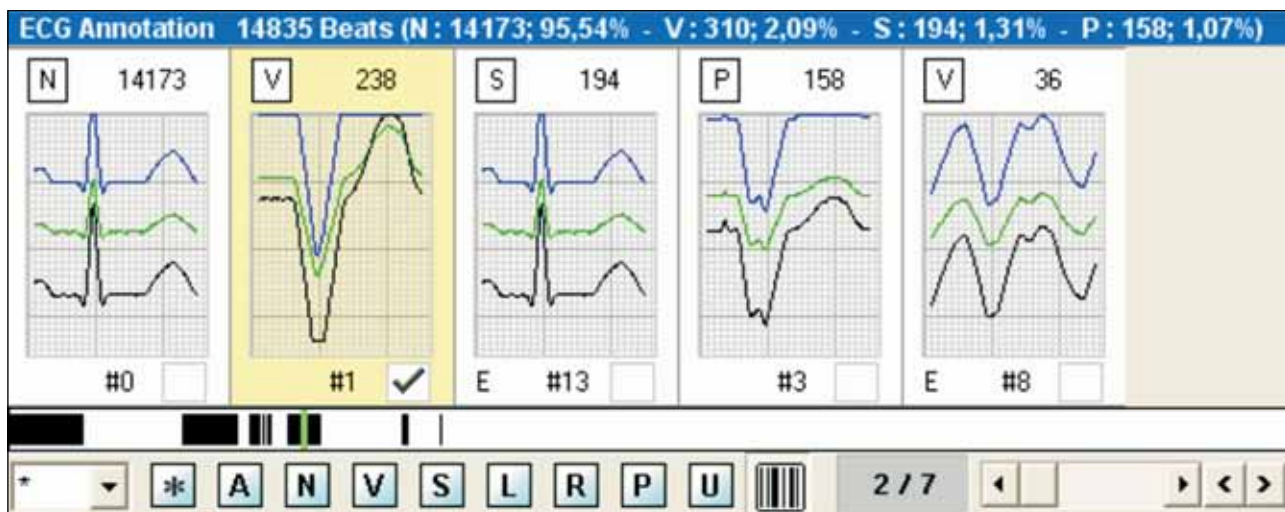


Figure 2. Ventricular disorder of cardiac rhythm

psychological condition, common daily activities or sleep. Essential part of the methodology in preparation of this part of the investigation is correlation of disorder with recordings from patient diary.



Figure 3. Supraventricular disorder of heart rhythm

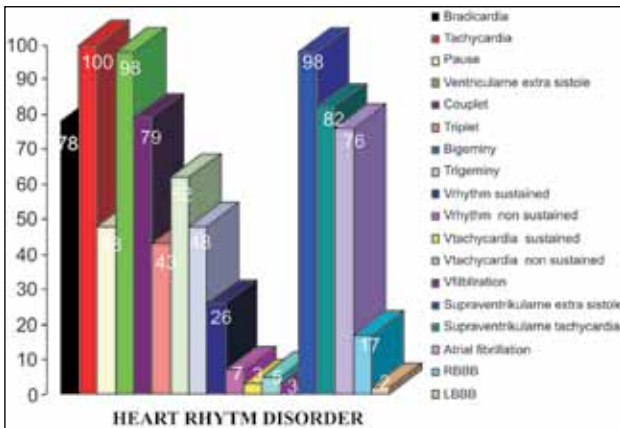


Figure 4. Display of patient activity through 24 hours

### Results of the study

Table 1. Display of all heart rhythm disorders in all patients

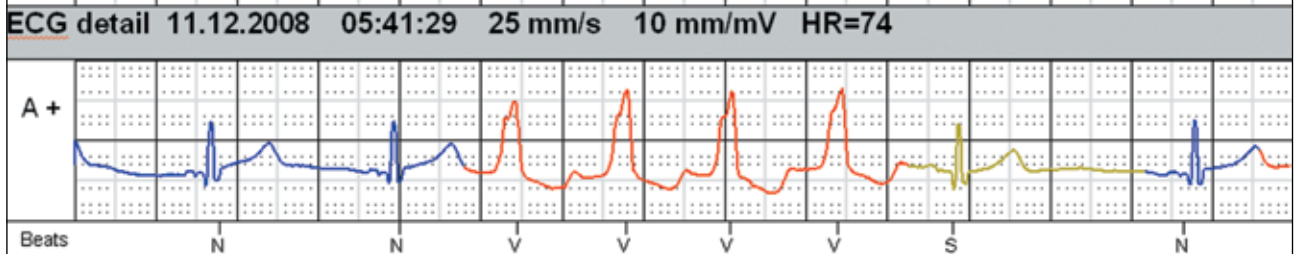
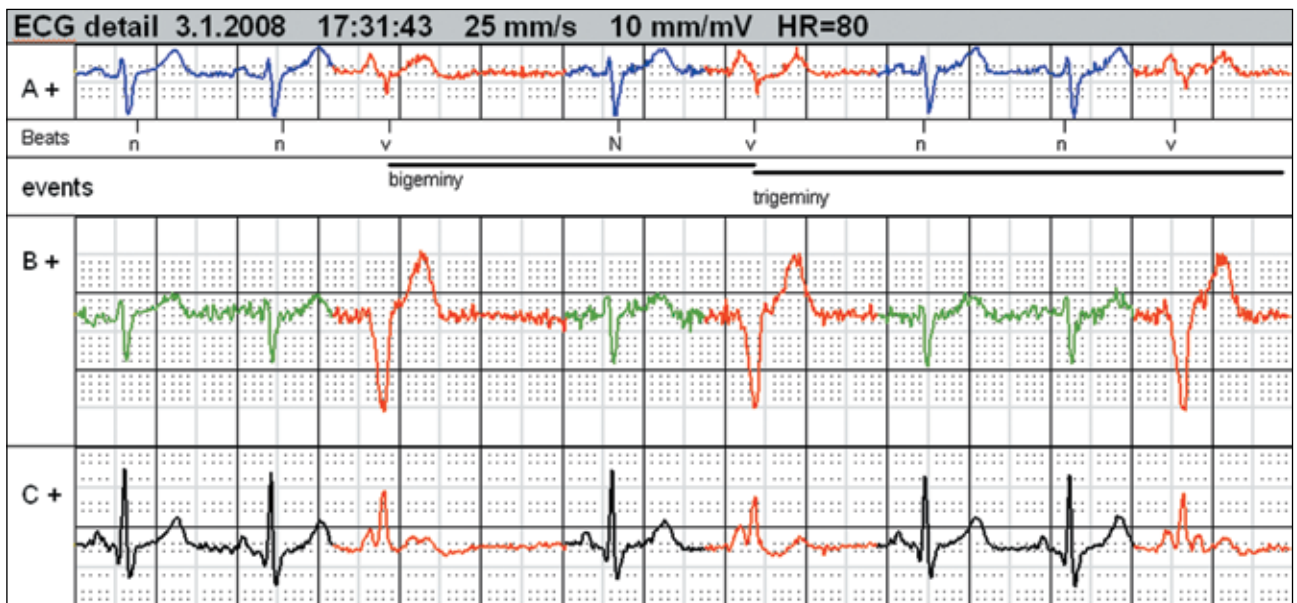
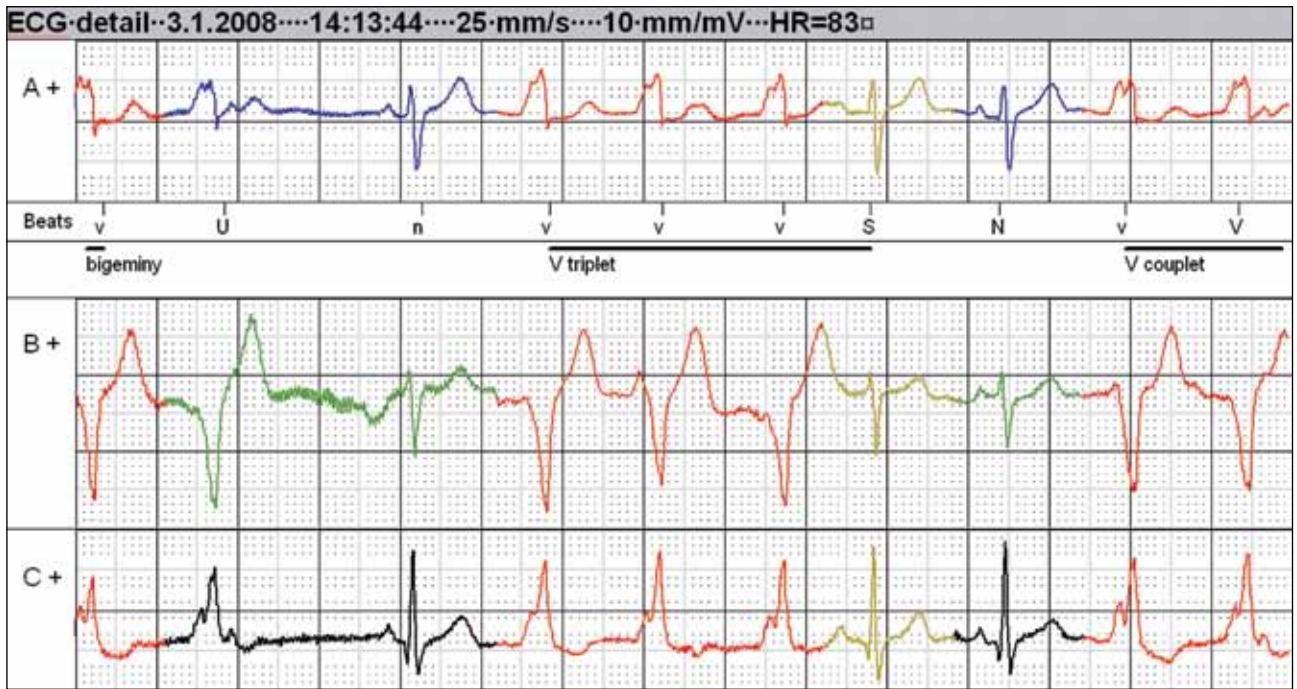
R/b	Type of disorder	Number of patients	%
1	Bradycardia	78	71,56
2	Tachycardia	100	91,74
3	Pause	48	44,03
	Ventricular extrasystole	98	89,08
4a	Couplet	79	72,47
4b	Triplet	43	39,44
4c	Bigeminy	62	56,88
4d	Trigeminy	48	44,03
5	V.rhythm sustained	26	23,85
5a	V.rhythm non sustained	7	6,42
6	V.tachycardia sustained	3	2,75
6a	V.tachycardia non sustained	5	4,58
7	V.fibrillation	3	2,75
8	Supraventricular extrasystole	98	89,90
9	Supraventricular tachycardia	82	75,22
10	Atrial fibrillation	76	82,84
11	RBBB	17	15,59
12	LB BB	2	1,83



der in all patients

Graph 1. Relation of type of heart rhythm disorder in all patients

Heart rates, RR intervals	Average	Max	Min	Max time	Min time	
HR [1/min]	80	139	53	15.5.2008 15:35	16.5.2008 06:04	
HR equivalent intervals [ms]	750					
RR filtered [ms]	778	1493	346	16.5.2008 09:26	15.5.2008 17:02	
RR unfiltered [ms]	741	2166	180	15.5.2008 21:25	15.5.2008 15:32	
Tachy / brady / pause	Number of events		Longest event			
			Time	Length		
Tachycardia	597		15.5.2008 15:30	5 min 17 s		
Bradycardia	3		16.5.2008 06:04	15 s		
Pause ( 2.5 s )	0					
QRS statistics						
	Total	Max/h	Longest		Highest rate	
			Duration	HR [1/min]	Duration	HR [1/min]
<b>Ves</b>						
Isolated	30517	1832				
Couplet	360	96				
Triplet	8	3				
V-tachycardia	0	0				
Bigeminy	640	103	6 min 6 s	78	0 s	180
Trigeminy	2232	175	2 min 55 s	82	2 s	135
V.rthym non s.	26					
V.rthym sus.	12					
RBBB	206					
LBBB	7800					
V.fibrillation	2					
<b>SVES</b>						
SVES	12935	1091				
SV-tachycardia	25	4	00:00:03	98	00:00:02	203
Atrial fibrillation	180					



Display of segment from 24 h Holter-monitoring report of heart and blood pressure in investigated students: table of registered heart rhythm disorder-ECG details - Bigeminia, Couplet, Triplet, Trigemina, ventricular rhythm

Table 2. Display of Bradycardia in all patients

Number of patients	Bradycardia	Recorded number	Duration in seconds
109	Maximal	1234	2935
	Middle value	116	153
	Minimal	0	0

Table 3. Display of Tachycardia in all patients

Number of patients	Tachycardia	Recorded number	Duration in seconds
109	Maximal	2383	7416
	Middle value	742	1056
	Minimal	22	25

Table 4. Display of frequency values in all patients

Number of patients	HR intervals	Heart frequency 1/min		
		Average	Maximal	Minimal
109	Maximal	102	191	72
	Middle value	81	161	50
	Minimal	61	100	30

Table 5. Display of HR equivalent in all patients

Number of patients	HR equivalent Intervals	Average value in milliseconds
109	Maximal	983
	Middle value	753
	Minimal	588

Table 6. Display of RR interval values in all patients

Number of patients	RR intervals	Heart frequency 1/min		
		Average	Maximal	Minimal
109	Maximal	968	2380	486
	Middle value	749	1539	331
	Minimal	584	1110	233

Table 7. Display of Pauses in heart action in all patients

Number of patients	Pause	Recorded number	Duration in seconds
109	Maximal	110	66
	Middle value	4	4
	Minimal	0	0

Table 8. Display of presence of Ventricular Extrasystole in all patients

Number of patients	Type of cardiac disorder	Recorded number	Max/sat
	Ventricular Extrasystole		
109	Maximal	30517	1956
	Middle value	1090	149
	Minimal	0	0

Table 9. Display of presence in all patients

Number of patients	Type of cardiac disorder	Recorded number	Max/sat
	Couplet		
109	Maximal	746	222
	Middle value	40,37	14,17
	Minimal	0	0



Table 10. Display of Bigeminy presence in all patients

Number of patients	Type of disorder Bigeminy	Recorded number	Max/ hour	Duration in seconds	Average frequency	Duration in seconds	Maximal frequency
109	Maximal	49,61	13,05	17,92	127,18	0,59	196,15
	Middle	1282	224	366	215	5	306
	Minimal	0	0	0	53	0	53

Table 11. Display of Trigeminy presence in all patients

Number of patients	Type of disorder Trigeminy	Recorded number	Max/ hour	Duration in seconds	Average frequency	Duration in seconds	Maximal frequency
109	Maximal	2232	175	440	201	4	229
	Middle	60,87	8,63	18,25	103,49	1,53	158
	Minimal	0	0	0	0	0	0

Table 12. Display of ventricular tachycardia presence in all patients

Number of patients	Type of cardiac disorder	Recorded number
	V-tachycardia	
109	Maximal	2
	Middle value	1,33
	Minimal	1

Table 13. Display of presence of Supraventricular Extrasystole in all patients

Number of patients	Type of cardiac disorder	Recorded number	Max/sat
	Supraventricular extrasystole		
109	Maximal	16284	1111
	Middle value	967	129
	Minimal	0	0

Table 14. Display of presence of Supraventricular Tachycardia in all patients

Number of patients	SV-Tachycar.	Recorded number	Max/ hour	Duration in seconds	Average frequency	Duration in seconds	Maximal frequency
109	Maximal	1006	85		175		234
	Middle	18,94	3,48		84,33		117,45
	Minimal	0	0		0		0

Table 15. Display of Atrial fibrillation presence in all patients

Number of patients	Atrial fibrillation	
109	Maximal	313
	Middle value	21
	Minimal	0

Table 16. Display of presence of right bundle brunch block in all patients

Number of patients	RBBB	Recorded number
109	Maximal	4921
	Middle value	383
	Minimal	32

Table 17. Display of presence of left bundle brunch block in all patients

Number of patients	LBBB	Recorded number
109	Maximal	7800
	Middle value	6351
	Minimal	4901

Table 18. Display of presence of shorter PQ interval, prolonged QT interval, nodal rhythm and torsade de pointes in all patients

Heart rhythm disorders	Male		Female		Total	
	Number	%	Number	%	Number	%
Pq interval (shorter)	3	7,69	12	17,14	15	13,76
Qt interval (prolonged)	7	17,95	0	0,00	7	6,42
Nodalni ritam	4	10,26	4	5,71	8	7,34
Torsade de pointes	3	7,69	2	2,86	5	4,59

## Discussion

Prolonged and continuous recording usually lasts for 24 hours. This length of recording time is most convenient because it allows observation of rhythm during various daily activities and during sleep. Recording time can be shorter if there is an established rhythm disorder and is not expected that such a rhythm change during prolonged observation. Usually the shorter time used in the estimate of treatment success. Recording can be longer if rhythm disturbances occur periodically or occasionally, if arise difficulties that can cause rhythm disturbances.

Insight into the patients' difficulties and rhythm disorders is enabled on the one hand with automatic recording time on an electrocardiogram, and the other hand by keeping a diary in which the patient records the exact time of any complaints, the types of problems, then the kinds of physical activities, as well as taking medication. Synchronizing the existence of subjective symptoms that the patient complains with rhythm disorders, confirms that the disturbance of rhythm disturbances causing patients complaints. It is also possible to notice that some transient disturbances of rhythm pass asymptotically, without patient's symptoms, and that there is arrhythmia that the patient feels not as arrhythmia, but as dizziness, dyspnea. Analyses of ECG recordings are done in the apparatus for analyzing tapes, reproduction of the electrocardiogram. In this part of the analysis is performed automatically in the camera, to the extent

to which pre-programmed, recognizes certain rhythm disturbances, classified them and qualify. Part of the analysis performed by the physician who the following the on-screen reproduction of the electrocardiogram, gain insight into the types of rhythm disorders that exist, resolves complicated rhythm disorders. The doctor, on the basis of seeing P-waves can determine the manner of atrial activation, as well as the relationship between activation of atria and ventricle. It is very important to distinguish between sinus arrhythmia from supraventricular extrasystole, aberrant conduction of atrial extrasystole to ventricular extrasystole, sinus pause from functional AV conduction disorders and various forms of AV dissociation, and to separate ventricular extrasystole from parasystole.

The advantage of continuous recording with Holter monitor is that it captures every electrocardiogram complex, which happened during 24 h, to obtain a full insight into the electrical events in the myocardium, seeing the impact of rhythm disturbances in the normal living conditions and activities, and activities by the have an effect on heart rhythm. Comparing the recorded onset of rhythm disturbances with the problems of patients, which was recorded in the diary we can found out if the arrhythmia is causing hemodynamic disturbances that are clinically manifested and what are these disorders, whether there are cerebral, or anginal interference or disorders in general circulation.

The evaluation of importance of symptoms is to determine it the problems that the patient feels could be caused by disorders of rhythm are really

a result of arrhythmias and what is the type of arrhythmia that causes them. The most significant symptoms whose origin should prove were caused by transient disturbances of circulation. Those are pre-syncope and syncope which are symptoms of CNS disorders, anginal disorders that arise spontaneously, unprovoked by physical exertion or some other identifiable cause, as a symptom of disorders in the coronary circulation induced by arrhythmias, then attacks of paroxysmal dyspnea that are not caused by physical exertion, and symptoms of functional arrhythmia disorders.

Indications for the application of long-term ECG recording are the complaints of patients to unpleasant sensations in the chest in the form of palpation. There is a wide range in frequency and severity of symptoms of early and rare heart skipping to frequent and long **jumping** and kicking in the chest to the right long-term attacks palpitations. The next group of patients is those with the possibility of organic disease that is known to be able to have a propensity for severe rhythm disorders. The task of recording is the assessment of the risk of serious rhythm disturbances and the recording is done even if the patient has no symptoms of rhythm disorders. The diseases that have a particular tendency to rhythm disorders are including: congestive and hypertrophic cardiomyopathy, mitral valve prolapse, prolonged QT-time, changes that indicate a weakness of the sinus node or AV conduction disturbances, particularly bifascicular block. Viitasalo et al. found that in the study group of young men of 20 years, more than 50% had ventricular extrasystole. Polymorphic ventricular extrasystole were rarely found (Viitasalo et al.) in investigated young athletes between 18-20 years and 35% of healthy elderly people. The greatest number was found in Brodsky et al. investigating students 6%, Sabotka et al. in 40% of young women. Sinus bradycardia during sleep is regular finding with minimal frequency of 31/min. for students between 18-21 years, (Marine et al.) sinus bradycardia out of sleep were found by Dickinson et al. in 40% of healthy young men under 20 years. Sinus pauses that lasted up to 2 seconds were found (Viitasalo. et al.) in 14% of young athletes. Brodsky et al. found sinus pause lasting between 1.75 sec.-3 sec. in 68% of tested students. In hypertrophic cardiomyopathy, arrhythmia is the common occurrence and the one of supraventricular origin and ventricular origin. So were found repetitive ventricular complexes of 15% to 41% and ventricular extrasystole in 47% to 64% (Podrido al. 2011). Compared with persons who have no signs of heart disease, which was conducted, it was found that there was no difference in the unaided ventricular extrasystole but it was found that there is a difference in complex forms, ventricular tachycardia occurs between 14% and 19% in hypertrophic cardiomyopathy, while rarely observed in those individuals who have signs of heart disease. Ventricular extrasystole, including single and complex forms was found in 83% and interrupted ventricular tachycardia in 60% of patients with idiopathic dilatative cardiomyopathy. In mitral regurgitation the most common disorders were atrial rhythm fibrillation in 22%, and the interrupted ventricular tachycardia in 50% of patients. (Miller et al. 2007).

tricular origin and ventricular origin. So were found repetitive ventricular complexes of 15% to 41% and ventricular extrasystole in 47% to 64% (Podrido al. 2011). Compared with persons who have no signs of heart disease, which was conducted, it was found that there was no difference in the unaided ventricular extrasystole but it was found that there is a difference in complex forms, ventricular tachycardia occurs between 14% and 19% in hypertrophic cardiomyopathy, while rarely observed in those individuals who have signs of heart disease. Ventricular extrasystole, including single and complex forms was found in 83% and interrupted ventricular tachycardia in 60% of patients with idiopathic dilatative cardiomyopathy. In mitral regurgitation the most common disorders were atrial rhythm fibrillation in 22%, and the interrupted ventricular tachycardia in 50% of patients. (Miller et al. 2007).

### Conclusion

The study of the heart rhythm abnormality that has been analyzed and proven via 24-h Holter monitoring of heart and blood pressure has resulted in many data on heart rhythm disorders including atrial, ventricular and rhythm disturbances in the AV nodes, as well as the clinical arrhythmia syndromes. Based on the survey results were recorded following an abnormal heart rhythm: bradycardia in 78 patients or 71.56%, tachycardia in 100 patients or 91.74%; pauses in 48 patients or 44.03%, ventricular extrasystole in 98 patients or 89.08%; Couplet in 79 patients or 89.08%; Triplet in 43 patients or 39.44%; Bigeminia in 62 patients or 56.88%; Trigemina in 48 patients or 44.03%; Ventricular rhythm interrupted 26 patients or 23, 85%; Ventricular uninterrupted rhythm in 7 patients, or 6.42%, ventricular tachycardia interrupted in 3 patients, or 2.75%; continuous ventricular tachycardia in 5 patients, or 4.58%, supraventricular extrasystole in 98 patients or 89.90%, supraventricular tachycardia in 82 patients or 75.22%; Atrial fibrillation in 76 patients or 82.84%, right bundle branch block in 17 patients or 15.59%; left branch block 2 or 1.83%, nodal rhythm in 8 patients, or 7.34%; Torsade de pointes in 5 patients, or 4.59%, and AV block in 35 patients or 32.11%.

Registered Heart rhythm disorders are presented in tables and graphs but also objectified with

ECG recordings from a report 24-h Holter monitoring of heart and blood pressure according to the etiopathogenesis or separately presented. During the study 24 h Holter-effective monitoring of the heart and blood pressure was performed to all patients, and during ongoing monitoring of the effects of therapy, and, if necessary one same patient had been subject to several Holter-findings. Disorders of heart rate were the guideline for further cardiac monitoring and observation, where echocardiography was the key method to detect the presence or absence of anatomic substrates of arrhythmias.

Analysis and interpretation of 24-h Holter monitoring of heart and blood pressure, presented in Holter-report is the result of multiple interdependencies and combination of modern medical computer technology achievements with individual abilities and knowledge of medical-practitioners. Our research has been done on one recorder, so that the weekly could be treated only two patients. All the footage is almost entirely technically correct. Due to monitoring the effects cardiotherapy two or more 24-h Holter monitoring of heart and blood pressure in the same patient were often performed, whose results are also presented in the study. The total number of analyzed 24-h Holter monitoring of heart in this study is the 105.

## References

1. *The heart's electrical system: Working and not.* American Heart Association. <http://americanheart.org/presenter.jhtml?identifier=34>. Accessed Dec. 1, 2010.
2. *Heart rhythm disorders.* Heart Rhythm Society. <http://www.hrsonline.org/PatientInfo/HeartRhythmDisorders/index.cfm>. Accessed Dec. 1, 2010.
3. *Long QT syndrome.* National Heart, Lung, and Blood Institute. [http://www.nhlbi.nih.gov/health/dci/Diseases/qt/qt\\_all.html](http://www.nhlbi.nih.gov/health/dci/Diseases/qt/qt_all.html). Accessed Dec. 1, 2010.
4. *Sick sinus syndrome.* Heart Rhythm Society. <http://www.hrsonline.org/patientinfo/hearthythmdisorders/sss>. Accessed Dec. 1, 2010.
5. Mehra R, et al. Association of nocturnal arrhythmias with sleep-disordered breathing: The Sleep Heart Health Study. *American Journal of Respiratory and Critical Care Medicine.* 2006;173:910.
6. *Diagnosing arrhythmias.* American Heart Association. <http://americanheart.org/presenter.jhtml?identifier=3>. Accessed Dec. 1, 2010.
7. *Arrhythmia medications.* American Heart Association. <http://americanheart.org/presenter.jhtml?identifier=18>. Accessed Nov. 30, 2010.
8. *Ablation.* American Heart Association. <http://americanheart.org/presenter.jhtml?identifier=6>. Accessed Nov. 30, 2010.
9. *Maze procedure.* University of Southern California Keck School of Medicine. <http://www.cts.usc.edu/mazeprocedure.html>. Accessed Dec. 1, 2010.
10. Connolly S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *New England Journal of Medicine.* 2009;361:1139.
11. Wann LS, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2010;123:104.
12. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS, et al. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices): developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *Circulation.* 2008;117:e350-e408.
13. Hayes DL, Zipes DP. Cardiac pacemakers and cardioverter-defibrillators. In: Libby P, Bonow RO, Mann DL, Zipes DP, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine.* 8th ed. Philadelphia, Pa: Saunders Elsevier;2007:chap 34.
14. Vereckei A, Duray G, Szénási G, Altemose GT, Miller JM: A new algorithm using only lead aVR for the differential diagnosis of wide QRS complex tachycardia. *Heart Rhythm* 5:89-98, 2008. *ology Clinics, Volume 26, Number 3, Ventricular Arrhythmias, WB Saunders, Philadelphia, 124:168,2008*
15. Miller JM, Bhakta D: The precordial thump: Convertio Cordis, Commotio Cordis, or neither? *Pacing and Clin Electrophysiol* 30:151-152, 2007.
16. Miller JM, Zipes DP: Therapy for Cardiac Arrhythmias. In Zipes DP, Libby P, Bonow RO, Braunwald E. (eds) *Braunwald's Heart Disease (8th edition)* Elsevier Publishing Co., Philadelphia, pp 779-823, 2007.
17. Podrid PJ. Clinical significance and treatment of ventricular premature beats. <http://www.uptodate.com/home/index.html>. Accessed March 4, 2011.

18. Podrid PJ. Prevalence and evaluation of ventricular premature beats. <http://www.uptodate.com/home/index.html>. Accessed March 4, 2011.
19. Arrhythmia. National Heart, Lung, and Blood Institute. [http://www.nhlbi.nih.gov/health/dci/Diseases/arr/arr\\_what.html](http://www.nhlbi.nih.gov/health/dci/Diseases/arr/arr_what.html). Accessed March 9, 2011.
20. Ventricular premature beats. *The Merck Manuals: The Merck Manual for Healthcare Professionals*. <http://www.merckmanuals.com/professional/sec07/ch075/ch075j.html?qt=premature%20ventricular%20contraction&alt=sh>. Accessed March 9, 2011.
21. Health encyclopedia – diseases and conditions. *The healthcentral network*. Accessed Feb 8th 2009.
22. Zimetbaum P, Josephson ME (May 2008), “Evaluation of patients with palpitations”, *N. Engl. J. Med.* 338 (19): 1369–73, doi:10.1056/NEJM199805073381907, PMID 9571258, <http://content.nejm.org/cgi/content/full/338/19/1369>
23. Meurs KM, Spier AW, Wright NA, Hamlin RL 2”Comparison of in-hospital versus 24-hour ambulatory electrocardiography for detection of ventricular premature complexes in mature Boxers”, *J. Am. Vet. Med. Assoc.* 218 (2): 222–4, 2007
24. Piktel JS. Cardiac rhythm disturbances. In: Tintinalli JE, et al. *Tintinalli’s Emergency Medicine: A Comprehensive Study Guide*. 7th ed. New York, N.Y.: The McGraw Hill Companies: 479-523, 2007. 2011. <http://www.accessmedicine.com/content.aspx?aID=6357092>. Accessed March 9, 2011.
25. Bredikis, *Cryoablation Role In Cardiac Arrhythmias*, WB Saunders, Philadelphia, 124:168,2011 ByCentrelFlorida Medicine.com

Corresponding author:

Zana Pozderac,

J.U.K.S. Institute for Health Protection of Students,

University of Sarajevo,

Sarajevo,

Bosna and Hercegovina,

E- mail: [zanapozderac@gmail.com](mailto:zanapozderac@gmail.com)

# Our attitude towards the treatment of the rectal cancer

Zuvdija Kandic<sup>1</sup>, Adis Kandic<sup>1</sup>, Alma Kandic<sup>2</sup>, Lejla Catic<sup>3</sup>, Enis Kandic<sup>3</sup>

<sup>1</sup> Clinic for Abdominal Syrgery, KCU Sarajevo, Bosnia and Herzegovina,

<sup>2</sup> Clinic for the Ginecology, KCU Sarajevo, Bosnia and Herzegovina,

<sup>3</sup> Clinic for the Plastic surgery, KCU Sarajevo, Bosnia and Herzegovina,

<sup>4</sup> „Alea dr Kandić“, Sarajevo, Bosnia and Herzegovina.

## Abstract

Malignant disease of the colon is the most often human neoplasm which comprises about 30% of all digestive tumours. Thereat, cancer of the lower end the colon (rectum) comprises 45 to 48 % of all CRC (colorectal cancers). According to 'American Society Cancer', only lung and prostate cancer in men and breast and cervix cancer in women are more frequent than CRC. The incidence of colorectal cancer is 15 to 30/100,000 citizens. Rectal cancer is the result of interection of disturbed genetic factors with external factors. The first surgical treatments began with Faget, who did the first rectal extraperitoneal excision in 1739. It was improved by Ernest Milles in 1908, and in 1923, Hartman did the resection without anamnesis. In the middle of 20th century, Dixon defined the resective interventions and in Litre did a colostomy.

The aim of this study is point out the necessity of early diagnosis and protocolar oncological approach to the treatment of this malignant disease which must be done before choosing any operative procedure in order to prevent postoperative morbidity.

On the material of the Clinic for Abdominal Surgery at the Clinical centre University of Sarajevo, during the four-year period (from 2006 to 2010), out of the 406 patients with CRC, 261 of them (64.3 %) had cancer of the final part of the colon. In this case, all the time of the treatment, protocol was strictly applied. Primary surgery was performed on the early stages of the disease. Radiochemotherapy (RKT) followed by operation after 6 to 8 week is applied in th progressive state of the disease with the penetration of the meso rectal fascia with positive lymph-gland assessment (NMR). Out of 261 operated patients, 5 of them (1.9 %) underwent transanal resections where the

tumour was up to 2 cm; 104 patients (39.8 %) underwent rectal resection with TME (II and III tumour states of recto-sigma); 24 patients (9.2 %) uderwent amputation; 156 patients (22.4 %) underwent left chemicolecotomy with rectal resection and 29 patients (11 %) underwent intersphincteric colo-transversal-anal anastomosis. The operation by Hartman was performed on 44 patients (16.8 %) and colostomy on 10 patients (3.8 %) in emergency service. In the tumours with low localisation we do low colo-transversal-rectal or ultra-low intersphincer colo-anal anastomosis. Total meso rectal excision and lymhadenectomy is our priority. We fully respect the oncologic approach, i.e. complete removal of the affected organ with the lymphovascular arcade.

Operative lethality up to 30 days was 2.5 % (comorbidity, thromboembolism). Owing to combined protocolar approach of surgical and radiochemotherapy of rectal tract, extirpational interventions are not so frequent any more compared with resections with low and ultra-low anastomosis.

Team work and close cooperation of oncologic team of physicians (surgeons, gastroenterologists, pathologists, oncologists, radiotherapeutists) as well as respect for the protocol of the treatment are the most important factors of a successful oncologic surgery.

**Key words:** rectal cancer, resection and extirpational intervention, protocolar approach

## Introduction and significance

Malignant disease of the colon and the rectum are the most often human neoplasm and as such comprises 30 % of all malignant diseases. Comparing with the malignant neoplasm of digestive tract, there are 50 % of colon and rectum cancer. Accord-

ding to the 'American Society Cancer', only lung cancer in men and breast cancer in women are more often than colon and rectal cancer. Rectal cancers comprises 50% of all colo-rectal malignant diseases. The incidence is 17 : 100 000 citizens. The incidence in USA is from 11 to 51: 100 000, with mortality up to 14 %. In USA, 50 000 patients die every year, and 20 000 in SRN (2, 3, 5, 7, 10).

Some of the most important factors in the formation of reactal cancer are Genetic predispositions, colon polyps, hereditary diseases, diet, Garder's, Turcot's, Peutz-Jehger's as well as inflame. In addition, there are geographical variations in the distribution of the disease. Surgical treatment of the rectal cancer began with Faget who did the first extraperitoneal excision in 1739 which is later improved by Ernest Milles in 1908. Hartman did the resection without anastomosis in 1923, and in the middle of the 20th century, Dixon defined resection interventions. In 1884, Meydl inaugurated moderne technique of colostomy (1, 3, 4, 9, 17).

**The aim of the study**

The aim of this study is to point out the necessity of early diagnosis and protocolar oncological approach to the treatment of malignant disease of the final part of the colon which must be done before choosing any operative procedure in order to prevent postoperative morbidity. It is also important to pay attention to the significance of the preoperative estimation of the disease state, which has a great influence on the life expectancy after the operation and the quality of life.

**Material and methodology**

On the material of the Clinic for Abdominal Surgery at the Clinical Centre-University of Sarajevo, 406 patients with colon malignant diseases who had undergone interventions were examined by retrospective-prospective analysis, during the four year period (from 2006 to 2010). Out of the total, 261 patients (64.2 %) had cancer of the final part of the colon. The sources of information were the history of diseases, operative protocols, tracking files of the specialist clinics as well as the methods of the dialogue.

*Table 1. Distribution of the malignant colon diseases*

Localisation	Number	% ratio
Colon ascendens	93	23,0
Colon trasversum	22	5,2
Colon descendens	30	7,4
Colon rectosigmoidei	69	17,0
Rectum	159	39,2
Anorectum	33	8,1
<b>Total</b>	<b>406</b>	<b>100,0</b>

Analysing the diseases in the first two years (from 2007 to 2008) and comparing that scope with the one from the other two years (from 2009 to 2010), we noticed that there is a significant increase in the number of patients in the other two year period (table 2).

*Table 2. Cancer of the final part of the colon*

Length of the observation (in years)	Number	% ratio
2007.- 2008.	114	43,7
2009.- 2010.	147	56,32
<b>Total</b>	<b>261</b>	<b>100,0</b>

All statistics contribute to the increase of colon malignant disease. (1, 3, 4, 7, 9)

*Table 3. Distribution of cancer of the final part of colon between the sexes*

Male	Number	%ratio
2007.-2008.	141	54,0
2009.-2010.	120	46,0
<b>Total</b>	<b>161</b>	<b>100,0</b>

As you can see from the table 3, male sex prevails (table 3).

Dukes (ABC) and Manson or histological variant of TNM system (p1 - p4) are guides for choosing a kind of protocol treatment (3, 4, 12, 25).

*Table 4. Tumour staging*

	Number of the examinee	% ratio
A/ B1-2	93	35,6
C 1,2	107	41,0
D	61	23,4
<b>Total</b>	<b>261</b>	<b>100,0</b>

In the state A and B1/2, there were 93 patients (35.6 %) who were treated with primary surgical procedure. In the state C and D, there were 168

patients (64.36 %) and 24 of them (9.2 %) underwent interventions in emergency service and 144 of them (55.2 %) were treated with neoadjuvant chemo and radiotherapy followed by intervention and radiotherapy. After the adequate diagnosis, every patient passes oncological consilium which prescribe the protocol of the treatment in order to heal, prevent the systemic spread, have local control, preserve sphincter and continency and maintain sexual and urinar functions by integrity of plexus of autonomous nerves (plexus hipogastriacus i n.pudendus).

Histopathologic verification is obligatory (3, 4, 12). There were 248 (95.0 %) examples of Adenocarcinoma; 12 (4.6 %) examples of mucinous adenocarcinoma (mucoid or colloid) and non-differential carcinoma. There was 1 lymphoma (0.4 %).

Table 5. Histopatological verification

	N	%
Adenocarcinoma	248	95,0
Adenocarcinoma mucinosum, nondifferential	12	4,6
Lymphoma	1	0,4
<b>Total</b>	<b>261</b>	<b>100,0</b>

“Conditio sine equanon” is presented by: histologic type, histologic degree of the malignment and morphometric parametres (table 5).

Table 6. Symptoms and diagnostic

	Number	% ratio
Blood in stool	188	72.0
Changes in the character of bowel movement	164	64.4
Abdomina pain	202	77.4
Clinic examination – RT	198	75.8
TU markers (CEA, CA 19-9, CA-50)	92	35.2
Colonoscopy with biopsy	261	100.0
Virtual CT and MR colonoscopy	201	77.0
Rectal UZ	26	1.0
NMR and CT	261	100.0

Bleeding in stool was detected in 72 %, changes in the habits of bowel movements were detected in 64.4 % and abdominal pain was detected in 77.4 %. Increased values of tumour markers were present in all patients with extensive process or recidive (35 %). Colonoscopy with biopsy were

done to all examinees as well as virtual CT and NMR colonography. We point out a great diagnostic importance of NMR because of the affected meso rectal fascia. Tumour gradus I, II, as well as tumour state B without the affection of mesorectal fascia and lymphoglandula require primary surgical procedure and all other cases require adjuvant radio and chemotherapy followed by an operation (1, 3, 4, 5, 17, 19, 22).

While treating rectal cancer, we strictly follow the protocol of the treatment.

Table 7. Rectal cancer

Tumour stage	Standard approach	Alternative approach
IUCC I<4 cm G I/II	Local excision	Local excision + RT
UICC I Resectabile	Resection	
UICC II/III Resectabile	RT+Resection	Resection +RCT
UICC III Progressive	RCT+Resection RCT+Resection + IORT	RCT+Resection +CT
Local relapse	RT+Resection + IORT	RCT+Resection + CT

### Radio-chemotherapy (RCT) and operative therapy of the rectal malignoma

In the treatment of malignant final part of the colon, we follow these recommendations (table 7): in the state of tumour UICC from 1 to 2 cm, we use local excision, in terms TER, TEM. In the state UICC II/III (resectabile) we indicate resective intervention followed by RKT. In progressive tumour state III: RCT + resection, alternative RCT + Resection + CT. In local relapse RT + Resection + IORT, alternative RCT + Resection + CT. Nowadays, we try to apply neoadjuvant RT (25 Gy) in the treatment of the early state of the tumour.

**The aim of the application of the neoadjuvant RT (radiotherapy) is:** to reduce the percentage of the local recidive and advantage the number of survivors in resectable cancer, to reduce the tumour, make the resection easier, to shorten the treatment and make the surgical treatment possible with non operative patients.

Neoadjuvant therapy has to enable the sphincter-preservative procedure in low rectal carcinoma. It is performed as: short-lasting (25 Gy in 5



Fr) and /or/ long-lasting (50 Gy in 25 Fr). It can be combined (“sandwich”), intraoperative and transluminal (15, 16, 21).

- Adjuvant RCT treatment like „gold standard“.
- Operation whenever it is possible
  - \* abdominoperineal extirpation, anus praeter
  - \* explorational laparotomy +/- biopsy
- monitoring - recidive - reoperation - palliative RT
  - \* Dukes A - without therapy
  - \* Dukes B - radiotherapy
  - \* Dukes C - radio-chemo therapy
  - \* Dukes D - chemotherapy

Table 8. Operative interventions

	Number	%ratio
Radical operations	200	76,6
Paliative operations	61	33,4
Total	261	100,0

Radical operations were done to 76,6 % and palliative to 33,4 % (table 8).

Out of the radical surgical procedures, there were 104 (39,8 %) anterior-posterior rectal resections, 24 (9,2 %) rectal amputations, 27 (10,3 %) colo transversal-rectal anastomosis, and 29 (11,1 %) ultra-low colo transversal-anal anastomosis and intersphincter anastomosis. There were 5 (1,9 %) transanal resections (table 9).

In most of the cases, Hartman’s procedure was applied in emergency service- 44 (16,8 %). Derivational colostomy was applied to 10 cases (3,8 %) - in non operative cases in emergency service because of the ileus.

In the treatment of a malignant rectal disease, we strictly follow the oncological principle of tumour resection of the affected organ together with its lymph-vascular way (TME). Total meso rectal excision (TME) requires completely removed rectum concoction with Denonvilliers fascia which shines shoothly on the concoction (1, 2, 3, 4, 5, 7, 8, 10). Resection of the whole mesorectum (TME) is a sharp dissection under eye control between parietal and visceral rectal fascia → “Holy plane” (table 10).

Lymphadenectomy is always done in the treatment of all states of diseases which actually stops its expansion. We noted that it is followed by prolonged treatment and recovery. In rectal tumours we put the

proximal rectali line on the transverse colon on the junction of left branch of the middle left colic artery and right branch of the lefr colic. We put the distal resective line in the middle and upper third of the rectum in the hight of the puborectal sling in terms of low colo rectal anastomosis. In more distal localizations, we do ultra low colo-anal, intersphincter anastomosis by hand or stapler. We specially pay attention to the preparation and preservation of the innervation responsible for sexual function as well as the function of urinary bladder (1,2,3,4,5,7,9,12,23). In all the cases, preparation of hypogastric plexus and pudendal nerve (sexual an urinary function) are obligatory.

Table 10. TME „Holy plane“

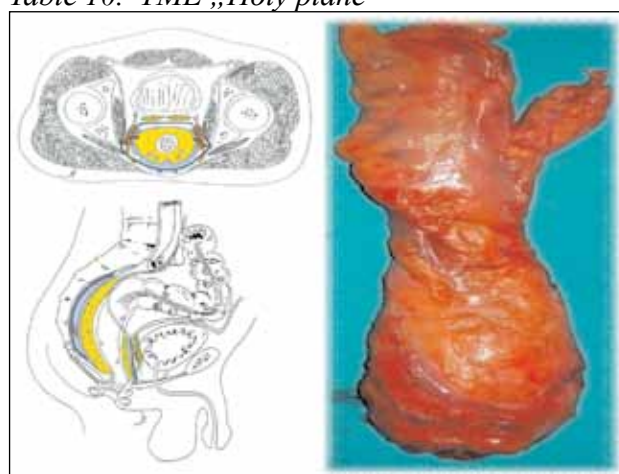


Table 11. Complications op. Th.

	Number	% ratio
Dehiscencio of anastomosis (surgical intervention)	5	2.7
Parcial deh. anastomosis (without s.i.)	12	6.5
Lethality	6	2.3
Inf. operate wounds	19	8.8
Thromboembolic manifestations	9	4.4

Out of all surgical comlications of the rectal cancer treatment (table 11), there were 5 (2,7 %) dehiscencia anastomosis. There were 12 (6,5 %) partial dehiscencia and 19 (8,8 %) infections of the wound. There were 9 (4,4 %) thromboembolic manifestations.

**Prognosis** of the patients treated for rectal cancer depends on the early detection and strict application of the protocol of the treatment.

An adequate pre-operative screening, strictly implemented protocol of treatment, regular con-

trols and monitoring of the patients greatly improve the treatment.

Treatment of malignant rectal diseases requires measures of primary and secondary prevention. It consists of : rectal touche (RT) once a year after the age of 40 as well as a a blood in stool test once a year, sigmoidoscopy and/or colonoscopy every 3 to 5 years after the age 45. Genetic stool tests on APC gene mutations promises an effective screening.

## Conclusion

Generally speaking, colon cancer has the highest morbidity rate of all carcinomas. In almost half of the patients with colo rectal cancer, the localization was done in the final part of the colon and the rectum. Successful treatment depends on the localization, biological tumour action, progression of the process and good knowledge of its surgical and radio-chemotherapeutic treatment. A strict application of the protocol of malignant disease treatment gives the chance for good results.

Surgery is the priority in the treatment of early disease stages (A i B), while stages C and D require neoadjuvant chemo and radiotherapy followed by the operation.

Team work and close cooperation of oncologic team of physicians (surgeons, gastroenterologists, pathologists, oncologists, radiotherapeutists) as well as respect for the protocol of the treatment are the most important factors of successful oncologic surgery.

## References

1. Beck D.E., Wexner S. D.: *Fundamentals of anorectal surgery*, New York: McGraw-Hill, 1992.
2. Goligher J. C.: *Surgery of the Anus, Rectum and Colon*, London, Baillere Tindal, 1984.
3. Kandić Z.: *Hirurgija anorektalnih oboljenja, univerzitetski udžbenik*, 2011. Sarajevo
4. Kandić Z., Bešlić Š., Kandić A., Kandić L.: *Evaluation and results in operative treatment of malignant disease, Medičinski arhiv*, 56 (1, Suppl.1) : 65, 2002. Sarajevo.
5. Milles W. E.: *Cancer of the Rectum*, London:Harrison, 1926.
6. Nissan A., Guillemm J. G., Paty P. B. et all.: *Abdominoperineal Resection for Rectal Cancer at a Specility Center. Dis. Colon Rcetum*, 2001, 44: 27-36.
7. Corman M. L.: *Colon and Rectal Surgery*, Philadelphia J.B, Lippincot, 1993; 99-104.
8. Goodsall D. H., Milles W. E.: *Disease of the Anus and Rectum (I)*, Longmans Green Co Harlow (Essex), 1900.
9. Goldberg S. M., Gordon P. H. nivatvomgs S.: *Essentials of Anorectal Surgery*. J. B. Lippincot, Philadelphia, 1980.
10. Huges E., Cuthbertson A.M., Killingbock.: *Colorectal Surgery*, Churchil Livingstone, Edinburgh, 1984.
11. Kraus U., Pahlman L.: *Abdominoperineal excision, World J Surg*, 6: 549-553, 1982.
12. Berman I. R., Cheung J., Weinberg S.: *Survilence after Coloorectal cancer Resection. Lancet* 2003; 355: 395-399.
13. Bieri S, Allal AS, Kurtz JM. *Sphincter-conserving treatment of carcinomas of the anal margin. Acta Oncol* 2001;40(1):29-33.
14. Cavaliere F., Pemberton H., Cosimelli M. et all.: *Coloanal Anastomosis for rectal cancer. Dis Colon Rectum*, 38: 807-812, 1995.
15. Douglas h. o.: *Adjuvant Treatment in Colorectal Cancer: An update. World J Surg*. 11: 478, 1987.
16. Ellenhorn JD, Enker WE, Quan SH. *Salvage abdominoperineal resection following combined chemotherapy and radiotherapy for epidermoid carcinoma of the anus. Ann Surg Oncol* 1994;1(2):105-10.
17. Goligher J.C.: *Surgery of the Anus, Rectum and Colon*, 4-th ed., London, Bailliere Tindall, 1979.
18. Mason Y.: *Malignant tumort of Rectum. Local Excision. Clin Gastroenterol*. 4:582-585, 1975.
19. Mason Y.: *Transsphincteric Sugery of the Rectum. Pro Surg*, 13:66, 1974
20. Nigro ND, Vaitkevicius VK, Considine B Jr. *Combi- nedy therapy for cancer of the anal canal: a preliminary report. Dis Colon Rectum* 1974;17(3):354-6.
21. Parks A. G., Percy J. P.: *Resection and Sutures Coloanal Anastomosi for Rectal Carcinoma. brit J Surg*. 69: 302, 1982.
22. Štulhofer M.: *Resekcije rektuma u: Štulhofer i sur.: Digestivna kirurgija, JAZU/GZH, Zagreb*, 1992. Štulhofer M.: *Abdominoperinelana amputacija rektuma, u: Štulhofer M.: i sur.: Digestivna kirurgija, JAZU/GZH, Zagreb*, 1992.
23. Thomas R., Lindblad S.: *Adjuvant postoperative Radiotherapy and Chemotherapy in Rectal carcinoma. Radiother Oncol*. 13: 245, 1988.
24. Utsunomiya J., Iwana T., Imajo M., et all.: *Total Colectomy, Mucosal Proctectomy and Ileoanal Anastomosis. Dis Colon and Rectum*, 23 : 459, 1980

Corresponding Author  
Zuvdija Kandic,  
Clinic for Abdominal Syrgery,  
KCU Sarajevo,  
Bosnia and Herzegovina,  
E-mail: kandic@bih.net.ba

# Cardiovascular risk factors in Banovići coal mine miners

Munevera Becarevic<sup>1</sup>, Esad Burgic<sup>2</sup>

<sup>1</sup> Public Health Centre Banovići, Department of occupational medicine, Bosnia and Herzegovina,

<sup>2</sup> Public Health Centre Lukavac, Department for laboratory diagnostic, Biochemical-hematological laboratory, Clinic for internal diseases, Bosnia and Herzegovina.

## Abstract

Global cardiovascular risk is probability to suffer heart attack or stroke in certain period of life and it depends on risk factors (RF) such as metabolic factors (total cholesterol, HDL cholesterol, glucoses metabolism disturbance), some biological factors (blood pressure) and some life style factors (smoking, physical activity).

The aim of this research is to determine the presence and tendency of certain cardio vascular (CV) risk factors (RF) as well as determination of hypertension prevalence, metabolic syndrome and depression among coal-miners in Banovići black coal mine.

**Materials and methods:** epidemiological study was conducted on 492 miners actively involved in working in mine pits. The analysis covered the following values: blood pressure, height and weight, BMI, waist, concentrations of total cholesterol, HDL and LDL cholesterol, triglycerides, blood sugar, determination of smoking status along with depression score based on Beks' scale.

According to NCEP ATP III criteria MS is defined. The results are as follows: 43.9% out of 492 testers have high blood pressure, 34,34% are with depression, 42,88% are with MS. The most frequent risk factors are high BMI (75,40%), high values of LDL-H (70,32%). The most of hypertensive miners had six (23,61%), and normotensive three (21,73%) risk factors.

**Conclusion:** there is high prevalence of diagnosing from hypertension, metabolic syndrome and depression with expressed tendency of risk factors grouping with high BMI as the most frequent one along with the high values of LDL cholesterol.

**Key words:** cardiovascular risk, arterial hypertension, metabolic syndrome, depression, miners,

## Introduction

Global cardiovascular risk is probability to suffer heart attack or stroke in certain period of life. Global cardiovascular risk presents absolute risk expressed as potential possibility of diagnosing of these illnesses in time period of 10 years. Factors related with coronary disease and strokes are metabolic factors (total cholesterol, HDL cholesterol, glucoses metabolism disturbance), some biological factors (blood pressure) and some life style factors (smoking, physical activity).

Hypertension is defined as systole increasment of blood pressure above value of 140 mm/Hg and/or diastolic increasment of blood pressure above value of 90 mm/Hg, measured with usual technique sitting position of tester according to proper protocol (1).

Recent analysis have shown that 2/3 of strokes and a half of all cardiac illnesses are caused by increased blood pressure, what causes 7 million of lethal cases and 64 million of cases with invalidity each year(2).

Systolic blood pressure reduction for 10 mmHg results with reduction of larger cardiovascular incidents for 20-25%, with expression of stroke reduction in comparing to coroner diseases.

The lipoprotein role as independent cardiovascular risk marker is under research for more than 20 years. Many epidemiological studies have proved positive concentration correlation of lipoproteins in blood with coronary disease(3).

Other studies didn't prove positive correlation between levels of lipoproteins in blood and arterial hypertension (4).

However, European Atherosclerosis Society (EAS) recently issued new guidelines that confirm needs for routine measurements of lipoprotein level in blood of patients with medium to high risk for diagnosing of cardiovascular diseases (5).

According to this are results of certain studies that confirm the role of lipoproteins as predictors for atherosclerosis, which suggests determining of lipoproteins level in patients with arterial hypertension, especially in those with atherogenic dyslipidemia. The reason for this is actual behavior of lipoproteins as predictive markers of serious coronary atherosclerosis (6).

Large differences are evident on level of aimed values of lipids which suggest various relevant organizations. However, there is general agreement that ideal aimed value of LDL-cholesterol is in range of 2,0 do 2,6 mmol / l (7).

The level of high density lipoproteins (HDL) in blood is in reversed correlation with risk of development of cardiovascular diseases. This relation can be explained with several antiatherosclerotic LDL cholesterol functions as follows: antiflogistic characteristic, capability for removal of extra cholesterol from cells such as macrophages in arterial wall using the reversed cholesterol transport (8), antioxidative and antithrombotic characteristic (9,10) and its functions of maintenance of endothells by inhibition of apoptosis of endothell cells and functions, "repairment" of damaged endothell (10,11).

Increase of triglycerides level in blood for 1 mmol/l increases the risk for ischemic coroner disease for 15 % in men and 37 % in women. Genetic changes on ENPP1/PC-1 gene are connected with hypertriglyceridemia in mail testers and can contribute development of insulin resistance/metabolic syndrome in this population (12).

Even though BMI and waist have very high correlation coefficient and can be used selectively, research have shown significant connection between high values of waist index and increased blood pressure (13). In comparing to BMI it highly probable that waist value is even more important parameter because of larger connection with metabolic syndrome and cardiovascular illnesses (14). BMI is usual measure used for identification of increased body mass. However, in comparing to BMI, waist value is better parameter for research of metabolic abnormalities such as hypertension and disturbance of glucoses metabolism (15,16,17).

High values of BMI, general and abdominal increase of body mass are inconsequential connected with increased risk of cardiac weakness, while medium or high level of physical activity

in all levels of BMI are connected with decreased risk of cardiac insufficiency (18).

Higher BMI and increased waist values increase risk of hypertension, diabetes, increase of cholesterol concentration even among physically active persons with normal body mass. Therefore, increased body mass is disease and risk factor for other illnesses.

Insulin resistance, is condition in which normal amount of insulin produces weakened biological response on aimed cells, which results with compensatory hyperinsulinemia.

It is most frequent in persons with diabetes type II and in persons with increased body mass and insulin response is significantly bigger in those with higher amount of visceral grease.

Insulin resistance advances towards hyperinsulinemia and hyperglycemia activating, in this way, periphery vasoconstriction and maintaining natrium in body. Liver also increases production of lipoproteins with very low density, what brings to hypertriglyceridemia, lower level of HDL cholesterol, increase of apolipoprotein B, increase of LDL cholesterol level along with atherosclerosis. As a result of such misbalance of lipids, persons with metabolic syndrome usually show protrombotic and antiinflammatory changes (19,20).

The fact that these metabolic abnormalities can be grouped in many cases, give sense to term "metabolic syndrome" i.e. construction adopted by some and rejected by other authors. Syndrome is primarily suggested and continued to be researched by Greald Reaven who suggested that risk factors for cardiac illness and diabetes come together and determined the term of "complex syndrome" (21).

From epidemiological point of view metabolic syndrome seems to slowly increase cardiovascular risk while, in those who don't have diabetes, efficiently shows the beginning of the same diagnose. Results of meta-analysis confirm strong connection of metabolic syndrome defined by NCEP definition with cardiovascular risk. Therefore, it is recommended to health employees to use metabolic syndrome as diagnostically tool for recognition of those with increased risk for cardiovascular happenings (22). Discussions about pathophysiological mechanism by which metabolic syndrome increases cardiovascular risk are presently actual (19).

Earlier definitions of metabolic syndrome enhance independent role of insulin resistance as basic component of metabolic syndrome. Certain research which analyzed 87 studies regarded topic on influence of metabolic syndrome on cardiovascular risk and which included 951 083 patients, have shown that metabolic syndrome double increases the risk of diagnosing of cardiovascular illnesses as well as for 1,5 times increases mortality of any cause (22). The same research has shown that patients with metabolic syndrome but with absence of diabetes also had high cardiovascular risk (22).

ACCF and AHA (American College of Cardiology Foundation, American Heart Association) have developed the guidelines with exact aim to initially assess the risk for development of cardiovascular illnesses related to atherosclerotic vascular changes in adult persons with objectively good health (23).

The aim of this early assessment of cardiovascular risk in asymptomatic individuals is to create the plan for aimed preventive activities for stopping or postponing of illness. It is grounded on creation of long-term concept of aimed action and treatment on patient regarding ones general risk (24).

In Systematic Coronary Risk Evaluation – SCORE, it is possible to determine ten-year risk for diagnosing cardiovascular diseases based on gender, age, values of blood pressure and concentration of cholesterol in blood, smoking status (25).

Relation between psychosocial stress and cardiovascular diseases is identified as important publicly known health problem (26).

Epidemiological proofs for connection between depression and cardiovascular risk factors are rather strong (27,28).

Behavioral changes such as intensifying of smoking, reducing of physical activity and bad feeding habits can appear as adaptation or response on psychological stress which points activation of other important risk factors for disease development (29).

Psychosocial stress primarily activates hypothalamus system, hypofysis and adrenocortical axis along with sympatic neural system, which activates pataphysiological mechanisms along with inflammatory processes, processes of hemostasis and changed metabolic and coroner self-control(26).

Depression and metabolic syndrome are in positive correlation and each of them is independent predictor of negative cardiac happenings (30).

Despite numerous and factual datas of many studies, it can not be claimed with certainty whether depression is the cause, consequence or just marker of metabolic syndrome. For example, physical barriers or social stigmas caused by overweight can cause depression, while emotional problems in overweight people can cause additional production of cytokine that can take part in depression etiology (31).

Even though depression is related to increase of cardiovascular morbidity and mortality, very few informations are available about whether risk exists among younger population.

Certain research has proven that among cases younger than 40, depression and suicidal attempts are significant and independent predictors of premature cardiovascular illnesses and lethality caused by ischemic cardio disease among both gender (32).

Depression also significantly increases the risk of stroke development. This increase is probably independent on other risk factors, including hypertension and diabetes (33).

### **The aim of the work**

1. Determination of arterial hypertension prevalence in coal miners,
2. Determination of metabolic syndrome prevalence in coal miners,
3. Determination of depression prevalence in coal miners
4. Determination of frequency and combination of certain risk factors in coal miners

### **Material and methods**

Epidemiological research is conducted in department of “Omazići” pit, black coal mine Banovići. The research included 492 miners, male gender, age 25 to 55 years, which are employed in department of coal mine pit “Omazići”, black coal mine Banovići.

All subjects was tested on blood pressure values, height and body mass, waist and BMI index.

Values of blood pressure were taken in medical department located in black coal mine Banovići

facilities with expected microclimatic conditions, noise excluded, in cozy sitting positions.

Measurement was conducted according to auscultator method by Korokotov, on both upper arms in time gap of 5 minutes and by the same person. The blood pressure instrument that is used was properly adjusted with dimensions of belt 13 x 45 cm and 16 x 70 cm depending on upper arm diameter. All subjects were submitted to laboratory tests including blood sugar, cholesterol concentration and triglycerides in blood, HDL and LDL cholesterol concentration. Laboratory analysis were processed in laboratory department of health facility in Luka-vac and clinical and university center in Tuzla. Subjects provided anamnesis data on smoking status. Stimulatingly, all subjects completed Becks' scale for determination of angisxiety level and depression. This questionnaire contained groups of various conditions. Subjects were warned to carefully read provided options before choosing one suitable for their subjective feeling regarding last week, including the fact how did they feel in the moment of completing the questionnaire by circling the number next to chosen condition.

If subjects find several provided condition suitable for them, then they would circle all of them. Adding of circled numbers resulted in assement of value of depression degree in subjects according the following criteria: 0-9 normal condition, 10-15 medium depression condition, 16-19 medium to slight state of depression, 20-29 medium to serious depression, 30-63 serious condition. Based on results adjusted to Beks' scale, frequency of depression among subjects is determined.

Based on values of blood pressure is determined prevalence of arterial hypertension among employees in this department. In processing certain guidelines recommended by European Society of Hypertension were used. According to these guidelines and according to values of blood pressure, there are following cases of hypertension: optimal pressure (systole < 120 mmHg and diastole pressure < 80 mmHg), normal pressure (120-129 mmHg /80-84 mmHg), highly normal pressure (130-139 mmHg/85-89 mmHg), first level of hypertension or low hypertension (140-159 mmHg/90-99 mmHg), second level of hypertension (medium) (160-179 mmHg/ 100-109 mmHg), third level of hypertension or hard hypertension

(systole > 180 mmHg and diastole pressure >110 mmHg) and isolated or systole hypertension (>140 mmHg systole < 90 mmHg diastole).

According to results of high levels of blood pressure, waist values, LDL cholesterol concentration, triglycerides and levels of sugar in blood, prevalence of metabological syndrome is determined. National Cholesterol Education Program, Third Adult Tretmant Panel, NCEP-ATP III criteria are used for diagnosing of metabological syndrome. Metabological syndrome requires existence of three or more of following five criteria: waist values >102 cm in men and 88 cm in women, serum triglycerides  $\geq 1,7$  mmol/l, HDL cholesterol >1.03 mmol/l in men and 1,29 mmol/l in women, blood in sugar  $\geq 6,1$  mmol/l and blood pressure  $\geq 130/85$  mm/Hg. Ideal value of LDL cholesterol was taken in range of 2,0 to 2,6 mmol / l (7).

Described epidemiological study, estimated frequency of certain risk factors among miners, grouping of these factors, presence of hypertension, metabological syndrome and depression among miners in department of coal mine pit "Omazići", black coal mine Banovići.

## Results

The research included 492 miners employed in department of coal mine pit "Omazići", black coal mine Banovići. All subjects are males concerning the fact that there are no female employees in this department of coal mine. Average age of subjects is 41,89 ( $\pm 6,08$ ) years.

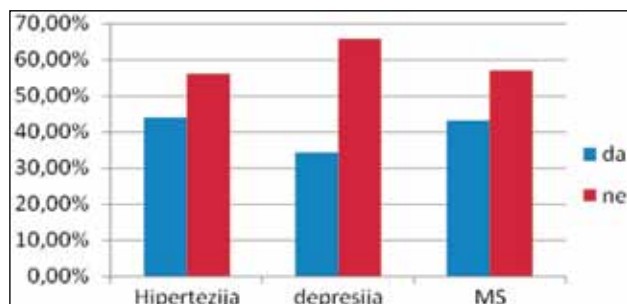
Average risk factors values which were examined are in normal range except LDL cholesterol values with average values of  $3.72 \pm 1.10$ , triglycerides with average values above referent values 1.89 (0.18-11.97), as well as values of BMI with average value of  $27.46 \pm 3.66$  (table 1.), while average values of blood pressure are in range of prehypertension (135/85 mm/Hg).

Out of 492 tested subjects, 216 (43,9%) of them were diagnosed with high blood preasure, according to Becks' selfevaluating scale 169 (34,34%) of tested subjects deals with some form of depression and according to NCEP-ATP III definition 211 of tested subjects 42,88% are dignosed with metabological syndrome (graphic 1).

Table 1. Average values of risk factors in miners

Parameters	Values
SKT	135 (95-240)
DBP	85 (60-140)
WV	98.58 ± 10.13
BMI	27.46 ± 3.66
Cholesterol	5.7 (2.7-10.4)
LDL	3.72±1.10
HDL	1.06 (0.9-3.20)
TGL	1.89 (0.18-11.97)
Sugar in blood	4.47 (2.70-15.6)
Becks' score	6.0 (0.0-47.0)
smoking	294 (59,75%)

Legend: SBP-systole blood pressure. DBP-diastole blood pressure. WV-waist values. BMI-body mass index. LDL-low density lipoprotein. HDL-high density lipoprotein. TGL-triglycerides. SIB-sugar in blood



Legend: MS-metabolical syndrome

Graphic 1. Hypertension and depression prevalence and metabolical syndrome in miners

Table 2. Groupation of risk factors in comparing to hypertension in pit miners

Br KV FR	without RF	one RF	two RF	Three RF	four RF	five RF	six RF	Seven RF	eight RF	nine RF
total n	7	20	49	75	83	88	80	53	29	8
total %	1,42	4,06	9,95	15,24	16,86	<b>17,88</b>	16,26	10,77	5,89	1,62
helthy n	7	19	45	60	59	42	29	13	2	0
healthy %	2,5	6,88	16,3	<b>21,73</b>	21,37	15,21	10,5	4,71	0,72	0
hypertensive n	0	1	4	15	24	46	51	40	27	8
hypertensive %	0	0,46	1,85	6,94	11,11	21,29	<b>23,61</b>	18,51	12,5	3,7

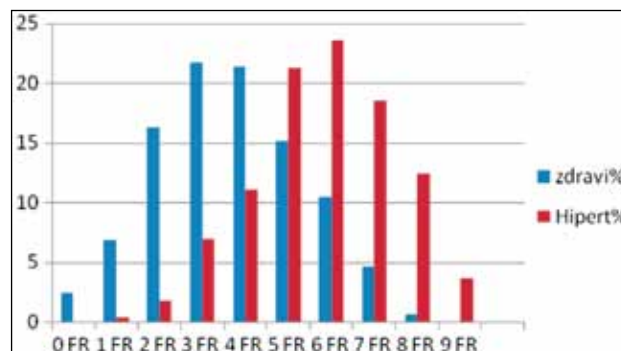
Legend: RF- risk factors; n-number

Table 3. Frequency of number of risk factors in pit miners

Risk factors	Total number		Normotensive		Hypertensive	
	N	%	N	%	N	%
Smoking	294	(59,75%)	169	(61,23%)	125	(57,87%)
Waist values	190	(38,61%)	73	(26,44%)	117	(54,66%)
BMI	371	(75,40%)	190	(68,84%)	181	(83,79%)
cholesterol	242	(49,18%)	115	(41,66%)	127	(58,79%)
Triglycerides	278	(56,5%)	138	(50%)	140	(64,81%)
HDL-cholesterol	194	(39,43%)	97	(35,14%)	97	(44,9%)
LDL-cholesterol	346	(70,32%)	189	(68,47%)	157	(72,68%)
Blood in sugar	13	(2,64%)	6	(3,26%)	7	(3,24%)
Depression	169	(34,34%)	73	(26,44%)	96	(44,44%)

Research have shown egzistence of tendency to risk factors grouping which is more evident among tested subjects with high blood pressure.

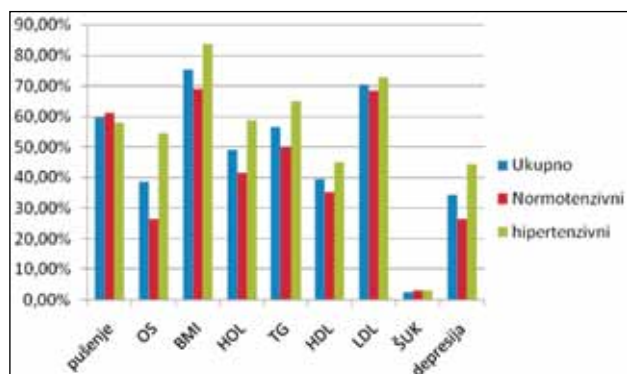
In normotensive group of patients dominant ones are those with 3 or 4 risk factors (out of nine tested subjects), and in tested group with high blood pressure, dominant ones were those with five, six and sevens joined risk factors. Regardless is the number of tested subjects with 8 risk factors joined together (table 1 and graphic 2).



Graphic 2. Frequency of number of risk factors in miners with and without hypertension

The most frequent risk factors among tested subjects are certainly BMI (75,40%) of tested subjects, high level of LDL-cholesterol (70,32%), and apart

from blood sugar level and smoking, all other risk factors are more frequent in group of tested subjects with high blood pressure (table 3 and graphic 3).



Graphic 3. Frequency of certain risk factors in pit miners

## Discussion

According to Nhanes, in period 1999-2004, evident increase of hypertension prevalence occurred from 26,8% in period 1999-2000 to 29,3% for period 2003-2004 (34).

Hypertension prevalence in USA in age group 18-39 is 7,3%, and in population 40-59 years is 32,6% (2007). Based on single measurement of blood pressure values, one of four adults world wide had pressure values 140/90 mm/Hg and higher (36).

Epidemiological study conducted in Vojvodina confirmed that prevalence of normal blood pressure was 46,5%, 4,9% of tested subjects had increased blood pressure in range, 48,7% were with hypertension and only 11,9% of tested subjects in Vojvodina in age of 45 years and more were with normal values of blood pressure.

Prevalence of metabolic syndrome among adult Americans was 23,7%, 24% were men and 23,7% were women (38), in Croatia in 2006 according to NCEP criteria 34,0% of adult Croats are with diagnosed metabolic syndrome (39), and in Germany prevalence of metabolic syndrome for men is 23,5% and for women 17,6% (40). Results of earlier study in the same mine coal conducted on 160 miners speaks of prevalence of metabolic syndrome in value of 51,87% (4). This research in coal mine pit shows that 42,88% of tested subjects are diagnosed with metabolic syndrome what presents each 2,5 tested subject which is more than in previous researches.

It is estimated that during lifetime unipolar depression is evident in 20% of women and 10% of men, while only 25% of tested subjects with disturbed mood take medical treatment (41).

Our research in department of coal mine pit have shown that on 33,94% of tested subjects each third subject was with evident depression criteria according to Becks' scale for self-evaluation. This research have shown much bigger prevalence of depression diagnosing in comparing to situation in America where 1 out of 5 adult persons of 42,1 million of Americans suffer from slight depression symptoms. This is the reason why depression represents large challenge even for American national health for it is often undiagnosed and inadequately and insufficiently treated (42).

Epidemiological evidence for connection between depression and cardiovascular risk factors are rather strong (27,28). Depression and metabolic syndrome are in positive correlation and each of them is independent predictor of negative cardiac happenings (30).

This confirms our research where out 216 tested subjects with high blood pressure 67 of them are with depression and metabolic syndrome in comparing to 9 tested subjects with both complications in group of tested subjects without high blood pressure. In period from 2007 to 2008 among adult Americans in age  $\geq 20$  years, it is estimated that 49,7% (107,3 million) were with at least one of following risk factors for cardiovascular diseases: uncontrolled hypertension, uncontrolled high level of LDL- cholesterol and smoking, where 21,3% were with two out of three risk factors and 2,4% were with all three (43).

Combination of presence  $\geq 3$  of metabolic factors and high values of waist, which is present in 15% of patients, is connected with 10 times larger risk of type II diabetes development (44). According to some results 10-15% are those which lacked any of risk factors (dyslipidemy, hypertension, disturbances in regulation of sugar in blood), between 32 and 37% are those with two risk factors and 12% and 17% were with joined risk factors (45). Research results in same facility in 2008 have proven that 11,25% of tested subjects were without any risk factors, 19,37% were with two risk factors and 17,5% with three risk factors while 31,17% were with four or five risk factors.



Among normotensive tested subjects the majority of them were with one risk factor (33,75%), and in hypertensive group the presence of four risk factors is in 46,25% of tested subjects (4). This research confirmed that hypertensive group holds those tested subjects with six (23,61%) and five (21,29%) risk factors in comparing to those without high pressure values with domination of tested subjects with three (21,73 %) and four (21,37%) risk factors, while total number of tested subjects shows the domination of those with five (17,88%) and four (16,86%) risk factors.

Research in India confirmed that among tested subjects with high risk of cardiovascular illnesses, 48% of them are with high body mass index (46) in comparing to our study where 75,40% were with high BMI . Among miners there were 83,79% of tested subjects with high BMI which is double of the value in India.

Epidemiological study conducted in Vojvodina confirmed that only fifth of tested inhabitants of Vojvodina were with proper waist values (37), while increased waist value in our research were in 38,61% of miners out of which 26,44% were with increased blood pressure and 54,66% were with evident hypertension.

In research (4) the most frequent factor of metabolic syndrome is increasment of triglyceride concentration (58,75%), increased waist values (49,37%), decreased concentration of HDL (46,25%). This research recognized increasment of triglyceride concentration in 56,5% tested subjects, increased waist values in 38,61%, decreasment of HDL concentration 39,43%. Slight fall in frequency of increasment of waist values and HDL concentration is evident in comparing to previous research, but the most significant difference is evident in concentration of sugar in blood in same population which is decreased in 2008 from 39,37% to 2,64%. This could be explained with more quality preparation of tested subjects. The most frequent risk factors in this research were increased BMI and increased concentration of LDL cholesterol which were not taken in consideration in previous study.

## References

1. Anonymous European Society of Hypertension – European Society of Cardiology guidelines for the management of hypertension. *J Hypertens* 2003; 21: 1011-1053.
2. Lawes CM, Vander Hoorn S, Law MR, Elliott P, MacMahon S, Rodgers A. Blood pressure and the global burden of disease 2000. Part 1: estimates of blood pressure levels. *J Hypertens* 2006; 24: 413–422.
3. Bennet A, Di Angelantonio E, Erqou S. Lipoprotein(a) levels and risk of future coronary heart disease: large-scale prospective data. *Arch Intern Med* 2008;168(6):598-608.
4. Becarevic M, Barakovic F, Ljuca F, Tulumovic A, Batic-Mujanovic O. Metabolic syndrome in miners with hypertension. *Health MED* 2009; 3(3): 273-279.
5. European Atherosclerosis Society (EAS) New recommendations from the European Atherosclerosis Society consensus panel resolve controversy about lipoprotein (a) and cardiovascular risk [press release]. 2010.
6. Şerban C, Drăgan S, Mozoş I, Noveanu L, Şuşan L, Christodorescu R, Păcurari A, Caraba A, Romoşan I. Lipoprotein(a): an emerging cardiovascular risk factor in hypertensive patients. *International Journal of Collaborative Research on Internal Medicine & Public Health*. 2011; 3(10):733-742.
7. Rutter MK, Nesto WR. Blood Pressure, Lipids and Glucose in Type 2 Diabetes How Low Should We Go? *Re-Discovering Personalized Care. European Heart Journal*. 2011; 32(18):2247-2255.
8. Lewis GF, Rader DJ. New insights into the regulation of HDL metabolism and reverse cholesterol transport. *Circ Res*. 2005; 96: 1221–1232.
9. Negre-Salvayre A, Dousset N, Ferretti G, Bacchetti T, Curatola G, Salvayre R. Antioxidant and cytoprotective properties of high-density lipoproteins in vascular cells. *Free Radic Biol Med*. 2006; 41: 1031–1040.
10. Mineo C, Deguchi H, Griffin JH, Shaul PW. Endothelial and antithrombotic actions of HDL. *Circ Res*. 2006; 98: 1352–1364.
11. Tso C, Martinic G, Fan WH, Rogers C, Rye KA, Barber PJ. High-density lipoproteins enhance progenitor-mediated endothelium repair in mice. *Arterioscler Thromb. Vasc Biol* 2006; 26: 1144–1149.
12. Tanyolaç S, Bremer AA, Hodoglugil U, Movsesyan I, et al. Genetic variants of the ENPP1/PC-1 gene are associated with hypertriglyceridemia in male subjects. *Metab Syndr Relat Disord*. 2009;7(6):543-548
13. Cheuk-Sing Choy, Wan-Yu Chan, Ta-Liang Chen, Chun-Chuan Shih et al. Waist Circumference and Risk of Elevated Blood Pressure in Children. *BMC Public Health*. 2011; 11:613

14. Hirschler V, Maccallini G, Calcagno M, Aranda C, Jadzinsky M. Waist circumference identifies primary school children with metabolic syndrome abnormalities. *Diabetes Technol Ther.* 2007; 9:149–157.
15. Hirschler V, Aranda C, Calcagno ML, Maccalini G Jadzinsky MC. Can waist circumference identify children with the metabolic syndrome? *Arch Pediatr Adolesc Med* 2005; 159:740–744..
16. Genovesi S, Antolini L, Giussani M, Pieruzzi F, Galbiati S, Valsecchi MG, Brambilla P, Stella A. Usefulness of waist circumference for the identification of childhood hypertension. *J Hypertens* 2008; 26:1563–1570.
17. Maffei CM, Banzato C, Talamini G. Waist-height ratio, a useful index to identify high metabolic risk in overweight children. *J Pediatr.* 2008; 152:207–213.
18. Hu G, Jousilahti P, Antikainen R, Katzmarzyk PT, Tuomilehto J. Joint Effects of Physical Activity, Body Mass Index, Waist Circumference, and Waist-to-Hip Ratio on the Risk of Heart Failure. *Circulation.* 2010; 121(2): 237 - 244.
19. Alberti KG, Eckel RH, Grundy SM. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation.* 2009; 120:1640-1645.
20. Onat A, Can G, Hergenc G, Yazici M, Karabulut A, Albayrak S. Serum apolipoprotein B predicts dyslipidemia, metabolic syndrome and, in women, hypertension and diabetes, independent of markers of central obesity and inflammation, *Int J Obes (Lond).* 2007; 31:1119-1125.
21. Reaven G. Metabolic syndrome: pathophysiology and implications for management of cardiovascular disease. *Circulation* 2002;106: 286–288.
22. Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P at all. The Metabolic Syndrome and Cardiovascular Risk: A Systematic Review and Meta-Analysis *J Am Coll Cardiol.* 2010; 56:1113-1132.
23. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: Executive Summary *J Am Coll Cardiol.* 2010; 56(25):2182-2199.
24. Califf RM, Armstrong PW, Carver JR. 27th Bethesda Conference: matching the intensity of risk factor management with the hazard for coronary disease events. Task Force 5. Stratification of patients into high, medium and low risk subgroups for purposes of risk factor management. *J Am Coll Cardiol.* 1996; 27:1007–1019.
25. De Backer G, Ambrosini E, Barch-Johnsen K. European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J.* 2003; 24: 1610.
26. Brotman DJ, Golden SH, Wittstein IS. The cardiovascular toll of stress. *Lancet.* 2007; 370:1089–1100.
27. Fan A, Strine T, Jiles R, Mokdad A. Depression and anxiety associated with cardiovascular disease among persons aged 45 years and older in 38 states of the United States, 2006. *Prev Med.* 2008; 46: 445-450.
28. Alboni P, Favaron E, Paparella N, Sciammarella M, Pedaci M. Is there an association between depression and cardiovascular mortality or sudden death? *J Cardiovasc Med (Hagerstown).* 2008; 9: 356-362.
29. Steptoe A. *Depression and Physical Illness.* Cambridge, United Kingdom: Cambridge University Press. 2007.
30. Vaccarino V, McClure C, Johnson BD, Sheps DS, et al. Depression, the Metabolic Syndrome and Cardiovascular Risk. *Psychosomatic Medicine.* 2008; 70: 40-48.
31. Raison CL, Capuron L, Miller AH. Cytokines sing the blues: inflammation and the pathogenesis of depression. *Trends Immunol.* 2006; 27:24–31.
32. Shah JA, Veledar, Hong E, Bremner JD, Vaccarino V. Depression and History of Attempted Suicide as Risk Factors for Heart Disease Mortality in Young Individuals. *Arch Gen Psychiatry.* 2011; 68(11):1135-1142.
33. Dong YJ, Zhang Y-H, Tong J, Qin LQ. Depression and Risk of Stroke. Published online <http://stroke.ahajournals.org/content/early/2011/10/19/STROKEAHA.111.630871>.
34. Ong KL, Cheung BMY, Man YB, Lau CP, Lam KSL. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999–2004. *Hypertension.* 2005; 49(1): 69–75.
35. Kwok LO, Bernard MY, Yu Bun Man, Chu Pak Lau, Karen L. Prevalence, Awareness, Treatment, and Control of Hypertension Among United States Adults 1999–2004. *Hypertension.* 2007; 49: 69-74.
36. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet.* 2005; 365: 217–223.
37. Novaković B, Jovičić J, Martinov-Cvejin M, Božin B, Grujičić M, Đurić D, Lakić N, Mijatović-Jovanović V. Prevalence of risk factors for non-communicable diseases. *International Journal of Collaborative Research on Internal Medicine & Public Health.* 2011; 3 (3): 220-221.

38. Ford ES, Giles WH, Dietz WH. Prevalence of the MetS among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*. 2002; 287: 356–359.
39. Kolcic I, Vorko-Jovic A, Salzer B, Smoljanovic M, Kern J, Vuletic S. Metabolic syndrome in a metapopulation of Croatian island isolates. *Croat Med J*. 2006; 47: 585–592.
40. Assmann G, Guerra R, Fox G, Cullen P, Schulte H, Willett D, Grundy SM. Harmonizing the definition of the metabolic syndrome: comparison of the criteria of the Adult Treatment Panel III and the International Diabetes Federation in United States American and European populations. *Am J Cardiol*. 2007; 99: 541–548.
41. Hotujac Lj. Depresija prepoznavanje i liječenje u ambulanti liječnika primarna zdravstvene zaštite. U: Hrvatska consensus grupa za depresiju i anksiozne poremećaje. Prepoznavanje i liječenje depresije i anksioznih poremećaja- uloga liječnika primarne zdravstvene zaštite. Zagreb. 2003; 10-11.
42. Shim RS, Baltrus P, Ye J, Rust G. Prevalence, Treatment, and Control of Depressive Symptoms in the United States: Results from the National Health and Nutrition Examination Survey (NHANES), 2005–2008. *J Am Board Fam Med*. 2011; 24:33-38
43. Valderrama AL, Loustalot F, Gillespie C, George MG, Schooley M et al. Million Hearts: Strategies to Reduce the Prevalence of Leading Cardiovascular Disease MG. Risk Factors. *Morbidity & Mortality Weekly Report*. 2011; 60(36):1248-1251.
44. Wassink AM; van der Graaf Y; van Haeften TW; Spiering W; Soedamah-Muthu SS; Visseren FL. Waist circumference and metabolic risk factors have separate and additive effects on the risk of future Type 2 diabetes in patients with vascular diseases. A cohort study. *Diabet Med*. 2011; 28(8):932-940.
45. Khot UN, Khot MB, Bajzer CT. Prevalence of conventional risk factors in patients with coronary heart disease. *JAMA*. 2003; 290: 898-904.
46. Auras A, Asha K, Muralidhar V, Suma N. Behavioural Risk Factors and Health Promotional Activities in Adults at Risk of Cardiovascular Disease in a South Indian Tertiary Care Teaching Hospital *International Journal of Collaborative Research on Internal Medicine & Public Health*. 2010; 2(8):280-290.

Corresponding Author  
Becarevic Munevera,  
Public Health Centre Banovici,  
Department for Occupational Medicine,  
Bosnia and Herzegovina,  
E-mail: munevera.b@gmail.com

# Quality of life of people with Diabetes Mellitus type 2

Nehra Mosorovic<sup>1</sup>, Selmira Brkic<sup>2</sup>, Sabina Nuhbegovic<sup>2</sup>, Nurka Pranjic<sup>2,3</sup>

<sup>1</sup> Health center, Lukavac- Occupational medicine, Bosnia and Herzegovina,

<sup>2</sup> University of Tuzla, Faculty of medicine, Bosnia and Herzegovina,

<sup>3</sup> Institution of Occupational Health – Health center “ Mustafa Šehović” Tuzla, Bosnia and Herzegovina,

## Abstract

**Background:** Diabetes mellitus is a disease which no longer has the classic symptoms, which develops complications very quietly and which disables many people during their productive life disrupting their quality of life.

**Aim:** To determine the quality of life in patients with diabetes mellitus type 2 in relation to gender and type of the applied treatment.

**Methods:** A cross-sectional study examined the quality of life of 100 respondents suffering from diabetes mellitus type 2, of both sexes, aged 19-59 in relation to sex and applied therapy. Respondents were divided into two groups based on therapy. The control group consisted of 50 respondents without diabetes mellitus. Assessment of quality of life was performed using the SF-36 questionnaire consisting of 8 segments, grouped in the dimension of physical and mental health.

**Results:** A total of 150 respondents, divided into 3 groups, were analyzed. In the first group were respondents with oral agents (38.7%), in the second on combined therapy (28%), while the third was a control group (33.3%). By the analysis of gender representation within the examined groups of subjects, significant differences were found with the domination of men in the second group, and women in the first and the third groups ( $X^2 = 2 \cdot df = 2, p < 0.001$ ). The values of SF-36 score expressed as the median of the studied groups were: 77.50, 62.64, 92.22 (Ht=104.41,  $p < 0.0001$ ). There is a significant difference between SF-36 score in relation to gender in the total sample ( $Z=3.29, p=0.001$ ), with higher values in women. However, within the examined groups there was not significant difference in the first and the third groups ( $Z=1.56, 1.53, p=0.12, 0.13$ ), while in the second one a significantly higher SF-36 was fo-

und among female subjects ( $Z=2.75, p=0.006$ ). Also, significant difference between physical and mental dimensions of SF-36 score was found and its different domains related to the control group (Ht=103.33; 97.98,  $p < 0.0001$ ; Ht=97.98,  $p < 0.0001$ ; Ht=36.571-105.9;  $p < 0.001$ ).

**Conclusion:** Quality of life of people with diabetes mellitus type 2 is exacerbated and associated with patient gender and type of the treatment.

**Key words:** Diabetes mellitus, Quality of life, SF-36 questionnaire.

## Introduction

According to the World Health Organization, diabetes is a chronic, incurable disease, state of chronic hyperglycaemia that occurs when the pancreas does not produce enough insulin or when the body can not effectively use the insulin it produces. Hyperglycaemia or elevated blood sugar is a common effect of uncontrolled diabetes and over time leads to serious damage to many body systems, particularly blood vessels and nervous system.<sup>1</sup> Diabetes mellitus is a disease that is no longer just an individual problem of the patient, but it is assuming psychological and socio-medical significance of mass disease. It is estimated that 195 million people worldwide have diabetes, and prevalence of diabetes worldwide has taken a dramatic, unexpected growth. It is expected that the number of cases doubles by 2030 although the awareness of population about the disease remains low.<sup>2</sup> Good glycaemia control, reducing blood pressure and concentrations of lipoproteins are three main therapeutic targets to prevent target organ damage and other complications of diabetes.<sup>3</sup> The therapy involves education of diabetes patients, rational nutrition, physical activity and medicament therapy.<sup>4</sup> Medicament treatment involves the application of oral hypoglycaemic and insulin preparati-

ons. A modern insulin therapy should be based on the use of human insulin and insulin analogues. By the effective treatment of hyperglycaemia, it is not only extended the life of a patient but it reduces the capacity of micro and macro vascular damage after long period of diabetes, and thus reduced the negative impact on quality of life. Serious studies have shown that diabetes has a very strong negative impact on quality of life, especially diabetes with complications.<sup>5</sup> Initially, studies of diabetes have been focused on studying the quality of life in patients with diabetes mellitus with severe complications of the disease, such as patients on haemodialysis treatment, who have had a kidney transplant or have had a foot or leg amputated. Later studies were more focused on the psychological impact of the disease on quality of life, where one seeks to understand the patient's ability to cope with the complicated and demanding regimen of treatment of disease. Quality of life is widely recognized as a very important component of health status in patients with diabetes mellitus, where patients are bearing the burden of a very demanding regimes and disease management.<sup>6</sup> Quality of life refers to the personal well-being and life satisfaction, including mental and physical health, material well-being, interpersonal relationships inside and outside the family, work and other activities in the community, personal development and satisfaction, as well as active recreation.<sup>7</sup> Diabetes mellitus require patients to possess daily responsibility and concern for their health by using insulin, tablets, careful monitoring of diet, exercise and checking blood glucose, daily, until the end of life. Adapting to diabetes mellitus often requires months, sometimes even years, and entails certain emotional responses that help in the successful battle with stress. A patient who suffered from diabetes for over twenty years once said, "At least once every fifteen minutes I have to deal with my illness, I have to stop and think about how I feel and what and when I ate last time, think about what I will do next, decide when I test my blood, and depending on results i.e. blood sugar levels to plan the next meal, and insulin doses." Of course the life of every person with diabetes is unique. Most patients manage the disease actively and effectively, but almost every person with diabetes mellitus strongly feels its influence on their lives and carries the burden of this very demanding disease.<sup>8</sup>

## Methods

We conducted a cross-sectional study, which covered the population of working age (19-59 years) suffering from diabetes mellitus type 2 who were treated on outpatient basis at Public Health Institution Health Centre Lukavac in the period from 01.02.2009 to 01.08.2009. The study included patients with proven disease duration of more than a year. We analyzed a total of 100 respondents of both sexes suffering from diabetes mellitus type 2, divided into two groups based on therapy. In the first group there were patients treated with oral anti-diabetic agents (38.7%), while the second group the patients were on combined therapy (simultaneously receiving insulin and oral anti-diabetic agents) (28%). The control group consisted of 33.3% of respondents who do not suffer from diabetes mellitus. The studies excluded respondents who had, besides diabetes, a diagnosed psychiatric, cancer or another serious illness that could significantly affect the quality of life. All respondents were familiar with the goals and nature of research, they were presented the manner of research and sought their approval and consent for participation in the study. Assessment of quality of life was carried out by the scale of quality of life SF-36.<sup>9</sup> This is a health status questionnaire consisting of 36 questions, grouped into eight dimensions, namely: physical functioning, limitations due to physical problems, limitations due to emotional problems, social functioning, mental health, vitality and energy; physical pain and general health perception. These eight areas are grouped into two dimensions: physical and mental health. Total score is calculated through microcomputer programme (SF-36.EXE) and has the value of 0-100 or bad to excellent quality of life.<sup>10</sup> The scale was completed by the examiner. The study was approved by the Commission on Ethics of Health Centre Lukavac.

## Statistical analysis

Statistical analysis was made in the software package SPSS 18.0 (Chicago, IL, USA) and MedCalc 9.2.0.1 (MedCalc, Belgium). The basic tests of descriptive statistics were made, showing a measure of central tendency and dispersion. Testing

of each variable for belonging to a normal distribution was amde, using the Kolmogorov-Smirnoff test, and the histogram display. Comparison of two mean values, due to the nonparametric distribution of variables, was made by Mann-Whitney test. Quantitative variables, in case of comparison of three medium values, were compared by one-way ANOVA test, where they have been distributed by a normal distribution. For variables that were not distributed according to the normal distribution nonparametric alternatives were used - Kruskal-Wallis test. Categorical variables were analyzed by X<sup>2</sup>-test. All statistical tests were conducted with a level of statistical probability of 95% ( $p < 0.05$ ).

## Results

A total of 150 respondents were analyzed and divided into 3 groups. In the first group there were respondents with oral agents (38.7%), the second on combined therapy (28%), while the third was a control group (33.3%). The average age in the total sample was 50 ( $\pm 7$ ) with a minimum of 32 and maximum of 59 years of age. By comparison of gender representation between groups, a significant difference was found ( $X^2=2$ ;  $df=2$ ;  $p < 0.001$ ) with the dominance of males in the second group, whereas the first and the third groups were dominated by women. Given that the value of SF-36 score was not distributed by a normal distribution, nonparametric tests were applied. There was a statistically significant difference of SF-36 score between male and female subjects (Mann Whitney,  $Z=3.29$ ,  $p=0.001$ ), with average higher values of SF-36 score among female respondents. In addition, separate comparative analyses of SF-36 score were made in the individual study groups in relation to sex. There was no statistically significant differences in average SF-36 score between men and women in the control (Mann Whitney,  $Z=1.56$ ,  $p=0.12$ ), and the first groups (Mann Whitney,  $Z=1.53$ ,  $p=0.13$ ), while the second group significantly higher value of the SF-36 score was found among female subjects (Mann Whitney,  $Z=2.75$ ,  $p=0.006$ ). A comparison of SF-36 scores between groups was made in relation to the type of the treatment. The median value of SF 36 score within the examined groups are given in Table 1.

Table 1. Median values of SF-36 score in respondents according to the type of the applied treatment (Kruskal-Wallis;  $H_t=104.41$ ,  $p < 0.0001$ ).

Group	Median	Interquartile range
The control group	92.22	90.83-93.61
Respondents in oral therapy	77.50	67.84-84.40
Respondents in combined therapy	62.64	57.56-70.03

As in the analysis for the total value of the SF-36 score, a comparison of the values of physical and mental health dimensions of SF-36 score between groups was made. The median values of the SF-36 score of physical health dimension are given in Table 2, and SF-36 score of mental health dimension in Table 3.

Table 2. The median value of the SF-36 score of physical health dimension according to the type of the treatment (Kruskal-Wallis;  $H_t=103.33$ ,  $p < 0.0001$ ).

Group	Median	Interquartile range
The control group	95.23	92.85-96.42
Respondents in oral therapy	82.74	73.50-88.39
Respondents in combined therapy	66.66	62.43-72.91

Table 3. The median value of the SF-36 score of mental health dimension by type of treatment applied ((Kruskal-Wallis;  $H_t=97.98$ ,  $p < 0.0001$ ).

Group	Median	Interquartile range
The control group	92.85	91.05-94.28
Respondents in oral therapy	74.29	61.78-82.59
Respondents in combined therapy	58.21	51,42-69-91

Using the Kruskal-Wallis test, a comparison was made between the 3 studied groups in terms of individual domain of SF-36 scales of quality of life. Tabular representation with values of comparison tests is given in Table 4.

## Discussion

Table 4. Values of the individual dimensions of SF-36 score in each group tested, and comparisons by Kruskal-Wallis test

Dimensions of SF-36 score	Respondent group	The median values	Kruskall-Wallis	df	p-value
Limitations due to physical problems	The control group	100.0	52.037	2	<0.001
	Oral therapy	100.0			
	Combined therapy	75.0			
Limitations due to emotional problems	The control group	100.0	36.571	2	<0.001
	Oral therapy	66.66			
	Combined therapy	66.66			
Physical functioning	The control group	90.0	73.666	2	<0.001
	Oral therapy	85.0			
	Combined therapy	75.0			
Vitality and energy	The control group	90.0	89.103	2	<0.001
	Oral therapy	70.0			
	Combined therapy	50.0			
Mental health	The control group	92.0	92.764	2	<0.001
	Oral therapy	72.0			
	Combined therapy	56.0			
Social functioning	The control group	100.0	67.291	2	<0.001
	Oral therapy	87.5			
	Combined therapy	62.5			
Physical pain	The control group	N / A	65.470	2	<0.001
	Oral therapy	75.0			
	Combined therapy	62.5			
General health perception	The control group	90.0	105.900	2	<0.001
	Oral therapy	65.0			
	Combined therapy	45.0			

N / A - not applicable because there are not any variations - all subjects were assessed with 100 points

In our study, diabetes mellitus type 2 had a significant impact on quality of life, and was closely related to the type of the treatment and sex of the respondent. Namely, respondents to combined therapy had statistically worse quality of life, i.e. they had significantly lower values of the total SF-36 score, its physical and mental dimensions, as well as all eight of his domains, compared to subjects who were taking oral therapy and the control group. The results also show that the quality of life is lower in male subjects in both the total sample and in the group of respondents who were in combined therapy. Studies of other authors who have used the same measurement instrument for assessing quality of life as in our study also showed that the quality of life of those suffering from diabetes mellitus is worse than the general population of. <sup>11</sup> Lasaite <sup>12</sup> in her study indicates a greater worsening of quality of life and emotional status of men relative to women, which is consistent with our

results. When it comes to treatment with insulin, other authors, as well as our study, demonstrated that insulin treatment is significantly associated with lower levels of pleasure and significantly increases the impact of this disease on quality of life.<sup>13,14,15</sup> Earlier studies also found significantly lower values of SF 36 score in the area of individual domains of quality of life.<sup>16,17,18</sup>

Obviously, the results indicate that the solution of problems related to quality of life of people with diabetes mellitus should be approached in time. Therefore, any physical illness in addition to organic disorders leads to changes in mental status of patients, which is particularly expressed in chronic diseases such as diabetes mellitus. Knowledge about the long-term, lifelong disease often strikes the person suddenly and requires mobilization of all the psychological adaptation mechanisms to help them to overcome disease and to integrate it into his personality. It is very important to detect it early and

treat it adequately, not only elevated blood glucose, but also all other changes in diabetics, both because of the quality of life and the general prognosis.

### Conclusion

Quality of life in patients with diabetes mellitus type 2 is exacerbated and in close relation with the type of the applied treatment and sex of the respondent. Treatment with insulin increases the negative impact of disease on quality of life. Women with diabetes who were receiving treatment with insulin have a better quality of life compared to men. The task of physicians is timely diagnosis and appropriate treatment which can reduce delay and complications, and thereby reduce the negative impact of disease on quality of life.

### References

1. *The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up Report on the Diagnosis of Diabetes Mellitus. Diabetes Care* 2003; 26:3160-3167.
2. Wild S, Roglic G, Green A, Sicree R, King H. *Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care.* 2004; 27(5):1047-1053.
3. Ménard J, Payette H, Dubuc N, Baillargeon JP, Maheux P, Ardilouze JL. *Quality of life in type 2 diabetes patients under intensive multitherapy. Diabetes Metab.* 2007; 33(1):54-60.
4. Lapčević M, Ilić D. *Diabetes melitus. (U): Žigić D, Lapčević M, Popović J, Ivanković D. General medicine- Family medicine. Beograd, 2003; 499-555.*
5. Coffey JT, Brandle M, Zhou H, Marriott D, Burke R, Tabaei BP, Engelgau MM, Kaplan RM, Herman WH. *Valuing health-related quality of life in diabetes. Diabetes care.* 2002; 25(12): 2238-2243.
6. Speight J, Reaney MD, Barnard KD. *Not all roads lead to Rome- a review of quality of life measurement in adults with diabetes. Diabet Med.* 2009; 26(4):315-327.
7. Niemi ML, Laaksonen R, Kotila M, Waltimo O. *Quality of Life 4 years after Stroke. Stroke.* 1988; 19(9):1101-1107.
8. Richard R, Rubin PhD. *Diabetes and Quality of Life. Diabetes spectrum.* 2000; 13:21.
9. Ware JE Jr, Sherbourne CD. *The MOS 36-item Short-Form health survey (SF-36). Conceptual framework and item selection. Med Care* 1992; 30(6):473-483.
10. Hays RD, Sherbourne CD, Marzel RM. *RAND 36-Item Health Survey 1.0. Health Econ.* 1993; 2(3):217-227.
11. Rubin RR, Peyrot M. *Quality of Life and Diabetes. Diabetes Metab Res Rev.* 1999; 15(3): 205-218.
12. Lasaite L, Lasiene J, Kazanavicius G, Gostautas A. *Associations of emotional state and quality of life with lipid concentration, duration of the disease, and the way of treating the disease in persons with type 2 diabetes mellitus. Medicina (Kaunas).* 2009; 45(2):85-94.
13. Koopmanschop M. *Code-2 Advisory Board. Coping with Type II diabetes: the patients perspective. Diabetologia.* 2002; 45(7):S18-22.
14. Nicolucci A, Cucinotta D, Squatrito S, Lapolla A, Musacchio N, Leotta S, Vitali L, Bulotta A, Nicoziani P, Coronel G. *Quality Study Group. Clinical and socio-economic correlates of quality of life and treatment satisfaction in patients with type 2 diabetes. Nutr, Metab and Cardiovasc Dis.* 2009; 19(1):45-53.
15. Mata Cases M, Roset Gamisans M, Badia Llach X, Antonanzas Villar F, Ragel Alcazar J. *Effect of type 2 diabetes mellitus on the quality of life of patients treated at primary care consultations in Spain. Aten Primaria.* 2003; 15; 31(8):493-499.
16. Clouet F, Excler- Cavaillher G, Christophe B, Masson F, Fasquel D. *Type 2 diabetes and short form 36-items Health Survey. Diabetes Metab.* 2001; 27(6):711-717.
17. Hervas A, Zabaleta A, De Miquel G, Beldarrain O, Diez J. *Health related quality of life in patients with diabetes mellitus type 2. An Sist Sanit Navar.* 2007; 30(1):45-52.
18. Goldney RD, Phillips PJ, Fisher LJ, Wilson DH. *Diabetes, depression and quality of life: a population study. Diabetes Care.* 2004; 27(5):1066-1070.

Corresponding Author  
Nehra Mosorovic,  
Occupational medicine,  
Health center Lukavac,  
Lukavac,  
Bosnia and Herzegovina,  
E-mail: nehra.mosorvic@bih.net.ba



# Effects of short-term octreotide therapy on TSH adenoma with atrial fibrillation - Case report

Salih Azabagic<sup>1</sup>, Amra Jakubovic Cickusic<sup>1</sup>, Edin Zukic<sup>2</sup>

<sup>1</sup> JZU Univerzitetsko Klinički Centar Tuzla, Tuzla, Bosnia and Herzegovina,

<sup>2</sup> JZU Dom Zdravlja sa Poliklinikom Tuzla, Tuzla, Bosnia and Herzegovina.

## Abstract

Secondary hyperthyroidism due to a thyrotropin - secreting (TSH) pituitary adenoma is a rare cause of hyperthyroidism, representing 0.5-2.0% of all pituitary adenomas. We report a case of a 36 year old female who presented with signs of thyrotoxicosis, elevated T3, T4, TSH, atrial fibrillation, as a result of TSH adenoma. She was successfully treated with Somatostatin analogue without surgical intervention. The investigation and treatment of this condition is discussed.

**Key words:** TSH adenoma, Octreotide, Atrial fibrillation

## Introduction

Thyroid-stimulating hormone (TSH)-secreting pituitary adenomas are rare, representing around 2% of all pituitary adenomas (1). There had been Fifty-two cases from 24 medical centers in nine countries reported between 1987 and 1991 (2). Thyroid-stimulating hormone-secreting pituitary lesions are often delayed in diagnosis, are frequently macroadenomas and plurihormonal in terms of their pathological characteristics, have a heterogeneous clinical picture, and are difficult to treat (3). The criteria that are required to confirm this entity are the following. The patient is clinically thyrotoxic while serum levels of free T4 and/or free T3 are elevated and serum TSH concentration is normal or increased. Visualization of the pituitary by magnetic resonance imaging shows a pituitary tumor. The concentration of TSH alpha-subunits in blood is above normal, as is the ratio of TSH alpha /TSH (4). Decreased or lack of response of TSH during the TRH test has a good sensitivity and excellent specificity in patients with intact thyroid, with a slight decrease in sensitivity after thyroidectomy (5). Although in principle this thyrotoxicosis is not accompanied by eye signs,

unilateral exophthalmus may ensue from a thyrotropin secreting pituitary tumor due to invasion of one orbit (6). Pituitary TSH adenoma produce normal forms of TSH but secrete them in variable amount and differing biological activity, explaining the variable degree of hyperthyroidism in these patients (7). Surgical resection remains the basis for definitive treatment of TSH adenomas (8). Losa et al. found a relapse in 3 of 5 operated and postoperatively irradiated patients without postoperative TSH inhibition (9).

Octreotide has been shown to reduce TSH secretion in almost all cases, normalize thyroid hormone levels, and shrink tumors in up to one third of patients receiving long term treatment (10). Long-term medical therapy with somatostatin analogs is indicated adjunctively in patients with TSH-secreting pituitary adenomas who failed to be cured after surgery or who were awaiting the effects of radiation. The use of somatostatin analogs as primary therapy was generally reserved to patients who refused surgery or who were poor surgical candidates (11).

## Case report

Patient M.M. 36-years-old, mother of two, was referred to Endocrinology department with classical signs of hyperthyreosis, elevated T3, T4, TSH, atrial fibrillation, popliteal vein thrombosis and pituitary macroadenoma confirmed by magnetic resonance imaging (MRI) scan. The patient was treated for hyperthyreosis since 1999, with antithyroid drugs (Thyamazol and Propiltiouracil) and was diagnosed as having diffuse goiter. The patient had elevated levels of thyroid hormones (T3=5,8 nmol/L - normal range 1,2-2,8 nmol/L and T4= 396nmol/L - normal range 60-160nmol/L) and TSH (TSH=9,6 mIU/L - normal range 0,17-4,05mIU/L). Thyroid antibodies

were negative (TgAt=12, TPOAt=5,2). The patient had regular checkups at the Department for Nuclear Medicine Tuzla, and at the same time received antithyroid drugs with occasional breaks, depending on the subjective symptoms and levels of thyroid hormones and TSH until 2005. Due to a suspicion of secondary hyperthyroidism a CT scan of neurocranium was performed in 2005 (at this time MRI was unavailable in our clinic). Also additional hormones of pituitary gland FSH, LH, prolactin were all in the normal range. CT scan did not reveal any pathological processes in the pituitary gland so it was decided to proceed with antithyroid therapy (low doses of Methiamazol). For the past eight years the patient suffered from atrial fibrillation and was treated with various combinations of antiarrhythmics including Propafenon, Verapamil, Propranolol and Metoprolol. In May 2009 she had popliteal vein thrombosis and was started on anticoagulant therapy.

In November 2009 MRI scan of the neurocranium showed the existence of macroadenoma of pituitary gland. Patient was then referred to the Endocrinology department.

Once she was admitted to the hospital additional test were done including ACTH, prolactin, progesterone, estradiol, FSH, LH, growth hormone, testosterone, HCG, IgF1, parathormone, 17-OH, 17-KS, cortisol, all were within normal range. Level of sex hormone binding globulin (SHBG) was elevated.

In order to differentiate between secondary and tertiary hyperthyroidism TRH stimulation test was performed. TRH test was negative confirming that this was a case of secondary hyperthyroidism. Based on the negative TRH test, MRI of the pituitary gland, serum levels of T3, T4 and TSH, and a complete endocrinological workup we were able to confirm the diagnosis of TSH-secreting adenoma of pituitary gland.

We were unable to determine levels of alpha subunit of TSH in our clinic.

Additional test were performed including electrolytes, microelements, CIC, immunoelectrophoresis, immunophenotyping, allergy tests. These tests revealed an increased value of IgE in plasma. Allergy prick tests were positive for multiple nutritional and inhalant allergens.

At the moment of admission ECG showed atrial fibrillation with fast ventricular rate of 180 per

minute (Figure 1). She was treated with maximum doses of Propafenon, Metoprolol and Warfarin. Warfarin was started due to popliteal vein thrombosis, but also due to atrial fibrillation.

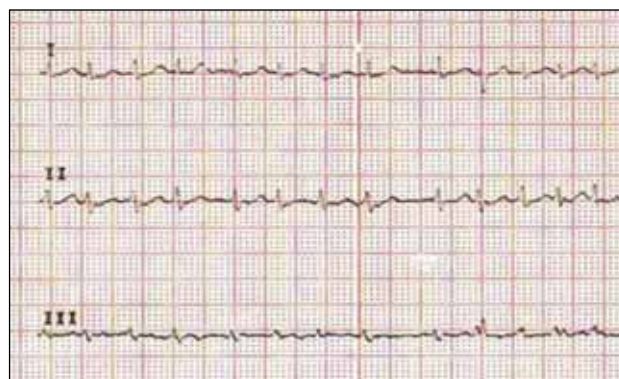


Figure 1. ECG tracing of atrial fibrillation with fast ventricular rate

Echocardiography showed tachycardial myopathy and dilatation of right ventricle, initial dilatation of the left ventricle, mild mitral regurgitation, and second-degree tricuspid regurgitation with pressure gradient of 35mmHg. (Figure 2).



Figure 2. Echocardiography longitudinal section of VCI and parasternal cross-section at the level of mitral valves

The patient refused the surgical treatment, so conservative treatment with octreotide was started with 0,1mg three times daily. After 8 days of therapy a significant drop in TSH and thyroid hormone levels was registered (T3=1.89; T4=153.19; TSH=0.80).

At the same time there was a significant reduction in ventricular rate of atrial fibrillation. Ventricular rate control was achieved with minimal doses of Metoprolol (Figure 3.)

The patient was discharged with normal levels of T3, T4, TSH, atrial fibrillation with normal ventricular rate, with recommended therapy of Octreotide 0,1mg s.c. bid, and minimal doses of Metoprolol 12,5mg bid.



Figure 3. Atrial fibrillation, with ventricular rate of 70/min

After two months of Octreotide therapy follow-up ECG revealed normal sinus rhythm. Atrial fibrillation was converted to sinus rhythm without any specific antiarrhythmic therapy. (Figure 4.)



Figure 4. Sinus rhythm, with rate of 80 bpm

Follow-up echocardiography registered normal morphology of the heart muscle with minor mitral end tricuspid regurgitation.

Control MRI scan of the pituitary gland showed cystic degenerative changes of macroadenoma (Figure 5).

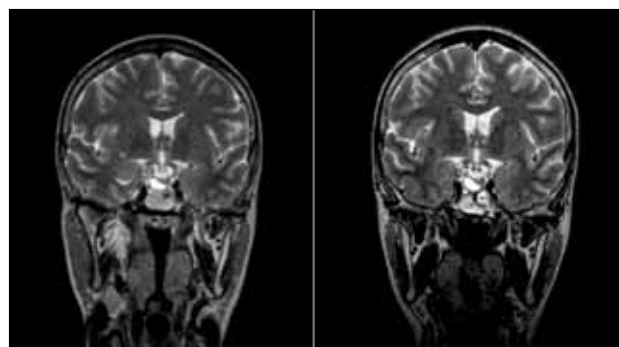


Figure 5. MRI of pituitary macroadenoma before (left) and after (right) two months of octreotide therapy.

The most significant effects after two months of therapy with octreotide are shown in table 1.

Therapy with Octreotide was continued with depot formulation once monthly.

During this period the patient did not have any adverse effects related to octreotide. After two months of therapy serum levels of thyroid hormones and TSH were in normal range, patient was free of any signs and symptoms of hyperthyroidism.

### Discussion

Thyrotropin - secreting (TSH) pituitary adenoma is a rare cause of hyperthyroidism, representing 0.5-2.0% of all pituitary adenomas (1, 2). Although rarely encountered in the past, TSH-secreting adenomas have been diagnosed in a gradually

Table 1. Effects of octreotide (after two months of therapy)

Before treatment	After treatment
Atrial fibrillation	Sinus rhythm
Echocardiography: tachycardial myopathy with sings of right ventricle dilatation and initial left ventricle dilatation.	Echocardiography: Normal morphological findings
T3, T4, TSH increased	Normal level of T3, T4, TSH
IgE: 1490 increased	IgE: 960 significantly lower
Thyrotoxicosis	Normal clinical findings
Irregular menstrual cycles	Regular menstrual cycles
Acuity weakened (reported by patient)	Acuity better (reported by patient-VOU was not determined)
MRI - pituitary macroadenoma	MRI pituitary macroadenoma with cystic degeneration (morphological changes)
SHBG elevated	SHBG within normal limits

increasing rate owing to the application of more sensitive measurement of TSH hormone (12). In these tumors there is an increased level of thyroid hormones and inappropriate level of TSH which is also high or not suppressed (12).

Due to low incidence of this disease, it is rarely included in the differential diagnosis of hyperthyroidism. Therefore, this disease remains unrecognized for a long time as a possible cause of hyperthyroidism, which unfortunately leads to wrong therapeutic approach. This was also the case with our patient where she was initially misdiagnosed as having diffuse toxic goiter and then treated with antithyroid therapy. Latency between the onset of hyperthyroidism and diagnosis of TSH-oma in our patient was 11 years. Similar results were reported by Kienitz et al., (13) where the mean period to proper diagnosis was 12.5 years (range 1-19 years). Therefore, we need to emphasize the importance of early detection of this disease, which can prevent serious complications (neurological compression syndrome caused by aggressive nature of these tumors - tumors to become large and invasive).

However, it is necessary to keep in mind that other clinical conditions may have similar clinical presentation such as pituitary TSH hyperplasia and thyroid hormone resistance. Therefore, it is necessary to perform additional hormonal measurements in differential diagnosis including serum level TSH,  $\alpha$ -subunit, molar ratio of  $\alpha$ -subunit / TSH, thyrotropin releasing hormone (TRH) stimulation test, T3 suppression test and sex hormone binding globulin (SHBG) as an indicator of peripheral effects of thyroid hormones. Brucker-Davis et al. suggested that a combination of negative TRH stimulation test, elevated  $\alpha$ -subunit, and  $\alpha$ -SU/TSH ratio is indicative of TSHoma. (14). In this case we were not able to determine  $\alpha$ -subunit, and  $\alpha$ -SU/TSH ratio. In our case we were able to diagnose TSH adenoma using elevated T3, T4, TSH levels, negative TRH test, and the presence of pituitary macroadenoma on the MRI scan. Therapy of TSH-secreting adenomas can be accomplished by surgery, irradiation therapy and medical treatment with somatostatin analogues or dopamine agonists. Although surgical treatment (transsphenoidal adenectomy) is essential, it doesn't guarantee complete cure of this disease.

Therapeutic options available for other types of pituitary tumors may also be valid for the treatment of TSH secreting tumor. As in the case of other pituitary tumors, there is no single treatment approach which can be effective in the treatment of TSHoma. Conventionally, preoperative management of this tumor involves restoring euthyroidism by suppression of TSH with somatostatin analogues. Somatostatin analogue octreotide acetate has also been used for treatment of many endocrine diseases. In addition it is very helpful tool in the diagnosis of some endocrinological diseases. Many studies reported that octreotide is an effective drug in reducing both TSH and thyroid hormones level as well as reducing tumor size in TSH-secreting pituitary adenoma (13, 15). A study by Lee et al. showed that octreotide therapy was effective in reducing both tumor size and serum level of TSH and thyroid hormones in 55 patients with TSH-oma (16). Another study by Gancel et al. (17) and Mayinger et al. (18), showed significant decrease in the levels of both thyroid hormones and TSH using a long-acting somatostatin analogues, lanreotide in 4 patients with TSH-oma. In our case the use of short-term octreotide therapy produced satisfactory results including the reduction of thyroid hormone levels and TSH, as well as morphological changes in adenoma (cystic degenerative changes). We also had a satisfactory response, using octreotide therapy, in reduction of clinical symptoms and signs of disease that include conversion to sinus rhythm from atrial fibrillation without using specific antiarrhythmic therapy and reduction of SHBG to normal limits. Based on the results of our study we want to emphasize the importance of short term octreotide therapy in preoperative preparation of patients for effective restoration of euthyroidism in order to minimize the risks of surgery and postoperative complications.

Elevated levels of IgE and positive allergen prick test revealed atopy predisposition of our patient. In this case it remains questionable if atopy could represent a possible etiological factor in the development of TSH adenoma, or if it is a part of pathological and clinical presentation of TSH adenoma. After octreotide therapy there was a significant drop in IgE from 1500 to 960. Also our patient had significant menstrual cycle disorders, which were resolved after Octreotide therapy.

Menstrual disorders can normally be seen in primary hyperthyreosis, but in this case it is possible that menstrual cycle disorder was produced by elevated levels of SHBG or alpha subunit (due to the fact that alpha subunit is biologically identical in TSH, LH and FSH hormones).

Octreotide is a cyclic octapeptide somatostatin analogue, which inhibits the production of growth hormone, TSH, gastrin, secretin, gastrointestinal polypeptides, motilin, enteroglucagone, insulin, glucagons, renin.

Cardiovascular effects of octreotide produce hypotension, systemic vasoconstriction, elevation of pulmonary arterial pressure. In patients with acromegaly which have left ventricular hypertrophy, octreotide therapy produces significant reduction of left ventricular mass.

With Octreotide therapy we have achieved sinus rhythm, without specific antiarrhythmic therapy, even after eight years of permanent atrial fibrillation.

In this case there has been a significant restitution of heart atria, and conversion to sinus rhythm. Exact mechanisms remain uncertain, but it is probably achieved with direct somatostatin effects to cardiovascular system, and possibly with indirect hormonal effects described above.

## Conclusion

Considering the effects of Octreotide therapy registered in this patient, we believe that there is a need for a review of similar cases of TSH adenoma with atrial fibrillation, that would evaluate the serum IgE and atopic predisposition.

Because various authors have also described long periods from the first symptoms to diagnosis, we believe that the diagnosis of TSH adenoma should be made without the need for radiological confirmation.

In our opinion elevated levels of T3, T4 and TSH, and a negative TRH test are indicative of TSH adenoma. Octreotide could be used as a first-line therapy if the TSH adenoma is indentified without radiological presence of macroadenoma, while being second line after surgery in case of radiological confirmation of macroadenoma.

## References

1. Mindermann T, Wilson CB, Thyrotropin producinh pituitary adenomas. *J Neurosurg* 1993;79:521-527.
2. Philipe C, Bruce DW, Alan GH, Octreotide Therapy for Thyroid-Stimulating Hormone-Secreting Pituitary Adenomas: A Follow-up of 52 Patients, *Annals of Internal Medicine* 1993; 119: 236-240.
3. Clarke MJ, Erickson D, Castro MR, Atkinson JL, Thyroid-stimulating hormone pituitary adenomas, *J Neurosurg*. 2008 Jul;109(1):17-22.
4. McDermott MT, Ridgway EC. Central Hyperthyroidism. *Endocrinol Metab Clin Nort Am* 1998; 27:187-203.
5. Brucker-Davis F, Oldfield EH, Skarulis MC, Doppman, JL, Weintraub BD. Thyrotropin-secreting pituitary tumors: diagnostic criteria, thyroid hormone sensitivity, and treatment outcome in 25 patients followed at the national institutes of health. *Journal of Clinical Endocrinology and Metabolism* 1999; 84: 476-486.
6. Yovos JG, Falko JM, O-Dorisio TM, Marlakey WB, Catalnd S, Capen CC, Thyrotoxicosis and a thyrotropin-secreting pituitary tumor causing unilateral exophthalmus. *J clin Endocrinol Metab* 1981 53:338.
7. Sergi E, Medri G, Papandreou M, et al. Polymorhpiism of thyrotropin and alpha subunit in human pituitary adenomas. *J Endocrinol Invest* 1993;16:45-55.
8. McCUtcheon IE, Weintraub BD, Oldfield EH, Surgical treatment of thyrotropin secreting pituitary adenomas. *J Neurosurg* 1990;73:674-683.
9. Losa M, Mortini P, Franzin A, Barzaghi R, Mandelli C, Giovanelli M, Surgical Management of Thyrotropin-Secreting Pituitary Adenomas, *Pituitary* 1999; 2:127-131.
10. Chanson P, Weintraub BD, Harris AG, Octreotide Therapy for Thyroid-Stimulating Hormone-Secreting Pituitary Adenomas: A Follow-up of 52 Patients, *Annals of Internal Medicine* 1993;119:236-240.
11. Caron P, Arlot S, Bauters C, Chanson P, Kuhn JM, Pugeat M, Marechaud R, Teutsch C, Vidal E, Sassano P, Efficacy of the Long-Acting Octreotide Formulation (Octreotide-Lar) in Patients with Thyrotropin-Secreting Pituitary Adenomas, *The Journal of Clinical Endocrinology & Metabolism* Vol. 86, No. 6 2849-2853
12. Kaimio M. Thyrotropin secreting adenoma. *Nippon rinsho* 1993;51:2701-2705 (Abstr).
13. Kienitz T, Quinkler M, Strasburger JC, Ventz M. Long-term management in five cases of TSH-secreting pituitary adenomas: a single center study and review of the literature *Eu J Endocrinol* 2007; 157: 36-46.

14. Brucker-Davis F, Oldfield EH, Skarulis M, Doppman JL, Weintraub WD. Thyrotropin-secreting pituitary tumors: diagnostic criteria, thyroid hormone sensitivity and treatment outcome in 25 patients followed at the national Institutes of Health. *Journal of Clinical Endocrinology and Metabolism* 1999;84:476-486.
15. Mannavola D, Persani LVannucchi G, Zanardelli M, FurgazzolaL, Verga U, Vacchetti M, Beck-Peccoz P. Different responses to chronic somatostatin analogues in patients with central hyperthyroidism. *Clinical Endocrinology* 2005;62:176-181.
16. Lee EJ, Kim KR, Lim SK et al.:Reduction in tumor size of thyrotropin-secreting pituitary adenoma treated with octreotid acetate (somatostatin analog). *Eur J Endocrinol* 1994;131:109-121.
17. Gancel A, Vuillermet P, Legrand A et al.: Effects of a slow releasing formulation of the new somatostatin analogue lanreotide in TSH-secreting pituitary adenomas. *Clin Endocrinol (Oxf)* 1994;421-428.
18. Mayinger B, Axelos DPavel M, Hahn EG, Hensen J. Monosymptomatische Hyperthyreose und TSH produzierendes Adenom:Erfolgreiche Therapie mit Octreotid. *Dtsch Med Wschr* 1999;124:73-78.

*Corresponding Author*

Salih Azabagic,  
JZU Univerzitetsko Klinički Centar Tuzla,  
Tuzla,  
Bosnia and Herzegovina,  
E-mail: zuka@bih.net.ba

# Instructions for the authors

*All papers need to be sent to e-mail: healthmedjournal@gmail.com*

Every sent magazine gets its number, and author(s) will be notified if their paper is accepted and what is the number of paper. Every correspondence will use that number. The paper has to be typed on a standard size paper (format A4), leaving left margins to be at least 3 cm. All materials, including tables and references, have to be typed double-spaced, so one page has no more than 2000 alphanumeric characters (30 lines). Sent paper needs to be in the form of triplicate, considering that original one enclosure of the material can be photocopied. Presenting paper depends on its content, but usually it consists of a page title, summary, text references, legends for pictures and pictures. Type your paper in MS Word and send it on a diskette or a CD-ROM.

## TITLE PAGE

Every article has to have a title page with a title of no more than 10 words: name (s), last and first of the author (s), name of the institution the author (s) belongs to, abstract with maximum of 45 letters (including space), footnote with acknowledgments, name of the first author or another person with whom correspondence will be maintained.

## SUMMARY

Second page needs to contain paper summary, 200 words at the most. Summary needs to hold all essential facts of the work-purpose of work, used methods (with specific data, if possible) and basic facts. Summaries must have review of underlined data, ideas and conclusions from text. Summary has no quoted references. For key words, at the most, need to be placed below the text.

## CENTRAL PART OF THE ARTICLE

Authentic papers contain these parts: introduction, goal, methods, results, discussion and conclusion. Introduction is brief and clear review of a problem. Methods are shown so that interested reader is able to repeat described research. Known methods don't need to be identified, it is cited (referenced). Results need to be shown clearly and logically, and their significance proven by statistical analysis. In discussion, results are interpreted and compared to existing, previously published findings in the same field. Conclusions have to give an answer to author's goal.

## REFERENCES

Quoting references must be in a scale in which they are really used. Quoting most recent literature is recommended. Only published articles (or articles accepted for publishing) can be used as references. Not-published observations and personal notifications need to be in text in brackets. Showing references is as how they appear in text. References cited in tables or pictures are also numbered according to quoting order. Citing paper with six or less authors must have cited names of all authors; if seven or more authors' wrote the paper, the name of the first three authors are cited with a note "et al". If the author is unknown, at the beginning of papers reference, the article is named as "unknown". Titles of the publications are abbreviated in accordance to Index Medicus, but if not listed in the index, whole title of the journal has to be written.

Footnote-comments, explanations, etc., cannot be used in the paper.

## STATISTICAL ANALYSIS

Tests used for statistical analysis need to be shown in text and in tables or pictures containing statistical analysis.

## TABLES AND PICTURES

Tables have to be numbered and shown by their order, so they can be understood without having to read the paper. Every column needs to have title, every measuring unit (SI) has to be clearly marked, preferably in footnotes below the table, in Arabian numbers or symbols. Pictures also have to be numbered as they appear in text. Drawings need to be enclosed on a white paper or tracing paper, while black and white photo have to be printed on a radiant paper. Legends next to pictures and photos have to be written on a separate A4 format paper. All illustrations (pictures, drawings, diagrams) have to be original and on their backs contain illustration number, first author last name, abbreviated title of the paper and picture top. It is appreciated if author marks the place for table or picture. Preferable the pictures format is TIF, quality 300 DPI.

## USE OF ABBREVIATIONS

Use of abbreviations has to be reduced to minimum. Conventional units can be used without their definitions.

# Uputstvo za autore

*Sve rukopise treba slati na e-mail adresu [healthmedjournal@gmail.com](mailto:healthmedjournal@gmail.com)*

Svaki upućeni časopis dobija svoj broj i autor(i) se obavještavaju o prijemu rada i njegovom broju. Taj broj koristit će se u svakoj korespondenciji. Rukopis treba otipkati na standardnoj veličini papira (format A4), ostavljajući s lijeve strane marginu od najmanje 3 cm. Sav materijal, uključujući tabele i reference, mora biti otipkan dvostrukim proredom, tako da na jednoj strani nema više od 2.000 alfanumeričkih karaktera (30 linija). Rad treba slati u triplikatu, s tim da original jedan prilog materijala može biti i fotokopija. Način prezentacije rada ovisi o prirodi materijala, a (uobičajeno) treba da se sastoji od naslovne stranice, sažetka, teksta, referenci, tabela, legendi za slike i slika. Svoj rad otipkajte u MS Wordu i dostavite na disketi ili kompaktnom disku Redakcijskom odboru, čime će te olakšati redakciju vašeg rada.

## NASLOVNA STRANA

Svaki rukopis mora imati naslovnu stranicu s naslovom rada ne više od 10 riječi: imena autora; naziv ustanove ili ustanova kojima autori pripadaju; skraćeni naslov rada s najviše 45 slovnih mjesta i praznina; fusnotu u kojoj se izražavaju zahvale i/ili finansijska potpora i pomoć u realizaciji rada, te ime i adresa prvog autora ili osobe koja će s Redakcijskim odborom održavati i korespondenciju.

## SAŽETAK

Sažetak treba da sadrži sve bitne činjenice rada-svrhu rada, korištene metode, bitne rezultate (sa specifičnim podacima, ako je to moguće) i osnovne zaključke. Sažeci trebaju da imaju prikaz istaknutih podataka, ideja i zaključaka iz teksta. U sažetku se ne citiraju reference. Ispod teksta treba dodati najviše četiri ključne riječi.

## SAŽETAK NA BOSANSKOM JEZIKU

Prilog radu je i prošireni struktuirani sažetak (cilj), metode, rezultati, rasprava, zaključak) na bosanskom jeziku od 500 do 600 riječi, uz naslov rada, inicijale imena i prezimena autora te naziv ustanova na engleskom jeziku. Ispod sažetka navode se ključne riječi koje su bitne za brzu identifikaciju i klasifikaciju sadržaja rada.

## CENTRALNI DIO RUKOPISA

Izvorni radovi sadrže ove dijelove: uvod, cilj rada, metode rada, rezultati, rasprava i zaključci. Uvod je kratak i jasan prikaz problema, cilj sadrži kratak opis svrhe istraživanja. Metode se prikazuju tako da čitaoci omoguće ponavljanje opisanog istraživanja. Poznate metode se ne navode nego se navode izvorni literaturni podaci.

Rezultate treba prikazati jasno i logički, a njihovu značajnost dokazati odgovarajućim statističkim metodama. U raspravi se tumače dobiveni rezultati i uspoređuju s postojećim spoznajama na tom području. Zaključci moraju odgovoriti postavljenom cilju rada.

## REFERENCE

Reference treba navoditi u onom obimu koliko su stvarno korištene. Preporučuje se navođenje novije literature. Samo publicirani radovi (ili radovi koji su prihvaćeni za objavljivanje) mogu se smatrati referencama. Neobjavljena zapažanja i lična saopćenja treba navoditi u tekstu u zagradama. Reference se označavaju onim redom kako s pojavljuju u tekstu. One koje se citiraju u tabelama ili uz slike također se numeriraju u skladu s redoslijedom citiranja. Ako se navodi rad sa šest ili manje autora, sva imena autora treba citirati; ako je u citirani članak uključeno sedam ili više autora, navode se samo prva tri imena autora s dodatkom "et al". Kada je autor nepoznat, treba na početku citiranog članka označiti "Anon". Naslovi časopisa skraćuju se prema Index Medicusu, a ako se u njemu ne navode, naslov časopisa treba pisati u cjelini. Fusnote-komentare, objašnjenja, itd. Ne treba koristiti u radu.

## STATISTIČKA ANALIZA

Testove koji se koriste u statističkim analizama treba prikazivati i u tekstu i na tabelama ili slikama koje sadrže statistička poređenja.

## TABELE I SLIKE

Tabele treba numerirati prema redoslijedu i tako ih prikazati da se mogu razumjeti i bez čitanja teksta. Svaki stubac mora imati svoje zaglavlje, a mjerne jedinice (SI) moraju biti jasno označene, najbolje u fusnotama ispod tabela, arapskim brojevima ili simbolima. Slike također, treba numerisati po redoslijedu kojim se javljaju u tekstu. Crteže treba priložiti na bijelom papiru ili paus papiru, a crno-bijele fotografije na sjajnom papiru. Legende uz crteže i slike treba napisati na posebnom papiru formata A4. Sve ilustracije (slike, crteži, dijagrami) moraju biti originalne i na poleđini sadržavati broj ilustracije, prezime prvog autora, skraćeni naslov rada i vrh slike. Poželjno je da u tekstu autor označi mjesto za tabelu ili sliku. Slike je potrebno dostavljati u TIFF formatu rezolucije 300 DPI.

## KORIŠTENJE KRATICA

Upotrebu kratica treba svesti na minimum. Konvencionalne SI jedinice mogu se koristiti i bez njihovih definicija.