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Nutritional transition of school children from low income families of a northeastern urban area, Brazil

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Abstract

Background: Evaluating child growth is, in practice, performed by measuring the development of a child's weight, height, and body composition in comparison to averages observed among a reference population.

Objective: To describe the nutritional status of children of low income families who live in urban region in northeastern Brazil.

Methods: This study is a population case series with a transversal and observational design. The study population consisted of 257 children, aged 5 to10 years, who were enrolled in a public school to children of low income families. We used the cutoff point for short stature of -2 Z scores for age, and underweight, overweight, and obese were classified as the 5th, 85th, and 95th percentiles, respectively, of the body mass index (BMI) for age, with both classifications in accordance with the Center for Disease Control and Prevention (CDC 2000). Comparisons by gender were performed for the measures of the central tendency and the frequency of diagnoses, in addition to the tendency of the evolution of BMI by age.

Results: The prevalence of short stature was 3.5% (95% CI: 1.9 – 6.5). In the evaluation of BMI for age, the prevalences found for underweight, overweight, and obese were 5.8% (95% CI: 3.6 – 9.4), 4.7% (95% CI: 2.7 – 8.0), and 2.3% (95% CI: 1.1 – 5.0), respectively. We found a significant trend in the reduction of BMI with the increase in age.

Conclusions: According to CDC references, the prevalences of underweight and short stature were higher than expected and for the overweight and obesity were lower than expected, indicating that the nutritional transition had still not reached, as commonly is described, these low income children from the urban outskirts of the Northeast region.

Key words: Nutrition assessment, anthropometry, nutritional transition, school health.

Introduction

Since 1987, the World Health Organization (WHO) has advocated for monitoring children's growth and development as part of basic health care because such surveillance best reflects the health of children[1]. Evaluating child growth is, in practice, performed by measuring the development of a child's weight, height, and body composition in comparison to averages observed among a reference population[2]. However, this evaluation goes beyond the technical perspective because the measured values also express, as an indicator, the social-emotional care experienced by the child[1].

The term nutritional transition, used in the analysis of populations, is defined by changes in the nutritional-epidemiological profile as a consequence of changes in diet[3], physical activity[4], conditions for access, and use of social goods and services that have repercussions on the body composition in a determined social, economic, and demographic context[5]. With nutritional transition, the simultaneous presence of two nutritional extremes is common; both the deficit and excess of weight in the same population may be observed, although there is a trend for the former to decrease and the latter to increase[6-10].

In Brazil, the coexistence of weight deficit and excess has already been observed[7,11-13]. These two extremes are associated with diseases and other adverse outcomes affecting psychosocial health during childhood, adolescence, and adulthood. Malnutrition during childhood is associated with an increase in the incidence and severity of infectious diseases, an increase in infant mortality rates, a retardation of psychomotor development, difficulties in academic performance, a decrease in height, and a decrease in productive capacity as an adult[14]. In turn, obesity among children and adolescents is associated with an increase in the prevalence of hypertension, dyslipidemia, hyperinsulinemia, cardiovascular and orthopedic diseases, and psychiatric disorders, among other problems, during multiple stages of life[15-18].

Our hypothesis is that nutritional transition, which is characterized by the displacement of the nutrition profile of a population towards higher z-score values for weight, occurs with a similar displacement in the z-scores for height among the poorest socioeconomic stratum of the population[7,13].

We evaluated the nutritional status of children enrolled in a public school to low income families located in the urban outskirts of a county from Northeastern Brazilian region. The decision to work with children 5 to 10 years of age have been encouraged by relatively few studies concerned with the nutritional transition in this age group[19-21]. Thus, the objective is to describe the nutritional status of children of low income families who live in urban region in northeastern Brazil.

Methods

This research is classified as a transversal epidemiological study with a case series study design. The study population was a group of children, ages 5 to 10 years, of low socioeconomic status based on the criterion of the IBGE (Brazilian Institute of Geography and Statistics): budged family less than two times the minimum wage[22].

All selected families had been assessed by local Government authorities as low family income group at the time of enrolment. These children were enrolled in the first four grade levels in a public elementary school located in the outskirts of the second large city of Bahia State (Feira de Santana). Only one child per family/household was considered in the analysis.

From a total of 295 students, 257 (87.1%) were selected in the final group to be analyzed; 38 children (12.9%) were excluded because they did not attend school during the entire week of data collection. An analysis of these 38 children suggested that they were similar to the analyzed cohort regarding the proportion of students distributed by grade levels (86% in the lower two grades), gender (55% boys), average age (8.5 ± 1.6 years), and income (same inclusion criteria as in the Prefecture registration), which suggested randomness in the excluded group.

The collection of the anthropometric data was performed according to the guidelines of the WHO[2]. To characterize the deficit in linear growth, short stature was defined as an index of height by age and gender (H/A) lower than -2 Z scores from the curves of the Center for Disease Control and Prevention (CDC) 2000[23].

For body mass index (BMI), the same reference was used. The BMI parameters used were as follows: underweight, children below the 5th percentile; overweight, children with measurements between the 85th and 95th percentile; and obese, greater than or equal to the 95th percentile of the reference curve[23].

To describe the weight trends by age among the population, we used the distribution of the Z scores of BMI. Data analysis was performed with Microsoft Excel 2003 and Epi Info 2000, which were used to calculate frequencies, ratios, and averages. Comparisons by gender were made for the averages of the central tendency and diagnosis frequency, in addition to the trends of BMI by age. For the ratios, we used the chi-square test or Fisher's exact test. The significance level was defined as 5% with Confidence Intervals (CI) of 95%.

This study was approved based on document number 094/07 by the 3rd/07 Ordinary Session of the Research Ethics Committee of the School of Public Health at the University of São Paulo.

Results

The distribution of students according to gender showed a slight male predominance (table 1). Regarding the number of people per household,

there was a predominance of households with six or more people, children included (Table 1). The household average number of persons was 4.9.

Table 1. Distribution of students by gender, age, grade level, and number of persons in the household. Feira de Santana-BA, Brazil, 2007

Characteristic	n	%
Gender		
M	140	54.5
F	117	45.5
Total	**257**	**100.0**
Age (years)		
5	10	3.9
6	36	14.0
7	46	17.9
8	56	21.8
9	51	19.8
10	58	22.6
Total	**257**	**100.0**
Grade level		
1st	110	42.8
2nd	72	28.0
3rd	40	15.6
4th	35	13.6
Total	**257**	**100.0**
No. of persons in household		
2	4	1.6
3	39	15.2
4	60	23.3
5	67	26.1
6	39	15.2
7 or more	33	12.8
No information	15	5.8
Total	**257**	**100.0**

Table 2 presents the anthropometric values by gender, including average weight, height, and BMI. In addition, Table 2 presents the minimum and maximum values for each studied variable. No statistical differences by gender were observed in any of the presented variables.

Table 3 shows that the prevalence of short stature was 3.5% (95% CI: 1.9 – 6.5). A greater proportion, 7.8%, was observed in children 7 years of age.

The observed prevalence of underweight was 5.8% (95% CI: 3.6 – 9.4). The prevalence of overweight was 4.7% (95% CI: 2.7 – 8.0) and of obesity was 2.3% (95% CI: 1.1 – 5.0), both less than half that expected in their interval of the percentiles. No significant differences by gender were observed in the classifications of nutritional status (Table 3).

We examined BMI by age and observed that the proportion of underweight varied from 5.5% to 11.3% (with a greater percentage in the 9-year-old age group). We observed that the prevalence of overweight began at 6 years of age, and obesity started in children who were 8 years old or older (3.8%, on average).

Figure 1 shows the frequency distribution curves for the weight for age (W/A) and height for age (H/A) indices. For W/A the mean ± standard deviation of the Z scores was -0.41±0.91 and for H/A -0.28±1.04. The 95% confidence intervals of the means where respectively of: 95% CI: -0.52 to -0.29 and -0.41 to -0.15. The mean and CIs suggested a statistically significant displacement of both curves toward lower values when compared with the reference distribution of those described by the

Table 2. Mean, minimum and maximum values, and standard deviations of the population characteristics, including age, weight, height, and BMI by gender. Feira de Santana-BA, Brazil, 2007

Characteristic	Gender			
	Female*	Male*	Total	p*
Age (years)	8.7 ± 1.5 (5.8 – 10.9)	8.4 ± 1.5 (5.6 – 10.9)	8.5 ± 3.8 (5.6 – 10.9)	0.065
Weight (kg)	27.3 ± 7.0 (16.8 – 55.8)	25.9 ± 5.8 (17.0 – 52.4)	26.5 ± 6.4 (16.8 – 55.8)	0.093
Height (cm)	129.9 ± 9.7 (110.7 – 155.4)	127.5 ± 10.4 (103.7 – 161.4)	128.6 ± 10.2 (103.7 – 161.4)	0.051
BMI (kg/m^2)	15.9 ± 2.2 (12.6 – 24.4)	15.8 ± 1.6 (13.5 – 24.0)	15.8 ± 1.9 (12.6 – 24.4)	0.545

n = 257 (117 girls and 140 boys)

** P value calculated from a comparison between genders for each independent variable.*

Table 3. Distribution of students by gender according to classification of nutritional status based on the BMI percentile and the H/A Z score. Feira de Santana-BA, Brazil, 2007

Nutritional status	Gender							
	Female*		Male*		Total			
	n	%	n	%	n	%	95% CI	p*
BMI (percentile)								
Underweight	9	7.7	6	4.3	15	5.8	3.6 – 9.4	0.519
Normal weight	98	83.8	126	90.0	224	87.2	-	-
Overweight	6	5.1	6	3.6	12	4.7	2.7 – 8.0	0.774
Obese	4	3.4	2	2.1	6	2.3	1.1 – 5.0	0.416
Total	**117**	**100.0**	**140**	**100.0**	**257**	**100.0**	-	-
H/A (Z score)								
Short stature	2	1.7	7	5.0	9	3.5	1.9 – 6.5	0.188
Normal height	115	98.3	133	95.0	248	96.5	-	-
Total	**117**	**100.0**	**140**	**100.0**	**257**	**100.0**	-	-

** P value calculated from a comparison between the genders.*

CDC[23]. Although the figure suggests a tendency of greater displacement to the left of W/A in comparison with H/A, the difference between their means was not statistically significant (p= 0.132).

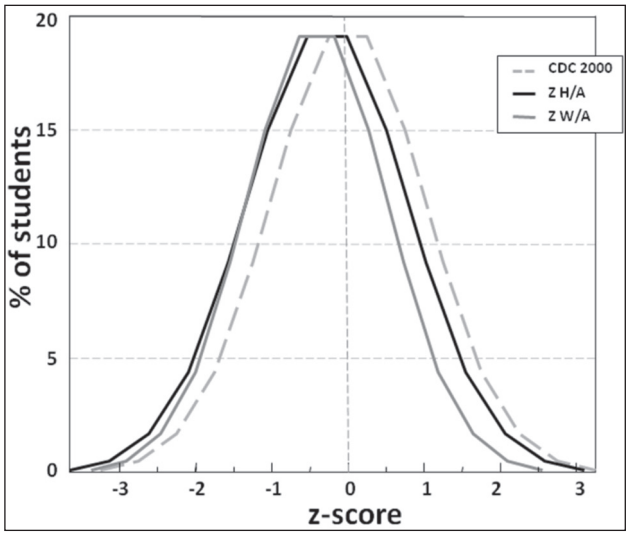

Figure 1. Frequency distribution curves of the students according to the H/A and W/A indices in Z scores. Feira de Santana-BA, Brazil, 2007

Figure 2 shows that the students presented a statistically significant trend (r^2= 0.016 and p= 0.045) of having a decrease in BMI with increasing age.

The analyses of correlation of W/A and H/A with increasing age were not significant (r^2= 0.013 and p= 0.066 for W/A and r^2= 0.002 and p= 0.503 for H/A).

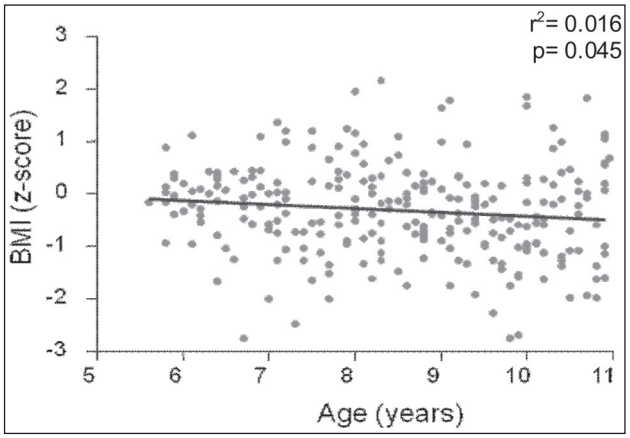

Figure 2. Trend of Z score for BMI by age of the students. Feira de Santana-BA, Brazil, 2007

Discussion

In this study, we used a case series study design and recruited students from families of low socioeconomic status. The observed prevalences do not represent all children in the region; but the growth and nutrition of the poorest ones.

Among children of this study, the prevalence of underweight and short stature were slightly higher than expected by CDC references[23], while was observed a decreasing trend in BMI with age. The frequency distribution of the school children according to their W/A and H/A indices as a whole showed a statistically significant displacement towards the left when compared with the z-score distribution of the curve provided by the CDC[23]. According to Waterlow[24] (1972) when observing an

impairment of weight and height for age and weight to height ratio, as observed in this study by means of BMI, it can be assumed that there is a chronic impairment of nutritional status in children.

In this study, the prevalence of short stature was four times lower than that observed in another study conducted in northeastern Brazil, with students aged 7 to 10 years of age[19], however, this rate was slightly higher than the prevalence found by Anjos *et al*[20] in Rio de Janeiro among children from 4 to 10 years of age (1.9% in girls and 2.8% in boys). The discrepancy between our observations and the data from the Northeast and Southeast regions may be partially explained by the socioeconomic characteristics of the Feira de Santana city and the study populations are from different group of ages.

Analysis of the nutrition indicators suggest that the values for the prevalences of overweight and obesity among children of this research may be considered lower than the expected according to the CDC reference[23]. At the other side of the data distribution, it was observed that the presence of underweight was slightly higher than the expected. Moreover, one can observe that there is worsening of the nutritional status of children as they grow older impairing their development.

Thus although we cannot generalize the results, another study, population-based study conducted in the same region with a population of public school students[21] reinforce the possibility that the nutritional transition had still not affected all low income children of this urban outskirt of the Northeast region[5,9].

The nutritional status observed in this study presents an epidemiological situation that is different from that observed by other authors[7,13,20,25]. In this study, the different intensities observed in the displacement of the W/A and H/A distribution curves suggest a different stage in the dynamics of the process of nutritional transition. This leads us to reflect on the dynamics and heterogeneity of the process of nutritional transition mainly among children and adolescents of low socioeconomic levels. Some studies have reported an increase of the weight excess prevalence coexisting with an high prevalence of short stature[11,26]. In this study, our population presented rates of short stature and underweight above the expected while those of overweight or obesity were lower than expected, indicating that the nutritional transition had still not reached these low income children[5,6,9]. In any case, the distribution of nutritional indicators seems to run opposite direction to that described by various authors on the process of nutritional transition population[7,13,20].

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Emotıonal burden of mothers of chıldren wıth developmental dısabılıty

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Abstract

Purpose: The purpose of this study is to determine the elements comprising the emotional burden of mothers of children with developmental disability.

Method: The research was conducted using the in-depth interview method, one of the qualitative research methods. In the study, the purposive sampling method was used to select the sample, 12 mothers were interviewed. The interviews were ended since data saturation was obtained. Inductive content analysis was performed.

Results: The themes identified in this qualitative study are as follows: motherly love, joy and sorrow, hope-hopelessness, anger, a constant and desperate problem, supervision and control, and challenge.

Key words: emotional burden, disability, developmental disability, mother.

Introductıon

Developmental disabilities or neurodevelopmental disabilities are a diverse group of chronic disorders that begin at any time during the development process up to 22 years of age and last throughout an individual's lifetime. Developmental delay is defined as late acquisition of developmental milestones. Children who achieve their developmental milestones two or more standard deviations later than the mean age of acquisition are considered delayed (1). Major categories of developmental disabilities are intellectual disability, learning disabilities, communication disorders, autism spectrum disorders, neurobehavioral disorders, neurogenetic disorders, neurometabolic disorders, neuromuscular disorders, cerebral palsy, other neuromotor disorders, sensory impairments, disabilities associated with chronic diseases, traumatic brain injuries, spinal cord injuries (2). Developmental delays stem from a variety of causes including adverse perinatal factors such as prematurity, genetic conditions, prenatal exposure to alcohol or drugs, social deprivation, or brain injury from trauma or infection, child abuse (1).

Having a child with a developmental disability causes mothers and families to have different experiences. After the diagnosis, many parents experience shock, trauma, and grieving for the loss of the normally developing child that they had planned for. Feelings such as denial about the diagnosis, anger about the unfairness of having to raise a child with developmental delays, and fear for the future of the child are all common reactions to the diagnosis (3,4).

The effects of developmental disability on the family can be defined through the Family Systems Theory (5). According to the systems perspective, the family is a complex structure, comprised of individuals who share a history, have emotional bonding, and develop strategies to meet the needs of individual members of the family and of the family as a group (6,7). The family system exhibits a coherent behavior. An individual's problem in the system affects the whole system. The presence of a child with a developmental disability in the family affects all the members and the functions of the family (5). There exists interrelation between the elements in the family system, which creates sub-systems in the family. There are three main sub-systems in the family: spousal, parental, and sibling subsystems (6,7). Both the subsystem in which the child with developmental disability is involved and the other sub-systems in the family are affected by the problems arising from the child with developmental disability (5). Another important feature of the family system is that the system is open and closed. The family system is neither an entirely open nor an entirely closed system. Fami-

lies sustaining their existence effectively have been able to develop a balance between being open and closed (6,7). Families having children with developmental disability are in relation with their environment and other systems. However, the reactions from the social environment negatively affect the relationship between the family and the environment, and thus change the family structure to a more closed one (8). Both the child's not being able to perform developmental assignments in due time because of his/her developmental disability and the delays experienced within the family lead to a negative impact on family life cycle, and create crises in the family (4).

Burden includes the feelings felt by a caregiver as a result of giving care, their physical health, social life and economic status. The concept of burden takes into consideration the effect an illness has on the caregivers' physical, psychological and socioeconomic wellness as a whole. Burden is a multidimensional phenomenon that affects the physical, social, emotional, material and economic aspects of the caregiver's life (9,10).

Studies conducted on families having children with developmental disability are often interested in the difficulties families undergo, and report that the family's burden is high (8,11). However, it is not clear what the elements constituting the emotional burden mothers suffer are. Geurtsen et al. (12) determined the factors which account for the emotional burden of caregivers of patients with brain injury as stress, supervision, anxiety, and encouragement. Sarı and Basbakkal (11) defined the emotional burden as depression and not being able to enjoy entertainment.

The purpose of this study is to determine the elements comprising the emotional burden of mothers of children with developmental disability.

Method

The research was conducted in a special education and rehabilitation center in Izmir in which children with developmental disability were trained. The research was designed as a descriptive one. The research was conducted using the in-depth interview method, one of the qualitative research methods. With the in-depth interview method; complex, touchy issues which have not been investigated previously can be examined in depth through one-on-one (face-to-face) interviews.

The longer-term impact of the child's disability varies across family members. Parents of children with an intellectual or physical disability have shown a greater stress level than is seen in the parents of children who are developing normally. The effect is usually greater in mothers than fathers (13). Therefore, the emotional burden of mothers was investigated in this study. The mothers agreed to participate after being fully informed about the aim and methods of the study.

In the study, the purposive sampling method was used to select the sample. Purposive sampling, one of the most common sampling strategies. Sample sizes, which may or may not be fixed prior to data collection, depend on the resources and time available, as well as the study's objectives. Purposive sample sizes are often determined on the basis of theoretical saturation (14). In this study, 12 mothers were interviewed. The interviews were ended since data saturation was obtained.

The data were collected during in-depth, face-to-face interviews with the mothers, usually in the suitable room at the training and rehabilitation centre. Interviews lasted between 60 and 90 minutes. Interviews were recorded with an audio recorder after the mothers' permission was obtained. In in-depth interviews, a semi-structured interview questionnaire prepared by the researcher in accordance with the literature was used.

In order for other people not to hear, audio tapes on which the interviews were recorded were transcribed in a room where the researcher was alone. When the records were transcribed, the names of the children and mothers were not used; letters such as A, B, C, D, E, F, G, H, I, J, K, L were used to represent the voice record of each child.

Immediately after the interviews ended, voice records were transcribed verbatim and analyzed. The data were analyzed using inductive content analysis. First, the data were coded by the researcher. (Open coding). The same data were encoded by two separate nurse faculty members, and then the codes were compared. Then, the themes and main themes were established. Inductive content analysis was performed as described by Elo and Kyngas (15). Below are listed the steps of the inductive content analysis.

Inductive Content Analysis Steps

1. Preperation Phase
   1.a. Selection the unit of the analysis,
   1.b. Making sense of the data and whole
2. Organising Phase
   2.a. open coding,
   2.b. Coding sheets,
   2.c. Categorization,
   2.d. Abstraction
3. Reporting the analyzing process and the results
4. Model, conceptual system, conceptual map or categories

Research Ethics Approval: There were no ethics or research committees in the nursing school and the university where the study was conducted. Therefore, written permission from special education and rehabilitation centers directors and informed verbal consent from all mothers were obtained after informing all parties about the purpose and the method of the study.

Results

Two of the children were in the 2-5 age group, five in the 6-12 age group and five in the 13-18 age group. In the 2-5 age group, one of the children developed developmental disability due to heart disease and the other children due to epilepsy. Children from the other age groups were diagnosed developmental disability due to intellectual deficiency, neurological diseases and congenital trauma. Half of the children were male and the other half female. Mothers' ages ranged from 26 to 56 years. While two of the mothers were working mothers, the others were housewives.

1. Motherly love

During the interviews, mothers of children with developmental disability especially stressed the love they have for their children. Mothers stated that they loved their children, they would not think of a life without their children no matter what problems they might face, and it was this love which provided the motivation for them to endure all those difficulties.

"It is hard to endure without the love I have for him. In fact, I am still happy with my child. I have never thought that I did not have such a child. You love your child, despite the difficulties you face." *(K, 15 years of age, intellectual disability)*

2. Joy and sorrow

Mothers emphasized that, although they have had joyful moments with their children in the process, there is more sorrow in their lives.

"I experience both joy and sorrow with my child. In our house, in our own castle, we are mostly happy. Even a delayed sound or a delayed movement by our child pleases us so much as to surprise other people in the environment. At home, everything is normal as if there is no problem. On the other hand, his being with other children always brings on sorrow. While even younger children can manage independently, my child cannot without my support. Being asked questions like "how old is your child" is the worst of all. Other people's questions make me face myself; face my child's developmental delay. Grief is the foundation of my life. Since my child's birth, I have almost always been sad, my joys, on the other hand, have been momentary." *(A, 2 years of age, developmental delay).*

"What makes me most distressed is his being called insane. This hurts me very much. I avoid meeting people. I cannot take part in social life. I feel as if others will look down on me and my child. " *(L, 12 years of age, developmental delay)*

"That state of hers or the way she looks at me so innocently and asks for help hurts my heart; makes me so sad. I am a mother, I cannot accept her having disability *(F, 8 years of age, epilepsy and intellectual disability)*

3. Hope and hopelessness

Mothers of children with developmental disability state that initially they had the hope that their children's development would be normal, but as the effects of developmental of retardation became worse, they fell into despair. Especially mothers whose children are younger stated that they kept their hopes alive for the future.

"I start each day with a new hope. Today, my child will be better than he was yesterday, maybe he will walk today, maybe a word will spill out

of his mouth today, maybe .... But all the hopes vanish at the end of the day. Disappointment once again. What I looked forward to did not take place. Then I say to myself "no more hope", which wears me away. Every morning a new hope, and then the facts .... *(A, 2 years of age, developmental delay).*

4. Anger

In the family, both parents and children with no history of developmental disability suffer anger. Anger is, in fact, targeted at the child's deficiency, but sometimes may be targeted at the child himself with developmental disability. Not able to control their anger, mothers and other individuals living at home may sometimes exhibit attitudes which hurt the child with disability.

"Sometimes we fly into a rage and even hold a grudge. We wish he did not have the disability; he were healthy. " *(C, 7 years of age, intellectual disability)*

"My child with no disability sometimes says: "I wish either my sister or I were not born". My child with no disability gets mad at her sister, beats her, flies into a rage, does not let her play with her friends. She asks "Do I have to look after my sister."" *(D, 7 years of age, intellectual disability).*

"When I go out, I compare other children with my own child. Then, I notice what my child cannot do. I become filled with anger. When I come back home, I leave my child alone, become very indifferent to him, sometimes get angry at him, and cry, and finally I get angry at myself. " *(A, 2 years of age, developmental delay).*

5. A constant and desperate problem

Mothers especially state that intellectual disability will never disappear in the future; they, together with their child, will forever suffer the same problem, and the problem will never end. Mothers' descriptions for the situation are as follows:

"A lifelong problem. There is nothing to do. it is impossible to treat it. This is a heavy burden; you become burnout, and there is no solution. If he walks, everything becomes normal when he turns two, then it is not a problem and you look after your child. But this is not the case " *(K, 15 years of age, intellectual disability)*

"In case of other diseases, they are treated; they improve. But there is no such thing in our case; it is with you for life " *(B, 11 years of age, intellectual disability)*

6. Supervision and Control

Mothers state that children, in particular those with intellectual disabilities, are in need of mothers' care, these children's independent living skills are insufficient, and even though the improvement in their independence is not at an expected level as the child's chronological age increases. Mothers also state that they should constantly supervise their children.

"If I had not looked after him, he would never reach his present age. He would have already died. For example, he would have rushed into the street and a car would have run over him. If you do not look after him, he cannot survive"

"You have to constantly take precautions: close the windows, remove the knives around, lock the front door, continuously watch over him, and check him. That makes me thoroughly burnout; even my brain gets tired." *(K, 15 years of age, intellectual disability)*

7. Challenge

Mothers of children with developmental disability state that, in order to provide medical care and education for the children, they have been in a huge and constant challenge in the process that began right after their children's birth. Problems, especially the ones arising from health system and education system, cause mothers to suffer and challenge difficulties more.

"I wanted to send my son to kindergarten, but they did not want to admit him due to his aggressive behavior. I struggled with them a lot; they finally agreed to admit him…. When he started the school parents of other children in the integration class did not want my son to attend the school"

"The staff in the guidance center overlooked the developments in my son and reported that my son was thoroughly uneducable, which infuriated me. I struggled. He learned how to read and write, and now works in a sheltered workplace " *(E, 13 years of age, intellectual disability)*

Discussion

The themes identified in this qualitative study performed to define the emotional burdens of the mothers of children with developmental disability are as follows: motherly love, joy and sorrow, hope-hopelessness, anger, a constant and desperate problem, supervision and control, and challenge.

Mothers of children with developmental disability stated that they loved their children a lot, and they were able to endure all the difficulties they faced thanks to this love. Landsman (16) evaluated the worlds of the mothers of children with developmental disability from a different perspective, and pointed at the fact that these mothers give their children their love from the heart. A mother who participated in Landsman's study (16) expressed her love and the paradox she experienced as follows: "I love you as you are" and "I would do anything to change you." In some cases, the imperfect child, who is perceived as a reflection of the parent's own competence, may represent a narcissistic injury. The stark contrast between the imagined parenting experience and the reality of caring for a child with autism and intellectual disability may lead to intense disappointment and self-blame (3). Despite all this paradox, motherly love provides the mothers with the strength they need. Therefore, these mothers should be given feedback about the positive aspects of their struggle, and their positive experiences they have shared with their children should be brought to the fore. These mothers should not be blamed for their negative feelings; their feelings should be appreciated.

Mothers emphasized that, although they enjoy joyful moments with their children, there is more sorrow and grief in their lives. Kearney and Griffin (17) reported that having a child with intellectual deficiency has two sides: joy and sorrow, and that families display transitions between these emotions. Reactions shown to children with disability differ in each family. Reactions are related to the meaning attributed to disability by mothers. In some studies, it has been determined that the child with intellectual deficiency contribute to the family with such positive effects as joy, loyalty and strength (9,18,19) On the aother hand, the parents of children with congenital anomalies suffer from sorrow more (20). Depression in mothers of children with disabilities are more often (21). Mothers who suffer from sorrow should be supported so that they can cope with the problem efficiently and continue their lives effectively. Nurses should identify mothers at risk and provide support for them.

Mothers stated that initially they had the hope that their children's development would be normal, but that as the effects of developmental delay became worse, they fell into hopelessness, which is supported by the paradox described by Landsman (16). While mothers love their children as they are, they keep their hopes alive that everything will change someday. A mother who took part in Landsman's study stated that she hoped that her child's developmental disability would one day disappear. Hope was largely considered to be a positive concept that can make a difference to people's lives. Hope was mainly presented as an expectation for the future. Hopelessness, defined as 'feeling no hope'. Hopelessness like dissatisfaction may be a separate concept that carries its own set of meanings and constructs (22). Whether mothers live in hope or hopelessness may cause them either to strive or to surrender. Therefore, nurses should realistically assess the situation mothers are in, and plan the efforts for the benefit of both the mother and the child.

In the family, both parents and children with no history of developmental disability suffer anger. Anger is a negative emotional state that varies in intensity and duration and usually is associated with emotional arousal and a perception of being wronged by another (23). Not able to control their anger, mothers and other individuals living at home may sometimes exhibit attitudes which hurt the child with disability. Especially parental anger is significantly associated with child abuse risk (23,24). Therefore, mothers of children with developmental disability should be considered in the risk group in terms of anger, and anger management interventions should be planned. In addition, these families should also be evaluated in terms of child abuse and neglect. Indeed, in a study, mothers of children with intellectual disabilities were trained on anger management and thus while the frequency of temper tantrums that mothers had reduced, their anger management skills increased (25).

There are mothers who state that their children's developmental disability would never dis-

appear, there is no cure, and it will remain with the child lifetime. While some mothers hope that their children's developmental disability will one day disappear, some other mothers realistically assess the situation they are in. The most agonizing factor for the parents is the fact that the disability is irreversible (26).

One of the themes determined in the research is supervision and control. Mothers stated that they should constantly supervise their children since the children are unable to carry on their living skills alone. In addition to supervision and control, mothers should deal with several other issues such as their children's medical care and education. Caring for a young child with a developmental disability can be a challenging experience for parents. Parents of children with developmental disabilities are faced with these same high risk parenting tasks, however, they are also required to complete additional tasks which are specific to their child's disability. These tasks may include assisting their children with self-care (e.g. bathing, feeding, toileting), providing ongoing supervision to prevent behaviors which may be a risk to self or others (e.g. road safety, choking), completing therapy to extend their child's learning and development, locating social and recreational activities in which children can participate independently, educating the public about disability, advocating for their children, and working with a range of professionals (27). In addition, the difficulties encountered in services offered to children with disability in Turkey cause mothers to struggle more. Even though several steps have been taken for the benefit of children with disability in Turkey over the last decade, problems still remain in such areas as education, health and social life (28).

Conclusion

Being a mother is a different feeling, but being a mother of a child with developmental disability is a completely different feeling. All mothers love their children, but mothers of children with developmental disability have not only love but also sorrow in their hearts. The mother of a child with developmental disability should spend more effort and time with her child than anyone else does. The most important thing which makes mothers hold on to life is the love they have for their children. Therefore, mothers of children with developmental disability should be encouraged at any opportunity by giving feedback about their love for their children and struggle they take part in, and they must be helped to realize their strength. Nurses should listen to and try to understand these mothers, and plan new anger management interventions for them.

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Effects of diurnal temperature changes on asthmatic children: an ecological study

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Abstract

Background and purpose: The prevalence of childhood asthma increased in Taiwan despite of air pollution control. This ecological study evaluates the effect of diurnal temperature changes on exacerbation of asthma and its possible mechanisms.

Methods: Data on both climate factors and air pollutants were obtained from the governamental agencies. Of the 365 days in the study period, the case group is defined as the days with admissions for asthma and the other days are classified as the control group. The days with admissions is defined as the days when patients under 18 years of age were admitted to hospitals with the chief problem of asthma. 7,623 patients with asthma (age ≤ 18) were assessed and the characteristics between these two groups were compared, including diurnal temperature changes. Multiple linear regressions were used to assess the effects of both temperature changes and air pollutants.

Results: The effects of diurnal temperature changes were relatively consistent in a given geographic area in a specific season. In winter, there were positive associations in regions southern to the Tropic of Cancer and negative associations in northern regions. In other seasons, there were positive associations in plain regions near the sea and negative associations in mountainous regions away from the sea.

Conclusions: Diurnal changes of temperature themselves may affect symptoms of childhood asthma in different ways, and the effects vary across different geographic areas and seasons. The varied effects may cause exacerbation of symptoms in children through the mechanism of physical accommodation.

Key words: asthma, temperature change

Introduction

Asthma is one of the most common diseases in children. The environmental level of dust mites might be related to the exacerbation of asthma symptoms(1), and air pollution appeared to have an impact as well(2,3). In Taiwan, the prevalence of asthma in school-aged children increased from 1.3% to 10.79% during past ten years even though air pollution has been controlled (4-6), which indicates there are some other important factors affecting the development of asthma. Some studies have shown that seasons and changes of temperature were associated with frequencies of hospital visit or admission in asthmatic patients (7,8). As global warming trend was found to be more prominent in Taiwan (9), the possible effects of climate factors on asthma needed to be studied further. A study in Japan demonstrated that the diurnal temperature changes were correlated with admission rate of asthmatic children (10). This study was conducted to further evaluate whether diurnal temperature changes may cuase exacerbation of asthma in Taiwanese children and what the possible mechanisms were.

Methods

Study subjects

The subjects of this study were hospitalized asthmatic patients under the age of 18.

The hospitalized patients were identified by the admission database obtained from the Bureau of National Health Insurance (BNHI), which is a government agency providing health insurance to majority of residents in Taiwan. For each case the BNHI database provided information on the date

of admission, code of the hospital, ICD-9 codes of principal and secondary diagnoses, gender and age of patients, and the category of the hospital. The diagnosis of asthma was confirmed by a physician and included ICD-9 codes 493.00, 493.90, and 493.91. Patients with coexisting fever, infection, heart disease, and underlying respirator diseases were excluded.

Assessments

According to the geographic characteristics and the locations of the 22 monitor stations of the Central Weather Bureau, Taiwan was divided into five zones. Zone 1 (north western Taiwan) included the Taipei City, Taipei County, Taoyuan County, Hsinchu City, Hsinchu County, Miaoli County, Taichung City, Taichung County, Changhua County, Yunlin County, Chiayi City, and Chiayi County. Zone 2 (south western Taiwan) included the Tainan City, Tainan County, Kaohsiung City, Kaohsiung County, and Pindong County. Zones 3 and 4, represented by Nantou County and Taidong County respectively, were mainly comprised of mountainous areas. Zone 5 (eastern Taiwan) included the Hualian County, Yilan County, and Keelong City. Weather data including temperature and humidity were obtained from the Central Weather Bureau, and the diurnal temperature change of each day was defined to be the difference between the highest and the lowest temperature measured on that day.

In order to account for the effects of air pollution, data on pollutant standards index (PSI) were obtained from 72 monitor stations of the Environmental Protection Administration (EPA). The PSI value reflected health effects related to PM_{10}, SO_2, NO_2, CO, and O_3 levels; values greater than 100 usually lead to exacerbation of respiratory symptoms.

The 365 days of the study period between January 1, 2001 and December 31, 2001 were divided into two groups: days with admissions for asthma (case group) and without admissions (control group). To account for time lag between exposure to diurnal temperature changes and hospital admission for asthma, the effects were evaluated by applying different gaps before the admission, from 1 to 7 days, and the case groups were defined accordingly. For example, when a gap of 2 days was applied, the group that was exposed to diurnal temperature changes two days before admission was defined as the case group.

When a gap was found to be statistical significant, further analyses for longer gaps were not performed. For example, if significant difference was found between the groups when a gap of 2 days was applied, further comparisons with gaps of 3 days or more were not performed. A study conducted by Ehara *et al*. in 2000 was adopted as the major reference in setting up this approach of data analysis.[10]

For analyses of meteorological data, spring is defined as days from March to May, summer as days from June to August, autumn as days from September to November, and winter as days from December to February. For analyses of PSI, data from hospitals within 2 km of detection stations only were included to ensure the accuracy of the measurements.

Statistical analysis

The temperature changes between groups were evaluated using the two-sample t-test, and the difference between daily highest and lowest temperatures of the same group was also tested. Partial correlation coefficients were applied to evaluate correlation between PSI and diurnal temperature changes. The linear regression model was used to evaluate the differences in effects on asthma admissions among diurnal temperature changes, PSIs and humidity after adjusting for seasons.

Ethics approval was provided by the Grant Review Committee of the National Science Council, Taiwan.

Results

A total of 7,623 asthmatic children were included in the analyses, most of them were between the age of 1 and 7 years (Figure 1) with male to female ratio of 1.7:1. Hospital admissions were highest in autumn with 2,525 (33%), followed by winter with 1,971 (26%), spring with 1,818 (24%), and summer with 1,309 (17%). Significant differences in diurnal temperature changes between the case and control groups in nine regions (cities or counties) (Table 1) were observed in spring. A positive association is defined as larger changes

of diurnal temperature observed in the case group when compared to the control group. Similarly, a negative associated is defined as larger changes of diurnal temperature observed in the control group. In Zones 1, 2, and 5, the case groups had the larger changes of diurnal temperature (positive associations between admissions and diurnal temperature changes), but in Zones 3 and 4, the control groups had the larger changes of diurnal temperature (negative associations). Similar results could also be found in summer (Table 2) and autumn (Table 3). The results in winter were very different from the other three seasons, with Zones 3 and 4 presenting positive associations and negative associations in Zones 1 and 5 (Table 4) (Figure 2). Furthermore, negative associations were observed in all zones during winter in the northern part of Taiwan with only one zone having positive association in the southern part.

There were limited data available on PSI for analysis because only the codes and categories (medical center, regional hospital, and local hospital) of hospitals, but not patient identities, were released by the BNHI. Therefore, PSI analysis was limited to six monitor stations, which were linked to nearby medical facilities. Only one (Changhua) station covered all the corresponding medical centers and regional hospitals in the region. The other five stations did not cover all the corresponding regional hospitals due to the restricted data access, although regional hospitals contributed the largest number of admissions among the three categories of hospitals. With a 3-day lag, the mean PSI measured was higher in the case group (61.81 *vs.* 56.75, p=0.03). In addition, at the Changhua Station, a positive correlation was found between average diurnal temperature changes and PSI on a weekly basis (correlation coefficient: 0.46, p<0.01). No statistical significant effects on asthma admissions were observed when the diurnal temperature change, PSI and humidity were put in to linear regression models, while the temperature change was generally found to have a relatively stronger effect as measured by standardized regression coefficient.

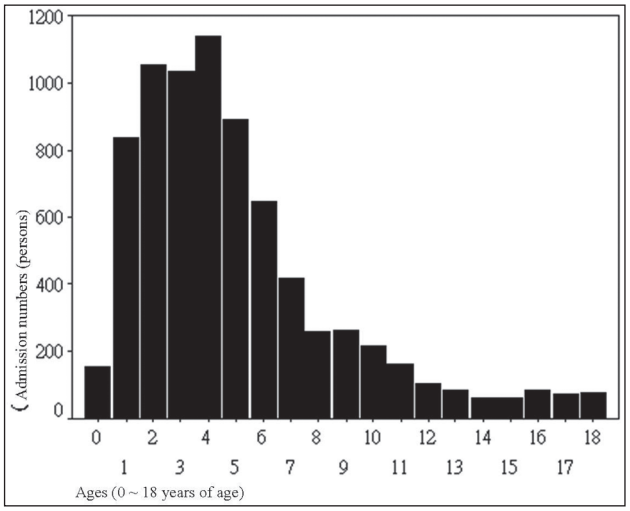

Figure 1. Distribution of admission numbers in different ages

Table 1. Regions with significant differences in diurnal temperature changes between case / control groups in spring

Region (Zone)	Gap (day)	T_{case} (°C)	$T_{control}$ (°C)	△T [95% C.I.](°C)	p
Taipei City (1)	0	5.74	4.59	1.15 [0.22, 2.08]	0.02
Taichung City (1)	3	8.00	6.71	1.29 [0.30, 2.27]	0.01
Taichung County* (1)	3	7.07	5.96	1.11 [0.38, 1.84]	0.00
Chiayi County (1)	1	9.45	8.18	1.27 [0.22, 2.31]	0.02
Tainan City† (2)	1	8.98	7.85	1.13 [1.18, 2.07]	0.02
Kaohsiung County (3)	4	8.58	7.67	0.91 [0.01, 1.80]	0.04
Nantou County (3)	1	7.32	8.39	-1.07 [-2.05,-0.09]	0.03
Taidong County† (4)	7	4.97	6.14	-1.17 [-2.23, -0.09]	0.03
Keelong City* (5)	4	6.72	5.01	1.71 [0.44, 2.98]	0.01

*Gap: the number of days between exposure to temperature change and admission (0 means the day of admission); T_{case}: average diurnal temperature change in the case group; $T_{control}$: average diurnal temperature change in the control group; △T: T_{case} - $T_{control}$; C.I.: confidence interval; p: p value for two-sample t-test; *: the mean daily lowest temperatures between the case and control groups was significantly different; †: the mean daily highest temperatures between the case and control groups was significantly different.*

Table 2. Regions with significant differences in diurnal temperature changes between case / control groups in summer

Region (Zone)	Gap (day)	T_{case} (°C)	$T_{control}$ (°C)	△T [95% C.I.](°C)	*p*
Taipei City† (1)	6	7.23	6.34	0.89 [0.10, 1.67]	0.02
Miaoli County† (1)	6	6.60	6.03	0.57 [0.19, 0.93]	0.00
Tainan County (2)	4	7.62	6.94	0.68 [0.12, 1.22]	0.01
Keelong City* (3)	4	7.39	6.18	1.21 [0.51, 1.90]	0.00

*Gap: the number of days between exposure to temperature change and admission (0 means the day of admission); T_{case}: average diurnal temperature change in the case group; $T_{control}$: average diurnal temperature change in the control group; △T: T_{case} - $T_{control}$; C.I.: confidence interval; p: p value for two-sample t-test; *: the mean daily lowest temperatures between the case and control groups was significantly different; †: the mean daily highest temperatures between the case and control groups was significantly different.*

Table 3. Regions with significant differences in diurnal temperature changes between case / control groups in autumn

Region (Zone)	Gap (day)	T_{case} (°C)	$T_{control}$ (°C)	△T [95% C.I.](°C)	*p*
Taipei County*† (1)	2	5.67	4.37	1.30 [0.41, 2.18]	<0.01
Taoyuan County* (1)	6	5.69	3.34	2.35 [0.01, 4.68]	0.04
Hsinxhu City (1)	4	7.47	6.26	1.21 [0.12, 2.29]	0.02
Taixhung County (1)	0	7.17	6.06	1.11 [0.02, 2.18]	0.04
Chiayi County (1)	0	10.24	8.44	1.80 [0.46, 3.11]	0.00
Tainan City* (2)	4	8.69	7.43	1.26 [0.18, 2.33]	0.02
Nantou County* (3)	4	7.78	9.17	-1.39 [-2.53, -0.24]	0.01
Taidong County (4)	2	5.74	6.67	-0.92 [-1.54, -0.30]	0.00
Hualian County* (5)	6	7.50	6.60	0.90 [0.07, 1.73]	0.03

*Gap: the number of days between exposure to temperature change and admission (0 means the day of admission); T_{case}: average diurnal temperature change in the case group; $T_{control}$: average diurnal temperature change in the control group; △T: T_{case} - $T_{control}$; C.I.: confidence interval; p: p value for two-sample t-test; *: the mean daily lowest temperatures between the case and control groups was significantly different; †: the mean daily highest temperatures between the case and control groups was significantly different.*

Table 4. Regions with significant differences in diurnal temperature changes between case / control groups in winter

Region (Zone)	Gap (day)	T_{case} (°C)	$T_{control}$ (°C)	△T [95% C.I.](°C)	*p*
Taipei County (1)	2	5.49	6.93	-1.44 [-2.57, -0.30]	0.01
Taoyuan County (1)	5	6.47	4.71	1.76 [0.02, 3.50]	0.04
Hsinchu City (1)	5	6.37	7.97	-1.60 [-2.92, -0.28]	0.01
Miaoli County (1)	4	5.52	6.91	-1.38 [-2.31, -0.44]	0.00
Taichung City (1)	6	8.22	9.56	-1.34 [-2.63, -0.05]	0.04
Yunlin County* (1)	2	8.84	10.82	-1.98 [-3.13, -0.82]	<0.01
Chiayi County (1)	0	8.59	10.02	-1.43 [-2.60, -0.26]	0.01
Tainan County† (2)	3	9.91	8.89	1.02 [0.07, 1.96]	0.03
Nantou County†† (3)	6	10.40	8.74	1.66 [0.34, 2.98]	0.01
Taidong County (4)	1	7.25	6.42	0.83 [0.02, 1.63]	0.04
Hualian County (5)	2	7.18	5.91	1.27 [0.23, 2.29]	0.01
Keelong City (5)	3	4.17	5.35	-1.18 [-2.23, -0.12]	0.02

*Gap: the number of days between exposure to temperature change and admission (0 means the day of admission); T_{case}: average diurnal temperature change in the case group; $T_{control}$: average diurnal temperature change in the control group; △T: T_{case} - $T_{control}$; C.I.: confidence interval; p: p value for two-sample t-test; *: the mean daily lowest temperatures between the case and control groups was significantly different; †: the mean daily highest temperatures between the case and control groups was significantly different.*

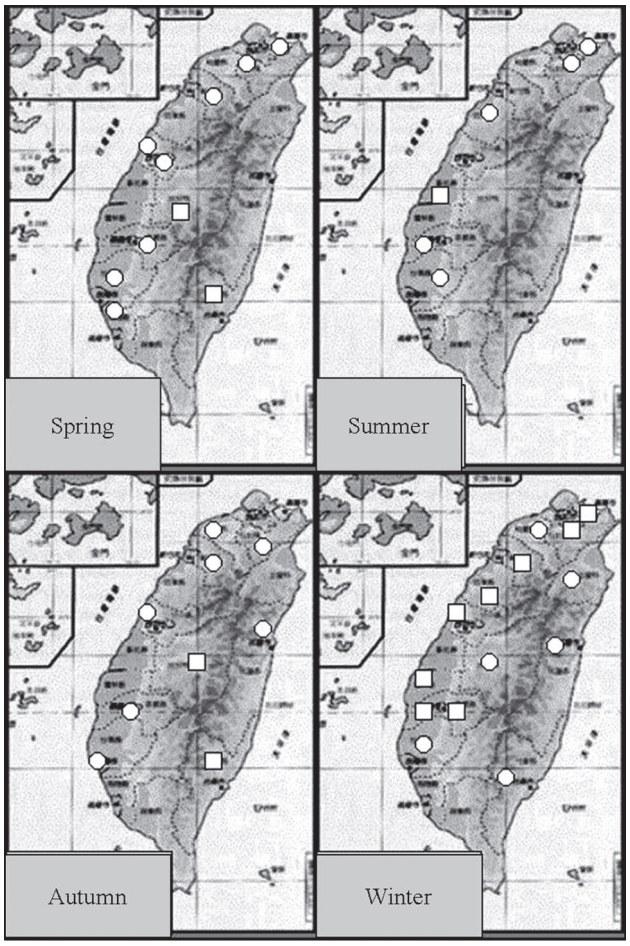

Figure 2. Regions with significant differences in diurnal temperature changes between case and control groups by season.
Circle=*Regions with significant positive association between diurnal temperature changes and child asthma admissions.*
Square=*Regions with significant negative association between diurnal temperature changes and child asthma admissions.*

Discussion

The prevalence of asthma in school-aged population in Taiwan was found to be 8.1% in boys and 5.6% in girls. Parental genetic constitution seemed to have stronger effect on asthma than environmental exposures to air pollution, fungus, and cockroach (11). However, the possible effects of diurnal temperature change were rarely, if ever, evaluated in Taiwan, although there is evidence showing such effects (6). In fact, in previous studies, climate factors including room temperature and air pollution could explain up to 69% of admissions for asthmatic children (2,12-17). Similarly, our study has revealed some associations between diurnal temperature changes and asthma admissions. Daily changes in the climate were found to contribute to the fluctuations of disease frequencies in humans (18). Some studies have shown that sudden onset of heat wave increased the incidence of cardiovascular diseases while the extreme cold climate exacerbated symptoms of asthma. It implies that such environmental changes may challenge human's innate ability to adapt and accommodate in a short period of time, which in turn lead to deleterious health effects.

In the current study, although there are both positive and negative associations between diurnal temperature changes and asthma admissions, and the gaps varied, there are relatively consistent trends in a given season within a given geographic zone. Specifically, from spring to autumn, positive associations were observed in plain regions, which are near the sea (both eastern and western Taiwan), while negative associations were observed in mountainous regions, which are away from the sea in central Taiwan with mountain ridges (Figure 2). In winter, positive associations were observed in regions southern to the Tropic of Cancer, while negative associations were observed in northern regions. The variations might be related to factors of wind direction, thickness of cloud, and geographical location in relation to Tropic of Cancer. In regions near the sea, daytime temperature on the land was higher than that in the sea, and winds moved from sea to land. These conditions reversed during the night, and winds had no effect on regions 300 meter or more above the sea level. In all seasons except for winter, the clouds are thin, and so the diurnal temperature changes in plain regions near the sea are smaller than those in the mountainous and inland regions. In contrast, during winter time, thicker clouds and shorter duration of daylight in regions northern to the Tropic of Cancer reduced the diurnal temperature changes in mountainous and inland regions.

There are some mechanisms that may be applied to explain the effects of temperature changes. The level of eosinophil cationic protein (ECP) was found to be positively correlated to the degree of asthmatic symptoms, and the ECP level in sputum decayed faster at room temperature than at 4 ^{o}C (19). It is possible that temperature changes affect

the symptoms of asthma by altering the ECP level. Similar studies have shown that the plasma level of basophil cells and temperature changes might also affect asthma by altering the level of leukotriene (20,21). Some studies of a single region simply claimed that a large change in temperature can induce asthmatic symptoms (7,10), but our study demonstrated that temperature changes could affect residents of plain and mountainous regions differently in the same season. Therefore, not only the seasons, but also the landforms should be taken into account in studying the effects of temperature changes on asthma. Estela et al. noted that residents living in tropical regions with very little temperature changes did not adapt larger weather changes well in comparison with residents living in regions with higher latitudes (18).

Asthmatic attacks in children usually lead to hospital admissions in Taiwan, but patients living in remote areas may visit hospitals out of their residential regions. Such events might lead to underestimation of the effects of temperature changes and partially explain why relatively less significant correlations were observed in Zones 3 and 4, which mostly consist of mountainous regions.

Acute and severe effect of temperature change on asthmatic children was what we concerned. That was why the maximal lag period was seven days in our study. We noted that some patients were admitted to the hospital only when they did not respond well to a short period of medical treatment initially, and the lags between the day of disease onset and the day of admission were various. It explained why we did not use consistent lag periods for analysis during each season. Because different lag periods were used for different regions and different dates, there was also a challenge for us to exclude the possibility that the findings resulted from chance only. P-P plots were constructed to evaluate the effects of testing of multiple hypotheses (Figures 3-4). The y axis was applied to plot all the 570 *p* values resulted from our tests, and the x axis was applied to plot the normal distribution of probabilities between 0 and 1. In order to avoid potential problem in curve estimation, cubic regression was applied between x and y, instead of linear regression. Results from both evaluations supported the rationality of our conclusions and explained that our conclusions were not derived due to coincidence or chance.

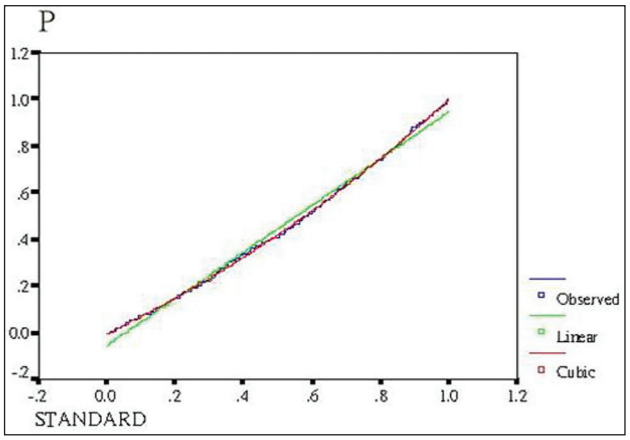

Figure 3. Test for spurious p values in multiple comparisons: Curve estimation method for regression model.
Y axis=*570 p values from multiple comparisons of diurnal change of temperature.*
X axis=*corresponding 570 probabilities of normal distribution from 0 to 1.*

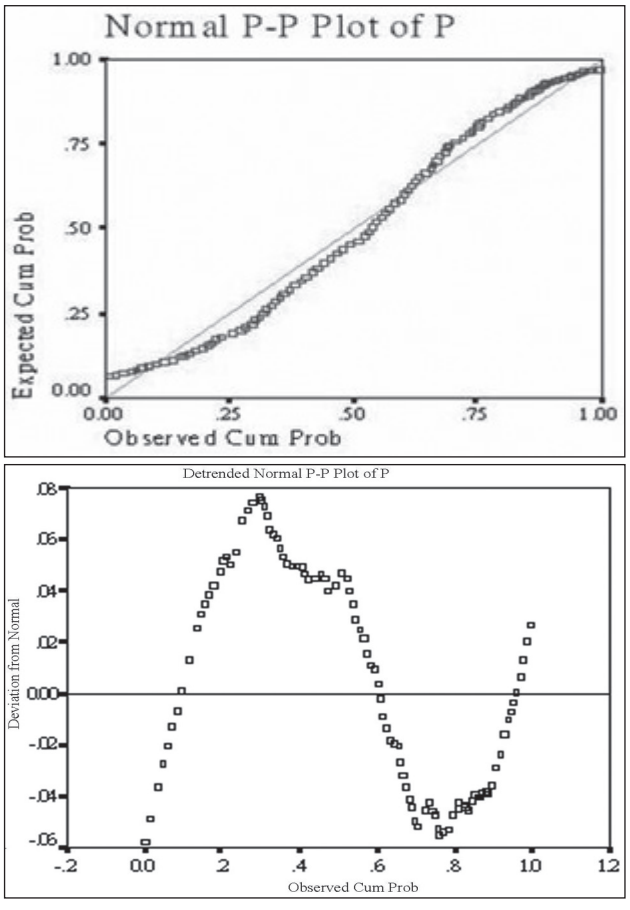

Figure 4. Test for spurious p values in multiple comparisons: normal P-P plot of p value.
Y axis= *570 p values resulted from multiple comparisons.*
X axis= *Corresponding 570 probabilities of normal distribution between 0 and 1.*

Although data on PSI were not readily available, a positive associative relationship between PSI and exacerbation of asthma was identified based on Changhua Station's data, which was also found in many other studies (6,13,14,22). However, we were unable to evaluate the effects on diurnal temperature changes with the adjustment for air pollution. Also, we were unable to account for other potential confounding factors such as health history and genetic constitution of parents due to the use of secondary data. The potential confounding effects from smoking is expected to be small in our study. The proportion of smokers is very small among children in Taiwan, particularly in those with asthma. Although some other confounding effects might occur, a study that was conducted at a local hospital, which had more control over confounders observed similar effects of temperature changes on asthma to those observed in our study (23).

In the current study, we observed associations between diurnal temperature changes and asthma admissions in Taiwanese children, but the associations varied across geographic areas and seasons. In winter, we observed positive associations in regions northern to the Tropic of Cancer and negative associations in southern regions. In other seasons, we observed positive associations in plain regions, which are near the sea, and negative associations in mountainous regions, which are away from the sea.

Because we were unable to control the effects of air pollution in the current study, further studies should be conducted to confirm our observations and evaluate the possible interactions between climate factors and air pollution. Additionally, it would be of great interest to evaluate whether there are such associations between diurnal temperature changes and asthmatic attacks in adults.

Conclusion

The relatively consistent trends in a given season within a given geographic zone indicate both seasons and landforms may affect the associations between diurnal temperature changes and asthma attacks. Accordingly, we believe changes in ambient temperature in short periods of time can induce exacerbation of asthma, and therefore asthmatic children should avoid such exposures. The diurnal change of temperature can be an important index to predict the acute onset of asthma, and it may cause exacerbation of symptoms in children through the mechanism of physical accommodation. This means that weather forecasts may offer important information to the prevention of asthma attack in children, and further studies should be conducted to identify other climate factors that may affect the exacerbation of asthma.

Acknowledgements

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Regression Model Analysis of Service Desirability in a Group of Mazandaran Hospitals

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Abstract

Background and purpose: Assessment of hospital services is the first essential step in improving service desirability, and a means to evaluate the clients' level of satisfaction. The main purpose of this research is to investigate the hospital service desirability in a group of hospitals in Iran.

Methodology: Analytic Hierarchy Process (AHP) which is a common multiple regression technique was used as the main method for organizing and analyzing data. Furthermore, the empirical model of service desirability was applied in the analysis process which has been carried out on 563 patients at the time of release in 15 hospitals of Mazandaran province in Iran.

Findings: The level of service desirability in hospitals was found to be at an average level with a mean score of 2.72. Besides, a significant relationship ($p < 0.05$) of the criteria and the sub-criteria at various levels of the model with the dependent variable desirability was confirmed.

Conclusion: Assessing hospital service desirability and determining the way it influences the customers' satisfaction is one of the most crucial issues in the planning for quality service provision and enhancing service desirability, hence it requires utmost attention by the health care decision makers.

Key words: service desirability, multiple regression, service quality, hospital services

Introduction

Securing customers' satisfaction is a fundamental element in organization's mission and is considered as the ultimate goal for any organizational strategy [1]. Identification of customers' needs and securing their satisfaction results in customer retention for the organization. A forward- looking organization needs to have a meticulous view to the issues associated with its customers [2]. Since customers differ in terms of personality traits, as well as intellectual and even physical attributes, they have varying perceptions towards each aspect of goods and services. Therefore, organizations are to contemplate two important elements when providing services to their customers: a) various dimensions and attributes of the offered services and b) customers' perception of each attribute of the offered services [3]. In fact, satisfaction is defined as a customer's evaluation and assessment of the experience he has after consuming a good or service. Hence, satisfaction result is introduced and specified as the consumption desirability [4].

Service quality has become a key strategic concept in the management field [5], yet for certain sectors it is of a greater significance. One of those sectors is health care where clients demand excellent hygienic and health care services from the service providers. Therefore, an emphasis on the quality of results, service quality and desirability, and client satisfaction with regards to the offered services is now a top priority in the health care system [6, 15]. The finding of a study in Korea showed a remarkable increase in the satisfaction rates in the country, jumping from 15.4% in 1989 to reach 40.5% in 2003. This trend in crude rates did not change even after adjusting for the patients' socio-demographic factors and health status. This improved satisfaction rate is in line with the finding of another study from Social Statistics Survey in 2002 where 30% of respondents reported that the health care services they received had gotten better when compared with those of the previous five years (47% reported no change, and 17% said that their health care services had gotten worse) (Korea National Statistical Office, 2003). Although a direct transnational comparison should be cautiously performed, the upward trend in satisfaction is notable when compared with trends in other countries [7]. Another study showed that there is an association between the level of

primary physicians' service productivity and patients' satisfaction with access to the services. These findings were in agreement with the widely-know findings of Blendon et al. in their study of the relationship between health care expenditure per capita in a country and satisfaction of the population with health services [8, 9]. Given the importance of assessing the critical factors associated to satisfaction and considering prior similar research works, the present study has applied a novel approach to investigate satisfaction levels for both general and particular services using statistical model and technique. Through assessing the factors involved in the satisfaction level by means of mathematical techniques and advanced statistical models, present research is expected to be a new step for introducing mathematical models to resolve the problems faced in the medical sciences. This study seeks to analyze the level of hospital services desirability by means of statistical regression technique.

Methodology

This is a descriptive-cross sectional research carried out on patients at the time of release in 15 hospitals of Mazandaran province in Iran during the year 2010-2011. A sample of 563 patients at the time of release who were willing to take part in the study, were selected and questionnaires were distribute to them over a one-week time span. The questionnaire consisted of the following main sections: demographic questions, general satisfaction over common services (items: employees' politeness and propriety, service quality, waiting time, cost and privilege which in turn includes hospital reputation, physician reputation, comfort facilities for patients and their attendants, information supply upon arrival and cleanness and silence of the environment), and particular satisfaction (items: clinical services, nursing services, medical services, Para-clinical services, reception and release services, and nutritional service). Data analysis was done using multiple regression analysis and Analytic Hierarchy Process (AHP). To do so, first by assigning some weights to independent variables, their relative effect on the independent variables was estimated. These weights (numerical values) are called "regression weights" or coefficients. Then these weights or coefficients were standardized and the beta coefficients were identified. Moreover, the independent variables were ranked and compared with one another [10]. The experimental model for measuring life quality consists of the following hierarchical structures: criteria, sub-criteria and effective criteria which form different levels of the model [11]. Finally, the desirability level on the two axes (general satisfaction and particular satisfaction with regards to hospital services) was measured. An empirical "upside-down" approach was used to set up the value tree for utility. In this model, utility is placed at the first level of the value tree. The second level is broken down into two criteria (categories): 1) General satisfaction level with hospital services 2) Particular satisfaction level with hospital services. The third level of the value tree is formed up the five sub-criteria for general satisfaction (namely, employees' politeness & propriety, service quality, waiting time, cost, and privilege) and six sub-criteria for particular satisfaction (namely, clinical services, nursing services, medical services, para-clinical services, reception & release services, and nutritional services). Finally, the model's fourth level was divided into more detailed indices of each of the third level's criteria specified using the direct method of questionnaire.

Findings

According to the findings extracted from the questionnaire, based on a single-sample t-test, mean score of hospital services desirability was equal to 2.72 and the variables of the model's four levels have a significant relationship with the satisfaction variable ($p < 0.05$) (Diagram 1).

Comparing the mean scores of satisfaction levels (general and particular) was done using the one-sample test of Kologroph- Smirnoph. The results showed that distribution of data in groups was normal ($p<0.03$). In addition, the mean score of satisfaction at the second level of the model was equal to 2.۶۵ and 2.79for general and particular satisfaction, respectively (Table1).

To rank the criteria and sub-criteria of the hospital services desirability, multiple regression analysis was applied. In this method, the "beta coefficients" to determine the criteria and sub-criteria that influence the satisfaction at the second

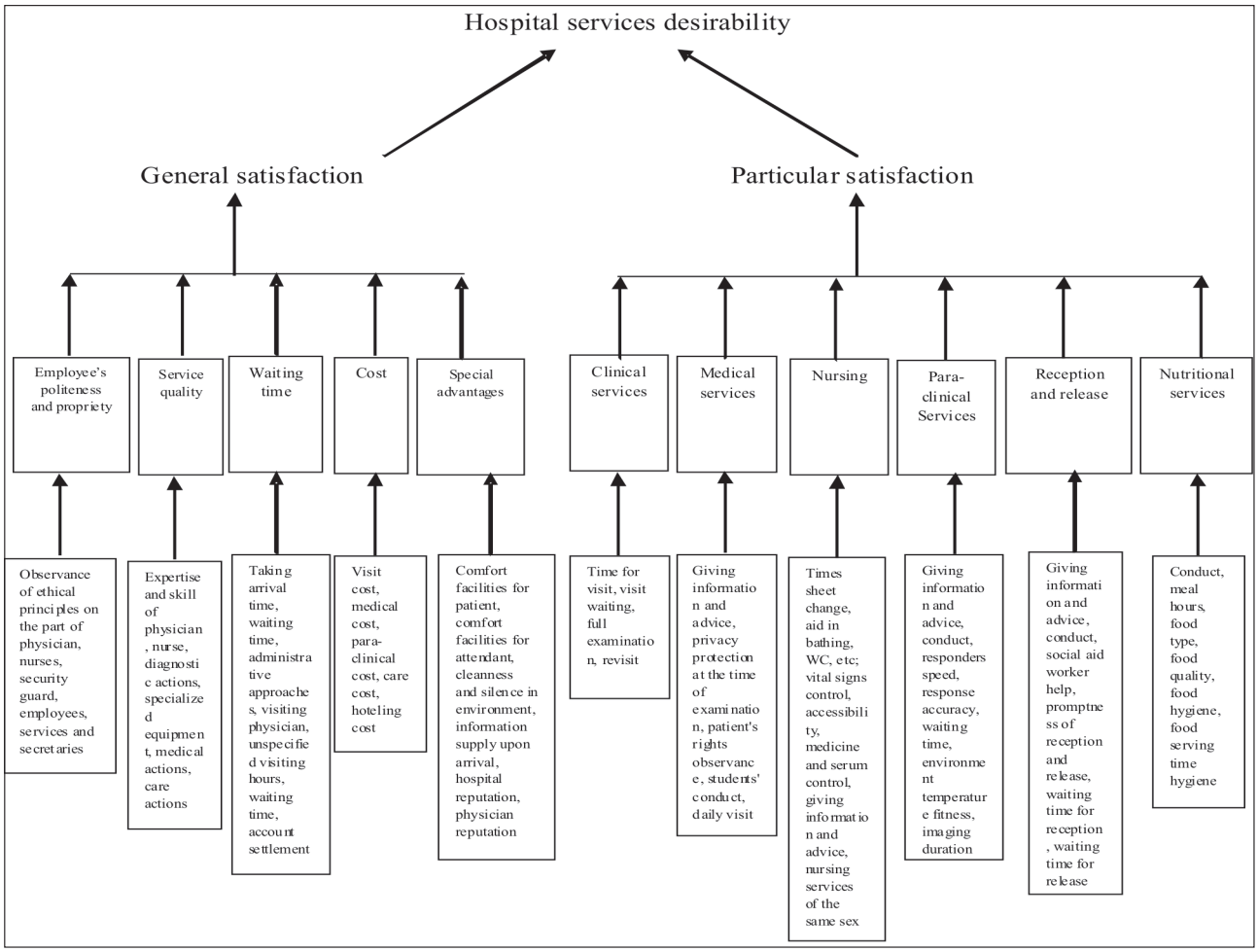

Diagram 1. Hierarchical prioritization of criteria and sub-criteria of hospital services desirability

Table 1. Hospital services desirability and satisfaction in understudy area as criteria and sub-criteria

First level	Second level	Satisfaction mean score 1>mean>5	Third level	Satisfaction mean score 1>mean>5
Hospital services desirability (Mean score: 2.72)	**General satisfaction with hospital services**	2.65	Employees politeness and propriety	2.27
			Service quality	3.47
			Waiting time	2.13
			Cost	2.46
			Privilege	2.92
	Particular satisfaction with hospital services	2.79	Clinical services	2.56
			Nursing services	3.01
			Medical services	2.9
			Para-clinical services	2.86
			Reception and release services	2.52
			Nutritional services	2.89

level were equal to 0.532 and 0.592 for general and particular satisfactions, respectively.

In addition, among the sub-criteria for the general satisfaction of hospital services, the item of employees' politeness and propriety (with β = 0.462) had the highest importance compared to the other items. And among the sub-criteria for particular satisfaction with hospital services, the item of nursing services had relatively higher importance with a Beta coefficient equal to 0.453 (Table 2).

Table 2. Ranking coefficients based on the importance of satisfaction's criteria and sub-criteria

First level	Second level	Beta coefficients (β)	Third level	Beta coefficients (β)
Hospital services desirability	**General satisfaction with hospital services**	0.532	Employees politeness and propriety	0.462
			Service quality	0.417
			Waiting time	0.406
			Cost	0.434
			Privilege	0.441
	Particular satisfaction with hospital services	0.592	Clinical services	0.438
			Nursing services	0.453
			Medical services	0.440
			Para-clinical services	0.435
			Reception and release services	0.430
			Nutritional services	0.436

Conclusion

Service quality and desirability analysis by means of quantitative techniques and empirical models is an approach used nowadays to identify general level of desirability, as well as the influential criteria and their relative importance in service desirability level and clients' satisfaction. In the meantime, obtaining reliable results close enough to reality can be used as the base for planning and decision making about action and interference solutions in organizations, provided that application of those group of desirability assessment approaches is based on assessment of service recipients' judgment about various aspects of desirability. By allowing for this reality, the results from current research indicate that patients' satisfaction with service desirability in hospitals of Mazandaran province is evaluated at average level (Mean score: 2.72). In addition, satisfaction levels at the second level (Mean score: 2.۶۵) and the third level (Mean score: 2.79) were also evaluated to be at average level. A comparative survey, conducted in five nations, reported that the proportion of citizens who believed that their health care system worked well and required only minor changes decreased from 1988-2001; namely in Australia from the percentage dropped from 34% to 25%, in Canada from 56% to 21%, and in the UK from 27% to 21%. Only in the United States, the proportion slightly increased from 10% to 18% [12].

With regard to the constituting sub-criteria of general and particular satisfaction of hospital services the greatest degree of satisfaction belonged to service quality with a mean score of 3.47 and nursing services with a mean score of 3.01; whereas the least degree of satisfaction belonged to waiting time with a as well as employees' politeness and propriety with the mean scores of 2.13 and 2.27, respectively. The study by Soleimanpour et al. [13] used an association analysis between waiting time and satisfaction levels to find out that those patients with longer waiting times were dissatisfied. Moreover, they discovered that the items with a high level of satisfaction consisted of physicians' courtesy and behavior with the patients (82.5%), security guards' courtesy (78.3%) and nurses' courtesy with the patients (78%); whereas the lowest level of satisfaction belonged to care provider's efforts to get the patients involved in making decisions about their own treatment (26.5%), waiting time (WT) for the first visit (26.2%), and cleanness and neatness (22.2%). Although the overall dissatisfaction rate for the night shift was less than that of other shifts, there was no meaningful statistical difference among different shifts. The data also indicate that living area, either urban or rural, had no meaningful relationship with the satisfaction level. The satisfaction levels for subjects with different educational background were calculated as it follows: those holding bachelor degrees and above (45.7%), associate degrees (51.5%), high school diplomas (53.7%), below high school level (76.3%), and finally those who were illiterate (65.8%) [13].

In another recent study by Otani et al., two-stage multiple linear regression analyses were conducted with several control variables (age, gender, perceived health, education and race). It was found out that patients' highest priority is to be treated with courtesy and respect by nurses and physicians. Be-

sides, the study suggested that an effective intervention program to improve patient satisfaction would include a training program, where care providers understand that patients want them to show courtesy and respect. Then, well-trained and empathetic nurses and staff members can comfort patients, and consequently improve patient satisfaction [14].

The current study results also show that the criterion of particular satisfaction with hospital services has a relatively higher importance to the patients (β = 0.592) compared to the criterion of general satisfaction with hospital services (β = 0.532). As for the satisfaction sub-criteria (items) the highest level of importance belonged to employees' politeness and propriety (β = 0.462) and privilege (β = 0.441), while the least importance were marked for waiting time (β = 0.406) and service quality (β = 0.417). Given that the satisfaction in all its criteria and sub-criteria was either low or average, corrective action needs to be applied in order to improve the desirability of health care services and satisfy patients. Moreover, organizing training to health care service providers and suppliers to empower them with effective relationship and communication skills should be emphasized by the health care policy makers and administrators.

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A graphical health report constructed as a KIDMAP Using Rasch Analysis of IRT Model

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Abstract

The health report was usually prepared by physician under the clinical decision with laboratory data, examinee personal characteristics of gender, age, race and even his/her occupation, on which the reference normal data were provided by laboratory technicians, and the examiners discriminated abnormal health results through computer programs initially

Rasch model with WINSTEPS software was applied to analyze the physical examination data from 462 workers of a regional hospital in southern Taiwan. The measurement items were examined to see whether they fit the Rasch model and whether they match a single construct in order to (1) estimate model parameters, (2) generate demographic comparison reports across items for the sample, and (3) depict the KIDMAP health report for the individual examinee.

The results showed that all 9 items fitted the model expectation reasonably well. Rasch analysis could be used to help physicians discriminate examinee health conditions by Fit statistics. We found that the norm-reference should be compared to an individual examinee as to plot KIDMAP to accurately explain health examination reports for patients.

The examinees are benefited from KIDMAP detection functions. KIDMAP produced in this study through item response theory was recommended as a monitor calibration of annual physical examinations in hospitals.

Key words: Rasch Analysis, single construct, health report, KIDMAP.

Introduction

Health examinations of different scales are performed in many healthcare settings. Every hospital conducts enormous numbers of diverse physical examination for their clients and customers. Even the simplest health examination requires a complete, clear and correct report. Professionals like physicians spend much effort and time in checking the physical examination results including many normal or non-significant abnormal ones and relatively fewer critical abnormal findings, which are usually emerged in the traditional examinees' health reports.

In this study, we apply Rasch-IRT (item response theory) model to generate a so-called KIDMAP[1-3] graphical health report as an auxiliary decision making for physicians to interpret the individual health results in which unexpected outlier values for the specific items will be disclosed while comparing with the sample norm-referenced of the counterparts. Aside from the new feature, we hope the KIDMAP health report can effectively and swiftly produce sophisticated report, increases the satisfaction of both professionals and customers, and even plays an important role in residents training.

Concepts gestated from KIDMAP and open access journals

KIDMAP[1], developed within the context of Rasch measurement[4], was devised by Benjamin D. Wright at the University of Chicago in 1978. It is a clever way of displaying academic performance. Four quadrants are used: items not achieved are plotted in the right-hand side of the map, items achieved are plotted in the left side, harder items are

on top, and easier items are on the bottom. Difficulty level is plotted in logits in the central column. Additionally, diagnostic errors that require more attention are plotted in both top left and bottom right quadrants. A complete map clearly highlights a person's overall performance, strengths and weaknesses [5-7]. Using KIDMAP as an individual diagnosis of health performance therefore becomes an interested and worth-pursuing topic.

Recently, many journals offer various kinds of on-line services for author's paper submission. Open access journal, all articles are accessible FREE of charge (as HTML file) and mostly funded by charges paid by the author (usually through a research grant), is one of them accepting three steps for authors to submit their manuscripts: (1) selecting the appropriate section for this submission; (2) nominating 2-4 external referees to review their manuscripts; (3) deciding whether the submission should be fast-tracked. For the patients' and authors' compared here, an immediate diagnostic diagram of health information could be generated once the payment (or request) is completed. The consultation for the examinee's health report will be arranged later like manuscripts dispatched to reviewers depending on the patient's choices of consultation or a fast-track service.

Internet is a very specific communication channel and effects of the educational program delivered could be viable. More research under real-life conditions should be executed to enhance our knowledge of how we can use the Internet effectively to promote health activity [8]. We wish to invent an open-access-journal-like approach on internet to help the examinee self-assessed the individual health levels and aberrant responses through the KIDMAP generation on web site in accordance with the development of medicine 2.0[9].

A flow of a graphical health report constructed as a KIDMAP

The steps for patients to submit the health examination report to a Medicine 2.0 website may be designed as: (1) selecting gender, age, race, body mass index (BMI) etc.; (2) assigning a doctor for consultation; (3) specifying whether there is urgency in getting doctor consultation, which is similar to those steps for authors to submit their manuscripts to an open access journal. The KIDMAP of the individual health auxiliary report will be immediately shown up on the computer screen once the payment by customers (or request by consultation physicians) is exactly allowed with permission from the hospital under certain security authentication.

Rasch-IRT based KIDMAP health report

How health items online which gathered through the item response theory (IRT) analysis and gave immediate diagnostic information was explained. The B. D. Wright-developed KIDMAP [1] which provided clear visual information was constructed after our internet module made. Different kinds of test banks for different groups by gender, age, race, BMI or even the global sample of the examinees were ready for selecting patients and immediately responded to an appropriate KIDMAP for detecting which items were unusually compared with the norm reference of the respective test bank. The banks like tester's items that would normally be placed in correct and incorrect columns in a KIDMAP were put on either side of the underlying interval scale for interpreting both the health performance and the measured health latent trait for every respondent, based solely on raw scores of the endorsed health-examination-item result submission.

Objectives of this study

In order to assess customer's health status and anomaly responded by both population-average and the individual examinees themselves across items, we illustrated a sample of 642 clinical workers (445 female and 197 male) of whom participated in an annual labors health examination of a regional hospital in southern part of Taiwan in 2006 and conducted this cross-sectional study attempting to apply the Rasch-IRT model (1) to estimate examinees' health abilities in term of unidimensionality, (2)to generate demographic comparison reports across items for the sample, (3)to depict the KIDMAP health report for the individual examinee.

Methods

Participants and Data

Data was obtained from all employees who underwent standard labors annual health examinations of a regional hospital in southern Taiwan in 2006. A total of 642 workers participated in this scheme (see in Table 1). According to the occupational health regulation of Taiwan's government, everyone must undergo a standard health examination every year. The contents of health examinations include a standard 14 x 14 inch CXR pictures, urine routine, complete blood cell count, biochemistry and regular physical examination, which were treated as a Likert-type [10] scale and classified according to respective criterion for each item responses, the healthier as coded the higher value as shown in Table 2.

Table 1. Demography for examinees of this study

Variables	count	%
Gender		
Female	445	0.69
Male	197	0.31
Total	642	1.00
Department		
Admist.	106	0.17
Nursing	190	0.30
Techni.	276	0.43
Physi.	70	0.11
Total	642	1.00
Age		
20+	96	0.15
30+	344	0.54
40+	147	0.23
50+	55	0.09
Total	642	1.00
Service tenure		
5-	66	0.10
10-	190	0.30
20-	348	0.54
20+	38	0.06
Total	642	1.00

Procedure and Data analysis

We took advantage of the Rasch model, using the software WINSTEPS [11], to analyze the physical examination data. The measurement items were examined to see whether they fit the Rasch rating scale model [12] and whether they match a single construct in order to (1) estimate model parameters, and to (2) develop a KIDMAP to help physicians accurately explain labors' health examination on internet. Statistical analyses such as t-test and ANOVA for comparing group health ability were performed using Statistical Package for the Social Sciences software (SPSS; Version 12.0; Chicago, IL).

Testing unidimensionality

We use the term unidimensionality to denote the fact that only a single person characteristic is involved in the responses [13-15]. The central idea is that we can delineate a domain of items for which holds that the correctness of the responses depends on a single person characteristic only. How this ability can be labeled, depends on the content of the items. That is that there exists a domain of items that is related in the sense that a correct response depends on the same person characteristic (ability). The way in which the correctness of the response is determined by this person characteristic, is a dominance relation between this person characteristic and an item characteristic (difficulty). The unidimensionality of the nine items of the physical examination data was inspected with WINSTEPS in order to see whether items fit the Rasch model.

To examine the unidimensionality of the scale, infit and outfit statistics were used to examine whether the data fit the expectation of the rating scale model. The infit mean square (MNSQ) is sensitive to unexpected behavior affecting responses to items near the examinee's performance measure (e.g., health status); the outfit MNSQ is sensitive to unexpected behavior on items far from the examinee's satisfaction status [16,17]. MNSQ can be transformed to a t statistic, termed the standardized Z value (ZSTD), which follows approximately the t or standard normal distribution when the items fit the model's expectation.

In this study items with both infit and outfit ZSTD beyond +/-2 and MNSQ beyond 0.6 and 1.4 were considered poor fitting [5, 16]. A factor analysis was conducted to verify whether any dominant component existed among the residuals (observed scores minus expected scores) which

Table 2. Liker-type scale for classification of item responses (healthier as higher value)

Item	Criteria		Low boundary		Up boundary		Coded
			Male	Female	Male	Female	
Chest X-ray	Normal, Abnormal						4,2
Urine dipstick test	- + 2+ 3+ 4+						4,3,2,1
WBC	Male	3.4-9.1*1000/ul	3.4-9.1	3.2-9.2			4
		-0.5	2.9-3.3	2.7-3.1	9.2-9.6	9.3-9.7	3
	Female	3.2-9.2*1000/ul	2.4-2.8	2.2-2.6	9.7-10.1	9.8-10.2	2
		-0.5	<2.3	<2.1	>10.2	>10.3	1
hematin	Male	13.5-17.5g/dl	13.5-17.5	11.6-14.8	□	□	4
		-2	11.5-13.4	9.6-11.5	17.6-19.5	14.9-16.8	3
	Female	11.6-14.8g/dl	9.5-11.4	7.6-9.5	19.6-21.5	16.9-18.8	2
□	□	-2	<9.4	<7.5	>21.6	>18.9	1
cholesterol	122-240mg/dl		122-240				4
	-50		72-121		241-290		3
	Meaningfulless if too low		22-71		291-340		2
			<21		>341		1
triglyceride	42-200mg/dl		42-200		□		4
	-50		0-41		201-250		3
	Meaningfulless if too low		251-300				2
□	□	□	>301		□		1
blood sugar	70-110mg/dl		70-110				4
	-20		50-69		111-130		3
			30-49		131-150		2
			<29		>151		1
Creatinine	0.6-1.3mg/dl		0.6-1.3		□		4
	-0.2		0.4-0.5		1.4-1.5		3
	Meaningfulless if too low		0.2-0.3		1.6-1.7		2
□	□	□	<0.1		>1.8		1
SGPT	10-50iu/l		0-50		□		4
	-50		51-100				3
	Meaningfulless if too low		101-1000				2
□	□	□	>1001		□		1

should be randomly distributed [18]. The unidimensionality assumption held if no dominant component was found [19].

Results

Unidimensionality analysis

Aside from the X-ray chest examination of dichotomy, others are of polytomy, 4 as normal, 1 as sever. The frequency and percentage of item responses are shown in Table 3. Besides the ZSTD of WBC beyond +/-2, all the MNSQ of infit and outfit are in the range of 0.6 and 1.4, indicating that data fit to the Rasch model's expectations. X-ray shows the most difficult (1.06 logits, SE=0.05) to be healthy in Table 4 with 27% of abnormality in Table 3, and Creatinine displays the easiest (-1.4 logits, SE=0.23) to be normal with 2% of abnormality in Table 3.

The person map of items shown in Figure 1 reveals that most of examinees present healthy in the left top of the Wrihgt's map. Person's average ability is 1.89 logits with 0.63 of standard error. The person reliability was 0.34 (which can be similarly interpreted as Cronbach's α), indicating that these items cannot sufficiently separate persons into more than two strata [13].

Table 3. Frequency for item responses

Item	scored	Freq.	%
Chest X-ray	2	173	0.27
	4	469	0.73
Urine dipstick	1	39	0.06
	2	29	0.05
	3	128	0.20
	4	446	0.69
WBC	1	18	0.03
	2	5	0.01
	3	15	0.02
	4	604	0.94
hematin	1	16	0.02
	2	12	0.02
	3	72	0.11
	4	542	0.84
cholesterol	1	0	0.0
	2	4	0.01
	3	60	0.09
	4	578	0.90
triglyceride	1	17	0.03
	2	12	0.02
	3	92	0.14
	4	521	0.81
blood sugar	1	1	0.0
	2	4	0.01
	3	22	0.03
	4	615	0.96
Creatinine	1	1	0.0
	2	2	0.0
	3	10	0.02
	4	629	0.98
SGPT	1	0	0.0
	2	15	0.02
	3	49	0.08
	4	578	0.90

To see the Wright' map in Figure 1, no enough more difficult items were matched with the most able persons as these items yielded less precise estimates for the persons (model RMSE= 0.66; real RMSE = 0.68)

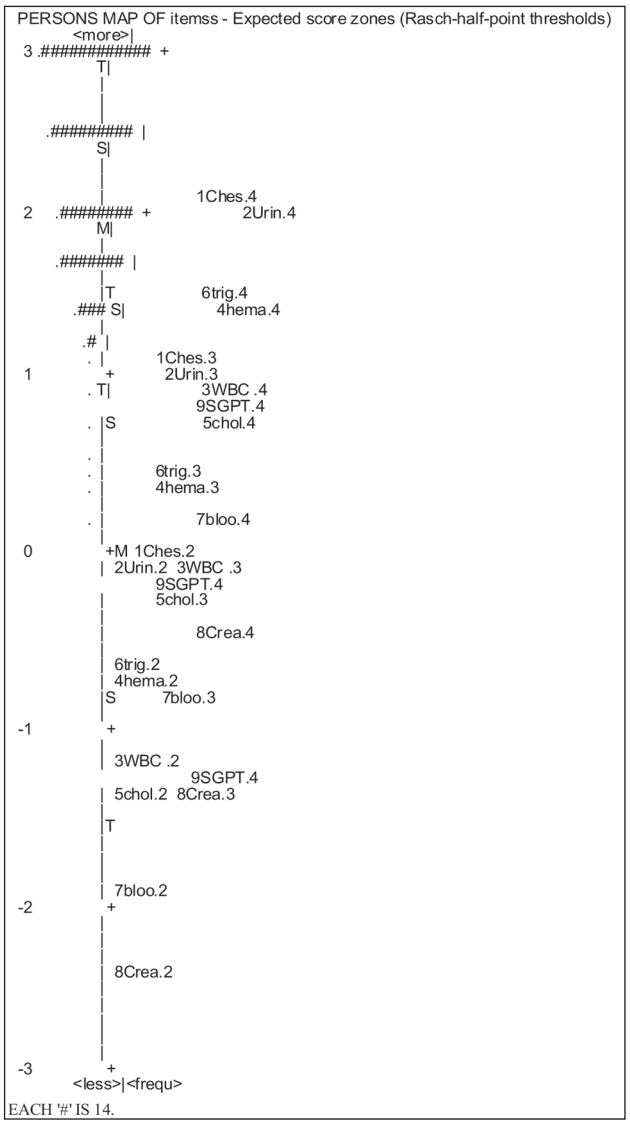

Figure 1. Wrihgt's map of Persons map of items

Table 4. Unidimensionality analysis

□	□	□	Logit		INFIT		INFIT	
No	Item	Raw score	Diff.	SE	MNSQ	ZSTD	MNSQ	ZSTD
1	Chest X-ray	1512	1.06	0.05	1.05	0.87	0.95	-0.62
2	Urine dipstick	1553	0.95	0.05	1.13	1.90	1.00	-0.01
6	triglyceride	1689	0.45	0.07	0.98	-0.13	0.97	-0.22
4	hematin	1713	0.32	0.07	0.86	-1.33	0.72	-2.2
9	SGPT	1777	-0.14	0.1	0.89	-0.72	1.01	0.13
3	WBC	1777	-0.14	0.1	1.39	2.36	0.61	-2.45
5	cholesterol	1788	-0.26	0.11	0.74	-1.74	0.97	-0.07
7	blood sugar	1823	-0.84	0.16	1.07	0.37	1.07	0.34
8	Creatinine	1839	-1.4	0.23	1.36	1.14	1.18	0.61

Comparisons for groups

Figure 2.1 shows that urine dipstick in Female and SGPT in male are statistically significantly worse than the opposite gender (t; p<.05). Age less 30 perform superior on X-ray, Age more than 50 significantly worse in Creatinine (t; p<.05). SGPT is displayed worst (t; p<.05) in those service tenure less than 5 years. Nurses present SGPT best, physicians exhibit SGPT worst and urine dipstick best (t; p<.05). What the most should be concerned is the SGPT occurred on those physicians who are male and serving for this hospital less than 5 years.

The results of ANOVA and Scheffe post hoc tests are disclosed that only service tenure of the employee exhibited statistically significant difference(F=3.912, df=3, p= .008) in health performance. The health abilities and SE for service tenure from less than 5 years to more than 20 years are (2.22, 0.10), (2.49, 0.06), (2.30, 0.05) and (2.09, 0.11), respectively, of which persons of service tenure less than 5 years merely performed better than the most senior group. Referring to Figure 2 previously discussed, poor SGPT for those new-comer and aged physicians may affect the average health level of sort service tenures.

KIDMAP health report for the individual examinee

The highest and lowest health abilities for persons are 2.51 and 0.25 logits, excluded the perfect response (i.e., extreme responded all items as 4) all valued at 3.51. Person's average ability including extreme and non-extreme is 2.34 (SE =0.93) logits, 1.89 (SE =0.63) logits for just the non-extreme, which show that the items are easier for those examinees who are not patients however, where as the log odds greater than the average item value of zero, or say examinee odds significantly greater than one.

A KIDMAP for the person whose health ability is 1.63 logits is shown in Figure 3 in which the item 8 (creatinine) exhibits outlier significantly unexpected response, Z-residual value is -12.89 (equal to observation of 1 minus expected value of 4 and then divide by the standard deviation of 0.23), indicating that the creatinine (difficulty=-1.4 logits) interacted with the person (ability=1.63 logits) very poor and needed to be further researched whether some things wrong with the data entry or the person really performed so poor in item 8 (creatinine). The other 8 items shown on the right side of Figure 3 are met with the normal level (Z-residuals are within +/- 2).

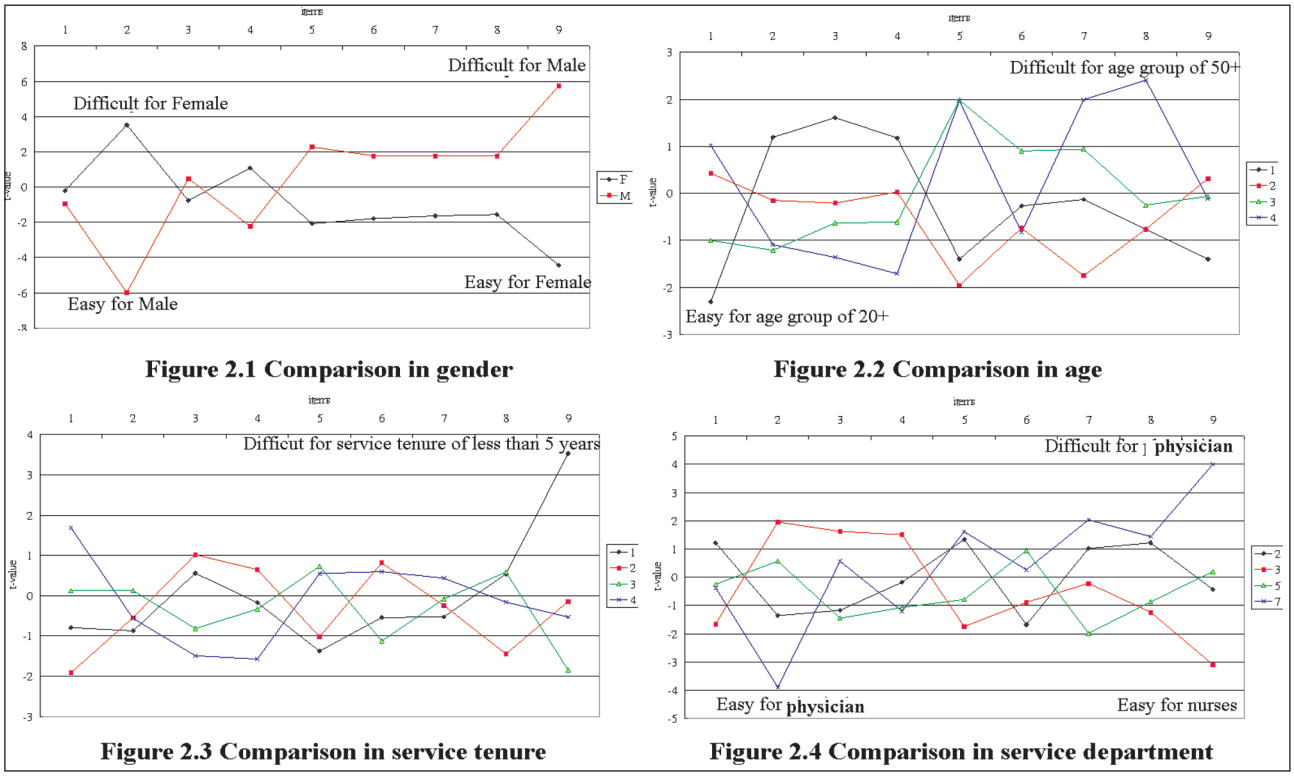

Figure 2. Comparisons of Groups
Note: t-values beyond +/- 2 deemed as significant differences

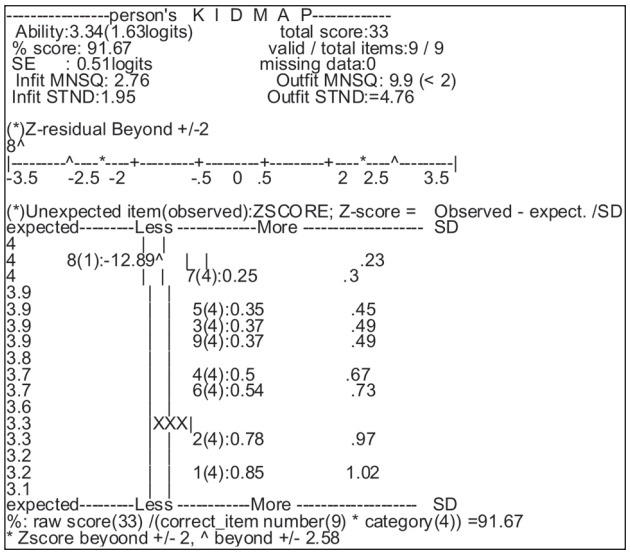

Figure 3. KIDMAP for the individual examinee

Discussions

Labor health protection through annual health examination is mandate for all employees in Taiwan, including the health care workers in hospital. The reference normal data were provided by laboratory technicians usually, and the examiners discriminated abnormal health results through computer programs initially. The final report was prepared by attending physician under the clinical decision with laboratory data, examinee personal characteristics of gender, age, race and even his/her occupation.

In tradition health report, professionals spend much effort and time in checking the examination results including many normal or non-significant abnormal ones and relatively fewer critical abnormal findings. Though the criterion of each item value had been appropriately set in computer database and easily shown the results of examined items with normality or abnormality. As we know that the criterion of each item should be met with the gender, the machine property of laboratory and even the age of each examinee. In this study, we recruited Rasch model, which derived from the IRT model, and analyzed the data of health examination. Many visualized diagrams were shown and interpreted through Rasch analysis. The difficult issues with regard to criterion setting for differently specific examinee can be solved in Rasch analysis due to the combined effects as formula 1 and 2 having been considered together in a model.

$$RM: \ln\left(\frac{P_{ni}}{1-P_{ni}}\right) = \theta_n - \delta_i, \quad \text{..... (1)}$$

$$RSM: logit_{nij} = \theta_n - (\delta_i - \tau_j), \quad \text{..... (2)}$$

Where, the probability of interaction between person's health ability (theta) and the specific item difficulty (delta) will be decided by the threshold difficulties of the item, i.e., the delta difficulty in formula 1 of Rasch model and the eta step difficulties on each item in formula 2 of Rasch rating scale model. The residuals (observed scores minus expected scores) could be examined as to detect the outlier effects through which the most unexpected response of a person's health examination can be highlighted.

Some ones may doubt that why the scale was set as polytomy instead of traditional dichotomy as the normality and the abnormality. The polytomous scale will be higher reliability than the dichotomous one and can be shorter item length according to the Spearman-Brown Prophecy formula [20].

The results showed that all 9 items fitted the model expectation reasonably well. Rasch analysis could be used to help physicians discriminate examinee health conditions by Fit statistics and personal health index estimation. We also found that norm-reference such as the sample of the study could be compared with the specific person's examination result so as to plot the KIDMAP as Figure 3 on internet to accurately explain health examination reports for customers. The examinees are benefited from outlier item alerting function in KIDMAP which produced in this study through item response theory and recommended as a monitor calibration of annual physical examinations in hospitals. KIDMAP is a fully web-based application and play important roles in preventive medicine in health examinations. Customers can also easily access the KIDMAP healthcare information from a hospital under certain security authentication. That is the graphical diagnostic map for the requested output being proposed after a self-scoring health report submitted.

Our developed shorten 9-item inventory of health examination was demonstrated to investigate

the examinees' health status online and present any difference beyond or under expectation. One parameter Rasch IRT model was for dimensionality, health ability and item difficulty distribution, and group gender difference. The online KIDMAP illustrated in this study showed the outcomes of online submission of the health examination items.

For future, we can develop broader items as test banks for different groups. The self-scoring KIDMAP, online consultation with or without fast-track service, could be useful for USERS-like Medicine 2.0, which is as the acronym of USER (Unconstraint, Service, Externality and Reward) referred to Web 2.0 features. Our graphical diagnostic map for the requested output was proposed after a self-scoring health report submitted.

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Factors Associated to Time of Arrival at the Health Service after Sexual Violence

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Abstract

Background: We aimed to describe the social, demographic and medical profile of victims of sexual violence and its association with the lapsed time between the aggression and the search for medical attention, in order to help professionals on the difficult task of minimizing the consequences of a painful situation, identifying the possible reasons for delay in access to hospital services.

Methods: We reviewed 439 female cases, voluntarily treated through the medical services of the Program for the Care of Violence and Sexual Abuse in Sao Bernardo do Campo, Brazil (PAVAS-SBC), during a seven years period, from 2000 to 2007. Of the 439 patients, 374 arrived at the hospital within 72 hours after the aggression. The average age was 24.5 years old and the most part of the population (45.1%) completed or were coursing high school. The most common form of sexual aggression was vaginal penetration in 43.9% of the cases, followed by multiple forms of penetration, like vaginal plus anal, or vaginal plus oral in 31.4% of the patients.

Results: Significant results among the patient group presenting after 72 hours was the absence of extra-genital injury (OR=2.58; IC95%: 1.04; 6.38), failure of notifying the authorities (OR=2.74; IC95%: 1.58; 4.78), and prior knowledge of the aggressor (OR=0.51; IC95%: 0.28; 0.96).

Conclusions: In summing, the extra-genital trauma and the police notification had been protective of the victims; while the known aggressor implied in the delayed arrival to the hospital. Public policies to qualify, make public and integrate the fields of action in this matter may reduce the complications involving such crime.

Key words: public health, women health, sexual violence, rape, sexual assault, , prevention and control, HIV infection, epidemiology

Background

Violence against women is defined by the World Health Organization (WHO) as "any act of gender-based violence that results in serious physical, sexual or psycho-emotional impairment to women, occurring in public or private life". It is a type of crime characterized as universal, covered by underreporting and lack of discussion with respect to this theme, although it is a serious public health problem due to its high morbidity (Krug et al, 2002).

The Pan American Health Organization estimates that 20% of women were sexually abused at least once in their lives, and the incidence of this type of aggression ranges from 13 to 28% (Krug et al, 2002; McIntyre, 2002). In Brazil, these data remain vacant due the lack of studies regarding this matter, but the minimum incidence rate is estimated at 7% in the general population (Ministério da Saúde, 2005).

Sexual violence can directly lead to unwanted pregnancies and sexually transmitted diseases (STDs), which include the Human Immunodeficiency Virus (HIV), other physical injuries and the impact on the psychological status of women. Thus, the health professional is in position to early diagnosis and to prevent problems resulted from such violence, noting that the health service does not obligate patients to report the police, furthermore, it is offered host and guidance.

According to the technical standard of the Ministry of Health, in the final version published in 2005 (Ministério da Saúde, 2005), the efficiency of the prevention mechanisms is higher when adopted earlier. In this case, it means that 72 hours after sexual aggression is the deadline for administration of drugs against unwanted pregnancy and STD/HIV (Faúndes et al, 2000; Ministério da Saúde, 2005; Draucker and Martsolf, 2009; Ahrens et al, 2009; Brozowski and Hall, 2009). It is under-

stood that the situation of sexual aggression imposes varied degrees of embarrassment to the victim, thus inhibiting their attendance to the police and even to the health service. It is therefore crucial to obtain data able to help professionals on the difficult task of minimizing the consequences of an unfair and painful situation, identifying the possible reasons for delay in access to hospital services.

Thus, the aim of this study is to describe the social, demographical and clinical profile of sexual violence victims and its association with the time lapsed between the aggression and arrival at the health service.

Methods

This is a retrospective descriptive study by free demand of 439 women attended at the Program for the Care of Violence and Sexual Abuse in Sao Bernardo do Campo (PAVAS-SBC), State of São Paulo (SP), Brazil, from 2000 to 2007. The study was conducted after approval of the Ethics Committee in Research of the College of Medicine of the ABC (protocol number 100/2008).

Sao Bernardo do Campo is a brazilian city in the state of Sao Paulo, in the Metropolitan region of Sao Paulo, Brazil. The total area of Sao Bernardo is 406 km² and its population is approximately 781,390 habitants (421,918 are female), according to the Brazilian Institute of Geography and Statistics (IBGE, 2007).

Data was withdrawn from patients files, which contained a semi-structured questionnaire and description of the victim clinical examination. The independent variables were listed: age, school degree, marital status, pregnancy at the time of the aggression, time of arrival at the hospital, previous use of contraception, previous sexual activity, identity of the aggressor, number of aggressors, type of crime, conducting police report and presence of physical trauma at the first examination. The dependent variable was the time between sexual aggression and the arrival at the hospital.

The age groups were divided into three groups after calculation of mean and standard deviation using quantitative data. For composition of the population, we used the following definitions: adolescence as the period between 10 and 19 years old (World Health Organization, 2002), reproductive age between 20 and 39 years old and peri or postmenopausal from 40 years old on (Li et al, 2002). The inclusion criteria was the free demand and the exclusion criteria was male gender and cases of chronic sexual abuse against children.

In order to evaluate normality of the variables we used the Anderson-Darling test. Tests of hypotheses for proportions used were chi-square or Fisher exact test. The odds ratio was calculated by logistic regression. We adopted the level of significance as $\leq 5\%$. All variables with a p-value ≤ 0.20 in logistic regression or chi-square test or Fisher were included in the hierarchical model. In the final model, we kept all the variables whose association with the time of arrival at health service remained ≤ 0.05, controlling for age. In order to analyze factors such as school degree and marital status, it was assumed that age would be a variable that modify the effect in logistic regression models. We analyzed two models: model A, with the independent variables not controlled by age, and a model B, variables controlled by age. It was considered statistically significant findings with p-value ≤ 0.05, with their respective confidence intervals (CI) of 95%.

Results

The total number of patients included in the study was 439. We observed that 374 (85.19%) arrived within 72 hours at the hospital, while 65 (14.81%) arrived 72 hours after the aggression. The average age was 24.5 years, 44.4% were between 10 and 19 years old and 47.3% between 20 and 39 years old (Table 1). Regarding school degree, the majority (45.1%) was studying or completed high school. Table 1 also shows that the most frequent crime was the vaginal coitus (43.9%), while the oral penetration was exclusively in 8.9% and anal penetration in 3.6%. The association of two or more crimes occurred in 31.4% of the cases. In 11.9% of women more than one aggressor was involved in the crime.

In relation to physical trauma we also noted in Table 1 that 14.8% of the victims suffered genital trauma whereas 18.6% suffered extragenital trauma. The aggressor was known by the victim in 18.4% of cases and 62.4% attended the police station to file a complaint officer.

The variables that did not present $p \leq 0.20$ during the univaried analysis were not presented in Table 1, which were: previous sexual activity, contraceptive use and pregnancy on the crime date. Table 2 presents the variables with $p \leq 20\%$ after multiple logistic regression for the dependent variable (time to arrival at the hospital after the crime), whereas in the model B we applied the control of variables by age. There was no statistical difference between the results of p and odds ratio (OR) between A and B models, which means that the high number of young women did not alter results in any variable.

According to Table 3, we may identify the variables associated to the interest event with $p \leq 5\%$. The non-genital trauma and the conducting police report presented as protective factors with respect to the interest event. The known aggressor was associated to delay in the search for the health service.

Discussion

Gender disparity affects women not only due their biological differences compared to men, but also by social, cultural and economic discrepancies (Bergamo et al, 2000). These differences generate discrimination, sometimes accompanied by physical violence, which contributes to the genesis of alterations of growth and development at the reproductive period (Oshikata et al, 2005; Casanueva and Martin, 2007). The physical and social comfort of women is essential to the development and maintenance of an equal and integral universal society.

The fight against sexual violence against women or children requires integrated actions of education, justice, social action, civil society and health. The last endeavors to protect the victim from pregnancy risk, sexually transmitted diseases and psychological damage.

The literature evidenced that women chosen by the aggressors were very young, ranging between 50 and 60% of girls younger than 19 years old (Oshikata et al, 2005; Andrade et al, 2001; Riggs et al, 2000). This is not explained only by the physical attraction for younger woman but also because their immaturity makes it more vulnerable to aggression (Oshikata et al, 2005; Brozowski, and Hall, 2009). Based on our findings, the average age of the population studied was 24.5 years old, 44.4% aged between 10 and 19 years old and 47.3% aged between 20 and 39 years old. After applied statistical tests we found, however, that the age group of victims does not contribute to advance or delay the search for the health service.

HIV infection is great concern for sexually aggressed women. Previous investigations showed that the risk of infection in these cases ranges between 0.8 and 2.7% (Ministério da Saúde, 2005), a risk comparable to other forms of sexual exposure, heterosexual single piercing or cutting accidents. The risk of infection depends on several conditions, including type of sexual exposure (anal, vaginal, oral), number of aggressors, susceptibility of women, trauma or genital lesions associated, viral status of the aggressor, but mainly the time elapsed between the contact with the infected person and the onset of prophylactic medications (Ministério da Saúde, 2005; Garcia-Moreno and Watts, 2000). There is consensus in the literature that anti-HIV prophylaxis must be initiated as early as possible (Andrade et al, 2001; Riggs et al, 2000; Garcia-Moreno and Watts, 2000; Drezett, 2002), after its penetration through the failure of the skin and mucosal barriers, the virus will reach the bloodstream and will be able to infect macrophages after about 48 hours, which determined that 72 hours would be the acceptable limit within which the antiretroviral drugs could exert a protective effect (Plata, 1988; Ball, 2001).

Although new and poor understood in the literature, prevention of HIV with the use of antiretroviral brings preceding success in situations such as the transmission during pregnancy and childbirth and in cases of occupational injuries (Ministério da Saúde, 2005). It is worth to remember that there are no reports regarding seroconversion in any patient who has correctly used the scheme after sexual aggression (Oshikata et al, 2005; Garcia-Moreno and Watts, 2000), and neither our patients.

The scheme suggested by the Brazilian Ministry of Health, in the final version of Technical Standards for Prevention and Treatment of injuries resulting from sexual violence against women published in 2005, was zidovudine, lamivudine and nelfinavir for 28 days (Ministério da Saúde, 2005). On the other hand, according to the anti-HIV therapy review in 2007, nelfinavir was replaced by the association between lopinavir and ritonavir (Ministério da Saúde, 2007).

In the same way, emergency contraception should be made within 72 hours, as suggested by the Ministry of Health, through two options: Levonorgestrel 1500 milligrams as a single dose as the first option, or the old "Yuzpe method", 200 milligrams of ethinyl estradiol plus 100 milligrams of levonorgestrel in two doses with an interval of 12 hours (Ministério da Saúde, 2005).

Although more flexible in the time recommended for its use, the prophylaxis for hepatitis B and non-viral infections (chlamydiosis, gonorrhea, syphilis and trichomoniasis) is also more effective when made earlier (Ministério da Saúde, 2005; Andrade et al, 2001).

In the literature concerning populations similar to ours, we observed numbers between 7 and 33% of patients coming to the health service after the first three days (Oshikata et al, 2005; Andrade et al, 2001), however, none of them examined the variables related to the delay. The lack of important technical details discussed before may have contributed to 14.8% of women in our study arrive after 72 hours, which avoided them from receiving appropriate care.

We reported with statistical significance that the aggressor, when known, is one of the factors that delay the search for the hospital. Besides the embarrassment and humiliation experienced by the victim, the fear of retaliation by an aggressor that may easily find the woman, scares her more than pregnancy and infection. It is worth to remember the difficult recognition of the "marital rape" when relationships ends in supposedly consensual aggression, however, it is rarely reported (Schraiber et al, 2007). The literature indicates rates around 70% of known aggressors, which the main aggressors were partners and from the own family (Oshikata et al, 2005; Drezett, 2005), however, great part of the researches regarding sexual abuse discusses attention to children or does not exclude them, which significantly alters the criminal profile, as shown by studies in several countries (Draucker and Martsolf, 2009; Riggs et al, 2000; Garcia-Moreno and Watts, 2000; Gomes et al, 2006; Grossin et al, 2003). In emergency room visits studies such as emergency rooms or reference services like ours, the numbers of known aggressors range from 10-20%, (Oshikata et al, 2005; Andrade et al, 2001) which supports the 18.4% of our data.

On the other hand, statistical analysis shows that the presence of non-genital trauma and police report were protective factors for the outcome studied, responsible for arrival of the patient in a period able to the prophylaxis. It is natural to suppose that professionals in police and emergency send post-sexual aggression as soon as possible to the reference service, which demonstrates an integrated and well coordinated municipal net in order to assist the victims of crime.

An interesting fact was observed in relation to the genital trauma that even in similar proportions to the extra-genital trauma did not influence the time of arrival of women. Whereas the vast majority of injuries were of small gravity, such as excoriation, bruises light, superficial hematomas and ecchymosis, it amazes us that genital injuries were not also served as a protective factor. It seems that the modesty and social taboos make it difficult for victims to exhibit the injuries in their intimacy, such as lacerations and vulvar or vaginal bleeding.

In conclusion, most of the victims arrived within 72 hours after the crime to the hospital. The average age was 24.5 years old, the great part was studying or completed high school. The vaginal penetration was the most committed crime, followed by the association of this with indecent anal or oral aggression. Considering that 72 hours after sexual abuse is the maximum time recommended for effective prophylaxis against STD / AIDS and unwanted pregnancies, two factors were shown to be protective for the victims: the presence of non-genital trauma and conduction of police complaint. Since the aggressor was known by the patient, it was noted delay in the search for the health service. Therefore, public policies aiming more preparation, dissemination and integration between the different sectors involved in the issue of sexual violence may bring positive impact in reducing and controlling the complications of this type of crime.

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Relationship between Helicobacter pylori virulence genes and clinical outcomes in Saudi patients

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Abstract

Helicobacter pylori has been strongly associated with gastritis, peptic and duodenal ulcers, and it is a risk factor for gastric cancer. Two major virulence factors of *H. pylori* have been described: the cytotoxin-associated gene product (CagA) and the vacuolating toxin (VacA. Since considerable geographic diversity in the prevalence of *H pylori* virulence factors has been reported, the aim of this work was to determine if there is a significant correlation between different *H. pylori* virulence genes (*cagA* and *vacA)* in 68 patients, from Saudi Arabia, and gastric clinical outcomes. *H. pylori* was recognized in cultures of gastric biopsies. *vacA* and *cagA* genes were detected by polymerase chain reaction (PCR). The cagA gene was obtained with 42 isolates (61.8%). The vacA s- and m- region genotype were determined in all strains studied. Three genotypes were found: m1/s1 (28%), m2/s1 (40%) and m2/s2 (26%). The m1/s2 genotype was not found in our study. The relation of the presence of cagA and the development of cases to gastritis and ulcer was statistically significant ($p<0.05$). The study showed a significant correlation between the *vacAs1m2* genotype and gastritis cases, and a significant correlation between *vacAm1/s1* genotype and peptic ulcer cases. The results of this study might be used for the identification of high-risk patients who are infected by *vacAm1/s1* genotype *H. pylori* strains.

Key words: H. pylori, CagA , VacA, gastritis, peptic ulcer

Introduction

Helicobacter pylori (*H. pylori*) is a gram negative spiral bacterium which colonizes in human stomach. Infection with *H. pylori* is linked with chronic gastritis, peptic ulcer, gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue lymphoma [1]. It is one of the most prevalent bacterial pathogens in humans [2]. There are two major bacterial virulence markers of *H. pylori*, the *VacA* (vacuolating toxin) and the *cagA* (cytotoxin-associated gene), which play a major role in determining the clinical outcome of *Helicobacter* infections [3]. The *VacA* gene is consider as a significant virulence factor encoding the vacuolating toxin and it is present in all strains [4]. This gene contains the signal(s) region and middle region (m). The middle region has m1 and m2 allelic types and the signal region has an s1 (s1a, s1b and s1c) or an s2 allele. The subtype s1/m1 strains give a higher level of cytotoxin activity than other genotypes, while s2/m2 strains do not secrete the vacuolating cytotoxin [5].

The *CagA* gene is considerably associated with cytotoxin production and the induction of interleukin 8 (IL8) by gastric epithelial cells [6]. This gene is an important marker for the most virulent strains which are associated with peptic ulcer, atrophic gastritis and adenocarcinoma [7]. The *cagA* is a marker for a pathogenicity island and associated with more severe clinical outcomes [8,9]. Atherton et al [5] reported a strong association between *cagA* and *vacA* signal sequence type s1.

In Saudi Arabia, there are no data for the pattern of *H. pylori* genotypes in patients; for that purpose, our study was the first to be done in Saudi Arabia. It aimed to investigate the prevalence of the cagA and vacA genotypes of *H. pylori* isolates from gastric culture to detect pathogenic *H.* pylori and their relations to clinical outcomes.

Materials and Methods

Biopsy samples were obtained over a 6 months-period (January to June 2010) from selected patients referred for endoscopy at different hospitals

in Riyadh, Saudi Arabia. Sixty eight (68) patients, who had *H. pylori*, were enrolled in this study. The mean age of the patients was 43 years (range, 14 - 84) and 45% were female. Histologically, patients were classified into gastritis in 37 cases (54,4%) and peptic ulceration in 31 cases (45.6%). One biopsy specimen taken from the antrum was used for the culture. All subjects data were collected from patients file. The study was approved by the Research and Ethical Committee (REC).

H. pylori Culture and DNA extraction

Antral biopsies were cut into small pieces, homogenized and were smeared on the surface of on *H. pylori* selective agar (Oxoid, UK) then incubated at 37°C in a BBL GasPak (Becton-Dickinson, USA) containing a Campy-Pak Plus microaerophilic system generator (Becton-Dickinson, USA) for 7 days. The identity of *H. pylori* clinical isolates colonies were smooth, translucent and small. Colonies that manifested the described characteristic morphologies were identified as *H. pylori* if they were Gram negative and shaped bacilli, and urease, catalase and oxidase positive. From the primary growth, seven or eight colonies were pooled together, and genomic DNA was extracted with the QIAamp DNA mini kit (Qiagen, Germany) according to the instructions of manufacture's. The isolated DNA was eluted in 200 µl of 1× TE buffer (10 mMTris-HCl, 1 mM EDTA [pH 8.0]) and stored at -20°C until use.

H. pylori genotyping for CagA and VacA

After DNA samples extraction, polymerase chain reactions (PCR) were carried out in a volume of 50 µl containing 1 µM of each primers, 1 µL of genomic DNA (approximately 200 ng), 1 mM of dNTPs mix, 2 mM of Mgcl2, and 0.05 U/µL Taq DNA polymerase. PCR amplifications were carried out in GeneAmp PCR system 9700 (Perkin Elmer; Norwalk, USA). Table 1 summarized the primer sequences and the expected size of PCR products. The following cycle conditions were used: for cagA: 1 min at 94°C, 1 min at 56°C, and 1 min at 72°C and for vacA: 35 cycles of 1 min at 94°C, 1 min at 53°C, and 1 min at 72°C. All runs included one negative and one positive DNA control. A 10 µL of amplified PCR products was then resolved by electrophoresis on 1.5 % agarose gels run in acetate EDTA buffer and stained with ethidium bromide. The PCR product was visualized under a short wave length ultraviolet light source (Figure 1).

Table 1. PCR primers for amplification of cagA and vacA sequences [10]

Region	Primer	Primer sequence (5'-3')	PCR product size (bp)
cagA	F1	GATAACAGCCAAGCTTTTGAGG	349
	B1	CTGCAAAAGATTGTTTGGCAGA	
vacA			
m1	VA3-F	GGTCAAAATGCGGTCATGG	290
	VA3-R	CCATTGGTACCTGTAGAAAC	
m2	VA4-F	GGAGCCCCAGGAAACATTG	352
	VA4-R	CATAACTAGCGCCTTGCAC	
s1/s2	VA1-F	ATGGAAATACAACAAACACAC	259/286
	VA1-R	CTGCTTGAATGCGCCAAAC	
s1b	SS3-R	AGCGCCATACCGCAAGAG	187
	VA1-R	CTGCTTGAATGCGCCAAAC	
s1a	SS1-R	GTCAGCATCACACCGCAAC	190
	VA1-R	CTGCTTGAATGCGCCAAAC	
s2	SS2-R	GCTAACACGCCAAATGATGC	199
	VA1-R	CTGCTTGAATGCGCCAAAC	

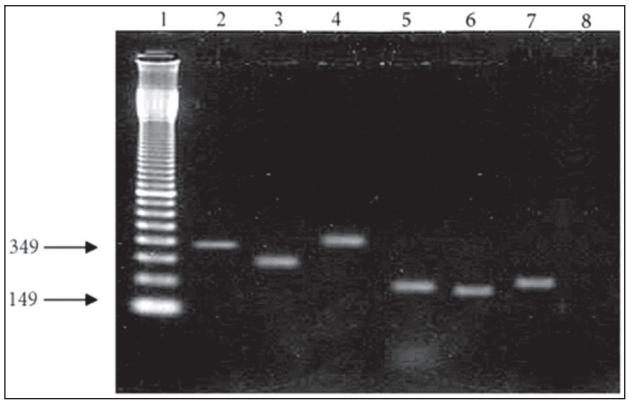

Figure 1. PCR genotyping of vacA and cagA status from different cases.Primers described in Table 1 were used for PCR reaction (Lanes-1= Molecular weight marker; 2= CagA+; 3= m1; 4= m2; 5= S1a; 6= S1b; 7= S2 and 8= Negative control (without DNA)).

Data analysis

Fisher exact test was used for analysis of data. A *P* value of < 0.05 was accepted as statistically significant.

Results

Prevalence of CagA v and VacA genotyping

The cagA gene was obtained with 42 isolates (61.8%) and 26 (38.2%) were negative. The vacA s- and m- region genotype were determined in all strains studied. In the m-region, 2 strains contained both m1 and m2 alleles. In the strains containing one single vacA m allele, the m1 allele was found in 19 isolates (28%) and m2 in 45 one (66%). For the s-region, in strains where a single vacA s allele was found, the minority 18 (26%) contained the s2 allele. In 46 isolates contained s1 allele (68%), 23 (34%) were subtype for each s1a and s1b. Considering strains with only one single vacA genotype, and taking vacA s- and m-region together, three genotypes were found: m1/s1 (28%), m2/s1 (40%) and m2/s2 (26%). The m1/s2 genotype was not found in our study. (Table 2).

Table 2. Prevalence of H.pylori genotype detected in 68 isolates

Genotype status		Patient (%)
cagA	cagA +	42 (61.8)
	cagA-	26 (38.2)
vacA	m1/m2	2 (3)
	m1/s1a	15 (22)
	m1/s1b	4 (6)
	m2/s1a	8 (12)
	m2/s1b	19 (28)
	m1/s2	0 (0)
	m2/s2	18 (26)

Table 3. Distribution of H. pylori genotype in gastritis and peptic ulcer patients.

Genotype status		Gastritis	Peptic Ulcer
		n=37 (%)	n=31 (%)
cagA	cagA +	20 (54)	22 (71)
vacA	m1/m2	0 (0)	2 (6)
	m1/s1a	2 (5)	15 (48)
	m1/s1b	0 (0)	4 (13)
	m2/s1a	6 (16)	2 (6)
	m2/s1b	16 (43)	3 (10)
	m1/s2	0 (0)	0 (0)
	m2/s2	17 (46)	2 (6)

Relationship between *H. pylori* genotyping in clinical outcomes

While estimating relationship between potentially virulent *H. pylori* strains and clinical outcomes, significant differences ($p<0.05$) were found between isolates from gastritis and peptic ulcer cases (Table 3). The results showed a high percentage of cagA (70%) in peptic ulcer cases compared to gastritis cases ($p<0.05$). The results showed a high percentage of m2/s1 with a distribution of 22 (59%) in gastritis cases ($p< 0.05$). In case of peptic ulcer, the highest rates were among m1/s1 with a frequency of 19 (61%) ($p< 0.05$).

Discussion

The geographic distribution of distinct *H. pylori* genotypes and the prevalence of virulent bacterial genotypes in several regions, particularly in Saudi Arabia, remain unknown. This study included

68 selected patients, of whom were infected with *H. pylori*. In the present study, we examined the distribution of the CagA and *vacA* genes and their relationship to clinical outcomes. The cagA gene was obtained with 42 isolates (61.8%). Our results were in agreement with other studies conducted in Europe, Central and South America, and East Asia where a higher prevalence (67% or more) of the cagA genotype was reported [11]. For the vacA genotype, and when considering a single combined genotype, the results showed that the vacA s1 allele was predominant (68%) followed by the vacA s2 allele (26%). These are in contrary with a study in Kuwait reported that vacA s1 and s2 types were detected in approximately equal numbers in biopsies obtained from patients of Middle-Eastern origin, while North Africans were predominantly infected with the s2 type [12].

The distribution of cagA was 54% in gastritis and 71% in peptic cases. The relationship of the presence of cagA and the development of gastritis and peptic ulcer is statistically significant ($p<0.05$), which further substantiate the role of cagA as a marker for increased virulence of *H. pylori*. These findings are in agreement with several previous studies [13, 14]. In this study, the prevalence of the vacA genotypes m1/s1 was detected in 28%, m2/s1 in 40% and m2/s2 in 26%. No single case for vacAm1/s2 genotype was detected in this study. This finding is in agreement with previous studies as this genotype was reported to be rare [15, 16].

In this study, the most pathogenic vacA genotype which is vacAm1/s1 was present in 61% of peptic ulceration sampled studied, these are in agreement with previous studies where they found association between this genotype and severe gastric outcomes. These findings support the role of vacAs1m1 genotype in severe clinical outcomes [17-19]. In conclusion, the results of this study might be used for the identification of high-risk patients who are infected by vacAs1m1 genotype *H. pylori* strains. These patients infected with such strains should have more tension regarding anti-Helicobacter treatment to prevent reoccurrence and prevent severe clinical outcome such as peptic ulcer and gastric carcinoma later on in their life.

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Measuring the Benefit Equity in China's Basic Health Insurance Schemes

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Abstract

Background: Although the health insurance has nearly achieved universal coverage in China, the co-payment ratio is still very high. Therefore, it is doubtful that the insured could get equitable benefit from the health insurance schemes. The purpose of this study is to evaluate the benefit equity which the insured residents with different economic levels get from the Urban Employee basic Health Insurance (UEHI), the Urban Resident basic Health Insurance (URHI) and the New rural Cooperative Medical Scheme (NCMS), respectively.

Methods: The data were from the household survey in Mei County, Shannxi Province, in which the number of the urban employees, the urban residents and the rural residents used in this study were 1258, 733 and 2870 respectively. The benefit equity was measured by the equity of benefit rate and the equity of benefit degree in health insurance scheme. By subtracting the concentration index of health care need from the concentration index of benefit rate/degree, the horizontal index of inequity of benefit rate/degree were generated.

Results: There were pro-rich horizontal inequities of benefit rate in UEHI, RUHI and NCMS, and the horizontal indexes of inequity of benefit rate were 0.061, 0.122 and 0.161, respectively. In terms of the benefit degree, the horizontal indexes of inequity of benefit degree for the residents covered by UEHI, URHI and NCMS were 0.027, -0.187 and 0.178 respectively, which means both the inequity of benefit degree in UEHI and NCMS were pro-rich and the inequity of benefit degree in URHI was pro-poor.

Conclusion: When the insured with different economic levels have the same health care need, the number of the rich who can get benefit from UEHI, URHI and NCMS is more than the poor; meanwhile the rich can get more compensation from the UEHI and NCMS than the poor.

Key words: UEHI, URHI, NCMS, the equity of benefit rate, the equity of benefit degree, horizontal index of inequity

Introduction

Three basic health insurance schemes have been established in China since the end of last century: the Urban Employee basic Health Insurance (UEHI) which was designed for the employees was implemented in 1998; the New rural Cooperative Medical Scheme (NCMS) which was designed for the rural residents was implemented in 2003 and the Urban Resident basic Health Insurance (URHI) which was designed for the urban residents was implemented in 2007. By the end of 2010, there were 257 million people covered by the UEHI and 432 million people covered by the URHI, which accounted for 39.5% and 59.3% of the total urban residents, and meanwhile, the coverage rate of NCMS even reached 96.3% (1). Although the health insurance has nearly achieved universal coverage in China, the co-payment ratio (the share of patients' out-of-pocket health expense in total health expense) is still very high. As the China's fourth Health Service Survey in Shaanxi Province shows, the co-payment ratios of the UEHI, URHI and NCMS were 43.0%, 81.6% and 68.7% respectively. The purpose of establishing the health insurance schemes is to compensate the insured and then release the residents' burden from the expensive medical care. Thus whether the insured can get equitable benefit from the health insurance schemes is the key for achieving this goal. However, due to the high co-payment ratio, it is doubtful that the insured could get equitable benefit from the health insurance schemes. On the one hand, when the co-payment ratio is high, the health insurance couldn't increase the poor's access to health service, therefore, the rich would use more health service than the poor; on the other hand, for the per-visit inpatient servi-

ce, the high co-payment ratio would make the rich utilize more health service source than the poor. Therefore, the rich would get more compensation from the health insurance schemes than the poor. The purpose of this study is to evaluate the benefit equity which the insured residents with different economic levels get from the three health insurance schemes. Some policy recommendations will be made for improving the benefit equity in China's health insurance scheme.

Since only if the residents utilize the health service, they will be able to benefit from the health insurance, the definition of the benefit equity is closely connected with the definition of the equity of health service. The equity of health service refers to that the distribution of the health service should be based on health care need, rather than the willingness and the ability to pay (2). In accord with this definition, the benefit equity in health insurance means the benefit which the residents get from the health insurance should be consistent with their health care need, rather than other factors, such as economic levels. If the only factor which may cause the inequity of benefit is the health care need, then the benefit equity will be realized, no matter whether there is the inequality of benefit (the inequality of benefit means the benefits the insured residents with different economic levels get from the health insurance are vary).

Some researches have been conducted to measure the inequality of benefit in China's basic health insurance scheme. Wang et al., firstly made a comparison of the benefits which the residents with different economic levels get from the NCMS (3). Zhuang et al., Chun et al. and Wang et al. analyzed the economic-related inequality of benefit for the insured NCMS residents by using the concentration index (4-5). However, the previous studies have a couple of limitations: first, these studies only focused on the situation of NCMS, few analyzed the benefit equity in UEHI and URHI; second, the previous researches mainly focused on the NCMS's inequality of benefit, nearly no studies reported the equity of benefit.

Data

The data used in this study were from the household survey in Mei County, Shaanxi Province. The UEHI, URHI and NCMS were implemented in 1999, 2007 and 2006 respectively in Mei County. Table 1 shows the compensation policy, the funds raising policy and the funds using policy of the three basic health insurance schemes. The compensation policies of three basic health insurance schemes mainly consist of the personal/family outpatient account and the inpatient compensation, and the personal/family outpatient account is paid by the insured residents themselves, which means when the residents utilize the outpatient service, they won't get any benefit from their health insurance. Therefore, the current study

Table 1. Comparison of three basic health insurance schemes in Mei County in 2009

	UEHI	URHI	NCMS
The year of implementation	1999	2007	2006
Compensation policy	Personal outpatient account, inpatient compensation	Personal outpatient account, inpatient compensation	Family outpatient account, compensation for inpatient and chronic-disease outpatient
Funds raising policy	The companies pay 6% of the individuals' total income and the individuals pay 2%	280RMB per person per year, in which the individuals pay 200RMB and the governments pay 80RMB	100RMB per person per year, in which the individuals pay 20RMB and the governments pay 80RMB
Funds using Policy	All the money paid by the individuals and 30% of the money paid by the companies is taken out as personal account; the rest is used for the inpatient compensation.	50RMB paid by the individual is taken out as the personal account and the rest is used for the inpatient compensation.	4RMB paid by the individuals is taken out as the family outpatient account and the rest is used for the compensation of the inpatient and the chronic-disease outpatient.

will only regard the inpatient compensation as the benefit which the residents can get from their health insurances.

Using the method of multi-stage stratified and random sampling, we conducted the household survey. 2134 households (6600 individuals) were selected in the survey, in which the urban households were 1192 and the rural were 942. According to the Labor Law of China, the working age is 16 or above, thus the age of the residents who participated in the UEHI were 16 or above. Therefore, we only chose the insured residents with the age of 16 and above as our study sample, and the final sample size of the urban employees, the urban residents and the rural residents were 1258, 733 and 2870 respectively. The questionnaire of this survey mainly includes the residents' demographic characteristics, health and diseases status, health service utilization, and household income.

Methods

Study design

In this study, the equity of benefit rate and the equity of benefit degree were used to measure the benefit equity in China's health insurance schemes. The benefit rate means the share of the number of residents who were compensated by health insurance last year in the total number of insured residents, which is used to measure the incidence of benefit. The benefit degree means the amount of money the insured residents get from the health insurance, which is used to measure the depth of benefit.

The concentration index was employed to calculate the inequality of benefit rate and benefit degree, and the method of analyzing equity which was proposed by Wagstaff (7) was applied to evaluate the equity of benefit rate and benefit degree.

Concentration index

The concentration index (CI) is one of the most common methods to measure the inequality (7), which is defined as twice the area between the concentration curve of benefit rate/degree and the diagonal in this study. The concentration curve plots the cumulative proportions of the population against the cumulative proportions of benefit. The concentration index, between -1 and +1, provides a measure of the extent of inequalities in benefit that are systematically associated with socioeconomic status (8). If benefit is equally distributed across socioeconomic groups, the concentration index will be 0. The positive concentration index means there is a pro-rich benefit inequality (benefit is concentrated in the higher socioeconomic groups), and the negative concentration index means there is a pro-poor benefit inequality (benefit is concentrated in the lower socioeconomic groups). The concentration index is (8-10):

$$C = 2\,\mathrm{cov}(x,b)/\mu \quad \text{..... (1)}$$

where cov(x,b) is the covariance between the relative rank x and benefit b, and μ is the mean level of benefit.

Method of measuring the inequity

The method of concentrated curves proposed by Wagstaff (7) was used in this study to measure the inequity of benefit. It takes places in two stages. Firstly, drawing the concentration curves of the benefit rate/degree and the health care need in the same graph; then, calculating the area between the two concentration curves in the graph, and twice the area is the horizontal index of inequity, which is used to measure the inequity of benefit rate/degree. As the concentration index is defined as twice the area between the concentration curve and the diagonal. The horizontal index of inequity of benefit rate/degree is:

$$HI_{LG} = C_{benefit} - C_{need} \quad \text{..... (2)}$$

$C_{benefit}$ is the concentration index of the benefit rate/degree, and C_{need} is the concentration index of the health care need. The HI_{LG} index will be positive if there is pro-rich horizontal inequity and negative if there is pro-poor horizontal inequity.

Method of measuring the health care need

The health care need can be predicted by the variables like self-reported health status, the chronic disease and some demographic characteristics, such as age and gender (11). In this study, the

Logistic regression model was employed to predict the inpatient care need. Since we focus on the inpatient care need in this study, the dependent variable is whether the insured were hospitalized and the independent variables are the age, gender, chronic diseases and self-reported health status. The dependent variables and the independent variables are described in Table 2, in which the self-reported health status was measured by the individual self-reported marks ranging from 0 to 100 (for the worst health status was 0 and the best health status is 100).

Results

Health care need

Table 3 shows the estimated results of three logistic regression models for the residents covered by the UEHI, URHI and NCMS, respectively. Through the estimated results, health care needs are predicted: the mean of health care needs of the residents covered by the UEHI, URHI and NCMS are 0.10, 0.11 and 0.11, and the range of health care needs (minimum and maximum value) are 0.03-0.57, 0.02-0.66 and 0.05-0.43 respectively.

The equity of benefit rate

The result shows that the benefit rates of the UEHI, URHI and NCMS are very close, which are 9.0%, 8.5% and 9.0% respectively. From table 4, we can see that the horizontal indexes of inequity of benefit rate for the residents covered by the UEHI, URHI and NCMS are 0.061, 0.122 and 0.161, respectively. This indicates that there are pro-rich horizontal inequity of benefit rate in UEHI, RUHI and NCMS, which means the number of the rich who were compensated by health insurance is more than the number of the poor when their health care needs are the same. Further more, we find that the inequity of benefit rate in NCMS is higher than the equity in URHI, and both of them are higher than the equity in UEHI.

Table 2. Description of the dependent variable and the independent variables (Percentage/means)

Variables	Description	UEHI	URHI	NCMS
Whether hospitalized	1 if the insured is hospitalized, 0 otherwise	10.3	11.2	10.6
Age 16-44 *	1 if age between 16 and 44,0 otherwise. Omitted group.	48.1	47.7	45.9
Age 45-59	1 if age between 45 and 49,0 otherwise	27.0	30.8	34.3
Age 60+	1 if age is 60 and above,0 otherwise	24.9	21.5	19.8
Male	1 if male, 0 otherwise	60.1	44.6	47.9
Female*	1 if female, 0 otherwise. Omitted group.	39.9	55.4	52.1
Chronic disease	1 if chronic disease, 0 otherwise	35.2	36.4	32.4
Not chronic disease*	1 if not chronic disease, 0 otherwise. Omitted group.	64.8	63.6	67.6
Self-reported health status	The worst is 0 and the best is 100	80.4	76.5	77.0

*Note: * Reference variable.*

Table 3. Estimated results of logistic regression models

	UEHI		URHI		NCMS	
	Coefficients	Standard errors	Coefficients	Standard errors	Coefficients	Standard errors
Age 45-59	0.50*	0.27	0.60*	0.33	0.09	0.16
Age 60+	1.07***	0.27	1.13***	0.34	0.46***	0.17
Male	-0.07	0.21	-0.38	0.27	-0.21	0.13
Chronic disease	0.92***	0.23	0.54*	0.29	0.60***	0.14
Self-reported health status	-0.02***	0.01	-0.03***	0.01	-0.01***	0.00
Constant term	-1.41***	0.53	-0.73	0.63	-1.34***	0.31
LR	95.75		63.88		90.79	
P value	<0.001		<0.001		<0.001	
Sample size	1257		729		2858	

The equity of benefit degree

The average amount of money which the insured residents were compensated by the UEHI, URHI and NCMS for every inpatient service last year was 3201RMB, 3079RMB and 1490RMB, respectively. This indicates that the insured of the NCMS got less compensation than the insured of the UEHI and URHI. From the table 5, we can see that the horizontal indexes of inequity of benefit degree for the residents covered by the UEHI, URHI and NCMS are 0.027, -0.187 and 0.178 respectively, which indicates two facts: first, both the inequity of benefit degree in UEHI and NCMS are pro-rich (when the health care needs are same, the rich benefit more than the poor), and the inequity of benefit degree in NCMS is much higher than in UEHI; second, the inequity of benefit degree in URHI is pro-poor (when the health care needs are same, the poor benefit more than the rich).

Discussion

The results of the equity of benefit rate indicate that the rich can benefit more than the poor from the UEHI, URHI and NCMS. Theoretically, only if the insured utilize the inpatient service, they could get the benefit from the health insurance, thus increasing the inpatient service utilization of the poor will be very crucial for improving the benefit equity; meanwhile, the cost of inpatient service, that is, the co-payment ratio, is the most important factors which may influence the poor residents' inpatient utilization (the higher the co-payment ratio is, the less the inpatient utilization will be used). Therefore, decreasing the co-payment ratio will improve the benefit equity. This is consistent with the results of this study: the co-payment ratios for inpatient service in UEHI, URHI and NCMS in Mei County are 39.2%, 60.4% and 63.5% respectively and the horizontal indexes of inequity of benefit rate are 0.061, 0.122 and 0.161, which indicates that the co-payment ratio and the equity of benefit rate have negative correlation (as the co-payment ratio decreases, the equity of benefit rate will be improved). In order to increase the benefit equity in China' basic health insurance schemes, we suggest that the government should raise the financing of UEHI, URHI and NCMS, and thus increase the compensation for the insured residents.

The results of the equity of benefit degree shows that there were pro-rich inequities of benefit degree in the UEHI and NCMS, and meanwhile, the inequity of benefit degree in the NCMS is much higher than the inequity in the UEHI. This may be caused by the excessive high co-payment ratio in NCMS. When the co-payment ratio is high, the poor couldn't fully use the health service resource when they were hospitalized. Therefore, the poor will get less compensation than the rich from the health insurance. As the high co-payment ratio would increase the pro-rich inequity of benefit degree, this study suggests that Chinese government should take decreasing the co-payment

Table 4. The equity of benefit rate for three basic health insurance schemes

	UEHI		URHI		NCMS	
	CI	**Standard errors**	**CI**	**Standard errors**	**CI**	**Standard errors**
Benefit rate	0.078	0.053	0.151	0.073	0.147	0.035
Health care need	0.018	0.014	0.029	0.020	-0.014	0.006
HI_{LG}	0.061		0.122		0.161	
Sample size	1323		715		2832	

Note: CI is the abbreviation of concentration index.

Table 5. The equity of benefit degree for three basic health insurance schemes

	UEHI		URHI		NCMS	
	CI	**Standard errors**	**CI**	**Standard errors**	**CI**	**Standard errors**
Benefit degree	0.010	0.051	-0.139	0.105	0.153	0.052
Health care need	-0.017	0.034	0.049	0.048	-0.025	0.019
HI_{LG}	0.027		-0.187		0.178	
Sample size	112		61		254	

ratio as an object when making the policy of health insurance.

In addition, we find that there was pro-poor inequity of benefit degree in URHI. As the Mei County just had implemented the URHI for more than one year when this study was carried out and most of the poor patients who couldn't afford the expensive medical cost before the implementation of URHI would like to take the opportunity to be hospitalized for treating their serious disease during this short period, the poor people's medical cost was higher than the rich, and then they could get more compensation than the rich from URHI.

There are a couple of limitations in this study. First, in this study, we used the variables of age, gender, chronic disease and self-reported health status to predict the residents' health care need (11). However, it is still controversial for what indicators could be used to measure the health care need (12-14). Second, self-reported health status can be considerably affected by the residents' health consciousness level and health knowledge level, which may make the self-reported health status is different from the real one.

Conclusion

The coverage rates have grown very fast since the UEHI, URHI and NCMS were implemented in China, but the benefit equity is comparatively poor. When the insured residents with different economic levels have the same health care need, the number of rich residents who can get benefit from UEHI, URHI and NCMS is more than the poor, meanwhile the rich can get more compensation from the UEHI and NCMS than the poor. As the poor benefit equity of China's health insurance schemes could frustrate the objective of "releasing the residents' burden from expensive medical cost effectively", in order to improve the benefit equity, Chinese government should pay more attention to the reduction of the co-payment ratio of inpatient service in UEHI, URHI and NCMS.

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Obstructive Sleep Apnea Syndrome in Adult Patients with Asthma

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Abstract

Objective and Introduction: Previous epidemiological studies have shown respiratory system diseases and obstructive sleep apnea syndrome (OSAS) to be frequently concomitant, and co-occurrence of OSAS with respiratory system disease increased the severity and complications of underlying lung disease. It is known that symptoms associated with asthma are generally more severe at nights. Obesity is a common risk factor for two prevalent disorders, namely asthma and obstructive sleep apnea syndrome, which are commonly observed in the society and are important at both individual and social levels. Similarly, anatomical and functional abnormalities of the upper airways and gastroesophageal reflux are other associated factors. Moreover, since upper airways, which is the focus of physiopathology in OSAS, is an important area affected also in asthma, it leads to research evaluating possible interactions of these two diseases with a mutual pathway in etiology. The objective of this study was to investigate the prevalence of OSAS in patients with asthma and its effect on the severity and the management of asthma.

Material and Methods: In this study, 50 consecutive adult asthma patients (35 female and 15 male) who applied to the Department of Chest Diseases and accepted to participate in the study, were included. All of these patients underwent full overnight polysomnography.

Results: The overall prevalence of OSAS was 40% (moderate and severe OSAS: 16%) in asthma patients. However, no significant difference could be determined between OSAS prevalence, based on the asthma severity. OSAS was determined at rates of; 52.9% (9/17) in full control asthma patients, 40.9% (9/22) in those with partial control, and 18.2% (2/11) in patients with no control. As better control levels were provided for asthma, prevalence of OSAS increased, however the differences were not statistically significant (p=0.185). Between OSAS severity and asthma control level, a weak reverse correlation was determined (p=0.05, r=-0.279). In all asthma patients with OSAS, snoring was present (negative predictive value 100%). In asthma patients with habitual snoring, witnessed apnea and daytime sleepiness symptoms, OSAS prevalence was significantly higher compared to those with no symptoms. As concomitance of major symptoms increased, OSAS prevalence also increased significantly ($p<0.05$). As neck circumference and body mass index of patients with asthma increased, apnea-hypopnea index and OSAS severity significantly increased ($p<0.05$). A significantly positive correlation was determined between triceps fat thickness and asthma severity (p=0.003, r=0.563).

Conclusions: Compared to the regular population, among adult asthma patients, OSAS prevalence was much higher. Especially asthma patients who are obese and have wide neck circumference should be examined regarding OSAS symptoms. In the presence of major OSAS symptoms, polysomnographic examination should definitely be conducted. The lack of snoring can be an important criterion in the exclusion of OSAS in asthma.

Further studies are necessary in order to produce concomitance, interaction and long-term results of these two diseases.

Key words: asthma, sleep apnea, obesity, snoring, obstructive sleep apnea syndrome, OSAS

Introduction

Asthma is a worldwide problem and affected individuals are approximately 300 million. Based on data from various countries, asthma prevalence was shown to be between 1-18%.[1] Kalyoncu et al. have determined asthma prevalence to be

6.2% among 210 adult individuals from different regions of Turkey.[2] In Trabzon, among 908 adults, within the last year, Özlü et al. have determined wheezing prevalence, except having a cold, to be 9.9%, chest tightness to be 12.6%, and difficulty breathing to be 13.7%. [3] Wheezing prevalence was determined to be 15.8% in Istanbul by Erkan et al., and 21.7% in Ankara, by Saraçlar et al. [4,5]

In patients with asthma, the idea of investigating polysomnographic parameters arose from the facts that indicated; sleep quality was impaired in OSAS and asthma patients, significant decrease in nocturnal oxygen saturation was observed and this was especially obvious during REM (rapid eye movement) sleep.[6]

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent episodes of upper airway obstruction during sleep and frequent decrease in blood oxygen saturation. OSAS is a frequently encountered serious health problem in a society, just like asthma.[7] Today, among the adult population, OSAS prevalence in considered to be between 1.2-2.5% in women and 1-5% in men.[8] Epidemiological studies conducted in our country also report OSAS prevalence to be 1.8%.[9]

In cases where OSAS plays a role in the nocturnal asthma pathogenesis, and concomitant OSAS and bronchial asthma are present, sleep apnea is suggested to provoke asthma attacks. Additionally, nasal CPAP, the classical treatment of OSAS, can be safely used in these patients, moreover, it is reported to possibly bring nocturnal attacks under control. Interestingly, in OSAS cases where this co-occurrence is not present, it is suggested that bronchial hyperreactivity (BHR) is present and moreover this can decrease through CPAP treamtent.[10,11]

These two individually and socially significant problems frequently observed in the society have common risk factors such as obesity. An increase in asthma symptoms at night is a known fact. Furthermore, since upper airways, which is the focus of physiopathology in OSAHS, is an important area affected also in asthma, it leads to research evaluating possible causal interactions of these two diseases.

This study aims to investigate the effects of OSAS frequency and OSAS, on asthma severity and control levels, in patients with asthma.

Material and Methods

Study Group

In this study, 50 consecutive adult asthma patients who applied to Düzce University, School of Medicine, between the dates of October 2006 and August 2007, and accepted to participate in the study, were included.

Asthma Diagnosis

Differential diagnosis of patients was conducted based on GINA (Global Initiative For Asthma-2006) criteria. General and occupational anamnesis was obtained from each patient. Physical examination was conducted. Routine biochemical tests, chest radiographs, respiratory function tests (spirometry and flow-volume curve) were conducted. Patient with differential diagnosis problems received DLCO (diffusion) test, PEF (Peak Expiratory Flow) follow-up, total IgE, and skin test.

Exclusion Criteria

Individuals who smoked, had low DLCO, used oral beta-2 mimetic, theophylline and systemic steroids besides attacks, those who had infiltration in their lung radiograph or had other systemic diseases, were excluded from the study.

Study Design

Prior to the sleep test, all asthma patients filled out a questionnaire regarding sleep problems in order to determine symptoms that might develop in their sleep disorder. Using this form, basic OSAS symptoms such as snoring, witnessed apnea and day time sleepiness were evaluated. In order to objectively evaluate excessive daytime sleepiness Epworth Sleepiness Scale was used. If the score obtained on this scale was above 10, excessive daytime sleepiness was considered present, and all patients received a ENT (Ear Nose Throat) examination.

After evaluating all patients included in the study, the patients were called for an overnight polysomnography test with an appointment, at the sleep laboratory. On the day of the laboratory stay, patients were recommended not to sleep during

the day, not to consume any caffeinated beverages or food, and not to use alcohol and drugs (antihistamines, antidepressants, hypnotics etc.) that would change their sleep patterns. Polysomnography (Somno-Medics Gmbh-8 Co.KG, Nonnengarten 8, D-97270 Kist Germany. Model: Somnoscreen-PSG, Ser-No: 0372 CAA5-OJ), EEG (electroencephalography), EOG (electro-oculography), chin EMG (electromyography), oral and nasal air flow (nasal-oral 'thermistor' and nasal cannula), thorax movements, abdominal movements, arterial oxygen saturation (pulse oxymetry instrument), EKG and snoring recordings (>6 hours) were obtained.

All records were scored manually in a computer environment.

Definitions

Asthma severity: Based on GINA guide, asthma severity was divided into four groups; intermittent, mild, moderate and severe persistent, depending on the level of symptoms and air flow restriction, and variability in lung functions.

Levels of Asthma Control: (table 1)

OSAS related definitions

Habitual snoring: Presence of snoring for at least 5 nights per week

Witnessed apnea: Spouse or relatives of patients with OSAS, identifying noisy and irregular snoring, and stopped respiration through the mouth and nose

Excessive daytime sleepiness: It was evaluated using Epworth Sleepiness Scale. It consists of 8 scores measuring the tendency of the individual to sleep throughout various day time situations. The score varies between 0 and 24. If the score is 10 or above, it is an indication of the tendency to sleep during the day.[12]

Apnea: Complete lack of air flow through the mouth and nose for 10 sec or more.

Hypopnea: At least 50% in the air flow for 10 seconds or more, along with 3% decrease in oxygen saturation or the development of arousal,

Apnea-Hypopnea Index: The ratio obtained by dividing the total duration of apnea and hypopnea observed during sleep, by the total length of sleep. [13,14]

OSAS Severity: When evaluated based on Apnea- Hypopnea Index (AHI);

- Normal AHI < 5
- Mild Sleep Apnea: AHI between 5-15,
- Moderate Sleep Apnea: AHI between 16-30,
- Severe Sleep Apnea: AHI > 30

Sleep Efficiency: Sleep Duration / Time in Bed

Statistical Analysis

Data was entered into SPSS 10.0 (Statistical package for Social Sciences for Windows) program. For the paired comparison of quantitative data, Mann Whitney U test; for the comparison of more than two numerical data, Kruskal-Wallis test were used. Chi-Square Test was used to compare categorical data. In order to analyze correlations, Spearman's Correlation Test was used. A p-value of $p < 0.05$ was considered to be the limit for statistical significance.

Table 1. Levels of Asthma Control (GINA 2006)[1]

Characterisric	Levels of Asthma Control		
	Controlled	Partly Controlled	Uncontrolled
Daytime symptoms	None (twice or less/week)	More than twice/week	Three or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms/awakening	None	Any	
Need for reliever/ rescue treatment	None (twice or less/week)	More than twice/week	
Lung function (PEF or FEV1)	Normal	< 80% predicted or personal best (if known)	
Exacerbations	None	One or more/year*	One in any week†

** Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.*

† By definition, an exacerbation in any week makes that an uncontrolled asthma week.

Results

Of the 50 asthma patients, 35 were female and 15 were male. Demographic and clinical features of the patients are summarized in Table 2.

Table 2. General characteristics of patients with asthma

	Mean (SD)	Min-Max
Age (year)	52 (12)	24-77
Body mass index (kg/m²)	32,5 (7,9)	18.7-62.2
Neck diameter (cm)	39,5 (3,5)	34-47
Triceps skin thickness (mm)	21 (8)	8-40
Hematocrit (%)	40,2 (3,4)	33-46.3
FVC (%)	86,5 (20,8)	37-123
FEV$_1$ (%)	76,0 (23,8)	32-115
OSAS symptom duration (month)	35 (41)	0-240
	N	**%**
Gender		
Female	35	70
Male	15	30
Alcohol	7	14
Hypertension	23	46
Ischemic heart disease	7	14
Gastroesophageal reflux	13	26
Allergic rhinitis	20	40

SD: standard deviation; FVC: Force Vital Capacity; FEV$_1$: Force expiratory capacity 1. second

The levels of severity of asthma cases and their levels of control are summarized in Figure 1 and 2.

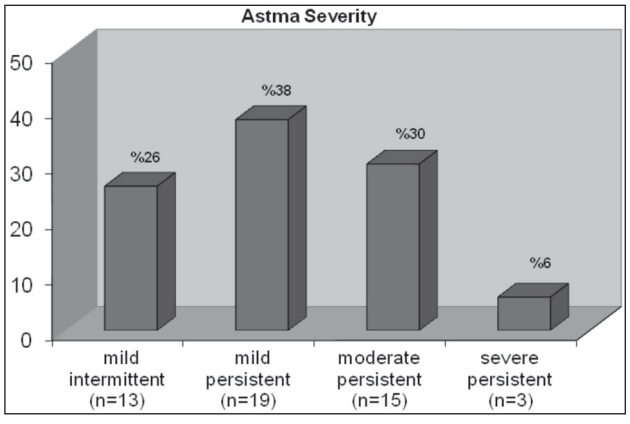

Figure 1. The levels of severity of asthma cases

When questioned about OSAS major symptoms, 88% (44/50) of patients had snoring, and in 54%, this snoring was determined to be habitual. Daytime sleepiness was found in 46% and witnessed apnea was found in 40%. While no major symptom was present in 36% of asthma patients, in 26%, 3 major symptoms were present concurrently (Table 3).

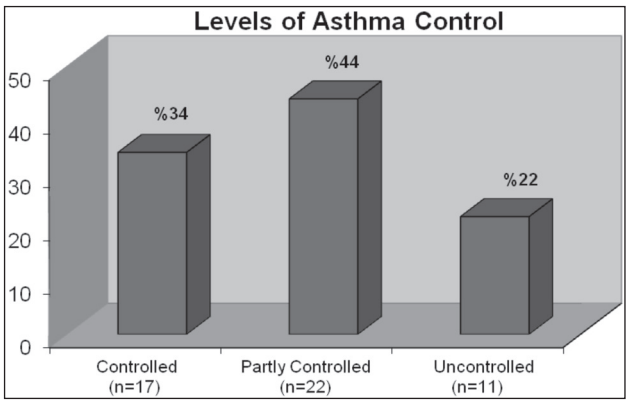

Figure 2. The levels of asthma control of cases

Table 3. Frequency of OSAS symptoms in patients with asthma

OSAS SYMPTOMS	N	%
Snoring	44	88
Snoring Severity		
No	6	12
Mild	12	24
Severe	32	64
Habitual Snoring*	27	54
Witnessed Apnea*	20	40
Daytime Sleepiness*	23	46
Major Symptoms		
No major symptom	18	36
1 major symptom (+)	7	14
2 major symptoms (+)	12	24
3 major symptoms (+)	13	26

** major symptoms*

As a result of the polysomnographicstudy, OSAS was determined in 20 (40%) asthma patients (AHI≥5). Among the asthma patients, 16% were clinically moderate and severe (AHI>15) cases (Figure 3).

When clinical features of patients with and without OSAS are compared, in those with OSAS, body mass index, neck circumference and symptom duration were determined to be significantly higher (Table 4). In regards to age and respiratory functions, no significant difference was determined between patients with and without OSAS.

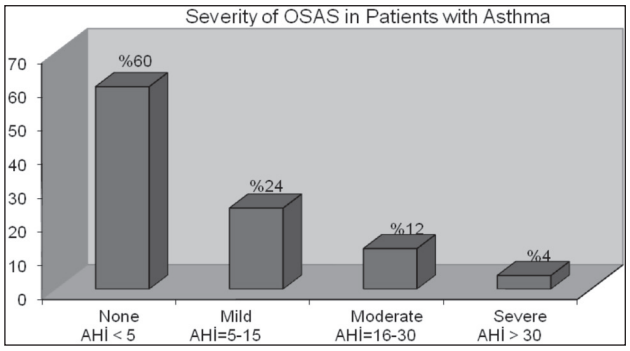

Figure 3. Frequency and severity of OSAS symptoms in patients with asthma

Also, in asthma patients with and without OSAS, no significant difference could be determined based on alcohol use, allergic rhinitis and other accompanying disease (Table 5).

In all asthma patients with OSAS, snoring was present. In other words, in asthma patients with no snoring (including simple snoring), OSAS was not found. As the degree of snoring increased, OSAS prevalence also increased significantly. In those with habitual snoring, witnessed apnea and day time excessive sleepiness, compared to those without them separately, OSAS prevalence was significantly higher (Table 6).

Table 4. The comparison of the features of asthmatic patients with and without OSAS

	OSAS (+)	**OSAS (-)**	**P**
	mean (SD)	**mean (SD)**	
Age (year)	54.9 (11.8)	50.3 (13.3)	*0.157*
Body mass index (kg/m²)	36.7 (17)	29.8 (5.6)	***0.002***
Neck diameter (cm)	41.6 (2.4)	38.4 (3.5)	***0.014***
Triceps skin thickness (mm)	22.7 (10.8)	20.7 (8.0)	*0.620*
Hematocrit (%)	40.9 (3.7)	39.7 (3.1)	*0.369*
FVC (%)	84.8 (21.8)	87.7 (20.4)	*0.647*
FEV (%)	80.3 (22.5)	73.1 (24.7)	*0.458*
Symptom duration (month)	52 (52)	23 (26)	***0.004***

SD: standard deviation; OSAS: obstructive sleep apnea syndrome; FVC: Force vital capacity; FEV1: Force expiratory volume 1. second

Table 5. The comparison of the features of asthmatic patients with and without OSAS

	OSAS (+)	**OSAS (-)**	**p**
	n (%)	**n (%)**	
Gender			
Female (n=35)	15 (%42.9)	20 (%57.1)	0.754
Male (n=15)	5 (%33.3)	10 (%66.7)	
Alcohol			
Yes (n=7)	1 (%14.3)	6 (%85.7)	0.219
No (n=43)	19 (%44.2)	24 (%55.8)	
Hypertension			
Yes (n=23)	11 (%47.8)	12 (%52.8)	0.388
No (n=27)	9 (%33.3)	18 (%66.7)	
Ischemic heart disease			
Yes (n=7)	4 (%57.1)	3 (%42.9)	0.416
No (n=43)	16 (%37.2)	27 (%62.8)	
Gastroesophageal reflux			
Yes (n=13)	3 (%23.1)	10 (%76.9)	0.197
No (n=37)	17 (%45.9)	20 (%54.1)	
Allergic rhinitis			
Yes (n=20)	8 (%40.0)	12 (%60.0)	0.839
No (n=19)	7 (%36.8)	12 (%63.2)	

Table 6. Frequency of OSAS symptoms in patients with asthma

SYMPTOMS	OSAS (+)	OSAS (-)	*p*
	n (%)	n (%)	
Snoring			
Yes (n=44)	20 (45.5)	24 (54.5)	***0.033***
No (n=6)	- (0)	6 (100)	
Snoring severity			
No	- (0)	6 (100)	
Mild (n=12)	3 (25)	9 (75)	***0.024***
Severe (n=32)	17 (51.1)	15 (46.9)	
Habitual snoring			
Yes (n=27)	16 (59.3)	11 (40.7)	***0.004***
No (n=23)	4 (17.4)	19 (82.6)	
Witnessed apnea			
Yes (n=20)	15 (75.0)	5 (25.0)	***<0.0001***
No (n=30)	5 (16.7)	25 (83.3)	
Daytime sleepines			
Yes (n=23)	14 (60.9)	9 (39.1)	***0.009***
No (n=27)	6 (22.2)	21 (77.8)	
Major symptoms			
No major symptom	1 (5.6)	17 (94.4)	
1 major symptom (+)	2 (28.6)	5 (71.4)	***0.001***
2 major symptoms (+)	8 (66.7)	4 (33.3)	
3 major symptoms (+)	9 (69.2)	4 (30.8)	

OSAS was determined to be at a rate of 5.6% if none of the major symptoms were present, and it was 69.2% if all major symptoms were present. As the concomitance of major symptoms increased, OSAS prevalence and AHI also significantly increased (Figure 4).

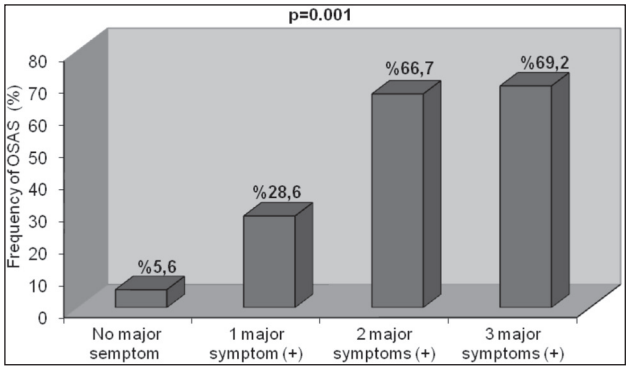

Figure 4. Frequency of OSAS major symptoms in patients with asthma

Based on asthma severity, no difference was determined in OSAS prevalence. As the asthma management levels decreased, OSAS prevalence decreased, however, the differences were not significantly different (Table 7 and Figure 5).

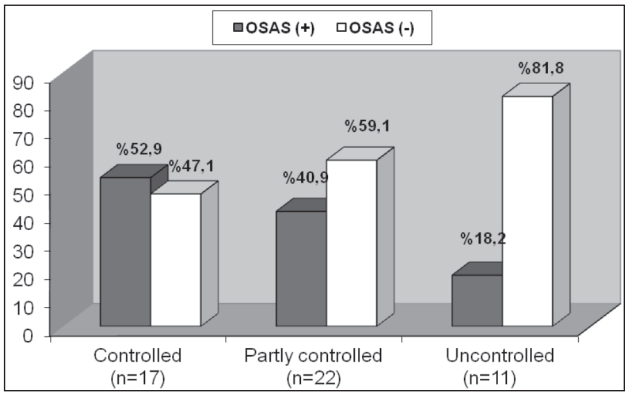

Figure 5. The ratio of OSAS according to levels of asthma control

As the body mass index of patients increased, AHI and thus OSAS severity significantly increased.

As the asthma management level was disrupted, thus OSAS severity decreased (Figure 6). A weak inverse correlation was determined between OSAS severity and asthma control level (p=0.05, r=-0.279).

Table 7. The ratio of OSAS according to asthma severity and levels of control

	OSAS (+)	OSAS (-)	p
	n (%)	n (%)	
Asthma Severity			
Mild intermittent (n=13)	6 (%46.2)	7 (%53.8)	
Mild persistent (n=19)	8 (%42.1)	11 (%57.9)	0.902
Moderate persistent (n=15)	5 (%33.3)	10 (%66.7)	
Severe persistent (n=3)	1 (%33.3)	2 (%66.7)	
Levels of Asthma Control			
Controlled (n=17)	9 (%52.9)	8 (%47.1)	
Partly controlled (n=22)	9 (%40.9)	13 (%59.1)	0.185
Uncontrolled (n=11)	2 (%18.2)	9 (%81.8)	

As the neck circumference increased, OSAS severity (p=0.009, r=0.486) and AHI (p=0.018, r=0.333) significantly increased. A significant positive correlation was determined between triceps fat thickness and asthma severity (p=0.003, r=0.563).

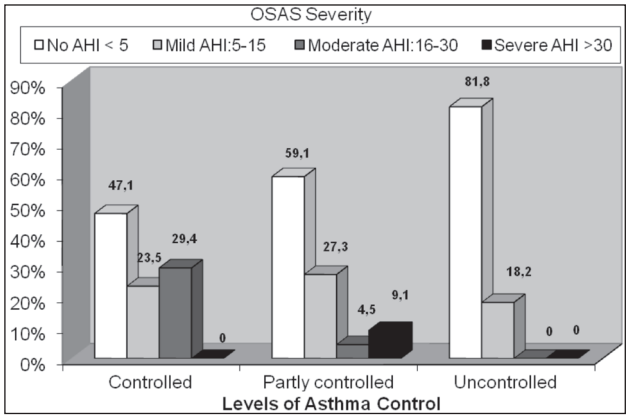

Figure 6. The ratio and severity of OSAS according to levels of asthma control

Discussion

In this study; 1) In asthma patients OSAS symptom and disease prevalence was determined to be higher than the normal population (40%) 2) Furthermore, clinically moderate and serve OSAS rate was quite high (16%) 3) No relationship was determined between asthma severity and OSAS 4) As asthma management level increased, OSAS frequency and severity was observed to increase.

In the literature, while frequent presence of OSAS in asthma patients is highlighted, there are no studies regarding the prevalence. However, the association of lung diseases with OSAS (overlap syndrome) is well known.[15-20] Mostly there have been studies on the association of COPD and OSAS, and OSAS frequency in COPD has been reported to be 45.8%.[17] Based on studies conducted with COPD patients in our country, OSAS coexistence is reported at a rate of 6.1% by Oguz Köktürk et al., and 69.7% by Oya İtil et al..[18,19] In interstitial lung disease, this OSAS overlap was reported to be 64.9% by Müge Aydoğdu et al.[20] In this study, OSAS frequency in asthma patients was determined to be 40%.

Age and obesity are among the most important defined risk factors for OSAS. [21-25] The study population consisting mainly of elder (mean: 54) and obese patients (mean BMI: 32) may have been one of the reasons for the prevalence being high. Also, the location of the study being the Department of Medicine and patients applying here consisting mainly of chronic and difficult to treat asthma patients, may be responsible for such a distribution. Frequent difficulties in treating old and obese patients are known.

On the other hand, OSAS is observed more frequently in men (man/woman ratio: 2.5/1) .[8] OSAS frequency is known to increase with advanced age, and especially during the post-menopausal period in women. [14,26] Our study population mainly consisted of women (70%). OSAS was found in 42.95 of women and 33.3% of men. This difference was not statistically significant.

Hypertension, which affects 20% of the adult population; is one of the most important risk factors for the development of coronary heart disease, cerebrovascular events and heart failure. In Sleep Heart Health study, a clear relationship between OSAS and hypertension was determined, independent of

other factors such as obesity and age.[27] In this study, in 47.8% of asthma patients who were determined to have hypertension, OSAS accompanies, in asthma patients without hypertension, OSAS was present in 33.3% of them. The difference between the two groups was not statistically significant.

OSAS was reported to cause numerous physiopathological changes increasing myocardial ischemia tendency and increase risk of coronary artery disease by 1.27 fold.[28,29] In this study, just like in the case of hypertension, in asthma patients with coronary artery disease, OSAS prevalence was found to be high, although not statistically significant (57.1% versus 37.2%).

As is the case in the general population, among asthma patients, the presence of major symptoms significantly increases OSAS probability. In a study by Maninder Kalra et al., including 677 women, a significant association between asthma and snoring was reported. In young atopic women, habitual snoring (more than 3 nights per week) was determined to be at a rate of 20.5%. This was compared with an epidemiological study from 1992, conducted in Denmark with a large population, which looked at the habitual snoring seen in young women (only 9%).[30] The study by Fitzpatrick et al., indicating higher prevalence of snoring in patients with asthma compared to those without asthma, also supports the study by Maninder Karla.[31] In this study, among patients with asthma, 88% simple and 54% habitual snoring was observed. The lack of OSAS in asthma patients with no snoring (including simple snoring), suggests it might be an important symptom for the exclusion of the disease. In almost all of OSAS related studies, snoring was emphasized to be the symptom that most frequently accompanies OSAS.[6,7,32] Snoring was reported to possibly have a role in nocturnal asthma by stimulating neural reflex leading to bronchoconstriction.[33] In this study, sensitivity in OSAS diagnosis and negative cut-off value of simple snoring was determined to be 100% (Table 4). In asthma patients, the high frequency of lack of sleep and excessive daytime sleepiness, has been stressed to possibly relate to underlying OSAS, besides nocturnal asthma symtpoms.[34] In this study, in almost half of asthma patients, excessive daytime sleepiness was determined. Consistent with the literature, the symptom with the highest specificity and general accuracy was determined to be witnessed apnea (specificity 83.3%, sensitivity 75%). Concomitance of 2 or more 3 major symptoms was close to 70% in asthma patients with OSAS.

Allergic rhinitis, an important component of asthma (40% in this series), and upper airway inflammation may be an important cause of the OSAS and asthma association.

Xu et al. have determined a relationship between BMI and atopy, and in their hypothesis, they suggest atopy affecting obesity in individuals who are associated with asthma and obesity.[35] In normal individuals, during sleep, respiration mainly provided through the nose. The nose constitutes 50% of the total respiratory resistance. In supine position, nasal polyp, acute and chronic rhinitis, there is a significant increase in nasal resistance. This increase leads oral respiration to be preferred, triggering nasal pulmonary reflex, at which time, peripheral pulmonary resistance increases and alveolar hypoventilation takes place. Additionally, apnea and hypopnea can be observed in seasonal allergic rhinitis and septum deviation.[36,37] The relationship between OSAS and upper airway inflammation has been shown. In children with OSAS, Leukotriene (LT) 1 and 2 receptors are significantly high; and in adenotonsillar tissue, LT B4/C4/D4/E4 are in high concentrations. In patients with recurrent rhinitis and no OSAS, LT B4/C4/D4/E4 are higher when compared to those with no rhinitis in adenotonsillar tissue. Oral use of LT antagonist for 16 weeks was found to have a significant effect on upper respiratory tract and be associated with improvement in the severity of sleep-related breathing disorder. When there is no treatment, this improvement was observed to decline.[38,39] However, in this study, no association could be shown between allergic rhinitis and OSAS.

Another potential mechanism that explains asthma and OSAS relationship is the induction of bronchoconstriction by gastroesophageal reflux forming due to intrathoracic negative pressure formed by OSAS-related upper respiratory tract obstruction.[30,40] Although 26% of the study group demonstrated reflux, this relationship could not be shown.

Obesity is a defined risk factor for both asthma and OSAS.[35,41] In 1997, World Health Organization (WHO) had defined adults with BMI: 26-30kg/m² to be "overweight", and those with BMI>30kg/m² as "obese".[42] When compared to those who

are not obese, in individuals with BMI above 29, OSAS risk is 8-12 fold higher.

Various mechanisms have been suggested regarding obesity leading to collapse of the upper respiratory tract through constriction. In general, obese patients with OSAS have a big tongue and a narrow upper respiratory tract passage.[22] Additionally, in obese patients with OSAS, muscle strength was shown to reduce.[23] For this reason, concomitance of central obesity and OSAS can be associated with abnormal upper airway muscle function. In patients with OSAS, studies conducted before and after weight loss, indicate functional changes in the upper respiratory tract, rather than structural changes.[24] Through weight loss, improvements is determined in OSAS clinic. Here, rather than general obesity, excessive fat accumulation in the lateral pharyngeal fat pillows located around the pharyngeal wall. MR (Magnetic Resonance) examinations have established the presence of a relationship between BMI and accumulated fat amount. In obese individuals, already reduced lung capacities also indirectly affect the upper respiratory tract. In other words, central obesity increases OSAS tendency by fat accumulation around the upper airway that affects upper airway passage and compliance, and abdominal fat accumulation that affects respiratory pattern. In this study, among both the general study group and asthma patients determined to have OSAS, BMI and neck circumference were found to have increased.

Obesity was also shown to be a risk factor for the development of asthma.[43,44] Additionally, asthma patients with morbid obesity are known to decrease their symptoms and asthma severity by losing weight.[45] In obese individuals, various mediators such as leptins, contribute to the development of asthma by affecting airway function.[1] Leptin is a peptide produced in the adipose tissue. Corticotropin-Releasing Hormone (CRH) stimulates its release. Since CRH stimulates respiration, leptin also controls respiration. Leptin has a central effect on respiration, independent of CO2 production and food intake. In obese individuals with hypercapnia, serum leptin levels are higher, when compared to those with eucapnia. Patients with OSAS have high serum leptin levels and can be reduced back to normal through nasal CPAP treatment.[46]

In obese individuals, serum leptin levels were reported to be significantly higher compared to those at normal weight, and they were twice as much in obese patients with asthma than obese patients without asthma.[47] Leptin is also thought to possibly have an effect on the formation of allergic respiratory tract inflammation. For instance, leptin increases the release of proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6) and interleukin-12 (IL-12), into the fat tissue. In case of asthma, tumor necrosis factor alpha (TNF-α) levels are thought to increase, and as allergen exposure continues, the synthesis is thought to continue, which subsequently increase the secretion of TNF-α adhesion molecules leading to the migration of inflammatory cells to the respiratory tract wall.[48] IL-6 is a proinflammatory cytokine and IL-6 amounts arising from fat tissues is thought to make up 25% of the total IL-6 level. IL-6, which has increased production during asthma, plays a role in airway remodeling. Additionally, it causes inflammation in obese people by increasing the secretion of acute phase proteins from the liver. The main responsibility of IL-12 is to antagonize TH2 differentiation and initiate antiviral host defense. In children with asthma, genetically decreasing IL-12 response capacity is considered to be associated with the disease severity.[49] In this study, although a correlation was present between the asthma severity and triceps skin fat thickness; no association could be determined between BMI, which seems directly related to OSAS, neck circumference, and asthma severity and management level. The reason for this may be the study group mainly consisting of obese patients.

Compared to healthy individuals, in OSAS, high TNF-α, CRP and IL-6, which are significantly correlated with OSAS have been shown; and through CPAP treatment decreased serum levels were reported.[35] This result indicates the important role of inflammation in the pathogenesis of the disease. CRP is an indication of an important systemic inflammation. It can be high in both adults and children with OSAS.[50-52] However, it is not clear whether the relationship between CRP level and OSAS can be handled independent of other possible factors such as obesity. In patients with OSAS, the circadian rhythm of TNF-α secretion is difference from that of healthy individuals. This shows the role of mechanical obstruction independent of inflammation in OSAS pathogenesis.[35] On the other hand, OSAS

is associated with increased bronchial response and this might be related to asthma attacks. Sleep apnea treatment improves PEF measurement and decreases night time asthma symptoms. In OSAS, improvement of lung volumes upon CPAP treatment may be associated with pulmonary capillary blood flow decrease during sleep, which is thought to be an important factor in precipitating nocturnal asthma symptoms.[53] Systemic inflammation and upper respiratory tract edema associated with OSAS may aggravate asthma. At the same time, steroid treatment may lead to the development of alkalosis. Alkalosis may contribute do increased hyperventilation during sleep. Shipley et al. have suggested that in patients with Cushing disease and syndrome, there is a relationship between high OSAS prevalence and abnormal endogen corticosteroid exposure. Changes of 10% in BMI were found to be associated with AHI in the general population. In Shipley's study, BMI increase with corticosteroid treatment was shown to aggravate or create OSAS.[54] In a study consisting of a small group of severe asthma patients, chronic or intermittent systemic steroid use was shown to increase OSAS prevalence by leading to upper airway collapse, however, this association could not be proved by the same researchers.[12,34] Indeed, in a study looking at hard to manage asthma patients receiving long-term corticosteroid treatment, Yigla et al. could not determine a relationship between BMI, neck circumference, respiratory disturbance index, and asthma. [55] In this study, patients with severe OSAS were observed to have more moderate asthma, and none of the patients were routinely receiving steroid treatment. However, in asthma patients, whether systemic steroids taken during acute attack and inhaled steroids used in routine treatment contribute to high OSAS prevalence can be a subject for further research.

Hypothetical association and overlap of cough and asthma, obesity and OSAS, rhinosinusitis and esophageal reflux is defined as **CORE** syndrome (**C**ough, **O**bstructive sleep apnea/ **O**besity, **R**hinosinusitis and **E**sophageal reflux). In asthma patients resistant to treatment, the necessity to keep CORE components in consideration has been emphesized.[35]

In recent studies, by showing CPAP treatment to have positive effects on nocturnal symptoms and life quality, OSAS was suggested to be a possible risk factor for nocturnal asthma attacks.[56-59] Similar to this study, in their study, Auckley et al. have reported OSAS to be more frequent in asthma patients, when compared with the normal population, independent of asthma severity.[53] However, in our study, among patients who had their asthma well under control, the presence of OSAS frequency and high severity suggests that asthma symptoms prevent apnea. During sleep, the decrease in upper respiratory tract dilator muscle activity possibly develops due to reduced stimulation of the related central motor neurons through (reduced central vent output).[60] Maybe in patients who cannot sleep well at night due to asthma, there is a reduction in the central ventilatory output and apnea is observed. In case of uncontrolled asthma, it could be preventing upper airway collapse causing apnea during sleep as a result of thoracic caudal traction[56], which is concomitant with increased respiratory motor output resistance and increased respiration in order to overcome airway constriction associated. Normally, the increase in the upper respiratory tract caliber during inspiration is a result of caudal traction of the thoracic inspiratory activity on the upper respiratory tract. This increase is proportional with thoracic activity and it is independent of upper respiratory tract dilator activity. Caudal traction can reflect sub-atmospheric pressure to soft tissues surrounding the upper respiratory tract though trachea and ventrolateral cervical structures. This ensures pharyngeal airway dilation by increasing transmural pressure. In individuals consistent with this mechanism, when lung volumes are increased through passive inflation, a decrease in upper respiratory tract resistance and an increase in retropalatal airway diameter were observed.[60] In addition to all of these, rather than a cause-effect relationship, asthma and OSAS association may be a result of common risk factors.

In conclusion, in asthma OSAS rates were determined to be very high, independent of the severity of the disease. Especially asthma patients who are obese and have a large neck circumference should definitely be questioned about OSAS symptoms. In the case of 2 or more major symptoms present in asthma patients, polysomnographic examination should be conducted. The lack of sleep could be important in the exclusion of OSAS.

In order to establish the association, interaction and long-term results of the two diseases, further studies are necessary.

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Systemic Lupus Erythematosus and Homocysteine: Is there any relationship?

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Abstract

Background: Systemic lupus erythematosus (SLE), is an inflammatory multi organ disease with unknown origin, variable clinical manifestations and laboratory findings. Coronary artery disease is an important cause of mortality and morbidity in these patients. This study was designed to evaluate homocysteine as a new risk factor for cardiovascular complications.

Methods: Sixty known case of SLE and 30 healthy controls were included. Disease activity in patients was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Age, sex, drug history, diabetes mellitus, hypertension(>140/90mmHg), Body Mass Index (>30kg/m2), early menopause(amenorrhea before 40 years old) and coronary artery disease,disease duration , duration of treatment with corticosteroids and anti malaria drugs were recorded in the questionnaire. Hematological and immunological tests were done along with lipid profile,24 hours urine protein and C-reactive protein in all individuals Analysis was done using chi-square tests, student's t test or Mann-Whitney test. Correlation was evaluated with Spearman's rank-order or Pearson's correlation coefficient.

Results: Homocystine level was significantly higher in patients than controls (P-value=0.001). Only LDL, HDL and TG had significant relationship with homocysteine level. Homocysteine showed no relationship with the disease activity (P-value=0.609).

Conclusions: Homocystine could be considerd as a potential risk factor for cardiovascular disease in subjects with an inflammatory condition such as SLE.

Keywords: Systemic lupus erythematosus (SLE), SLE disease activity index,homocysteine.

Introduction

Systemic Lupus Erythematosus (SLE) is an inflammatory multi organ disease with an unknown etiology that shows variable clinical manifestations and laboratory findings. Coronary artery disease is an important cause of mortality and morbidity in these patients.

The overall prevalence of coronary disease in SLE patients has been estimated 6-10% (1).

Atherosclerosis is an inflammatory disease that occurs prematurely in patients with SLE (2); although in SLE patients traditional risk factors for cardiac events is higher than control group but risk of cardiovascular disease in 10 years (with Framingham score) is equal in controls (3.2%) (3).

Therefore; we need more sensitive and specific markers for cardiovascular risks to explain cardiovascular events in lupus patients.

Homocysteine (Hcy) is a sulfur containing amino acid product of methionine metabolism. Its plasma levels are under the control of both environmental and genetic factors. In subjects with genetically induced markedly elevated total plasma Hcy levels (tHcy) with homocysteinuria, a high incidence of premature occlusive vascular disease has been reported, thus suggesting a potential role for hyper homocysteinemia (HHcy) in the development of cardiovascular (CV) disease(4).

The normal homocysteine range is 5-15μmoL/L, and it is approximately 10-15% lower in women than men (5).

Hyperhomocysteinemia has been classified as mild (0-15 μmoL/L), moderate (15-30 μmoL/L),

intermediate (30-100 μmoL/L) and severe (>100 μmoL/L) (6).

Patients with systemic lupus erythematosus (SLE) have a 4-10 fold greater risk of atherosclerotic cardiovascular disease (ASCVD) compared to the general population (7). In a case-control study in Brazil (2006), serum concentration of homocysteine was compared in children with SLE and a control group and revelead a positive correlation between plasma Homocysteine concentration and SLE (11). In another study in USA (2008), mean homocysteine level significantly higher in women with SLE (9.88 ± 3.8 micromol/l) than in women without SLE (12).

Therefore, in this study we measured cardiac risk factors (traditional and non traditional) such as homocysteine and their relationship to SLEDAI (Lupus activity).

Methods

In this cross sectional study, 60 SLE patients (including 9 males and 51 females) and 30 healthy persons (4 male and 26 female) as the controls (age and sex matched) were included. The control group was selected randomly from those without SLE disease.

Inclusions criteria: at least four criteria of lupus disease according to ACR (10) and duration of disease at least 5 months.

Disease activity was assessed by SLEDAI so that if the score was higher than 10, lupus was considered active.

Information of the patients such as age, sex, drug history, diabetes mellitus, HTN (>140/90mmHg), BMI (>30kg/m^2), early menopause(amenorrhea before than 40 years old), coronary artery disease, disease duration, duration of treatment with corticosteroids and anti malaria drugs were recorded in the checklist. An informed consent was taken before entering into the study.

Subjects were considered to have hypertension if they were taking antihypertensive agents or had a systolic blood pressure of at least 140 mmHg or a diastolic pressure of at least 90 mmHg.

We examined all patients carefully and ECG was done for them. Patients with other systemic disease, malignancy, overlap syndrome and pregnant women were excluded from the study.

We measured complete blood count (CBC), complements such as C3 and C4, anti nuclear antibodies (ANA), and AntidsDNA, renal function tests, fasting blood sugar (FBS), lipid profile and 24 hours urine protein in all.

Ten milliliters of venous blood samples was obtained and immediately was centrifuged; then serums were stored in -800C. Thereafter, Hs-CRP, CBC, AntiDNA, C3, C4, Low density lipoprotein (LDL), cholesterol, FBS and triglyceride were measured. We measured homocysteine with CRP high sensitive ELISA kits manufactured by Bender Med System Company (eBioscience, Ltd. United Kingdom). ANA calculated with immunoflorescent technique and amounts higher than 1/40 were considered as positive. We measured C3 and C4 with nephelometry technique.

Patients with history of cardiovascular diseases such as hospitalization with unstable angina or myocardial infarction approved by electrocardiography (ECG) or angioplasty or angiography had been considered as positive history.

The following cardiovascular risk factors were assessed: Diabetes, hypertension, early menopausal status, history of ASCVD (i.e., previous myocardial infarction (MI), coronary artery bypass surgery, or proven stenosis in angiography), a remarkable family history of heart disease (i.e., MI, sudden cardiac death, or a revascularization procedure in a first degree male relative younger than age 55 years or a first degree female relative younger than 65 years), and current-smoker status.

We used SPSS software version 16 for analyzing data.Values have been stated as mean (±SD) median and range. Factor were compared between the two groups using chi-square tests. Differences between numeric variable were tested with student's t test or Mann-Whitney test. Correlation was evaluated with Spearman's rank-order or Pearson's correlation coefficient. Significant level had been considered as P-value<0.05.

Results

We studied 90 individuals in "Rheumatology Center of Mashhad", East of Iran; including 60 patients with SLE and 30 healthy individuals as the control group.

Average age was 28.8±10.3 years in patients group and 33.8 ±9.13 years in control.The mean duration of disease was 56 months (5-288 months).

Mean of disease activity score was 15.37. In the present study, 44 patients (73.3 %) had SLEDAI score lower than 10 (inactive disease) while 16 patients (26.8 %) had higher than 10 (active disease).

All patients were treated or under treatment with prednisolone, the minimum duration was 2 months and the maximum was 228 months (average of 49 months).

Nine patients (15%) with premature ovarian insufficiency (amenorrhea before 45 years) but control group didn't have this disorder.

Mean (±SD) of homocysteine was not significantly different between males (24±3.24) and females (24.35±7.99) in cases (P-value=0.812).

As shown in table 1, mean level of Homocysteine, FBS, HDL, LDL, TG and cholesterol was significantly different between cases and control (P-value<0.001).

Mean of body mass index (BMI) was not significantly different between two groups (P-value= 0.679).

Hypertension (HTN) was more common among the patients than the control (21.7 percent vs. 6.7 Percent) (P-value=0.007).

Serum level of triglyceride, LDL and HTN had significant correlation with homocysteine (P-value<0.05).

The median of SLEDAI score in patients was 15.37 and there was no correlation between homocysteine and SLEDAI (P-value=0.609).

These variables were not significantly different between cases of active and inactive SLE.

Discussion

In the present study, it was seen that homocysteine level is significantly higher in casese (24 ± 8.13 mmol/l) compared to controls (12.3±1.93 mmol/l).

From the other hand, it has been said that homocysteine is strongly related to sex, and its concentration in men is higher than in premenopausal women (9), but in our study we didn't find a significant difference (P-value=0.812).

do Prado in Brazil (2006) showed that there is a positive correlation between plasma

homocysteine concentration and SLE (11). Rhew in USA (2008) reported a significantly higher mean of homocysteine level in women with SLE (9.88 ± 3.8 micromol/l) compared to those without SLE (12). Comparing the present results and other reports, there has been much higher homocysteine level both in cases of SLE and healthy controls. Maybe hyperhomocysteinemia is more prevalent in our area or a higher normal range sho-

Table 1. Comparing the serum level of Homocysteine and other variables between cases and controls

Variables	Mean ± SD		P-value
	Case	Control	
Homocysteine (μmoL/L)	24 ± 8.13	12.3±1.93	0.000
FBS (mg/dl)	84.4±18.1	74±18.4	0.004
HDL (mg/dl)	43.5±4.72	44.7±9.2	0.867
LDL (mg/dl)	120.93±32.29	95.56±42.88	0.002
TG (mg/dl)	135±45.5	73.9±37.7	0.000
Cholestrol (mg/dl)	181.65±43.03	187.36±181.12	0.009

**Means compared with Mann-Whitney U test.P-value<0.05 considered significant.*

Table 2. Comparing the serum level of Homocysteine and other variables between inactive and active cases of SLE

Variables (Mean±SD) SLEDAI	TG	Homocysteine	FBS	Cholestrol	HDL	LDL
Inactive	137.74±54.95	24.91±8.67	84.97±21.67	180.22±41.9	46.06±10.68	118±29.89
Active	131.88±27.04	23.14±5	86.05±11.29	184.76±51.25	40.71±5.99	129.29±39.31
P-value	0.612	0.548	0.380	0.891	0.098	0.43

**Means compared with Mann-Whitney U test.P-value<0.05 considered significant.*

uld be defined in this district of East Iran. More population-based studies are necessary.

As it is discussed in other studies, detection of Hyperhomocysteinemia in SLE patients could play an important role in decreasing mortality and morbidity (10).

Traditional cardiovascular risk factors such as FBS, LDL triglyceride and blood pressure in lupus patients were higher than controls; This situation maybe caused by prednisolone therapy; and this correlation could increase cardio vascular risk.

Premature menopause (before 45 years) in patients was higher than controls; maybe this correlation is affected by disease activity, corticosteroid and cyclophosphamide therapy.

Premature ovarian failure is one of the causes of atherosclerosis in SLE patients.

In this study, only LDL, hypertension and triglyceride had significant correlation with homocysteine; so maybe correcting hyperlipidemia and hypertension could decrease cardiovascular risks to some extent.

Elevation in homocysteine concentration could be an important risk factor for recurrent cardiovascular events. This hyper homocysteinemia can be considered a minor risk factor for CHD but; interacting with the traditional ones (i.e. smoking, diabetes mellitus, cholesterol levels, arterial hypertension), can become an important player in the development of new events in patients with known CAD.

Homocysteine levels may be an excellent test in especial groups such as those referred for CVD who are not explained with the traditional risk factors.

Conclusion

Simple, safe and inexpensive tests such as homocysteine could be used to determin sub clinical cardiovascular disease. Homocystine could be considerd as a potential risk factor for cardiovascular disease in subjects with SLE.

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Measles outbreak and its contributing factors in an Iraq governorate, Diyala

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Abstract

Introduction: Measles is one of the serious infectious diseases that cause high incidence of mortalities and morbidities. Although, there are many steps done to stop measles, but the measles outbreaks still presented in many countries. Few studies of measles conducted in some countries like Iraq. Objectives of study were to determine the incidence of morbidity and mortality of measles outbreak in one of Iraq's governorates (Diyala), and the contributing factors of the outbreaks.

Method: A survey conducted retrospectively from April 2008 to March 2009, based on the recorded data of patients with measles in Iraqi governorate, Diyala. Diagnosis of measles depended on case definition (macula-papular rash ≥ 3day) with fever and either cough, coryza or conjunctivitis, which done by doctors in the Primary Health Care Centers (PHCcs) and Hospitals. SPSS version 18 and Excel used to analyze the collected data.

Results: In Diyala, it found 1302 cases were reported over 52-week period. The incidence rate of measles cases was 80.3 per 100.000 populations. For Diyala districts, Al-Moqdadia occupied the highest incidence rate compared to the others. The incidence rate of mortality because of the measles was seventeen patients. Most of them was children and unvaccinated, while the main complications found were pneumonia and chest infections. Percentage of coverage for monovalent measles vaccine (MVCV) was higher than measles, mumps and rubella vaccine (MMR), and they varied in the needs for these vaccines among districts.

Conclusion: High incidence rate of measles in Diyala when compared to other governorates. Age, effective type and the date of vaccination contributed to increase the incidence of measles outbreaks. Pneumonia and chest infections were the most common complications of measles.

Key words: Measles outbreaks, mortality and morbidity, pneumonia and coverage rate.

Introduction

Many types of vaccines are used to control measles, but it still considered one of serious infectious diseases contributed in the mortalities and morbidities of children and women[1]. Several factors associated to measles' mortality such as low or moderate incomes of patients, lack of medical services and needed therapy, contaminated water and loss of sanitation, or poor in awareness and education[2].

Many countries and World Health Organization (WHO) took on to control the outbreaks of measles [3-5]; however, it seems still difficult in other countries like Iraq[6,7]. In Iraq, two-doses routine measles vaccinations carried out in all Iraqi governorates, are; monovalent measles vaccine (MVCV) and measles, mumps and rubella vaccine (MMR) which given at nine months and 15 months, respectively. Few studies related to measles conducted in Iraq, especially in poor districts. Objectives of study were to determine the incidence of morbidity and mortality of measles outbreak in one of Iraq's governorate (Diyala), and the contributing factors of the outbreaks.

Method

A survey conducted retrospectively from April 2008 to March 2009, based on recorded data of patients with measles in Iraqi governorate, Diyala, which situated in the North Eastern to Iraqi Capital, Baghdad. Diagnosis of measles depended on case definition (macula-papular rash ≥ 3day), with fever and either cough, coryza or conjunctivitis, which done by doctors in the Primary Health Care Centers (PHCcs) and Hospitals. Serological tests for IgM,

which is specific to measles, collected in the specialized hospitals: Al-Batual Maternity Hospital, Pediatric Hospitals and Baquba Teaching Hospital. Analysis of these samples performed in the National Measles Laboratory (NML) and Central Public Health laboratory (CPHL), while Enzyme Linked ImmunoAssays (ELISA) conducted only in the Teaching Hospital. SPSS version 18 and Excel used to analyze the collected data.

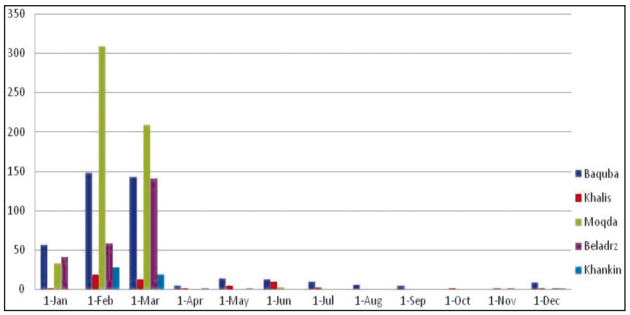

Figure 1. Distribution of measles cases according to the districts in Diyala, during outbreak April, 2008 - March, 2009

Results

About 1302 cases were reported with measles over 52-week period (from April - 2008 to March – 2009). The incidence rate of measles cases in Diyala was 80.3 per 100.000 populations, and it increased depending on time in February and March, as shown in Figure 1. Also, it differs among Diyala districts depending on populations. Al-Moqdadia district had the highest incidence rate compared to others (163.5 per 100.000 pop), followed by Beladruz district (131.8 per 100.000 population), as shown in Table 1.

Incidence of measles infections between children and their mothers totally found nine patients. About 46% of them were aged between 1-4 years old, and 55% were mothers aged 20 – 30 years old, and 64% were unvaccinated, as shown in Table 2. Mortality of the measles outbreak in Diyala was 17 patients (fatality rate = 1.3), which highly found in patients; aged younger than one year, unvaccinated, Baquba and Beladruz districts. Pneumonia and other chest infections contributed to the highest mortality, followed by encephalitis, as shown in Table 3.

Table 1. Incidence rate of measles cases in Diyala districts during outbreak 2008-2009.

District	Population	No. of cases	Incidence rate /100.000 pop.
Baquba	609.272	401	65.8
Al-khalis	274.925	50	18.2
Al-moqdadia	336.300	550	163.5
Beladruz	198.800	262	131.8
Khankin	201.990	47	23.5
Total	1.621.287	1302	80.3

Table 2. Concomitant measles infection between infected children and their mothers, in measles outbreak, Diyala 2008-2009.

Characteristics	No.	%
Child age group		
Less than 1 year	4	44%
1-4 years	5	46%
More than 5 years	-	
Mother age		
Less than 20 years	1 (pregnant)	11%
20-30 years	5 (2- pregnant- abortion)	55%
More than 30 years	3	36%
Child vaccination status		
Vaccinated	3	36% (history of vaccin 1-wk)
Un-vaccinated	6	4%
Total	9 (1-Baquba, 2-Khalis, 2-Moqdadia, 4-Beldruz)	

Table 3. Mortality of measles outbreak in Diyala 2008-2009.

Characteristics	No .	%
Age group		
Less than1 year	9	52.8%
1-4 year	7	41,2%
More than 5 year	1	5.5%
Vaccination :		
Yes	2	22.2%
Un-vaccinated	15	88.2%
District:		
Baquba	7	41.2%
Al-khalis	1	5.5%
Al-Moqdadia	2	22.2%
Beladruz	7	41.2%
Khanakin	0	0.0%
Complication :		
Encephalitis	5	29.4%
Pneumonia & other chest infection	7	41.2%
Kala –azar	3	17.6%
Other	2	22.2%
Total	17*	100%

**Fatality rate = 1.3*

To control the outbreaks of measles, the coverage rate of measles vaccination in the last three months of 2009, January, February and March, increased by 69.7%, 142% and 222.8% respectively, when compared to 2008 (65.2%). For vaccines types, the percentage of coverage for MVCV was higher than MMR vaccines, and their needs varied among districts. The coverage increased in Khanakin district higher than others, as shown in Table 4.

Discussion

Worldwide, measles is one of serious diseases related to vaccine-preventable deaths among children, more than two hundred thousand children died because of measles in 2006. Measles outbreaks reappeared to be serious cause of mortality in industrialized nations. Thus, measles cases and outbreak remind us the importance of vaccination of adults and children to reduce the incidence of death and protect them against this contagious disease[8, 9].

Outbreak of measles found in Iraq, particularly in Baquba, must consider as motivation for giving the support to stop or reduce incidence and the complications of measles[10]. Outbreaks did not only involve children, also there is a serious impact on the pregnant women. High mortality and serious complications found depending on the collected data. Seventeen patients were died because of measles and thousands hospitalized. Thus, control and surveillance services carried out, included vaccination campaigns, and health educations to improve the knowledge of people about measles by conducting training courses, and announcements in communicating media (like T.V and radio). As result for these achievements, the incidence of endemic virus reduced and the vaccination coverage increased, less unvaccinated children have had contact with wild type MV and higher number of adolescents at risk for outbreak[11,12]. Mathematical model used and threshold value for susceptible individuals found around 4.3%, which only minor outbreaks may occur[13]. Most of these cases ranged 1-4 years old, and the main reason is the loss of maternal immunity at the end of the first year. If infants were vaccinated there will be 27% primary vaccine failure, and 57% failure after the first birthday[14]. To give examples, in Switzerland, about

Table 4. Coverage rate of measles virus containing vaccine (MVCV) in Diyala districts, 2009

District	Measles vaccine coverage (%)			MMR vaccine coverage (%)		
	Jan.	Feb.	Mar.	Jan.	Feb.	Mar.
Baquba	71.1	86.9	210.8	22.8	28.8	44.7
Al-khalis	91.1	94.1	96.8	26.7	26.1	79.6
Al-moqdadia	61.7	185.4	177.6	15.8	59.4	72.4
Khanakin	68.2	254.2	421.2	23.2	69	37.6
Beladruz	43.8	229	309.5	50.7	199.7	58.6

58% of 1405 patients reported between November 2006 and February 2008 were aged 10 years or more. In 2007, in Bavaria and Germany, about 95 cases presented; 31% of them were aged 20 years and above, and 97% found among unvaccinated individuals.[15,16]

Several challenges found for the control strategies of infected adults because they are mobile and socially contacts to others in school or home than young children[17,18]. Although US government declared that measles eliminated in 2000, but it is still endemic and easy to get outbreaks again. In 2005, one of largest outbreaks of measles in US, because of 17-year old unvaccinated young woman was incubated to this disease when retuned from Romania [12]. Motivation of patients' families for the vaccination reduced because of related adverse effects of the vaccines and the lack of knowledge about this disease. As inverse risk for measles, reducing of the human vaccine - induced immunity against the wild virus, it as well considered as explosive outbreaks, which can happen anytime. [19]

WHO not recommended the supplementary immunization activities (SIAs) in Diyala, while it approved in other governorates of Iraq. However, it recommended performing vaccination campaigns in the closed communities by emphasizing the Reaching Every District (RED) to follow vaccinating children in uncovered areas of Diyala.

Conclusion

Measles is a serious infectious disease, and the outbreaks still presented everywhere and anytime. The incidence rate found higher when compared to previous recorded data in Diyala governorate. As contributing factors to the outbreaks; age, the effective vaccine, and date of vaccinations (first dose from nine months to one year and second from four to six years). Pneumonia and chest infections found to be the most common complications of measles. It recommended to conduct national studies in Iraq about measles for assessing sero - conversion rate after MVCV and evaluate the efficacy of given vaccines and duration needed for immunity. Besides, it needs to prepare educational programs to improve the knowledge and awareness of families to avoid the measles and its complications in future.

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Road Traffic Injuries in Shanghai, China

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Abstract

Road traffic injuries are major public health social and economic problem. In China road traffic injuries are increasing rapidly. Objective of the study was to assess the risk factors for road traffic injuries and the relationship between the individual and environmental factors and the severity of injury in a designated Safe Community in Shanghai, China. Data were retrieved from a Safe Community surveillance system including hospital, police and fire brigade records. Chi-square test and multivariate logistic regression were used. Total 568 was injured due to road accidents in 2008 (43% were mild injured and 9% severely injured) .Violation of traffic rule was major problem among drivers of motorized vehicles. Police has identified 15 major causes of road accidents. Age over 45 years and cloudy/rainy road conditions were major cause of accidents at the individual and environmental level factors. Findings are important for policy makers and Safe Community planning.

Key words: Road traffic injuries; Risk factors; Safe Community; China.

Introduction

Road traffic injury is a major public health problem constituting significant proportions of health, social and economic burden. Over 1.2 million people die each year on the world's roads, and between 20 and 50 million people suffer non-fatal injuries[1, 2]. In most regions of the world the epidemic of road traffic injuries is still increasing. WHO predicts that road traffic injuries will rise to become the fifth leading cause of death by 2030 [1].

Globally, road traffic accident deaths are projected to increase from 1.3 million in 2004 to 2.4 million in 2030, primarily due to the increased motor vehicle ownership and use associated with economic growth in low and middle-income countries[3]. Pedestrians, cyclists, and drivers of motorized two-wheelers and their passengers account for almost half of global road traffic deaths [1]. In China from 1951 to 2002 the road traffic injury had been increasing at an increasing rate. Since late 1980s this trend was getting worse with more motorized vehicle's accidents[4]. While higher motorization in the transportation brought convenience to the people it also brought an increasing trend in road traffic accidents[5]. The traffic death due to motorized vehicles in China accounted for 8.3% of the total death of the world, and accounted for 1.3% of total death of Chinese residents[4]. According to the report of the Ministry of Public Security since 2000 the number of traffic fatalities every year was around 100 000 while the number of injured was around 500 000. However, a hundred fold increase in road traffic mortality during previous 55 years[6].

Risk factors of road traffic injuries were explored by a worldwide report in different aspects: factors influencing exposure to risk, risk factors influencing crash involvement, severity and severity of post-crash injuries. The general factors contain growing number of motor vehicles, social deprivation, demographic factors, insufficient planning of transport, land use and road network. The risk factors affected crash involvement are divided into two groups: individual factors including young male, excess speed, presence of alcohol, medicinal o recreational drugs, fatigue, as well as poor road user eyesight, and circumstance factors (travelling in darkness, vehicle factors, defect road design, and inadequate visibility due to environmental factors). The factors specially contribute to the severity of road traffic injuries include scarcity of vehicle crash protection, lack of roadside protection, non-use of protective devices in vehicles (for example, seat-belts and air bags), non-use of helmets, inappropriate speed and alcohol intake [2].

Community is a setting where people share a common purpose interest or need, express their relationships and reflect diversity as well as local characters [7,8]. The community-based approach to injury prevention programs was developed in the 1980s and has since become an essential component of injury prevention [9]. Community-based programs are characterized by collaboration among different community sectors and the involvement of community members to define the safety problem and find solutions [10, 11]. Safe Community (SC) program aiming to reduce injury and create supportive environment has been operated for the last two decades[12].

The Safe Communities (SC) concept began its formal existence at the First World Conference on Accident and Injury Prevention held in Stockholm, Sweden in September 1989. There are six indicators for International Safe Communities[13] .

1. An infrastructure based on partnership and collaborations, governed by a cross-sectional group that is responsible for safety promotion in their community;
2. Long-term, sustainable programs covering both genders and all ages, environments, and situations;
3. Programs that target high-risk groups and environments, and programs that promote safety for vulnerable groups;
4. Programs that document the frequency and causes of injuries;
5. Evaluation measures to assess their programs, processes and the effects of change;
6. Ongoing participation in national and international Safe Communities networks.

Safety Community has started in China since early 21 century in Shandong province, named Youth Park Community. So far 35 communities successfully fulfilled the six indicators and became the member of International Safe Community Network in Mainland China[13]. In China the safe community is more likely a kind of top-down model that means the government takes the main responsibility of initiative, promote, coordinate and funding. Traffic injury has drawn attention of local governments that they would like to reduce traffic injury in their community through SC movement. The traditional approach of traffic injury reporting only provides limited information. So some SC communities try to make use of WHO's injury surveillance guidelines to improve their reporting. This paper is based on one pioneer community where SC office works closely with local police authority regarding traffic injury surveillance and prevention.

Objective of the study was to assess the risk factors for road traffic injuries and the relationship between the factors and the severity of injury in a designated Safe Community in Shanghai, China.

Materials and methods

Data collection

The safe community was situated in Shanghai, China. Each designated Safe Community has a surveillance system including hospital records, police records and Fire brigade records. In some Safe Communities the stakeholders also perform household surveys. In the current study, data was used from the police records. Data was extracted from the Road Injury Report (RIR) by local police station for a period of one year from 1st January 2008 to 31st December 2008.

When traffic accident happened there are different ways to report to local police station including report by people in person, by 110 police hotline, interphone and petrol car et al. Then the policeman will rushed to the event site as soon as possible to take care of the situation. It is required by the municipal police authority that for every road traffic event a form should be filled but it is very simple with only limited information about injury. Since this community is carrying out SC experts were invited to develop Road Injury Report (RIR) which guided by the ICECI and ICD10 and combine with the original form.

Dependent variables: Severity of injury was the main variable of interest. According to the severity of injured the subjects were divided into three groups with coding: no injury=1, minor injury=2 and severe injury/death=3.

Independent variables: Two main factors, individual factors and environmental factors were analyzed as independent variables in order to explore the relationship between the factors and the severity of injury. Environmental factors con-

tain seven variables: place of accident, whether condition, visibility, road surface, time of a day, region of road and partition. Individual factors include four variables: gender, age, migrated population and transportation mode. Codes for independent variables are shown in table 1.

Also violation of traffic rule (yes/no) and 15 causes of road injuries according to police records were considered in the study.

Statistical analysis

Pearson Chi-square test was used to determine relation between violation of traffic rule and road users (driver of motorized/non-motorized vehicle, pedestrian and vehicle occupant). Multivariate logistic regression was used to explore the relationship between severe injuries and all independent environmental and individual variables. Due to a very few numbers of detah register in the system we did not consider death in the regression analysis. A significance level of 0.05 was employed.

Ethical consideration

The study has used secondary data without assessing the identity of the victims. Furthermore, only the researchers concerned with the study had accessed the data. So anonymity was maintained. For such studies with secondary data, the concerned university had waived for ethical permissions.

Results

In 2008 there were 568 traffic accidents in total in the community in relation to 641 motor vehicles and 1205 individuals. Among which 504 events were reported to police by 110 phone calls which accounted for 88.7%. Five people died on the spot, 14 people died after first aid was conducted, and 563 people were injured.

Figure 1 shows the percentage of severity of road traffic injuries. As the severity was defined into three groups (no injury, minor injury and severe injury/death), 48% of the cases were without injured, following by mild injured, 43%. Only 9% of the traffic accidents accounted as severe injuries and dead.

Among 1205 individuals, involved in the accidents, 632 violated the traffic rules which accounted for 52.45% in total (table 2). The most common violation was drivers of motor vehicle not allowing vehicles or passengers going straight to go first when it was turning at road corners

Table 1. Independent variables

Variables	Codes for variables
Environmental factors	
Place of accidents	1= road for non-motorized vehicle 2= road for motorized vehicle
Whether condition	1=sunshine 2=cloudy/rainy
Visibility	1=>200m 2=100-200m 3=<100m
Road surface	1=dry 2=wet/icy/snowy/seeper
Time of a day	1=day time 2=night
Region of road	1=straight road 2=crossing road
Partition	1=no 2=partition between motorized vehicle road and non-motorized vehicle road 3=others
Individual factors	
Gender	1=male 2=female
Age	1= <25 2= 25-45 3= > 45
Migrated population	1=no 2=yes
Transportation mode	0=driver of motorized vehicle 1=driver of non-motorized vehicle 2=pedestrian 3=vehicle occupant

(28.01%). The second one was drivers of motor vehicle had disturbed other moving vehicles (13.92%). The third one was non-motorized vehicles drove on restored road (9.18%). Drivers of motor vehicle had highest percentage in terms of violating the traffic rules (P<0.05).

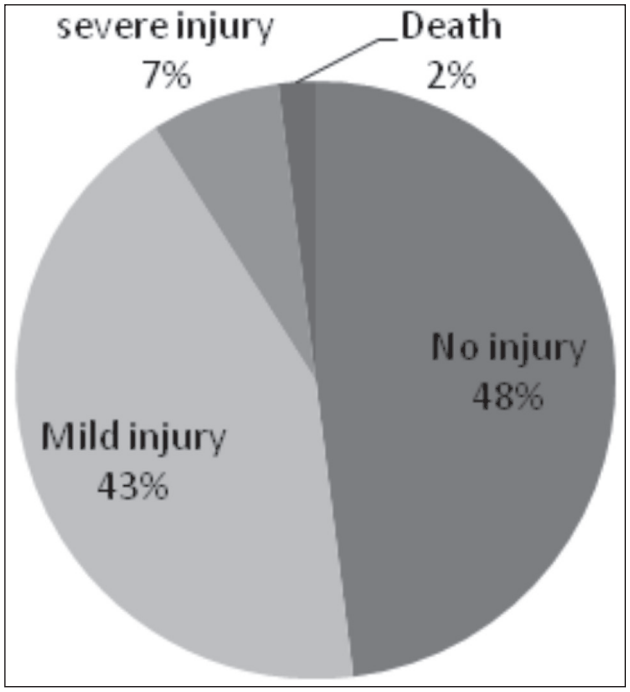

Figure 1. Distribution of severity of injured

Table 3 reflects the causes of injuries identified by police authority. The leading three causes constituted over 50% of the accidents. 'When motorized vehicles tuning corners without allowing other vehicles or passengers going straight to go first' was accounted 30.11%, of all accidents. Top two cause of injuries was 'Behavior of drivers of motor vehicles in ways of disturbing other vehicles driving' (12.67%), followed by 'Non-motorized vehicles drove in restored road' (8.62%). 'Overtaking vehicles when possible to meet the vehicles in other side' associated lowest number of accidents, sharing 1.23%.

Table 3. Causes of injuriesidentified by police authority

Causes	No. of accidents	Percentage (%)
When motorized vehicles tuning corners not allow vehicles or passengers going straight to go first	171	30.11
Behave of drivers of motor vehicle in ways of disturbing other vehicles driving	72	12.67
Non-motorized vehicles drove in retrorse road	49	8.62
Drivers of motor vehicle not follow the traffic light	34	5.99
The short distance between two vehicles	33	5.81
Others	28	4.93
When turning round disturbing other vehicles and pedestrians	20	3.52
When changing lanes disturbing other vehicles	15	2.64
When non-motorized vehicles tuning corners not allow vehicles or passengers going straight to go first	15	2.64
Inappropriate control of accelerograph	15	2.64
When non-motorized vehicles overtaking other vehicles disturbing other vehicles moving	13	2.29
Drivers of non-motorized vehicles not following the traffic light	11	1.94
Motorized vehicles moving in retrorse road	10	1.76
Motorized vehicles moving in non-motorized vehicles road	8	1.41
Overtaking vehicles when possible to meet the vehicles in other side	7	1.23

Table 2. Comparison of different transportation regarding violating of traffic rules

Traffic rules	Driver of MV	Driver of NMV	Pedestrian	Vehicle occupant
	Number (%)	Number (%)	Number (%)	Number (%)
No violation	186(32.46)	303(52.88)	24(4.19)	60(10.47)
Violation	470(74.37)	145(22.94)	17(2.69)	0(0.00)
Total	656(54.44)	448(37.18)	41(3.40)	60(4.98)

X^2=204.21 P<0.001 (Pearson Chi-square Test)

Table 4. Multivariate logistic regression analysis

	Odds Ratios (95% C.I.)
Personal factors	
Gender	
Male (968)	1.0
Female (237)	0.928(0.667 - 1.290)
Age	
< 25 (148)	1.0
25-45 (828)	0.968(0.656 1.427)
> 45 (229)	1.613(1.003 - 2.595)*
Floating population	
No (704)	1.0
Yes (501)	1.897(1.349 - 2.666)***
Transportation mode	
Driver of motorized vehicle (656)	1.0
Driver of non-motorized vehicle (448)	14.318 (9.696 - 21.143)***
Pedestrian (41)	53.164 (25.538 - 110.675)***
Vehicle occupant (60)	42.382 (22.642 - 79.332)***
Environmental factors	
Place of accidents	
Road for non-motorized vehicle (348)	1.0
Road for motorized vehicle (857)	3.021 (2.139 - 4.267)***
Weather condition	
Sunshine (859)	1.0
Cloudy/rainy (346)	1.445(1.009 - 2.071)*
Visibility	
> 200m (272)	1.0
100-200m (548)	1.065(0.766 - 1.481)
<100m (385)	0.753(0.496 - 1.144)
Road surface	
Dry (996)	1.0
Wet/icy/snowy/sleeper (209)	0.762(0.498 - 1.164)
Time of a day	
Day time (873)	1.0
Night (332)	1.093(0.773-1.546)
Region of road	
Straight road (690)	1.0
Crossing road (515)	1.186(0.893 - 1.576)
Partition	
No (336)	1.0
Partition between motorized vehicle road and non-motorized vehicle road (32)	1.097(0.499 - 2.413)
Others (837)	0.972(0.718 - 1.314)

*The contrast category was denoted by OR =1.0. *p<0.001, **p<0.005, *** p<0.010*

Table 4 shows the association between factors and severity of injury. There are no significant differences within environmental factors, except road for motorized vehicle and weather condition ($p < 0.05$). In the individual level factors, gender has no significant role on road traffic injuries in the study. Contrarily, age over forty, migrated population and transportation modes reflect significant relation with severe road injuries. At the environment level factors, road for motorized vehicles and rainy/cloudy weather have significant effect on road accidents.

Discussion

This study researched the risk factors of road traffic injuries and the relationship with the severity of injury in a designated Safety Community in Shanghai, China. Age over 45 years, migrated population, transportation mode, road condition and weather condition were revealed as significant risk factor for severe road traffic injuries.

Over 50% of people involved into road accidents suffered from injuries suggest that road accidents are highly related with injuries which is higher than the rate in general[2]. The drivers had high percentage of violating the traffic law. From the top 15 causes identified by police authority there were 12 items related to behaviors of the drivers of motorized vehicles, accounting for about 80.31% of total. This indicates that it is necessary to promote road safety and traffic rules to the public. Furthermore, drivers of motorized vehicles should be the key target population. A research investigated 1340 drivers about their unsafe driving behaviors for the last one month showed that the frequency of unsafe driving behaviors in rural areas was much higher than in urban areas and the number in male was much higher than female. Driving without seatbelt, drink diving, fatigue driving and driving without licenses were the main causes of injuries [14]. Through SC program, data

would be shown to them to demonstrate that how traffic injury happened, what they can do to prevent it. Also, let them imagine if they can change their behavior how many lives will be saved and how many people will not suffer from injury any more. Additionally, law enforcement can be enhanced strongly by the governmental administration. Punishment would be a good way to lead the drivers to obey the traffic safety law.

Most of environmental factors were not the main reason for the road traffic injuries as reflected by the logistic regression analysis with no significant influence. However, road for motorized vehicle was the risk place. Cloudy and rainy weather condition would affect the severity of injury distinctly. So in general the road traffic injuries are mainly influenced by individual factors. The results of logistic regression analysis represents that the risky populations for road traffic injuries are migrated people who come to Shanghai from rural areas. Drivers of non-motorized vehicles, pedestrians and vehicle occupants are also in the risk of road injuries. On the other hand, some previous researches reported that most of the injured people were male, aged between 21 - 45 years, with an increasing proportion of people aged over 60. The majority of the victims were passengers, motorcyclists and pedestrians. Road accidents mainly occurred at night between 19- 20 pm being peak hours, and most deaths occurred at 3- 5am. Road traffic injuries were caused mostly by motor vehicles, mainly passenger cars, motorcycles and vans. Electric bicycles were the main type of non-motor traffic vehicles that caused crashes. The crashes and casualties showed an upward trend every year. RTIs crashes caused by motor vehicle driving were due to law violations. The five leading causes of RTI crashes were: over speed, not giving way as required, driving without license, retrograde driving and alcoholic driving[15-18]. Safe Community can promote road safety education to the high risk population. Work places, schools, residential committees can be targeted by the Safe Community programs to improve the risky people's knowledge and to correct their attitudes and road using behaviors. Construction companies where most of the migrated population works should also be targeted to improve their awareness of road safety and to improve their road safety behavior. In addition, organizations which are responsible for management of car parking at residential areas should be targeted to figure out more effective way to promote road safety.

Limitation of this study: The study has considered only 15 causes of traffic injuries defined by police authority. They can help to explore the risk factors of traffic injuries however with an open end questionnaire study can provide us many more risk factors of road injuries. The study is a secondary data analysis. A firsthand investigation can provide us more accurate research base. Traffic rule violation should be more wide studied in absence of such information for the researchers and policy makers. It should be investigated to better understand the actual cause of such traffic rule violation.

Conclusion

During renovation of community road the local government should consider the results and suggestions from this kind of study. The roads should be prepared for and/or awareness should be provided to the drivers that cloudy or rainy weather conditions are dangerous for the road occupants. Drivers of motorized vehicles are mostly the violator of the traffic rules. Therefore, Safe Community should specifically emphasize strategies for the migrated people, drivers of motorized vehicles, pedestrians and vehicle occupant. Also the study suggests that local area based studies are important to specifically setting the traffic injury prevention activities. Injury surveillance at the local level is very important to decide the priority interventions [19].

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Spondylodiscitis – Current Diagnosis and Treatment

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Abstract

Introduction/Objective: Spondylodiscitis is an inflammatory process, which simultaneously afflicts the intervertebral disc and body of vertebra. Increasing incidence of the disease is linked to the rising number of acquired immune deficiencies. The objective is to identify the most frequent symptoms, clinical and neurological findings in these patients, basic laboratory features, average disease duration, localization of the inflammatory process, etiology, outcome and sequelae. We also suggest a diagnostic algorithm and an adequate empiric antibiotic therapy as well as the necessary length of treatment.

Methods: A retrospective study included 33 patients diagnosed with spondylodiscitis who were for the first time hospitalized at the Infectious Diseases Clinic of the Clinical Center of Vojvodina. We used descriptive statistics to identify the patients' demographic characteristics, clinical and laboratory indicators of inflammation, predisposing factors, the most frequent localization of the disease in respect to the spinal regions, as well as the use of appropriate diagnostic methods. We also noted the efficiency of the used combinations of antibiotics.

Results: Most of the patients were male, aged between 31 and 65 years. 94% of patients had an increased sedimentation rate, 33% had high fibrinogen, 73% had high C reactive protein (CRP), while 27% had alpha 2 hyperglobulinemia. Lymphocytosis was noted in 42% of patients, and neutrophilia in 9%. The most common predisposing factor was previous surgery, which was registered in 24% of cases. The inflammation was most frequently localized in lumbosacral region (30%). MRI was successfully used to confirm the diagnosis in 91% of cases. 97% of patients were successfully treated with conservative therapy.

Conclusion: There is a higher incidence of spondylodiscitis among men of working age. The disease has a predilection for lumbar and sacral region, and symptoms and clinical findings are non-specific. In most cases one cannot identify the causative agent; however, empiric combinations of broad spectrum antibiotics have proven to be adequate in majority of patients. MRI is the best imaging method to confirm the diagnosis of spondylodiscitis.

Key words: spondylodiscitis, diagnosis, antibiotics.

Introduction

Spinal infection implies the following diseases: spondylitis, discitis, spondylodiscitis (SD), epidural infections, meningitis, polyradiculopathy, myelitis and pyogenic arthropathy [1].

Septic discitis is an infection of intervertebral disc space; however, it often afflicts vertebral edges and spreads to the vertebral body. The simultaneous infection of the intervertebral disc and vertebral body implies the existence of SD[2].

SD is a rare disease with an annual incidence than ranges from 1/250 to 1/100 000[3]. It affects about 2% -7% of patients with osteomyelitis and it is 1.5 to 3 times more common in males[2, 3]. Our research illustrates a *bimodal age distribution* with the first peak in early childhood and another peak during the fifth and sixth decades of life[3]. Increased incidence of the disease is noted recently, which is linked to the rising number of acquired immune deficiencies such as malnutrition, drug abuse, alcohol, and also to the extended life expectancy [1, 3].

The following conditions are identified as the main predisposing factors for SD: diabetes mellitus (DM), HIV infection, chronic renal failure, liver cirrhosis, alcoholism, use of intravenous drugs, septicemia, chronic steroid use, gastrointestinal (GIT)

and genitourinary (GU) infections, malignancies and chemotherapy[4]. Inflammation can develop as a result of spinal surgery or it may be idiopathic [1].

The SD etiology, in general, is attributed to one isolated pathogen, while polimicrobe infections correlate with the presence of decubital ulcers and immunosuppression[2]. The most frequent pathogens are: *Staphylococcus viridans*, *Escherichia coli* (*E. coli*), *Staphylococcus epidermidis*, *Brucella mellitensis*, *Proteus spp*., *Pseudomonas aeruginosa* (*P. aeruginosa*) and *Candida albicans*[4]. Strains of *Staphylococcus aureus* are sensitive to methicillin, and were isolated in 15% -84% of patients with nontuberculous infection [2].

Gram negative bacilli (*E. coli, Proteus spp*. and *P. aeruginosa*) are noted in immunocompromised patients, patients with diabetes, syndrome of dependency, GIT and GU infection. Streptococcal infection is associated with endocarditis and dental treatment[2].

Mycobacterium tuberculosis is the causative agent characteristic for certain population groups – immunosuppressed patients, homeless, prisoners, alcoholics and drug addicts. Brucella SD still has a high incidence, especially in the Mediterranean (Italy, Spain) [2].

Fungal infections are typical for immunodeficient patients, and can occur as a late complication of long-term use of catheters or broad spectrum antibiotic treatment. While in children blood vessels penetrate into the nucleus pulposus allowing bacterial emboli to remain in the disk, in adults they only reach anulus fibrosus. In adult patients, emboli are deposited in the final arterial arcades between the vertebral metaphysis, leading to bone ischemia, infarction, and spreading of pathogens in the disc space area. Infective process can affect paravertebral area, epidural space and adjacent vertebral bodies[2].

Due to the mostly non-specific symptoms and signs of the disease, diagnosis is usually delayed. In 90% of cases patients complain of long-term neck and lower back pain, which wakes them up at night and does not respond to analgetics[3]. Fever occurs in 60-70% of patients with pyogenic infection. Other symptoms and signs listed are: anemia, night sweats, weight loss and neurological deficit, as a consequence of ischemia or a mechanical compression[4].

Physical examination shows the tenderness of the affected spine region, para-spinal muscle spasm and decreased range of motion. Neurological signs of radiculopathy and myelopathy may also be present. The symptoms of "psoas" abscesses and retropharyngeal abscess with dysphagia and trismus are rarely identified.

Differential diagnosis includes degenerative or metastatic disease of the spine, disc herniation, compressive fracture and inflammatory spondyloarthropathies (ankylosing spondylitis and reactive arthritis).

The laboratory findings in 90% of cases include increased sedimentation rate and high CRP levels. Radiologic changes due to pyogenic SD are usually identified between 2 and 8 weeks after the onset of symptoms. Computerized tomography (CT) enables the identification of changes in the early stages of disease (after 2 weeks), which is manifested by hipodensity, flattening of the affected disc and vertebral body erosion. Magnetic resonance imaging (MRI) is the most sensitive and specific method for early diagnosis of SD, and it additionally distinguishes between pyogenic discitis, neoplasms and tuberculosis[2].

The primary treatment are the broad-spectrum antibiotics. Most commonly used combinations are: levofloxacin and rifampicin, teicoplanin and rifampicin, vancomycin and rifampicin. Patients who do not respond to conservative treatment are referred for surgical treatment[3].

Adequate diagnostic procedures (especially CT and MRI), and adequate antibiotic therapy have reduced the mortality and morbidity from SD[4].

Objectives

1. To identify the most common symptoms, clinical and neurological findings in patients with SD.
2. To establish the main laboratory characteristics in patients with SD.
3. To determine the average time period that elapses between the first symptoms to the diagnosis and initiation of therapy.
4. To identify the most common localization of SD.
5. To identify the most frequent pathogens.
6. To propose an adequate diagnostic algorithm.
7. To identify the efficient empiric combinations of antibiotics and duration of treatment.
8. To determine the outcome and sequelae in patients with SD.

Materials and Methods

This is a retrospective study in which we analyzed the medical records of all patients treated for SD at the Infectious Diseases Clinic of the Clinical Center of Vojvodina in the time period from January 1, 2006 to December 31, 2009. The total of 33 patients were initially diagnosed based on the clinical and laboratory findings, while final diagnosis was confirmed by radiological methods (CT and/or MRI). Only patients who were hospitalized for the first time were included in the study.

We registered the following parameters: demographic characteristics of patients, leading symptoms, duration of symptoms until hospital admission, fever, laboratory indicators of inflammation (sedimentation, fibrinogen, CRP and WBC), potential predisposing factors for SD, sensitivity of the imaging methods such as CT and MRI, localization of inflammatory process, the type of antibiotics used and the length of treatment, outcome and the length of hospitalization.

In addition to standard bacteriological tests (blood cultures), we conducted testing for *Brucella, Mycobacterium t.* and ASTO titer, in attempt to identify the causative pathogens. Descriptive statistics included frequency analysis (percentages) for categorical variables and means and standard deviations or medians and interquartile ranges (IQRs) for continuous variables. The key results were presented as tables and graphs.

Results

Among the total of 33 patients with SD, there were 20 males (61%) and 13 females (39%). Mean age of patients was 54.5 years (SD ± 13.1). Most patients were between 31 and 65 years of age. Distribution of patients by age and sex is shown in Figure 1.

The median duration of symptoms before hospitalization was 68 days (IQR 42-79) for female patients and 51 days (IQR 40-68) for male patients, which adds up to 57 day median for all patients. The mean length of hospitalization for women was 29.5 days (SD ± 4), and 38 days (SD ± 5.5) for men – the total average of 35 days for all patients.

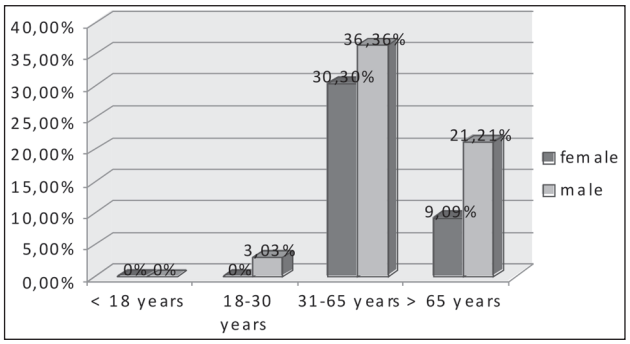

Figure 1. Demographic distribution of patients

The symptoms which all patients had before hospital admission were pain and paravertebral muscle spasm. 13 (39%) of patients were treated as out-patients: 10 (30%), were prescribed nonsteroidal anti-inflammatory drugs and other analgesics, 3 (9%) received antibiotics; while 4 (12%) were initially hospitalized at the Internal Medicine Clinic.

We investigated the presence of fever in patients with SD prior to admission to hospital, at the admission and during hospitalization. These results are shown in Figure 2.

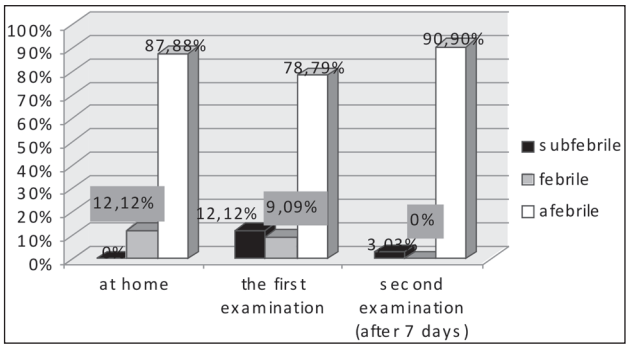

Figure 2. Febrile response in patients with SD

We examined the following markers of inflammation: sedimentation rate, fibrinogen, CRP, alpha-2 globulin; lymphocyte and neutrophils count. Results showed that 31 (94%) patients had an increased sedimentation rate, 11 (33%) had high fibrinogen, 24 had high CRP levels, and alpha 2 hyperglobulinemia was noted in 9 cases (27%). 14 (42%) patients had lymphocytosis, and 3 (9%) had neutrophilia. Neutropenia was present in 12 patients (36%).

Considering predisposing factors, we looked for tuberculosis, urinary infections, diabetes mellitus, osteoporosis, substance abuse, previous surgeries and injuries. In 12 patients (36%), no predisposing factor was determined. In other ca-

ses, at least one of the listed predisposing factors was confirmed. Previous surgery was present in 8 cases (24%), while 5 (15%) patients had tuberculosis. In the remaining two cases (6%), one person had a confirmed diagnosis of tuberculosis in combination with the dependence syndrome, and the other patient had been was previously diagnosed with tuberculosis and osteoporosis.

In order to confirm the diagnosis of spondylodiscitis, MRI was used in 30 patients (91%). CT was used to confirm the diagnosis in additional two patients (6%), and biopsy was performed in only 1 patient (3%).

The most common localization of SD was in the lumbar vertebrae - in 17 patients (51%), while lumbosacral area was affected in 10 patients (30%). The exact percentage of the affected region is shown in Figure 3.

The antibiotic protocols used to treat patients with SD and the cost of respective treatments is shown in Tables 1 and 2.

We opted for the antibiotics that can diffuse well into the bone tissue for 14 days, and then we rotated antibiotics. The total duration of antibiotic therapy was 6 weeks in hospital. Dring that time antibiotics were administrated parenterally, and then we switched to oral antibiotics for two weeks after the discharge. Only 1 patient (3%) was referred for surgery due to failure to respond to antibiotic therapy. The conservative treatment outcome for the rest 32 patients (97%) was satisfactory, with no registered sequelae in the sense of neurological deficit.

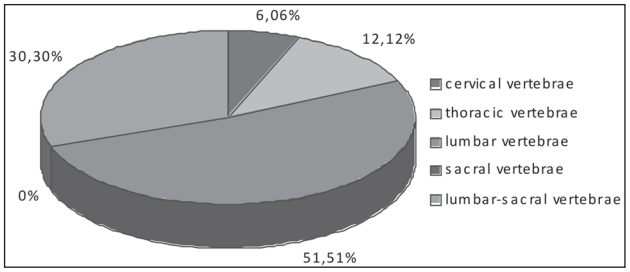

Figure 3. Anatomic distribution of SD

Discusion

Spondylodiscitis is a rare infectious disease whose incidence in Western countries ranges from 0.4 to 2.4 per 100.000 inhabitants[1, 2].

Group of authors from Turkey found an increased incidence of SD in the last 10 - 15 years. The

Table 1. Antibiotics used in Protocol I and the total cost for the period of six weeks

Antibiotics	Price (EURO) DDD	In total (EURO) 14 DDD for antibiotics treatment
Ceftriaxon	8,85	187,60
Amikacin	4,26	
Rimfampicin	0,29	
Imipenem	21,54	395,54
Klindamycin	6,71	
Piperacillin- tazobactam	49,58	880,94
Vancomycin	13,35	
TOTAL		**1.464,08**

DDD – defined daily doses

Table 2. Antibiotics used in Protocol II and the total cost for the period of six weeks

Antibiotics	Price (EURO) DDD	In total (EURO) 14 DDD for antibiotics treatment
Metronidazol	5,19	332,58
Ceftiaxon	8,85	
Ciprofloxacin	9,71	
Ciprofloxacin	9,71	437,54
Imipenem	21,54	
Meropenem	71,24	1.184,29
Vancomycin	13,35	
TOTAL		**1.954,41**

DDD – defined daily doses

reason is linked to a higher prevalence of bacteremia and septicemia, which is a direct consequence of the use of invasive diagnostic procedures and therapeutic methods [1].

According to the research conducted in Portugal during 2002-2007, mean age of patients was 63.5 years and 71% of hospitalized patients were from rural regions[5]. In our study, mean age of patients was 54.5 years. 30% of patients were over 65 years old, and only 3% were under 30. The age distribution in our study show that the highest percentage (67%) of patients was within working-age category, between 31 and 65 years old. Our results show the greatest similarity with the results scientists from Taiwan, where mean age was 52.8 years and only 30% were female[6]. Our study also showed predominance of male patients with 61%.

Data from the above mentioned study in Portugal showed the highest incidence of tuberculous SD (21%), followed by *Staphylococcus aureus* (14%) and *Brucella mellitensis* (14%). In 39% of cases the cause was not isolated[5]. In our study, the etiologic agent is isolated in only 8 cases (24%) – 7 patients diagnosed with tuberculosis (TB) and 1 with *coagulase negative Staphylococcus spp*. (blood culture). Unfortunately, etiology was not determined in the rest 76% of patients with SD at the Infectious Diseases Clinic in Novi Sad, and the main reason is a minimal practical availability of the biopsy of vertebral bodies as a diagnostic method. This practical limitation has prevented us from implementing the Guidelines for sampling nonpyogenic SD in adults, given by a group of scientists from France, which proposed the biopsy as necessary measure in patients who had a negative haemoculture results[7].

Abid, DeSilva and colleagues conducted a ten-year research in which they had 77% positive blood cultures. Leading pathogens were Gram-positive bacteria (especially *Staphylococcus aureus*) [8]. In our study, blood cultures results were negative in 97% of patients. In only 1 patient (3%) blood culture was positive for *coagulase negative Staphylococcus spp*.

Brucella SD still has a high incidence in many regions of the world and it is typical of the Mediterranean belt (Italy, Spain) [2]. Yet, we were not able to confirm Brucella in our patients with SD. Agglutination test for *Brucella* was done in 85% (28/33) of our patients and gave negative results.

Due to its non specific symptoms, SD is a disease that is rarely diagnosed during the first examination of the patient[9]. Departments of neurosurgery, orthopedics, ophthalmology and radiology of the General Hospital in Tokyo, concluded in their joint research that most of the patients were originally referred to the internal medicine department[10]. In our study, only 12% patients had been previously hospitalized at the Internal Medicine Clinic.

Cottle and Riordan found that more than 90% of patients had been complaining of persistent back and neck pain, which is resistant to painkillers, and woke them at night[2]. Turunc in his study pointed out that the paravertebral muscle spasm was also present[1]. Data from these study are similar to ours, since pain and paravertebral muscle spasm were present in all patients.

Our study showed that diagnosis was delayed and that the average number of days from onset of symptoms until hospitalization was 57. On the other hand, Cottle and Riordan found that diagnosis was delayed for 2 to 6 months after the first symptoms[2, 3, 9].

Italian scientists from Udine showed that 37.5% of patients had fever, while neurological symptoms and signs were present in 18% of cases[5]. Our findings significantly differ – there were only 9% of febrile patients at admission and another 12 % were subfebrile. This concurs with the findings of Abid and DeSilva whose majority of patients were not febrile and had normal levels of white blood cells[8]. As many as 55% of our patients had normal neutrophils count, while neutropenia was noted in 36% and lymphocytosis in 42%.

Majority of patients in pour study had increased markers of inflammation. Sedimentation rate were elevated in 94% patients, which corresponds to the results given by Cottle and Riordan[2].

Anatomical distribution of the inflammatory process in our patients *coincides* with the literature - in most cases (51% in our study) lumbar region is affected; followed by lumbosacral (L/S) region.

Untreated TB is an important predisposing factor for development of SD. With 90 million new infections in the last decade, TB is an important clinical entity. As many as 10% of these infections affect bone structure due to haematogenic spread[11].Our research has proven tuberculous SD in 21% of patients. Even though Turunc and co-

lleagues emphasized that tuberculous SD involves compression of spinal tract, nerve root and cauda equina, our study did not confirm that[1].

Invasive procedures are a suitable portal for direct entry of infectious agents and development of SD. Taiwan's team of researchers point to the certain procedures as essential, such as: stomatological intervention, lip laceration, epidural catheterization, and lumbar puncture[6]. Our patients were not subjected to these procedures; however, we found that as many as 24% of our patients had postoperative SD, as a result of neurosurgical decompression.

Renker and colleagues have found that the GU tract infections caused SD in 6.8% of cases[12]. Similarly, our study has showed that urinary infection was preceded by SD in 6% of cases.

Roentgen (X-ray) images of the spinal column according to Bettini should be applied in all patients with suspected infection of vertebra[3]. Still, in our study only 27% of patients were subjected to the X-ray. The rationale is that the changes due to pyogenic discitis are detectable on X ray only 2-8 weeks after the onset of symptoms and the use of this method cannot exclude the diagnosis of SD [2]. Superior imaging methods such as CT and MRI, on the other hand, have enabled an earlier diagnosis of SD[1]. MRI is the gold standard for diagnosing pyogenic spinal infection, especially in the early stages when the X-ray and scintigraphy are negative. In 50% of cases, the changes typical for SD are visible during the first 2 weeks[3, 5]. MRI is the most sensitive and very specific diagnostic method that was performed in 91% of our patients. Bettini and colleagues emphasize that each patient included in their study was subjected to MRI. This method allows the differentiation between pyogenic discitis, neoplasms and tuberculosis of the bones. There is a noticeable difference even between early postoperative infections and those that result from invasive diagnostic procedures[2].

Most experts agree that antibiotic therapy without surgical treatment is the best solution for most patients with SD. Conservative treatment has a priority, while surgical procedures are reserved for the selected patients who fail to respond to antibiotic regimens[3, 5, 6]. Cottle and Riordan have described successful recovery after conservative treatment, with the withdrawal of pain, in 50% - 75% of patients, which is similar to our results[2].

It is suggested that two bactericidal antimicrobial drugs should be initially administered in a large dose intravenously during the first 2 weeks, or until CRP is decreased to the normal level [7,13,14]. Our patients were treated with 2 or 3 broad-spectrum antibiotics simultaneously for 14 days after which we rotated antibiotics, during our current protocols. The total duration of antibiotic therapy was 4-6 weeks in hospital, and additional at least two weeks after discharge. The literature states that the following antibiotics are best diffused into the bone tissue: fluoroquinolones, clindamycin, rifampicin, fusidin acid and metronidazole[5, 7]. Our study showed the use of the following combinations of antibiotics: ceftriaxone + amikacin + rifampicin, piperacillin-tazobactam + cefepime, imipenem + clindamycin, imipenem + ciprofloxacin, meropenem + vancomycin, ceftriaxone + metronidazole + ciprofloxacin (vancomycin). The total duration of antibiotic therapy was 6 weeks in hospital (parenteral). The cost of antibiotics prescribed for the treatment of one patient cost 1.464 euros in case of Protocol I or 1.954 euros in case of Protocol II. However, had we been able to regularly perform bone biopsy, that would allow us the use of targeted therapy which would approximately cost 173 euros. The patients with tuberculous SD also received combined antituberculosis therapy - isoniazid, rifampicin, ethambutol and pyrazinamide, which was continued at home. The treatment of tuberculous SD was carried out in accordance with the National guidelines - loading dose of tuberculostatic drugs were used during the first 2 months and after that therapy regime was changed with combination of isoniazid and rifampicin.

Bettini and colleagues point out that indications for surgery are: peripheral neurologic deficit, cauda equina syndrome, paravertebral abscess, progressive vertebral deformity[3]. According to our records, only 3% of patients at our Infectious Diseases Clinic were referred for surgical treatment, while 07% of patients were successfully treated conservatively with antibiotics.

After the hospital discharge patients were recommended to rest and wear a bodice. Most authors emphasize that the use of bodice in a 3 moth period following the discharge can ensure stability and improve the quality of patients' life[2,7]. In our study 7 patients (21%) received a TLSO bodice,

and another 12% were referred to the Medical Rehabilitation Clinic.

Conclusion

Spondylodiscitis is a disease more frequent among working age men. Lower segments of the spinal column (lumbar and sacral) are more often affected. When patient complains of the back pain, spondylodiscitis should always be considered in order to make a timely diagnosis of this rare but serious disease, and to start an adequate treatment, reducing the sequelae to a minimum. MRI is the best tool to confirm the diagnosis of spondylodiscitis. Subjective symptoms and clinical findings are often non-specific. Laboratory parameters of inflammation, especially sedimentation rate and CRP level are good indicators of severity of spondylodiscitis. The conservative treatment for spondylodiscitis is usually sufficient, and surgical intervention is required only in selected cases. Although the causative agent mostly remains unidentified, empiric antimicrobial therapy has proven to be efficient as long as it covers the broad spectrum of potential pathogens and is given for an adequate period of time. In conclusion, prognosis of SD depends largely on the early diagnosis and appropriate antibiotic treatment.

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In Turkish Elderly Population Elder Abuse and Neglect: A Study Of Prevalence, Related Risk Factors and Perceived Social support

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Abstract

Introduction: In this study ıt was aimed to find out the relationship between the perceived social support levels, to determine the prevelance of elder abuse and neglect(EAN) among Turkish population aged 60 and over and to detect the risk factors leading to EAN.

Materials and method: A total of 452 elders were enrolled in this study. Data were collected by interviewing the subjects and by using Information Form on the experience of EAN, Socio- Demographic Information Form and Multidimensional Scale of Perceived Social Support (MSPSS)

Results: Prevalence rates of 28.5% for abuse and neglect. Among the abused and neglected, 58.9% were male. The Mean ± s.d. total MSPSS for the EAN group was 37, 14± 11, 13 and for the Non- EAN group it was 76, 39 ± 5, 751.There were statistically significant differences between those groups($p<0.001$). A higher social support level was observed in Non- EAN group. After binary regression, only perceived social support (OR, 0.763, CI, 0.708–0.823, P<0, 001) was found to be associated with elder abuse and neglect.

Conclusion: Higher social support may be a protective factor against Elder abuse and neglect in this population.

Key words: Elder abuse and neglect, Social Support, Turkish elderly population, Risk factors

Introduction

Elder abuse and neglect (EAN) is a pervasive global health issue and a violation of basic human rights. EAN is a multidimensional structure that encompasses the infliction on older people of physical abuse, abandonment, emotional/psychological abuse, financial /material abuse, and/or neglect. The inability to more precisely estimate the scope of elder abuse in the community has been related to poor construct definition and the variability of risk factors for different types of abuse (1).

With the aging of the population in Turkey, elder abuse is now recognized as a significant problem. However, health care providers lack knowledge regarding detection, reporting, and appropriate interventions in cases of suspected or substantiated abuse. Unfortunately, our current global understanding of EAN is limited, especially in Turkish cultures, where traditionally it has been thought that EAN is uncommon.(2,3)

EAN may be seen among almost every elderly. However, if the factors related to abuse are known widely, this may lead to the avoidance of abuse (4). The people in the risk group are especially the ones who lack physical and cognitive capabilities and are dependant on other people for their basic needs, thus they are easily abused. Lack of social support and inefficiency of similar social support systems, poverty, inadequate social circumstances, and the bad conditions in the household also increase the probability of abuse (4,5). The familial and social dynamics and social support networks are established to be among the factors detecting the violence (6).

One protective factor may be social support. For the last 25 years many studies have been conducted showing that social support is a source of coping, a protective element against illnesses and risks (7-11)

Social support is broadly defined as the existence or availability of people on whom one can rely; people who let one know that one is cared about, valued and loved (7-9).

Researchers state that the people or the institutions that make up one's social network can not always be positive and supportive, instead a

strong social network can sometimes have an adverse effect and prevent other supports. Thus, it is emphasized that the support one feels and perceives himself is more beneficial for the person than the social network(12,13).

In the few researches on EAN the effect of perceived social support level has not been studied. This study will be one of the first studies on the prevelance of EAN and the effect of perceived social support and also on searching the other probable risk factors.

In the light of this information, this study aims to find out the relationship between the perceived social support levels, to determine the prevelance of EAN among Turkish population aged 60 and over and to detect the risk factors leading to abuse.

Materıals and method

Design and Sample

This study, defining and cross-sectional, is conducted in Sakarya and its central districts in 2005–2006. The Table of Acceptable Sampling Sizes is used in order to determine the appropriate sample size for the study(14)The data were collected from a total of 452 elderly people who were living in the region of the chosen primary health care unit and they were the patients presented just for general health problems without any acute health disorders that would hinder or restrict the administration of the survey protocol. In order to find out how clear the questions were, a pre-administration on 15 elderly people outside the space was carried out. Thus, the first two forms were put into their latest state.

Particular attention was given to the sensitivity of the elder abuse and neglect. In the consent documentation (1,4,15), respondents were informed as follows: "In addition, you may be asked about elder abuse. We are required to report any incidents of elder abuse learned as a result of this interview to your state reporting hotline. This report would include your name, a list of service providers and medical resources Another adult was present during one third of the interviews conducted; 28% of these adults were spouses or children. 72% of the elderly were alone during the interviews conducted. Approximately 15 minutes were given to fill in the protocol form and to conduct the interview.

Ethical Considerations

Necessary official permissions were obtained from the Provincial Directorate of Health.The elderly who volunteered to participate in the survey were informed about the aim and the procedure of the study.

Instruments

1. It contains the information such as the age, sex, marital status, level of education, the state of having any savings or real estate etc.
2. **Information Form on the experience of EAN:** The information was gathered by literature scanning (4,16,17) and by a question form that was prepared by revising the most appropriate questions measuring abuse and neglect.

The questions on abuse and neglect were collected under three headings:

a - Presence and type of abuse and neglect
b - Performers of abuse and neglect
c - Thoughts upon abuse and neglect; behaviours and attitudes after suffering abuse and neglect

Presence and type of abuse and neglect: Five groups of questions were determined (Table 1).

3. Multidimensional Scale of Perceived Social Support (MSPSS)

The scale, aiming to detect the individual's perceived social support factors, was developed by Zimmet and his colleagues in 1988 (10). The studies on its reliability and dependability were conducted by Eker and Arkar in Türkiye in 1995(11).

Data Analysis

In evaluation of the data, percentage, Chi-Square, Student t tests and Binary Regression were employed. This analysis was made in order to detect the efficiency levels of variables that were found out to be effective in elder abuse.The "enter" method was used after the whole variables were dealt with. Data analyses were performed using SPSS 16.O version. The significance level was accepted as $p<0.05$.

Table 1. Information Form On Presence And Type Of Abuse And Neglect

1. The state of being exposed to abuse and neglect
Have you experienced any abuse or neglect from any of your relatives or acquaintances in a year? ..... YES NO
2. The state of being exposed to emotional abuse and neglect
Have you experienced any condition in which you were daunted, threatened, insulted or your needs being neglected by any of your relatives or acquaintances? ..... YES NO
3. The state of being exposed to physical abuse and neglect
have you experienced anything like being beaten or being roughed up or any deliberate injuries by any of your relatives or acquaintances? ..... YES NO
4. The state of being exposed to sexual abuse and neglect
have you experienced any sexually intended touch or a similar condition without your own will (by any of your relatives or acquaintances? ..... YES NO
5. The state of being exposed to financial exploitation
Have you had any relatives or acquaintances who tried to use your income or other financial resources illegally or improperly for their own benefits? ..... YES NO

Fındıngs

In the study conducted over a total of 452 people; average age of the participants were 66.49±4.59, a total of 54,0 % of whom were men and 46,0 % were women. EAN prevelance was found to be 28,5 %. A total of 58,9 % of the ones who had an experience of EAN were found to be men. A total of 57,4 % stated that they had experienced emotional abuse, 14,7 % had physical and 27,9 % had economic abuse. None of the participants stated that they had experienced any sexual abuse. The performers of abuse were investigated and they were found to be 40,3 % children, 41,1 % spouses, 12,4 % other people living in the house, 11,6 % relatives out of the house, 8,5 % friends and neighbours.

Average age of the elderly experiencing EAN is 67, 89 ± 5,428, and the ones who hadn't experienced EAN is 65, 93 ± 4,092 and thus, it can be seen that there is a statistically meaningful difference between them ($p<0.001$) (Table 2). Total MSPSS point for the ones who had experienced EAN is 37,14± 11,13, and 76,39 ± 5,751 for the ones who hadn't. Among the sub-groups of MSPSS, family support mean points for the ones who had experienced EAN is 14,81 ± 4,808, friend support mean points is 11,88 ± 4,247, significant other people mean points is 10,06 ± 3,850; the ones who hadn't experienced EAN had an average of 26,41 ± 2,312 points for family support, 25,41 ± 2,491 points for friend support and 24,08 ± 2,928 points for significant other people. The difference between them is found statistically meaningful ($p<0.001$) (Table 2).

The relationship between the state of being exposed to EAN and socioeconomic condition, having assets or savings and the trust object is found to be statistically meaningful ($p<0.001$) (Table 2). According to this, a total 10,9 % of the ones experiencing EAN and a total 23,2 % of the ones who hadn't experienced EAN have good economic conditions, whereas a total 47,3 % of the ones who experience EAN have some assets and savings but a total of 72,1 % of the ones who hadn't experienced EAN have those. The ones who experience EAN state their "family and parents" as their trust objects, and they have a percentage of 27,1. Trust objects for a total 42,6 % are stated as "myself and my moral values" and a percentage of 24,8 stated these objects as nothing. As regards to the ones who hadn't experienced EAN, these percentages are 66,6, 30,0 and 0 respectively.

A total of 68,2 % of the ones who experienced EAN, and a total of 56.0 % of the ones who hadn't were detected as having cognitive and mental problems and the difference was found statistically meaningful.($p<0.05$) (Table 2).

Binary logistic regression analysis is made in order to find out the efficiency levels of the factors known to be effective in EAN experience as well as to examine the relationship between the existence of EAN and the independent variables (age, sex, marital status, education level, the people living with the elderly, economic conditions, savings and assets, trusted objects, cognitive and mental problems and MSPSS) in terms of risks

Table 2. Comparison of Multidimensional Scale of Perceived Social Support and demographic variables among abused, neglected and non abused, neglected ages

Variable	non abused, neglected (N=323) Mean ± s.d. / n(%)	abused, neglected (N=129) Mean ± s.d. / n(%)	t test	Significance
Age,	65,93 ± 4,092	67,89 ± 5,428	-3,704	**0,000***
MSPSS*	76,39 ± 5,751	37,14± 11,13	38,053	**0,000**
Family support	26,41 ± 2,312	14,81± 4,808	26,211	**0,000**
friends	25,41 ± 2,491	11,88 ± 4,247	33,934	**0,000**
significant other	24,08± 2,928	10,06 ± 3,850	37,287	**0,000**
Sex				
Male	168(52.0)	76(58.9)		
Female	155(48.0)	53(41.1)	$\chi^2 = 1.768$	0.351
Education				
Nonliterate	79(24.6)	44(34.1)		
Literate and	213(65.9)	72(55.8)		
elementary level	31(9.6)	13(10.1)	$\chi^2 = 4.677$	0.096
Marital status				
Married	207(64.1)	74 (57.4)		
Single	9(2.8)	3 (2.3)		
Divorced or widowed	107(33.1)	52 (40.3)	$\chi^2 = 2.096$	0.351
Socioeconomic status				
Good	75 (23.2)	14 (10.9)		
Moderate	190 (58.8)	74(57.4)		
Low	58 (18.0)	41 (31.8)	$\chi^2 = 15.240$	**0,000**
People in same household				
Alone	62 (19.2)	32 (24.8)		
With spouse	63 (19.5)	25 (19.4)		
child and other family person	198 (61.3)	72 (55.8)	$\chi^2 = 1.861$	0.394
Saving and real-estate				
Yes	233 (72.1)	61 (47.3)		
No	90 (27.9)	68 (52.7)	$\chi^2 = 25.036$	**0,000**
Trusted persons or objects				
My family and children	215 (66.6)	35 (27.1)		
Public body and private establishment	11 (3.4)	7 (5.4)		
Self-confidence and coloration	97 (30.0)	55 (42.6)		
Nothing	0 (00.0)	32 (24.8)	$\chi^2 = 1.113$	**0,000**
Cognitive and mental problems				
Yes	181(56.0)	88(68.2)		
No	142(44.0)	41(31.8)	$\chi^2 = 5.676$	**0,017****

involved. When the efficiency levels or their meaningfulness is examined, it is seen that the scale points are statistically meaningful (OR, 0.763, CI, 0.708 -0.823) (Table 3). Thus, a single unit increase means a proportion of 0,763 decrease in the probability of being exposed to abuse. This means that the more scale points are, the less probable it is to experience abuse.

Dıscussıon

This study is not enough to profile Turkish population in terms of abuse and neglect. However, it is one of the most detailed studies compared to the few ones conducted in Türkiye, regarding the determination of risk factors and their relation to the perceived social support level. This study is believed to be a reliable one in terms of measuring elderly abuse and neglect.

Table 3. Binary Regression: Finaly Model.Prediction of Likelihood of EAN

Variables in the Equation									
		B	S.E.	Wald	df	Sig.	Exp(B)	95,0% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	Age	-,167	,829	,041	1	,840	,846	,167	4,293
	Sexuality	1,401	,813	2,972	1	,085	4,059	,825	19,957
	Marital status	,380	,826	,212	1	,646	1,462	,290	7,381
	Education	-,040	,870	,002	1	,964	,961	,175	5,283
	Socioeconomic status	-,646	1,205	,287	1	,592	,524	,049	5,567
	Saving- real-estate	-,238	1,018	,054	1	,815	,789	,107	5,797
	Trusted persons,objects	,892	,816	1,195	1	,274	2,440	,493	12,070
	People in same home	,369	,752	,241	1	,623	1,446	,331	6,312
	Cognitive-mental probl	,475	,714	,444	1	,505	1,609	,397	6,514
	MSPSS	-,270	,038	49,364	1	,000	,763	,708	,823
	Constant	14,168	2,678	27,995	1	,000	1,423E6		

N:452, P<0,001

MSPSS: Multidimensional scale of perceived social support

Ağe:*65-69: 0,70 and:1,***Sexuality***: 0:Women, 1:Male, ,* **Marital status:** *married:0,divorced or widoved:1,***Education:** *literate:1,nonliterate:0,* **Socioeconomic status:***good and moterate:0,low:1,* **Saving and reel-estate:Y***es:0,No:1***Trusted persons or objects:** *My family and children and my job:0,Nothing and nobody: 1,* **People in same household:** *family person and other person:0,single:1,* **Cognitive and mental problems:***No:0,Yes:1***, MSPSS:maximım :84,Minumum:12**

This model is found out to be available for the estimation of the presence of abuse when it is analysed by Hosmer-Lemeshow Goodness-of-Fit test (X^2=10,228, df=8 ve p=0,249, p>0.05).

A logistic regression is carried out in order to determine which variable is the most important of the ones that are thought to be risk factors related to EAN and it is seen that only the perceived social support level is a primary determinig risk factor (OR, 0.763, CI, 0.708 -0.823). Thus, it can be said that a single unit increase in the scale points lessens the probability of being exposed to abuse in a proportion of 0,763. This means that the higher points we get from the scale, the lower probability of being exposed to abuse the elderly has.

Total point of MSPSS from the ones who are not exposed to abuse and neglect and mean points of the sub-group family support, friends, significant other are found to be nearly two times more than the mean points got from the general scales and sub-scales of the ones who are exposed to abuse and neglect. The difference of mean points between the groups has been found statistically meaningful (p<0.001). According to these findings, it can be said that there is a contrary relationship between MSPSS and EAN. MSPSS being a primary predictory factor and its relationship to EAN are also supportive findings.

This information may be important because there is limited systematic information about the relationship between social support and EAN in the current literature No single factor is thought to be effcetive in EAN. Despite the fact that loss of physical and cognitive well-being constitutes a risk, it is stated that social support helps protect the elderly (19,4).The findings are consistent with what literature there is in a 2008 study (4). In this study greater social support was found to be associated with a 59% lower risk for EM (OR = 0.41 (0.19–0.90). In another study(20) low social support was stated as strongly predicting reporting abuse and neglect. In another study, (19) 701 subjects, aged 60 and over (mean 77.8 8 8.5), who were seeking home and community-based services in Michigan were examined. That study found out that those with a brittle support system may pose an increased risk for EM (OR = 3.76 (1.58–8.93). In an Indian population, (16) examined 400 community-dwelling adults aged 65 and over. In the binary regression analyses, the study found that low levels of social support may be associated with an increased risk of EM (1.07 (1.04–1.09)). Our current understanding of the temporal relationship between elder abuse and neglect and perceived social support remains limited.

Evidence suggests that perceived low social support may pose as a risk factor for elder abuse and

neglect The results of our study are consistent with prior findings in other countries, and further demonstrate that perceived higher social support may be protective against EAN in a Turkish population.

The results of this study show that the prevalence rate of elder abuse and neglect in Turkish population is 28.5 % in various types of abuse. These rates are higher than the rates in the USA (19.2 %) and China (20%) (21,6). Also, in two different studies conducted in China, it is reported that a total 36 % and a total 35.2 % were subject to elder mistreatment (20,4). From the findings of this study, it can be deduced that almost one in three elderly experiences abuse and neglect.

Nurses in acute care and outpatient settings are in an ideal position to detect abuse and neglect. To act as patient advocates, they must have increased awareness of the problem, as well as pertinent knowledge and skills to assess and intervene appropriately in cases of elder abuse.

The finding in this study that older men are more likely to experience abuse than women is contrary to the findings from other studies (22). This may be related to the tradition as well. Caregivers may find it more difficult to care for males than for women. Similarly, it may be because the Turkish men outspeak EAN than women or the women are more tolerated than males against negative behaviours of caregivers. However, it is similar to the result from a study in China (20). Those findings were that of the 145 EAN victims, 41% were women, and 59% were men.

Although China and Türkiye have great differences, in both countries women, at any age and situation, are more tolerating. The fact that they are both tradition-based countries may be playing a crucial role in this situation.

In this study, emotional abuse was the most frequent type while physical abuse was the least. Although the abuse rates and types vary in different studies, psychological and physical abuse are respectively reported to be the most common (21).It is estimated that approximately 3% of older Americans (21). 4% of older Australians and 6% of older Dutch experience some form of abuse. In a national study of over 12,000 Australian women aged 70–75, the prevalence of vulnerability to psychological abuse was estimated to be between 1% and 6%, and coercive behavior involving physical abuse was experienced by 1%–4% **(17).** It is reported in a study by Yan and colleagues that (6) verbal abuse is the most common (%20,8).

In this study, where types of abuse and neglect show social differences, psychologic abuse and neglect can be said to be the most common. Physical abuse and neglect is the type which is seen the least. Since the idea of pilial piety is still explicitly dominant in Türkiye, physical negative behaviour and bad treatment to old people is a taboo.

There were no elderly people expressing sexual abuse in this study. The fact that sexual abuse is not identified as abuse by the elderly may be due to absence of it in reality. On the other hand, it may also be due to inadequate knowledge of the elderly on this subject or to the fact that they don't regard these behaviours as abuse. Similarly, probable sexual abuse between husband and wife may not be regarded as abuse in marriage or in the family and this may be regarded as a private matter that should not be shared with anyone else.

The number of elders stating emotional abuse is higher. It may be because this kind of abuse is more widespread in the society. In another study conducted on elder abuse in Türkiye (23), it is reported that a total of 0,4 % of the elderly is exposed to sexual violence. It will be possible to have more clear information on the rate of sexual abuse as the studies on elder abuse increase.

On the examination of the information, it is seen that performers of abuse and neglect consist of many people (family members, relatives, neighbours and friends), but family members, mostly the children, are found out to be in the first place as performers of abuse This kind of elder abuser in Turkey is similar to the results of a study in Korea (22) in which a son or a daughter is the most frequent abuser.

In the study, the elder's being male or female, having a good education, being married, living alone or with family members are found to be risk factors not related to abuse.In Shugarman and his colleagues' study (19), the relationship between age, sex, marital status, education level and abuse is also not found significant. The findings of these two studies seem to be correlated. However, there are other studies which have different findings. Buchwald and colleagues (24) state in their study that the ones who experience physical abuse are

the women and old people who have health problems. There are also some studies showing that living together increases the occasion of abuse (25), as well as the studies showing that people living alone are more prone to experiencing abuse (22).

It is detected that the state of having good economical conditions and some income, assets and savings is related to abuse ($p<0.001$). Karaoğlu & Aydın (2008) (23) in a study conducted among the elderly aged 65 and over, stated that the elderly who have a registered real estate of their own and a good income have a significantly lower rate of abuse.The findings of both studies seem to be in accordance and indicate that the state of having a good income and assets may be a factor lessening abuse. This situation may result from the fact that the people having better economic conditions are respected more by the people they are in contact with. Another reason may be that the elder is able to use his/her economic wealth without being dependent on other people.

Lımıtatıons

The results of our findings limit the generalizability to the entire population of older adults in Turkey. This is a cross-sectional study limited with the examination of the association of perceived social support and other effective factors with elder abuse and neglect, limiting inference on causal direction. Further prospective study is needed to longitudinally quantify the temporal relationship of risk factors and elder abuse and neglect. On the other hand, this study does provide valuable insight to self- reported elder abuse and neglect and it is associated with factors in this Turkish population.

Conclusıon and suggestıons

In Turkey now there are laws regarding the abuse of older people, that include mandatory reporting and prescriptions for treatment of the abusers within the criminal justice system. Healthcare providers now recognize elder abuse as a real and serious problem. Nevertheless, there is a clear need for more provider education and outreach to train providers to recognize the signs of abuse and neglect of older people.

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Effects of selected combined training on muscle strength in Multiple Sclerosis patients

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Abstract

The purpose of this study was to determine the effect of eight weeks combined training on muscle strength in multiple sclerosis patients. Twenty volunteers men were randomized into two groups, experimental group (N =10) and control group (N=10).The experimental group participated in selected combined training program 3 times a week for 60 minutes and the control group did not participate in training protocol and performed routine program. Participants completed pretest (included testing on all muscle strength measures: chest press test, knee extension and paddle test), before begin of the intervention and after 8 weeks, completed posttest. The data were analyzed with SPSS18 software and t- test for paired samples significant with level at (P≤0/05). The result of this study showed that combined training on all muscle strength measures in experimental group were significantly increased (P<0/05). But improvement in all muscle strength measures in control group MS patients did not significantly increased (P>0/05). However, the result suggests that combined training program can increase muscle strength in multiple sclerosis patients.

Key words: combined training, multiple sclerosis, and muscle strength.

Introduction

The Multiple Sclerosis (MS) is the most prevalent disease of the central nerve system. MS is a chronic disease which effects on different aspects of individual life.[1] The prevalent symptoms of MS include reduction of ability in the walking and balance, increase of skeletal muscle weakness and tiredness that leads to reduction of movement, and the reduction of movement in these individuals leads to atrophy of muscular fibers, which the consequence is the muscular fibers reduction of slow twitch fibers [2].

MS can have a negative impact on both physical and psychological well being [3,4], and individuals with this disease often report lower quality of life scores than when compared to healthy individuals [3]. Fatigue and depression levels are higher in MS patients than healthy individuals, and these conditions may negatively impact upon quality of life. However, participation in regular physical activity has been suggested to positively influence feelings of fatigue [5,6] and depression [7], as well as modify quality of life [8,9] in persons with MS. Fatigue is the most common symptom reported by persons with MS [3,10], and has been negatively associated with quality of life scores [11]. In many MS patients show reduced physical activity levels and suffer from inactivity- induced muscle atrophy and loss of muscle strength, reducing daily life physical functioning as indicated by Motl et al.[12] To date, resistance training may also improve contractile characteristics, cellular respiration, quality of life and walking speed and distance, which have been reported to be deficient in MS.[13,14,15,16] Cross-sectional analyses in non-MS populations suggest that individuals who participate in regular exercise are less likely to suffer from depression [17]. If regular physical activity also positively influences depression in persons with MS, then it follows that associated improvements in quality of life may be observed.

As a consequence, MS patients are neither able to fully activate muscles in the lower limbs [18-19] nor to drive active motor units at high firing frequencies (rate coding) [20]. Accordingly, the muscle strength of MS patients is 30-70% lower compared to healthy control subjects, stating that muscle

weakness is a common symptom of MS [21-19]. Strength training has been shown to increase the neuromuscular activity in skeletal muscles through the use of surface electromyography [22].

Chronic mild to moderate stroke patients often have a non-paretic and paretic body side caused by upper motor lesions resulting in asymmetric muscle strength.[23,24] Because in a healthy population resistance training induces greater neuromuscular adaptations in weaker versus stronger muscles,[25] progressive unilateral resistance training has already been applied in stroke patients to optimize training stimulus. As observed by Chung et al., many MS patients also develop asymmetric leg strength.[26] However, given the underlying disease mechanisms such as increased central conduction time[27] and reduced motor unit recruitment and firing rates,[28] it is unclear if unilateral strength training in MS has similar effects.

In a study of the time of walking at short distances (7.62m) 12% and high distances (500m) 16% and 10% showed increase of knee flexor and had no effect on knee extensor, aerobic power, balance, Expanded Disability Status Scale (EDSS) and life quality of these patients [29].

De Souza–Teixeira et al have studied of the effect of an eight-weeks progressive resistance training on different strength manifestations, muscle mass and functionality in multiple sclerosis. The exercise was done during 8 weeks 2 times in a week. Intensity ranged from 40-70% of their maximum voluntary contraction. After 8 weeks strength training period, isometric strength 16%, muscles endurance 84%, and maximum power 51%, muscular hypertrophy from slice 6.27 to slice 11.67 of both things and functionality improved significantly [30].

Widener et al have studied resistance training effect on the balance on functional capacity of 16 of MS patients. They divided the patients to two groups of light and heavy, the light group wore a waistcoat with the weight of 0.23 kg and the heavy group wore a waistcoat with a weight of 1.5% of body weight while training. The results from investigation showed improvement in balance and functional capacity at the both of groups [31].

Dalgas et al have studied effect lower extremity progressive resistance training during 12 and 24 weeks on improvement of muscle strength and functional capacity of 38 MS patients. The exercise group completed a biweekly 12-week lower extremity progressive resistance training program and was afterward encouraged to continue training. After the trial, the control group completed the progressive resistance training intervention. Muscle strength of the knee extensors and functional capacity improved after 12 weeks of progressive resistance training in the exercise group, and the improvements were better than in the control group. The improvements of knee extension and functional capacity in the exercise group persisted at follow-up after 24 weeks [2].

Current research is demonstrating overwhelming benefits when people with Multiple Sclerosis exercise. Aerobic exercises and strengthening program improve maximal aerobic capacity [32] and muscular force production, power, work and endurance [33, 34].

Further benefits of exercise for people with MS include improved fatigue, cognitive ability and energy [35, 36]. Published exercise program have shown the benefits of specific strengthening regimens [37, 34], aquatic [33] and aerobic program [38, 32].

The duration of this program vary from four to fifteen weeks, with most participants attending three times a week. In a single case study of a person with MS Van Sint Annaland & Lord (1999) showed that a combined program of aerobic, strengthening and balance exercises was beneficial but again the participant attended the program three times a week over a five-month period [39].

Combined training is advanced type of exercise which is not specified its effects on the physiological adoptions of body, few researches used the combined training their executive protocol was executed at home and was not under the observation and gathered information was the result of participants feeling in the research, which the results of research should be studied carefully. Also primary results show that the tolerance of MS patients to combined training is better than endurance and resistance training and also this should be studied carefully. So with regard to existence of intensive protocols and the number of different frequencies and alternations in this type of exercise, extensive studies should be done to all of the aspects related to this way of exercise be reviewed. To the authors' knowledge

the reported resistance training studies in MS all use 'classical' bilateral training methods.[21,22] Unilateral resistance training applying relative workloads to investigate strength gains in weaker versus stronger legs has not been applied in this population yet [13].

The present study compared functional capacity, balance and muscle strength in persons with MS who did regularly participate in physical activity. It was hypothesized that persons with MS who participated in regular physical activity would report favorable functional capacity, balance and muscle strength when compared to those with MS who were classified as Non-exercisers.

The purpose of this study was to assess the effects of a 8-week selected combined training on muscle strength in subjects with EDSS. So researcher wants to answer following question: Does the combined training increase muscular strength of MS patients?

Methods and Materials

Twenty of MS male patients, free from any other known disease, were recruited while attending a selected combined training at Mazandaran in Iran. All subjects participated in daily physical activity for six months prior to the study (3 times per week). EDSS score in the participants were ranged from 2 to 3.5, indicating moderate disability and consumed interferon α. Subjects gave informed written consent prior to participation.

The volunteers were randomized into two groups, experimental group (N =10) and control group (N=10).The experimental group participated in selected combined training program and the control group did not participate in training protocol and performed routine program. Before testing, each participant completed a familiarization period (2 sessions), which included testing on all muscle strength measures: chest press test, knee extension and paddle test. After the familiarization period, participants completed pretest before begin of the intervention and after 8 weeks, completed posttest. The scores of pretest and posttest were registered by researcher. All testing sessions were performed at approximately the same time of day.

Procedures

The muscle strength training consisted of eight weeks of selected combined training performed three times per week. Subjects in experimental group performed four different exercises (combined training) after 5 minutes warm up.

A training protocol can be described in terms of sets, repetitions and load. Between set and exercises a rest period of approximately 2-3 minutes was allowed. The program was to increase the absolute level of peak torque of the muscles throughout repeated maximum strength. The principle of the program was to have low-load, relatively long pauses of rest between exercises and at least 1 day of rest between the training sessions. The intention was to perform 3 sets of exercises, with 10 repetitions of each exercise per set (3x 10), and exercised at least 3 days per week for 60 to 90 minutes per session. If the subjects managed to perform the exercises against resistance, the load throughout the training was 40% to 50% of 1 repetition maximum, defining 1 repetition maximum as the maximum load a subject was able to sustain throughout the range of motion.

The resistance training protocol was adopted from American College of Sports Medicine's resistance-training guidelines and recognized criteria for load assignment in older individuals.[40] The training protocol for experimental group were included strength exercises, aerobic fitness (stationary cycling) and balance exercises, and were done three times per week for eight weeks under the supervision of one physiotherapist. The resistance used in the strengthening exercises was progressed by increasing the number of repetitions performed.

Statistical Method

Data were expressed as mean and standard deviation. Data analysis was performed using pretest to posttest changes that assessed by t- test for paired samples. $P \leq 0.05$ was considered statistically significant. SPSS version 18.0 was used for all statistical analyses.

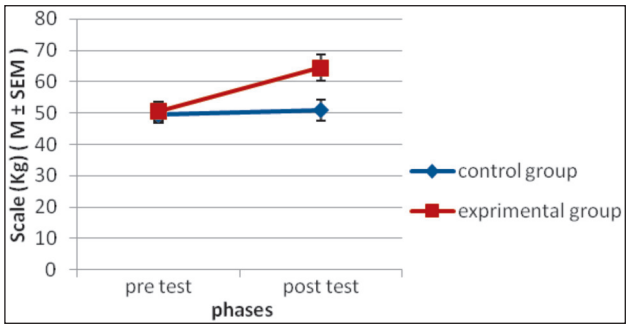

Figure 1. Mean ratings of pretest and posttest during chest press test

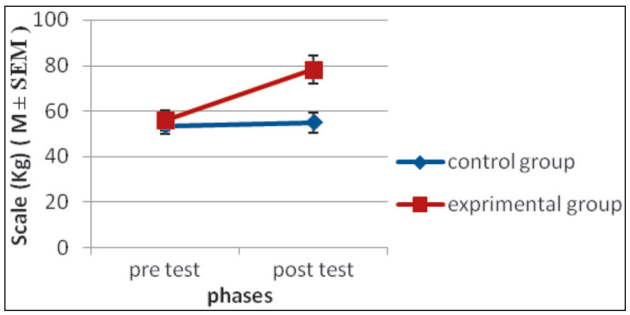

Figure 2. Mean ratings of pretest and posttest during extension knee test

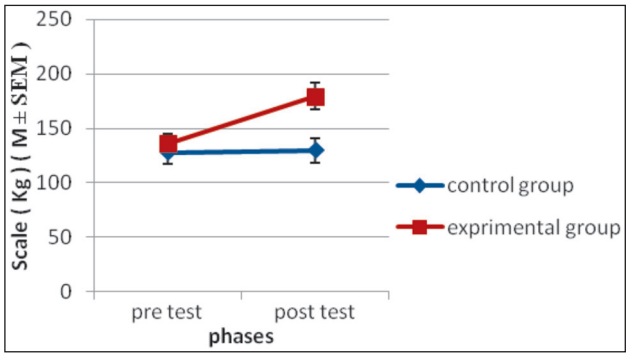

Figure 3. Mean ratings of pretest and posttest during paddle test

Results

There were no differences between the groups in any of the pretest measures. All patients in the experimental group were able to complete 24 sessions during the 8-week period.

The Figure1 showed the relationship between the pretest and posttest scores in chest press. Correlation of the experimental group between pretest (50.60±3.07) and posttest (64.50±4.16) was statistically significant and for the control group did not significant changes between pretest (49.45±2.74) and posttest (50.95±3.40) in chest press test (P≤0.05). The Figure 2 showed the relationship between the pretest and posttest scores in knee extension test. Correlation of experimental between among pretest (55.89±4.36) and posttest (78.23±6.03) was statistically significant and for the control group did not significant changes between pretest (53.48±3.54) and posttest (55.00±4.39) in knee extension test (P≤0.05). The Figure 3 showed the relationship between the pretest and posttest scores in paddle test. Correlation of experimental group between pretest (135.70±8.87) and posttest (179.10±12.21) was statistically significant and for the control group did not observe significant changes between pretest (127.65±10.62) and posttest (129.62±11.31) in paddle test (P≤0.05).

Pretest and posttest results for the measures of muscular strength tests were presented in above Figures. No differences between training modes (resistance-exercise and routine exercise) were found for any of the measures of muscular strength tests in pretests. However, analysis of the data found that all measures of experimental group significantly improved with 8- week combined training protocol.

Discussions

It is obvious that MS patient have deficits in various areas of physiological profile. In theory, optimal rehabilitation aiming at a normalization of the physiological profile would therefore require the application resistance training. Presently, the concept of combined training is however so sparsely investigated in MS patients that solid evidence-based recommendations cannot be provided [13].

In this study, significant increases for experimental group in chest press, extension knee and paddle test were found and no significant differences for control group in chest press, extension knee and paddle test observed. These changes are more indicative of normative tests of subjects without known impairments and thus support our hypothesis. Furthermore, our subjects showed improvements in chest press, extension knee, paddle test and isotonic muscle strength.

Limited research has been conducted on strength training in persons with MS. Kraft et al, found improved function, strength, and psychosocial well-being in 8 MS patients who strength trained for 3 months [41]. Debolt and McCubbin found

that a home-based resistance-training program was well tolerated by persons with MS and improved their leg extensor muscle power [42]. McCartney et al. found improvements in arm (19_/34%) and leg (11_/50%) strength after a nine week strength-training program [43]. In addition, Spector et al. found large increases in muscle strength in post polio patients [44]. For example, increases in knee extension (41_/61%) and elbow extensor (54_/71%) strength were observed following 10 weeks of strength training [44]. All subjects in this study completed the 8-week program with no appreciable musculoskeletal problems or exacerbation of MS symptoms. In addition, isotonic strength indices improved with training, suggesting that persons with MS can safely participate in a resistance-training program. These results are in agreement with those reported [1, 5, 15, 30, 45].

However, in that they observed improvements in muscle strength as a result of combined training program. In neither study, cartel et al. found that 12 weeks of twice weekly combined training were well tolerated, that muscle strength was improved, and that the level of effect of walking was reduced (46). In addition, Romberg et al. and Surakka et al. found that combined training was well tolerated by MS patients. Surprisingly, none or only small (10%) improvements were seen in knee extensor and knee flexor muscle strength after the training intervention, and no significant differences were noted when compared to the control group [29, 46].

The results of this preliminary study suggest that combined training program cause increase in muscle strength in MS patients. Brief moderate physical exercise improved physical fitness in the study by Bjarnadottir et al. [47].

The physiological reasons for the improvement in strength observed in this program were most likely due to neural changes. In the normal population it has been suggested that short-term training program, similar to that in the current study, have lead to more efficient muscle recruitment, increased neural activation and motor unit synchronization and a decrease in golgi tendon organ inhibition [48]. Harvey et al reported improvements in quadriceps maximum voluntary contraction (MVC) of 28-48%, this was not significant, which is probably a result of a small sample size (n=7) and suggested that people with MS undergo neuromuscular adaptations during strengthening program [37]. A further reason for observed changes in muscle strength in people with MS may be due to increased willingness and confidence of participants to participate in physical activity [34].

In this study, the isotonic strength in chest press, knee extension and paddle test improved significantly after training for experimental group. Although not statistically significant were observed in control group after routine daily training for all muscle strength tests. Also, results suggested that the routine daily training did not effect on muscle strength in MS patients. However, with a small sample size, additional studies are needed to confirm these observations. In addition, the combined training protocol used in this study may not have highlighted the full benefit or dangers of strength in persons with MS. Strength gains observed in this study should be interpreted cautiously because subjects trained isotonically, whereas strength testing were isotonic and performed on major limbs; therefore, the strength gains reported may not represent the entire strength. Despite these limitations, there were significant improvements in all parameters in experimental group that performed combined training protocol for 8- week. More studies that include muscle strength measures, with larger sample size, EDSS with high score, and increased duration and intensity of training, are recommended.

In conclusion, this paper reported on the effects of a combined training program on muscle strength for in MS patients. The results of the present study suggest that an 8-week selected combined training program can increase muscle strength in MS patients.

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An overview of chemoprevention of cancer

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Abstract

Chemoprevention is the therapy of cancer in which the cancer neoplastic cells or carcinogenesis is delayed, reversed or suppressed by means of chemical agents. Twenty different classes of chemo preventive compounds have been discovered, which are divided into two categories. These agents include the bioactive antioxidants and dietary compounds. Bioactive antioxidants are retinoids, carotenoids, selenium etc. Retinoids are compounds which resemble retinoic acid and maintain normal growth and epithelial differentiation. The anti cancerous activity of carotenoid is due to vitamin A activity, because a canthaxanthin in not a pro-vitamin-A but has chemopreventive affect. Selenium, an antioxidant dietary component is effective in cancer prevention during its initiation phase. Dietary compounds from plant source are photochemical e.g. polyphenolic and isothiocyanate (ITC) containing compounds occur in natural dietary sources. These are found in fruits, vegetables and herbs e.g. cactus, pear and green tea.

Chemoprevention is proving most appropriate and most protected therapy leaving less harmful effects than others therapies. Due to less toxic effects, this is a rational and most appealing strategy for the cure of carcinogenesis. The agents used in this therapy work at different steps either as antimutagenic or anti proliferative agents.

Key words: Cancer, Chemoprevention, natural Chemopreventive agents

Introduction

The most basic and possible way of preventing the cancer is to avoid the exposure and contact with carcinogens such as soot, cigarette smoke etc. by change in life style. But once the cancer is initiated, it can be prevented to develop fully by utilization of chemo preventive compounds (1;2).

Cancer chemoprevention is the therapy to delay or inhibit the development of cancer in the normal preneoplasic tissue by the use of drugs, vitamins or plant bioactive compounds. These agents reverse the cancerous process in the early stages of progression that leads to malignancy. Carcinogenesis is a long multistep process which takes about 10-30 years for its completion. It involves initiation, promotion and progression. **Initiation** includes the change in normal genetic events, **promotion** comprises of stimulation of cellular signals and expansion of initiated cells. The **progression** includes the malignancy due to the colonal cell expansion which is produced in the promotion stage (3;4).

The carcinogenesis can be prevented by targeting the initiation and ceasing the promotion and progression. The initiation of carcinogenesis can be targeted to avoid the exposure of cells to the carcinogens while the promotion and progression of cancer can be stopped by interfering the signaling pathways of the oxidative stress, inflammation and proliferation of cells (5). The cancer chemoprevention acts in two different routes. One is antimutagenic and other is anti proliferative. In anti mutagenic chemoprevention, specific drugs are used which block the uptake and activation of carcinogens. It can also be effective after the carcinogen activation by its carcinogen conjugation, thus leading to its inactivation and removal. The second is (COX) and lipooxygenases (LOX) activities, which lead usually to the procarcingenic activation into ultimate cancer. COX and LOX inhibition resumes apoptosis and reduces the angiogenesis thus leading to the cancer inhibition (6;7).

There are different compounds which play a vital role in chemoprevention. These are divided into two categories, natural dietary compounds and the synthetic compounds or drugs. The plant dietary compounds are natural bioactive compound e.g. antioxidants (8;9).

Natural dietary compounds are rich source of chemo preventive agents that have significant anti cancerous effect. Polyphenolic and isothiocyanate (ITC) containing compounds occur in natural dietary sources. Polyphenole has phenolic functional group and ITC has sulfur containing N=C=S functional group that are characteristics of these

compounds for being chemo preventive. Phenolic compounds are present in green tea and curcumin, while ITC containing compounds are present in cabbage, mustard, brassicas etc .Some compounds are not bioactive themselves but used in chemoprevention by their conversion to ITC through hydrolysis process e.g. Glucosonolates (10;11).

PEITC and SFN are included in ITC these chemicals play major role in the cell cycle arrest, apoptosis and inhibit the pathways. These are potent inducer of apoptosis. PIETC and SFN targets many pathways e.g. phase I and phase II. Drug metabolizing enzyme which carries out the oxidation in phase I and in phase II, the detoxifying enzymes are involved that conjugate with the endogenous substrates e.g. glutathione (SGH); SFN induces the phase II expression (12;13).

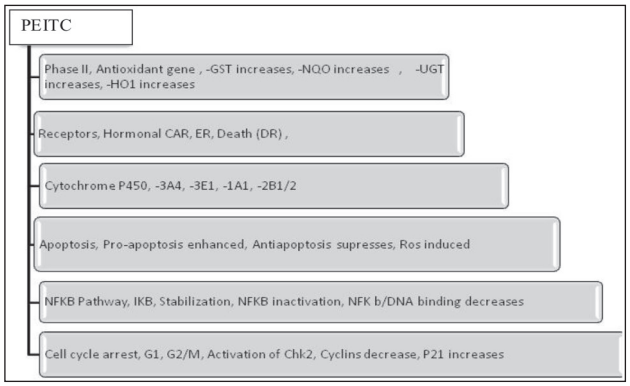

Figure 1. Potential molecular pathways targeted by PEITC. PEITC affect various molecular targets and pathways [Adopted from (14)].

Today 20 different classes of chemo preventive compounds have been discovered, which are divided into two categories. One which is effective against complete carcinogens and the second class eliminates the tumor promoters. Carcinogenic inhibitors are further divided into three sub classes. First prevent the formation of carcinogens from precursor compounds. Second are the blocking agents e.g. ascorbic acid which prevent the carcinogens to reach at target sites. Third class includes suppressing agents which inhibit the expression of tumor formation such as retinoids and carotenoids (15).

Retinoids are compounds which resemble retinoic acid and maintain normal growth and epithelial differentiation. These are often used singly for patients with very less mutations. Otherwise patients with high mutations are treated with combination of agents. Retinoids have the ability to regulate expressions via nuclear transduction. Signal modulation mediated by nuclear retinoid receptors of retinoids are thus helpful in chemoprevention of cancer because many types of cancer is caused by non expression of retinoid acid receptor e.g. head and neck cancer. Retinoids however have some limitations. They only work when cancer is in its promotional phase and their activity is also reversed when further doze is not given. The retinoids are toxic compounds thus their long term use is risky. Fenretinide is a synthetic retinoid which is experimentally proved to be preventive against breast cancer (16).

Carotenoids are also pigments found in plants when carotenoid are administered, they are degraded to retinol. An important dietry carotenoid, B-carotene is found to be anti cancerous. Skin and urinary bladder are found to be more effected by chemo preventive effects of B-carotene but it is under contradiction whether the anti cancerous activity of carotenoid is due to vitamin A activity, because a canthaxanthin in not a pro-vitamin A but has chemo preventive affect. A recent finding against vitamin A as a chemo preventive agent is that it is now found to be associated with the development of prostate cancer. But this carcinogenesis is most probably site concerned (17;18).

Selenium, an antioxidant dietry component is effective in cancer prevention during its initiation phase but like retinoids, its toxicity leads to further consideration about its use. Now it is found that there is a concentration range within which selenium shows its preventive activity i.e. 2ppm – 5ppm. Below 2ppm, selenium loses its activity and above 5ppm it becomes risky (19).

Some vegetables, fruits and other edible products are also found to be chemo preventive. Such as *Ganoderma lucidum*, an edible mushroom is utilized for this purpose. The bioactive compounds present in its extract cause inhibition of cancer invasion. The lucidenic acid present in it causes activation of extra cellular kinases which are involved in cell signaling. kinase activation then leads to the suppression of interleukin (IL-8), transforming growth factor (TGF) and endothelial growth factor (EGF), in order to prevent the cancer to invade (20;21).

Other compounds from plant source are phytochemicals. These are found in fruits, vegetables and herbs. They induce apoptosis by anti inflam-

mation and inhibit the metastasis in more developed tumors (22).

Cactus pear is also a natural product that is used for chemoprevention of cancer. Cactus extracts are useful for the treatment of cervical, bladder and ovarian cancer. These extracts are dose and time dependant and increase the apoptosis and growth inhibition in cancerous cells and immortalized epithelial cells. It interferes the phase G1, G2 and S phase and increases its duration in cell cycle. Cactus pear extract enhances the annexin IV and suppresses the VEGF expression in animal's tumor also. Annexin IV is a membrane binding protein and its binding depends upon Ca^{++} ions and has important role in apoptosis early stages (23;24).

Green tea is cultivated abundantly in many countries of the world and is consumed as a beverage. Before now, green tea was just appreciated for its taste and other health saving properties. But within the last 10 years, convincing evidences have obtained about the presence of polyphenolic antioxidant compounds in green tea which are responsible for cancer chemoprevention. The most important of which are epigallocatechin 3-gallate (EGCG); The (EGCG) in green tea inactivates carcinogens by inhibition of cytochromes P450 and urokinase enzymes by binding or blocking them. EGCG also causes induction of apoptosis, thus prevents the cells to enter in the uncontrolled cell division. The most important aspect of EGCG is that it is specific in its activity. It only inhibits the growth of cancer cells while the other surrounding cells remain unaffected (25).

Tamoxifen is an oral selective anti estrogen agent which reduces the rate of contra lateral breast cancer by 40-50% in ER+ women (estrogen receptor); Thus today, food and drug administration (FDA) approved the use of tamoxifen for primary prevention of breast cancer in ER+. However due to its toxicity as it can cause endometrial cancer, today research is being done to find out some novel and non toxic SERM's (Selective estrogen receptor modulator. Now-a-days, many other compounds are investigated which are considered to be chemopreventive such as leutinizing hormone releasing hormone. Other effective agents against breast cancer include raloxifene (6) and 4-hydroxifen (5) retinamide (7); Dietary calcium has also proved to be chemo preventive against colorectal adenomas. Besides this, non steroidal anti inflammatory agent e.g. aspirin is given in a specific concentration (80mg) which reduces the risk of colorectal cancer upto 40% (26).

The chemo preventive compounds however have some limitations in their use. The administration of dose, its recruitment is a complex process and a matter of careful consideration. The toxicity of the drug may also cause some risky situations. Also many of these compounds have proved to be anticancerous by their administration to mouse and some other animal models and thus they are not as effective on human body. The evaluation of the activity of chemo preventive agents at target sites is also a complicated process and intermediate markers must be developed before evaluation. Disappearance of these biological markers is usually associated with the decrease in cancer (27;28).

Retinoids and carotenoids are also under discussion today. These are effective against neoplasic cells but their administration is risky as they produce toxicity. In primary prevention trials, many agents which show remarkable preventive effect fail in secondary prevention. Even some agent e.g. B-carotene showed 18% increase in lung cancer, thus, it should be considered carefully that at which level and stage chemo preventive agent being used is effective (29).

Some drugs in this respect are under investigation e.g. EGFR inhibitors, VEGF-R inhibitors, demethylating agents, farnesyltransferase inhibitors, celocoxib, vitamin E and bowman – birk inhibitors. Today those compounds are considered to be ideal having little toxicity and high effectiveness against neoplasia. These both characteristics are not found in a single compound. Thus, to chose the appropriate compound for application against cancer is a matter of consideration today (30-32).

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Muscle lesion treatment in Brazilian soccer players: Theory vs. Practice

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Abstract

Background: In this study we evaluated the rehabilitation profile of Brazilian soccer players which underwent lower limb muscle lesions.

Methods: This is a descriptive investigation. We evaluated 139 professional soccer players (17-24 years old). We evaluated the following variables: muscle lesion diagnosis, symptoms, non steroidal anti-inflammatory used, physiotherapy treatment, which physiotherapy recourses was used if treated and train adaptation.

Results: In great part of the athletes muscle lesion remained between 2 weeks and 1month. Around 54% were diagnosed by a physician; the other part was diagnosed by a physical therapist. Non steroidal anti-inflammatory were prescribed by physicians in 42% of the cases; in 7% the physical therapist prescribed the medication while in 49% of the cases the masseur prescribed the drug. More than1/4 of the athletes received physiotherapy treatement between 48 hours and 5 days. Isometric exercise therapy was applied in 15% of the cases. 63% were not accompanied by the physiotherapist on their return to the field. 48% received massages immediately after injury.

Conclusion: We presented discrepancy between the recommended theory described by several researches and the practice. We indicate the necessity of recycling in a general context the rehabilitation of muscle injuries.

Key words: Sport; Sport Medicine; Athletic Therapy; Clinical Evaluation; Clinical Research; Injury Management.

Introduction

Skeletal muscle fatigue is an inevitable phenomenon in the training and competition routine for most athletes and may impair their performance and predispose the athlete to a variety of musculoskeletal disorders. This kind of harm may be transient, lasting minutes or hours after exercise, but it can also last for several days [1-5]. In the first few hours physical performance is impaired by metabolic disturbances that occur after high-intensity exercises [2]. Besides this type of musculoskeletal damage, traumatic lower limbs lesions are common in impact sports, such as soccer, which cause high incidence of muscle lesions [3].

Sports injuries in soccer games are still matter of concern for professionals. More so when faced with poor conditions of training, causing the athlete to their highest degree of performance for achievement of great results [6]. Although it is well described in the literature ideal rehabilitation methods in cases of muscle lesion in soccer players [7, 8], it is possible that some soccer clubs do not follow muscle lesions treatment protocols in the theory.

In order to verify if Brazilian soccer clubs follow this regulation, we endeavored to evaluate the rehabilitation profile of Brazilian soccer players which underwent lower limb muscle lesions.

Methods

Study Population

This is an exploratory cross-sectional descriptive research. We evaluated 139 male professional

soccer players (17 – 24 years old, 20.5 years old) from São Paulo teams. After we collect all the material it was performed to frequency analysis for further evaluation. All volunteers were informed about the procedures and objectives of the study and upon agreement they signed a consent letter. All procedures were approved by the Ethics Committee in Research of our University and followed the resolution 196/96 of the National Health Council 10/10/1996.

Inclusion Criteria

We considered the following inclusion criteria: Subject older than 16 years old, professional athlete according to Brazilian soccer laws, the athlete stayed away from sports for at least 1 week, present pain due to injury for at least 3 days, the injury must have occurred during training or competition and the athlete should be effectively linked to the club for at least 1 year.

Exclusion Criteria

Athletes who were younger than 16 years old, not registered in the Professional Soccer Paulista Federation, did not stay away from sports for at least 1 week, did not present pain due to injury for at least 3 days, which the injury was not occurred during training or competition and who were not linked to the club for at least 1 year were excluded. Among the 139 athletes, 16 athletes were excluded from the study according to our exclusion criteria.

Variables Evaluation

An interview was elaborated according to the advice of 5 technical specialists professional. Data collection was conducted through an interview survey developed especially for this study, consisting, in general, identification of the athlete, school degree, time of sports practice, a position in which it he plays, the occurrence of injury during practice sports, athlete rehabilitation before the injury and period of return to sports. The interview was administered only in athletes who presented muscle damage, they answered objectively to all issues of the instrument made directly by the researcher.

We evaluated the following variables:

- Muscle lesion diagnosis: which clinical professional made the diagnosis and complementary examination;
- Symptoms: Period the pain spent (more than three weeks, more than one week, more than two weeks and more than one month);
- Non steroidal antiinflammatories: The period when it was used (immediately after the injury, 24 hours after the injury, 48 hours after the injury and five days after the injury) and who prescribed it (physician, physical therapist or masseur);
- Physiotherapy treatment: Immediately after the injury, 48 hours after the injury, five days after the injury, one week after the injury or it was not treated;
- Which physiotherapy recourses it was used if treated: Ice treatment (immediately after the injury, 24 hours after the injury, 48 hours after the injury or five days after the injury), massage with the masseur (immediately after the injury, one day after the injury, two days after the injury or three days after the injury), ultrasound, microwave or short wave (immediately after the injury, one day after the injury, two days after the injury or three days after the injury), micro currents (immediately after the injury, one day after the injury, two days after the injury or five days after the injury), isometric exercises with or without pain;
- Train readaptation: how many days the athlete spend to return to train (one week after the injury, two weeks after the injury, one month after the injury or more than one month after the injury).

Statistical analysis

We performed descriptive analysis by using Microsoft Office Excel®. For each variable we classified in percentage.

Results

Among all soccer players evaluated (123), the majority (68%) presented injury on the right leg. Table 1 presents the period which the pain spent; in great part of the athletes muscle lesion remained between 2 weeks and 1month. Approximately 54% of the cases were diagnosed by a physician, while the other part was diagnosed by a physical therapist. Around 39% of the cases received complementary examination.

Table 1. Period which the pain spent

Period	%
< 3 days	24
1 week – 2 weeks	23
2 weeks – 1 month	39
> 1 month	14

Among all cases, non steroidal anti-inflammatory were prescribed by physicians in 42% of the cases; in 7% the physical therapist prescribed the medication while in 49% of the cases the masseur prescribed the drug. The majority of the cases received the medication immediately after the injury (Table 2). We observe in Table 3 that almost 60% of the sample remained more than 1 month away from training and sports activity.

Table 2. Non steroidal anti-inflammatory treatment onset

Period	%
Immediately	46
24 – 48 hours	9
48 – 5 days	14
After 5 days	29
Did not use	2

Table 3. Period which the athlete remained away from sports and training activity

Period	%
≤ 1 week	10
1 week – 2 weeks	15
2 weeks – 1 month	18
> 1 month	57

Table 4. Period when the athlete started to receive physiotherapy treatment

Period	%
Immediately	19
48 hours – 5 days	33
5 days – 1 week	11
After 1 week	28
No physiotherapy treatment	9

In relation to physiotherapy treatment, we observed that more than1/4 of the athletes was treated between 48 hours and 5 days. Physiotherapy recourses are presented in Figure 1 (Cryotherapy), Figure 2 (Laser therapy), Figure 3 (Microwave) and Figure 4 (Deep heat treatment). Isometric exercise therapy was applied in 15% of the cases. With respect to athlete's rehabilitation, we found that 63% were not accompanied by the physiotherapist on their return to the field. With respect to massages, 42% did not received massages, while 48% received immediately, 6% one day after injury, 2% three days after injury and 2% two days after injury.

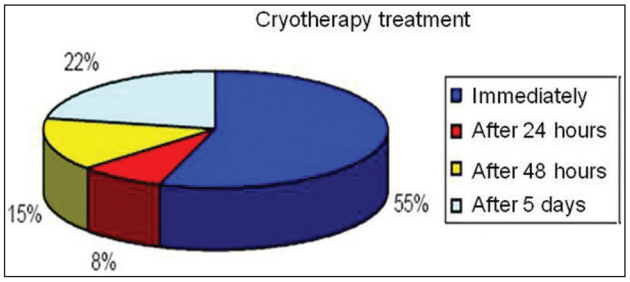

Figure 1. Cryotherapy treatment onset after muscle lesion

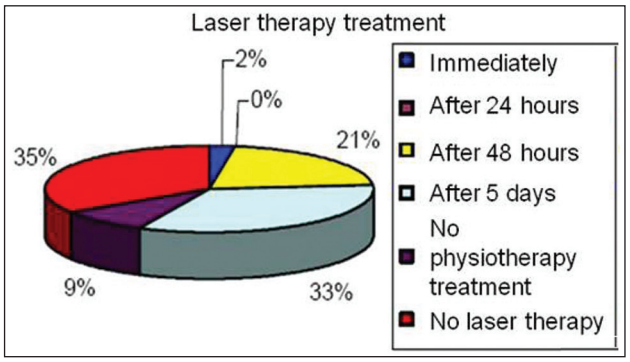

Figure 2. Laser therapy treatment onset after muscle lesion

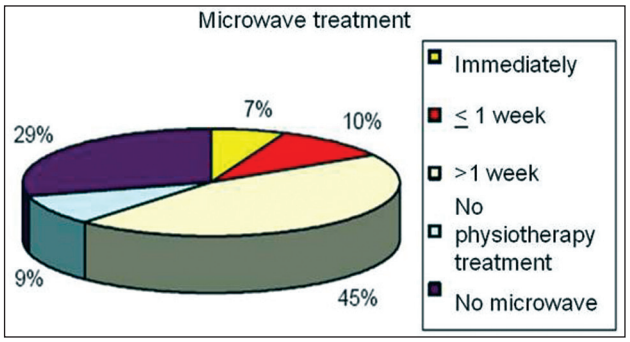

Figure 3. Microwave treatment onset after muscle lesion

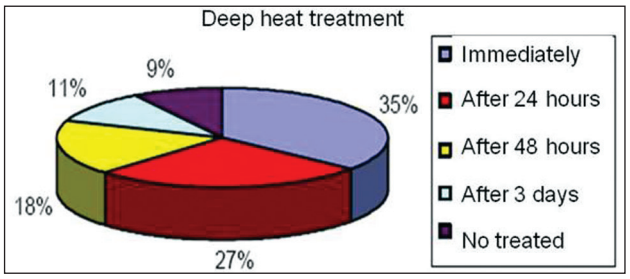

Figure 4. Deep heat treatment onset after muscle lesion

Discussion

The treatment of muscle injury is diversified if we consider the several achievements that we observed in this study. However, it is almost impossible to confront and discuss with the current literature, which is clear and relevant [9-11]. According to the muscle injury location, our results are supported by the literature, which shows hamstring muscles as the most affected chain [12, 13].

The diagnosis is an inevitable issue in our study because it is well known that doctors are responsible for complementary examination solicitation. Conversely, we reported that 46% of the requests were made by physiotherapy professionals. It leads us to believe that the physiotherapy professional often takes decisions on diagnosis. We suggest that a multidisciplinary team involvement should be discussed.

Pain is strictly subjective and very important for muscle injury diagnosis and treatment, since the success of any rehabilitation is closely linked to the pain that the athlete presents, leading to almost all clinical outcome [14, 15]. We observed that most of the athletes had severe pain, further solidifying the importance of pain in the treatment of muscle injury. This pain remained for more than two weeks, suggesting a lesion in the second degree, which causes edema formation and imminent functional disability.

The use of anti-inflammatory drugs was made in more than a peculiar form, because its applicability varied significantly, contrary to the literature that is very clear when it states its use immediately to injury [16, 17]. It is obvious the question regarding our results, which do not support the literature and in some cases it was administrated five days after the injury. The literature is objective as regards the regeneration of skeletal muscle tissue, making it clear that after five days the healing process is already often in the chronic phase [19], which does not indicate the use of anti-inflammatory drugs.

Another very relevant issue that we found and which should be also be discussed is anti-inflammatory prescription by the masseur. The question is very easy because we know that the masseur has no academic formation and therefore he is not able to clearly understand the collateral effects that many anti-inflammatory cause, which must be specified and prescribed only by the professional who gets the right and authority, i.e. the physician.

In relation to the therapy used, we found contradictory expressive and numbers compared to the literature. We reported that 33% of the athletes started to be treated 48 hours after muscle lesion, according to the physiological effects of cryotherapy, i.e. cryotherapy loses its efficiency when it is not applied immediately, it loses its ability to control secondary hypoxia [20]. Another factor found in our investigation that contradicts the literature is the finding that that 48% of the athletes receive massages immediately after injury. In the acute phase of any injury massage is contraindicated by the literature [21]. It is noteworthy that massages were made by the masseur and not by the physiotherapy professional.

According to our data, the applicability of microcurrent and laser were not in agreement with the literature, since the literature is very clear about the physiological effects of heat in the acute phase of injury. Microcurrent and laser therapy if applied immediately cause numerous undesirable outcomes such as vasodilatation and increased permeability of blood vessels [22].

Regarding isometric exercise, our results do not support the literature. Pain is often a limiting factor for certain procedures and sometimes it is a powerful clinical mediator, especially when we emphasize muscular injuries in soccer players. The numbers presented in this study are alarming because isometric exercise should never be performed when the patient relates pain, mainly of muscular origin [23], extremely relevant in this case.

With respect to athlete's rehabilitation, we found that 63% were not accompanied by the physiotherapist on his return to the field, which undoubtedly is of paramount importance for a safe return. Recurrences are responsible for leave athletes away from their activities [24], causing sometimes invaluable prejudice to the club. We propose to recycle archaic concepts and customs, where soccer is inserted. It is the time to bane the empirical moment from professional soccer which will consequently lead to scientific consciousness and cause a major benefit to the athlete, and therefore the club. Furthermore, new devices are being developed in order to improve athlete's rehabilitation [25].

Although the total incompatibility of the numbers in this study compared to the ideal in the literature, the athletes in our study remained in average one month away from games. Our data deserve relevance since we showed that 46% of the athletes underwent injury in the right thigh, while in 81% there was no complementary examination. We also emphasize that 57% of the athletes stayed away from sports activities, the 35% of the athletes who underwent deep heat immediately after the injury and the 45% who used microcurrent a week after the injury. Cryotherapy was evidenced in 22% which were treated five days after injury and 76% of the athletes performed isometric exercise therapy with pain.

In conclusion, our investigation presents discrepancy between the recommended theory described by several researches and the practice. Our results show the necessity of recycling in a general context the rehabilitation of muscle injuries, emphasizing consistency as a major factor, an important item in front of the complexity of muscle injuries in professional soccer players.

Acknowledgement

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The Relation between Air Pollution and Respiratory Tract Diseases in Duzce City by Months

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Abstract

Aim: In this study, it's aimed to investigate the relationship between the levels of particulate matter (PM_{10}) and sulphur dioxide (SO_2) and the admittance of the patients with the diagnosis of COPD, asthma, respiratory tract diseases to policlinics in the central part and counties of Duzce.

Materials-Methods: Between 1 January 2009 and 31 December 2009 in Duzce Ataturk State Hospital, the patients diagnosed as COPD, asthma, acute bronchitis, pneumonia, acute nasopharyngitis, acute pharyngitis, acute tonsillitis, allergic rhinitis at chest diseases, internal medicine, ENT, pediatric polyclinics were retrospectively evaluated. The monthly average values of SO_2 and PM_{10} of Duzce had been obtained from the official data of Ministry of Environment and Forests.

Results: Fifty-three percent (15,606) of total 29,367 cases were female. 64.4% of the cases were adults. The average SO_2 and PM_{10} concentration of Duzce city was highest in November, December, January and those were the lowest in July, August, September and October. The applications with the diagnosis of acute bronchitis were higher than the remaining applications in January (26.9%) and December (25.4%), while those were the lowest in July 16.4%) and September (20.4%), respectively. The applications with the diagnosis of COPD were more frequent in January (10%), February (10.9%), March (13.1%), but less in September (5.9%). The cases with asthma were most admitted in December (10.6%), January (9.6%) but less frequently in September (6.1%) ($p = 0.000$). Also the pneumonia cases were frequently admitted in November (10.6%), January (9.6%). The admission rates of the patients with COPD, asthma, acute bronchitis were similar among the central part, seaside and far from seaside. The most common admittance was due to the allergic rhinitis at the seaside part (119/479, 24.8%) ($p = 0.000$). Upper respiratory tract disease applications (58%) were higher than the lower respiratory tract diseases applications in the months that the air pollution was the highest ($p = 0.000$).

Conclusion: It was speculated that polyclinics admissions of COPD, asthma, acute bronchitis, pneumonia, acute nasopharyngitis, acute pharyngitis, acute tonsillitis, allergic rhinitis seemed to be associated with air pollution and also living in the seaside may lead to more increase in applications regarding allergic rhinitis.

Key words: air pollution, Duzce, COPD, asthma, respiratory tract diseases.

Introduction

In this study, it's aimed to investigate the relationship between levels of particulate matter (PM_{10}) and sulphur dioxide (SO_2) and the rate of the admittance of patients with COPD, asthma, respiratory tract infection in the central part and counties of Duzce. A number of studies have shown that the levels of PM and SO_2 are associated with mortality, hospital admissions, respiratory diseases (1, 2, 3). The most of these studies are included emergency department visits. Although the level of SO2 and PM declines in developed countries, it continues to threaten developing countries such as Turkey (4). On 17th August and 12th November 1999, two earthquakes occurred in Duzce. The first measured between 7.4 and 7.8 on the Richter scale. Duzce exhibits a remarkable diversity in placement and living conditions as a result of these two earthquakes (5). Increase in population and industrialization using fossil fuel in domestic settings and also vehicle exhaust emission are re-

asons of air pollution in Düzce. Also natural gas used recently. Ministry of Environment and Forestry make measurements of SO2 and PM, and these data are published officially (6).

Materials and methods

Between 1 January 2009 and 31 December 2009 in Duzce Ataturk State Hospital the patients diagnosed as COPD (J44), asthma (J45), acute bronchitis (J20), pneumonia (J18.9), acute nasopharyngitis (J00), acute pharyngitis (J02), acute tonsillitis (J03), allergic rhinitis (J30.3) at chest diseases, internal medicine, ENT, pediatric polyclinics were retrospectively evaluated using the International Classification for Diseases,(ICD-10). The monthly average values of SO_2 and PM_{10} of Duzce had been obtained from the National Air Quality Monitoring system archive of Ministry of Environment and Forests. The value of sulfur dioxide were considered zero in July, August and October, because they were not measured in those months. Data analysis was performed using the SPSS 13.0 for Windows software package Associations between air pollution and policlinic applications were investigated using statistical methods of multiple linear regression and bivariate correlation, Spearman's Rho test.

Results

53.1% (15,606) of total 29,367 cases examined from records were female. 64.4% of the cases were adults (18,903, mean age: 47.5 ± 17.9), 35.6% of cases (10,464, mean age: 6.1 ± 4.9) were children**.** COPD, asthma, pneumonia, acute bronchitis, acute allergic rhinitis and nasopharyngitis were observed in adult patients, whereas acute pharyngitis and acute tonsillitis were more common in children (Figure 1).

Acute bronchitis (21.2%) and acute pharyngitis (26.4%) were most commonly diagnosed while pneumonia (2.1 %) was less. Table 1 shows the observed incidence of diseases in all age groups.

The number of patients according to months has increased in March, December, January, February, November respectively (Table 2).

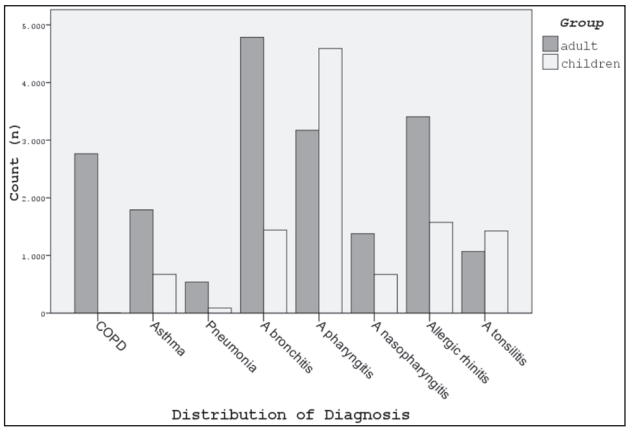

Figure 1. The diagnosis of adult and children patients

Table 1. Distribution of Diagnosis

Diagnosis	N	%
COPD	2767	9.4
Asthma	2465	8.4
Pneumonia	626	2.1
Acute bronchitis	6224	21.2
Acute pharyngitis	7762	26.4
Acute nasopharyngitis	2048	7.0
Allergic rhinitis	4981	17.0
Acute tonsilitis	2494	8.5

Table 2. Applications of patients according to months

Months	n	%
January	2979	10.1
February	2814	9.6
March	3127	10.6
April	2668	9.1
May	2393	8.1
June	2156	7.3
July	1911	6.5
August	1704	5.8
September	1565	7.5
October	2201	7.5
November	2779	9.5
December	3070	10.5

The average levels of sulfur dioxide (SO2) and particulate matter (PM10) of Duzce city were higher in November, December, January and were lower in July, August, September, October (Table 3).

The applications of patients with lower respiratory tract diseases regarding the months with the higher and lower air pollution levels were seen in Figure 2.

Table 3. The monthly measurements of SO2 and PM in Duzce

Months	SO_2	PM10
January	11	166
February	8	75
March	6	84
April	2	73
May	2	52
June	1	46
July	0	41
August	0	45
September	0	43
October	0	71
November	27	184
December	23	163

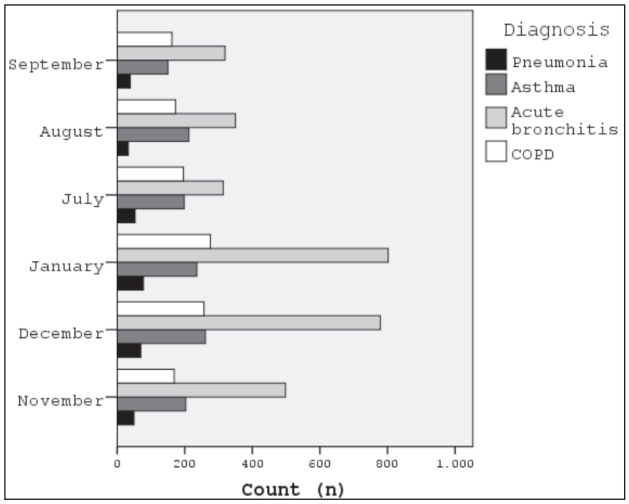

Figure 2. Distribution of lower respiratory tract diseases according to months

The applications of cases with acute bronchitis were higher than the remaining applications in January (26.9%) and December (25.4%), while those were the lowest in July (16.4%) and September (20.4%), respectively. The applications with the diagnosis of COPD were more frequent in January (10%), February (10.9%), March (13.1%), but less in September (5.9%). The cases with asthma were most admitted in December (10.6%), January (9.6%) but less frequently in September (6.1%) Also the pneumonia cases were frequently admitted in November (10.6%), January (9.6%) ($p = 0.000$). The distribution of upper respiratory tract diseases according to months with the highest and the lowest air pollution has shown in Figure 3.

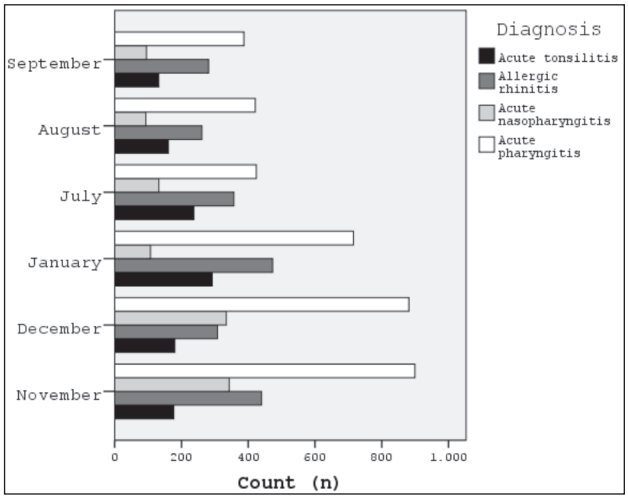

Figure 3. The distribution of the upper respiratory tract diseases according to months

The most frequent admission in patients with acute pharyngitis were in November (11.6%) and December (11.4%). Acute nasopharyngitis were frequently admitted in November (16.7%) and December (16.3%). Allergic rhinitis applications were the most common in January (9.5 %). Also tonsillitis was mostly admitted during January (11.7 %) ($p<0.001$). Upper respiratory tract disease applications (58%) were higher than the lower respiratory tract diseases applications in the months that the air pollution was the highest ($p<0.001$).

COPD, pneumonia, acute pharyngitis, acute tonsillitis were observed more frequently in males, whereas asthma, acute bronchitis, acute nasopharyngitis, allergic rhinitis were seen in women (Table 4).

Application rate of the patients with COPD among Düzce city center (2145/23835; % 9), the

Table 4. The frequency of diagnosis according to gender

	COPD	Asthma	Pneumonia	Acute bronchitis	Acute pharyngitis	Acute nasopharyngitis	Acute tonsillitis	Allergic rhinitis
Male	1941 (70.1%)	731 (29.7%)	355 (56.7%)	2746 (44.1%)	3806 (49%)	839 (41%)	1251 (50.2%)	2092 (42%)
Female	826 (29.9%)	1734 (70.3%)	271 (43.3%)	3478 (55.9%)	3956 (51%)	1209 (59%)	1243 (49.8%)	2889 (58%)

seaside (36/479, 7.5%) and towns away from the sea (586/5053, 11.6%) were considering similar. Asthma admittance rates were also similar among the center of Duzce city (1928/23835;% 8.1), the seaside (45/479, 9.4%) and towns away from the sea (492/5053, 9.7%). Also the rates of the patients diagnosed as acute bronchitis close to each other in the city center of Duzce (4995/23835, 21.0%), in the seaside (94/479, 19.6%) and towns away from the sea (1135/5053, 22.5%)

However, allergic rhinitis was observed much more at the seaside town (119/479, 24.8%) than in the city center of Düzce (4001/23835, 16.8%) and away from the sea (861/5053, 17%).

According to the regression analysis age (p=0.000, beta=-0,613, t=-69,637), gender (p=0.000, beta=-0.065, t=12,317) and living place (p=0.024, beta=-0012, t =-2,262) have had independent effects on the type of respiratory disease.

Discussion

A growing number of epidemiological studies investigating the relationship between air pollution and respiratory system have been done in Turkey. In a study made in Istanbul, a relationship was found between the application of patients to hospital because of acute respiratory tract diseases and the level of PM (7). In our study, pneumonia, acute bronchitis, pharyngitis, acute nasopharyngitis and acute tonsillitis were found associated with air pollution. Berk and his colleagues in Ankara have found a relationship between the concentration of SO2 and PM and emergency applications due to asthma (8). Keles and colleagues showed that air pollution is associated with allergic rhinitis symptoms (9). Significant associations were found among the SO2 levels and the upper and lower respiratory tract infections and the applications for emergency hospital because of COPD in Eskisehir (10). Furthermore a relation with asthma applications and the concentration of PM was observed in a study from Izmit (11). There was a relationship between the SO_2 levels and the upper and lower respiratory tract infections and also applications for emergency department have been increased due to COPD in Eskisehir (10), a relation with asthma applications and the concentration of PM in Izmit (11). In another study by Fişekçi et al, SO2 and PM values were found to be correlated with COPD-related emergency hospital applications (12). In our study, admission to clinic due to COPD and asthma were high in the months which the SO_2 and PM values were high. A study by Stieb and their colleagues in Canada found a strong association between PM 10 levels and the emergency department applications with asthma (13). In the United States, a significant relationship was determined between emergency administrations of 5416 asthmatic patients between the ages of 5-34 and the PM10 and SO_2 levels (14).

Also, Tolbert and colleagues reported the relationship between PM10 levels and emergency department visits with respiratory symptoms in the United States (15). Furthermore, Peel and his friends were observed a significant association between the increase in particulate matter and the patients with increased emergency service applications due to the lower respiratory tract infections, asthma and COPD (16). The present study showed similar results as the studies discussed above. Especially emergency visits and/or hospitalization rates due to the lower respiratory diseases increased regarding increased PM levels.

In a Japanese study planned to determine the prevalence of several allergic diseases among 2795 children in 12 elementary schools located in urban, seaside and mountainous areas, the prevalence rate of allergic diseases among school children was found as 24.6%. The common types of allergic diseases among boys were allergic rhinitis (11.3%), atopic dermatitis (9.7%), and bronchial asthma (5.7%), and those among girls were atopic dermatitis (9.7%); allergic rhinitis (6.5%), and bronchial asthma (3.7%). Analysis by residential area of the children, showed that the prevalence rate of allergic diseases in total was increased in the order of mountainous (20.8%), seaside (24.1%) and urban area (28.7%). The most common type of allergic diseases was atopic dermatitis in urban and mountainous area, while allergic rhinitis was most common in seaside area (17) In our study, allergic rhinitis, was observed most common in the seaside of the county (24.8%) while in Düzce city center (16.8%) and towns away from the sea (17%) were found to a lesser extent. COPD, asthma and acute bronchitis patients' applications were similar in the central city of Duzce, towns

in the seaside and away from the sea. There were some limitations in our study. First, it was a retrospective study performed in one center. We didn't examine individual exposure to air pollution. Contributory factors as occupational exposures, smoking and diseases were not evaluated in our study.

Conclusion

It was speculated that polyclinics admissions of COPD, asthma, acute bronchitis, pneumonia, acute nasopharyngitis, acute pharyngitis, acute tonsillitis, allergic rhinitis seem to be associated with air pollution and also living in the seaside may lead to more increase in applications regarding allergic rhinitis. Multicenter studies will produce more reliable results. Further studies are needed to clarify the association between particulate air pollution and respiratory diseases.

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Diagnosis and treatment of pediatric intussusception: 5-year experience

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Abstract

Introduction: Intussusception is relatively common cause of intestinal obstruction in children. The aim of this study was to evaluate the diagnostic value of applied diagnostic procedures and to define the most appropriate treatment option for intussusception.

Methods: Retrospective study included all children clinically suspected of having intussusception in a 5 year period, from 1-january-2005 to 31-december-2009. As data base were used features from hospital charts, ultrasound reports and surgical notes.

Results: Among 378 patients with clinically suspected intussusception, it was confirmed in 76 patients. The average age of patients with a positive finding was 1 year 7 months. Predominant signs and symptoms were abdominal pain (94.7%), vomiting (61.8%) and red currant jelly stool (53.9%). Previous infection was reported in 17 (22.36%) patients. There was no seasonal distribution of appearance of invaginations. Ileocecal form was found in 71 patients (93.42%). The head of the intussusceptum was mostly localized in the area of the hepatic flexure (28.94%). Pathologic lead points were indentified in 3 cases. Hydrostatic reduction was successful in 61 out of 74 patients (82.43%). Surgical treatment was required in 15 patients (19.73%). The average hospital length of stay for patients who had hydrostatic reduction was 3.4 days, while for patients undergoing surgery was 7.7 days. Diagnostic accuracy of clinical diagnosis was 96,5%, and of ultrasonographic diagnosis 97,5%.

Conclusion: Ultrasonography, as a safe procedure, has become a gold standard in diagnosis and minimally invasive treatment of intussusception in pediatric patients.

Key words: Intussusception; hydrostatic reduction; children; ultrasonography

Introduction

Intussusception is relatively common cause of intestinal obstruction in children, with the pick of incidence between 4 months and 2 years,[1] and male-to-female ratio of 2-4:1.[2,3] In up to 90% of cases intussusception seems to be idiopathic. Pathologic lead points occur most frequently in infants younger than 3 months and in children older than 3 years.[4] Intussusception occurs most often in well-fed boys with bright hair, after or during an inflammatory process of respiratory or gastrointestinal tract.[5] Clinical presentation is typical in most cases and physical examination alone can reveal a suspicion of intussuspection. For confirming of this diagnosis ultrasound (US) has been shown to be the first-line choice due to its efficiency and high diagnostic accuracy.[6] Immediately after the diagnosis of intussusception is made, this emergency condition needs to be treated. Since 1836, when the first case of nonoperative treatment of intussusception was reported, there have been attempts to avoid invasive treatment methods such as surgery, as well as the roentgenoscopy which involves ionizing radiation. Rectal air insufflation and the barium enema have been used for management of this condition, but sonographically guided hydrostatic reduction with normal saline has been shown as the best technique.[5]

The aim of this study was to determine the diagnostic value of the applied diagnostic procedures and to evaluate the efficiency of certain tratment methods and, based on that, to define the most appropriate treatment option for intussusception.

Material and methods

The retrospective study included of all children suspected of having intussusception presenting to the Institute for Children and Youth Health Care of

Vojvodina, Novi Sad between 1 January 2005 and 31 December 2009. The Institute for Children and Youth Health Care of Vojvodina provides tertiary pediatric care for Autonomous Province of Vojvodina which has a population of about 2 milion (about 27% of Serbia's total).

After initial clinical examination, all patients suspected of having intussusception were reffered to ultrasonographic examination. Clinical criteria for the clinical diagnosis of intussusception were the presence of at least two of following three clinical parameters: a history of intermittent abdominal pain, 'red currant jelly' stool and palpable abdominal mass. Sonographic criteria for intususception were the presence of the target sign seen on transverse sections (Figure 1.) and the pseudokidney sign on longitudinal sections. Hydrostatic reduction was performed directly after sonographic diagnosis of intussusception and a team include pediatric surgeon, anesthesiologist and radiologist who were always present during the procedure. The reduction was carried out in short intravenous anesthesia (midazolam 0,1mg/kg of body weight). A Foley catheter of the largest appropriate size (16- to 24-French) was inserted into the rectum, the balloon inflated with air, and the child was placed in the supine position with the thighs pressed together manually to ensure a tight anal seal. The catheter was connected to an intravenous fluid line and free flow of normal saline (pre-warmed to normal body temperature) was allowed into the rectum. The saline bottle was suspended at about 100 cm from the bed level. Gradual distention of colon and the retrograde movement of intussusceptum toward the ileocecal valve were monitored sonographically. The sonographic criteria for successful reduction were disappearance of the intussusceptum and reflux of fluid and air bubbles from the cecum into the terminal ileum through the ileocecal valve (Figure 2A,B). Procedure took approximately 15 minutes. Afterwards, the saline was drained and Foley's catheter was removed. In case of failure of progress of reduction, the procedure was repeated up to three times, in prolonged sedation. If hydrostatic reduction was unsuccessful, the child was taken to surgery. After reduction, a course of antibiotic therapy was started and patients were observed for at least 24 hours in the department of pediatric surgery, and were discharged when oral feeding and bowel movements were normal.

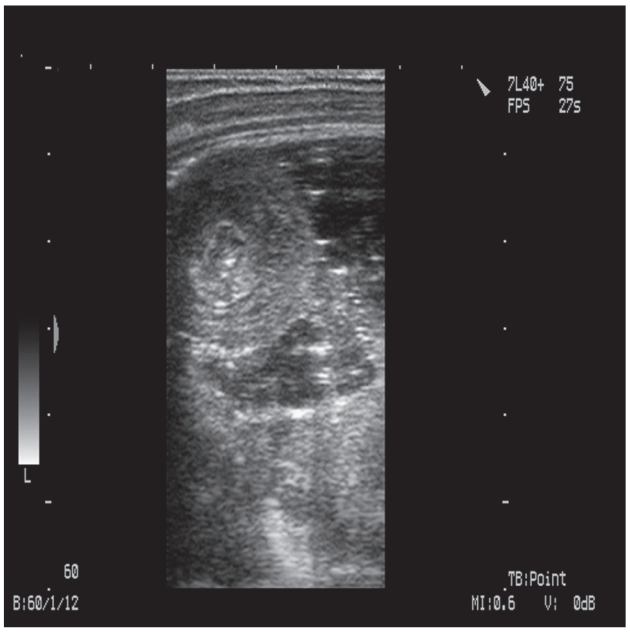

Figure 1. Sonogram shows the target sign seen on transverse section

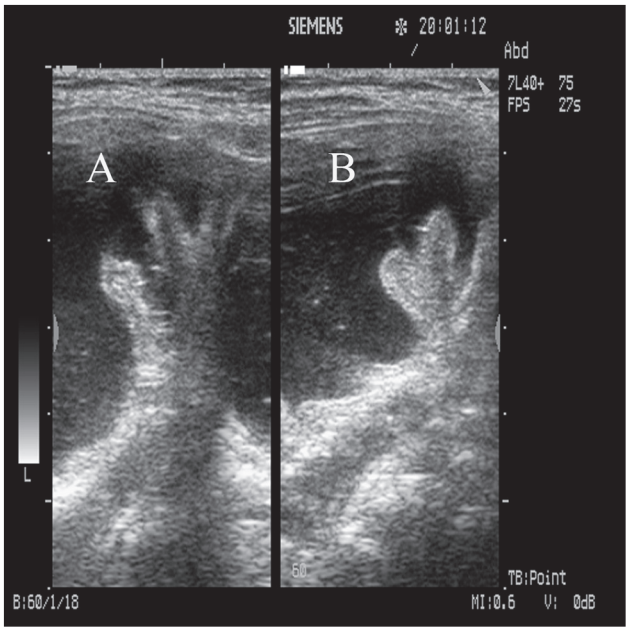

Figure 2. Sonogram shows the opened (A) and closed (B) ileocecal valve during the hydrostatic reduction

For our analysis, the following features were noted during review of the hospital charts, ultrasound reports and surgical notes: age at onset and the sex of the patient, presenting symptoms, duration of symptoms, seasonal distribution of intussusception, existence of a previous infection, a form

of intussusception, the site of intussusception, presence of leading points, treatment modality and treatment duration.

The chi-square test was used for the statistical analysis and differences at $P < 0.05$ were considered to be significant. We used Bayes' theorem to assess the diagnostic value of clinical and ultrasonography diagnostic methods, determining the sensitivity (Se), specificity (Sc), accuracy, predictive value of the positive test (PVPT) and predictive value of the negative test (PVNT) by defining true-positive, true-negative, false- positive and false-negative samples for both diagnostic methods. For clinical diagnosis: true positive were all patients in whom clinical findings indicated that there was intussusception and it was confirmed with ultrasonography; true negative were all patients in whom clinical findings indicated that there was no intussusception, which was confirmed by some other diagnostic method (US, rendgenography); false positive were all patients in whom clinical findings indicated that there was intussusception, but the US ruled out its existence; false negative were all patients in whom clinical findings indicated that there was no intussusception, but the US confirmed its existence. For ultrasonography diagnostic method: true positive were all patients in whom US revealed an intussusception, afterwards desinvagination was performed; true negative were all patients in whom US revealed that there was no intussusception, desinvagination was not performed, children were sent home and did not return to the clinic within next 48 hours; false positive were all patients in whom US revealed an intussusception, but during the desinvagination procedure it was shown that the presented formation was not the intussusceptum and saline solution smoothly passed through the ileocecal valve into the terminal ileum; false negative were all patients in whom US revealed that there was no intussusception, children were sent home but returned to the clinic within next 48 hours and underwent desinvagination.

Results

In the 5-year period 378 pediatric patients were admitted with clinical presentation which as a differential diagnosis could include intussusception. The same was confirmed in 76 patients, while in the remaining 302 patients intussusception was excluded. Two hundred forthy-three patients were referred for ultrasound examination.

Among 76 patients with confirmed diagnosis of intussusception, a significant male predominance was observed (56 males and 20 females) ($p<0.001$)). The average age of patients with a positive finding was 19 months (ranged from 4 months to 11 years). Occurrence of intussusception peaked in the age group of 7 to 12 months (Figure 3.).

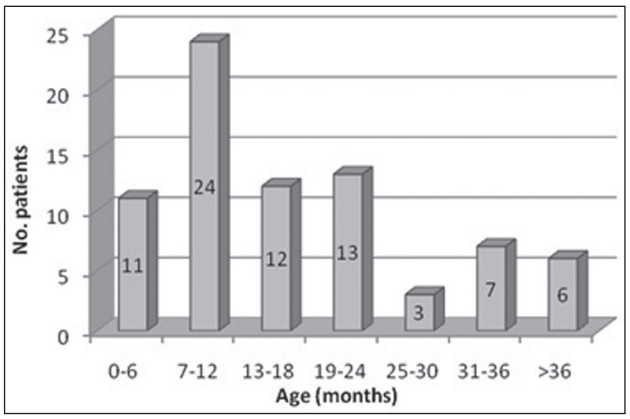

Figure 3. Age distribution of 76 patients with intussusception

The most common presenting features were intermittent abdominal pain (94.7%), vomiting (61.8%) and 'red currant jelly' stool (53.9%). Irritability/crying (22.36%), palpable abdominal mass (21.05%), fever (15.78%) and diarrhoea (9.2%) occured less frequently. Previous infection was reported in 17 (22.36%) patients (respiratory tract infection in 14 cases and single cases of gastrointestinal infection, middle ear infection and urinary tract infection). Intussusception occured consistently throughout the year, but peaked in June (17.10%). In relation to the seasons, the peak was in the summer (32.81%).

Of the 76 cases, 71 corresponded to ileocecal (93.42%), 3 to colocolic (3.94%), and 2 (2.63%) to ileocolic intussusceptions. There were no cases of small bowel intussusception. The initial location of the head of the intussusception is shown on the Table 1.

Ultrasound-guided hydrostatic reduction was attempted in 74 out of 76 patients (97.36%), and it was successful in 61 out of 74 patients (82.43%).

The majority of intussusceptions (55 (90.16%) of 61) were reduced on the initial attempt. Five reductions (5 (8.19%) of 61) required two attempts for success, and one reduction (1 (1.63%) of 61) required three attempts for success. Surgical treatment was required in 15 patients; in 13 after failed conservative treatment, while 2 patients were considered clinically unsuitable for hydrostatic reduction and proceeded directly to surgery. Most surgeries were performed in children under the age of one year (5 operations at the age of 0-6 months and 6 surgeries at the age of 7-12 months). Both types of treatment were equally represented between both sexes, the conservative with 80%, and surgical with 20%.

Table 1. Initial location of the head of intussusception

Initial location of intussusception	n	%
Cecum	11	14,47
Ascending colon	10	13,15
Hepatic flexure	22	28,94
Transverse colon	18	23,68
Splenic flexure	10	13,15
Descending colon	4	5,26
Sigmoid colon	1	1,31
Total	**76**	**100,00**

A significant correlation was found between a longer duration of symptoms and an increased rate of open surgery ($p < 0.001$), while hydrostatic reduction was significantly more often performed when duration of symptoms was less than 24 hours ($p<0.001$) (Figure 4). Association between initial location of the head of the intussusception and the treatment required is shown on the Figure 5.

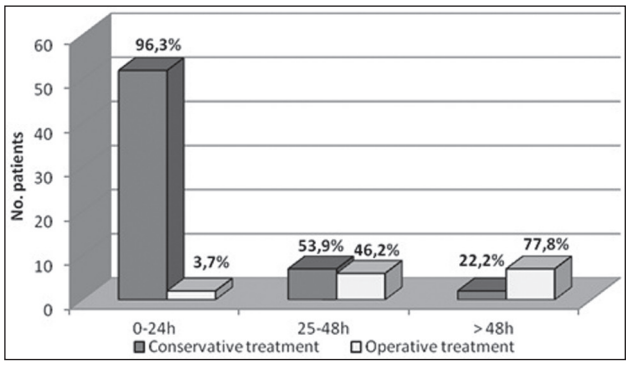

Figure 4. Type of treatment with regard to duration of symptoms

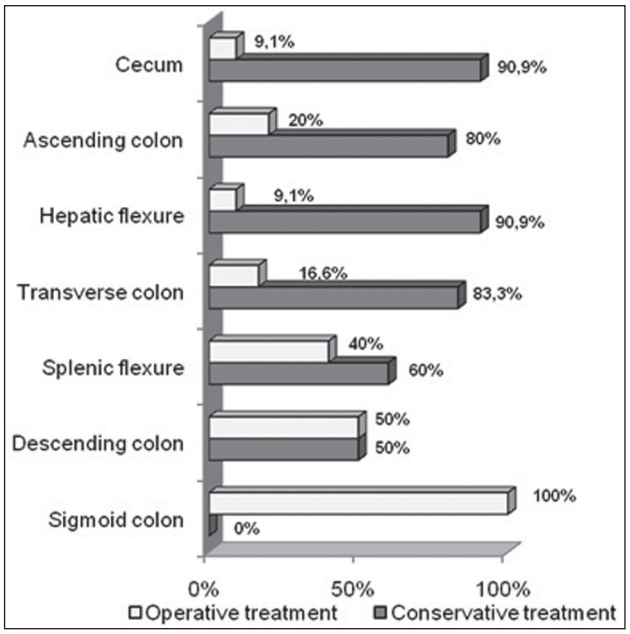

Figure 5. Relation of initial location of the head of the intussusception to the treatment required

Pathologic lead points were indentified in only 3 cases (3.95%). In one case it was the polyp, in the second the enlarged mesenterial lymph node, and in the third the thickened Peyer's patches.

Occurrence of a reccurences in relation to the sex of patients, time of occurrence and duration of symptoms before the first successful desinvagination is shown in Table 2. After successful conservative desinvagination, reccurence of invagination was registered in 10 cases (13.15%), the same day at 3 boys and 2 girls, and the next day also at 3 boys and 2 girls. Five reccurences occurred in children to whom desinvagination was carried out within the first 24 hours of onset of symptoms. Nine recurrences were resolved with repeat hydrostatic enemas, and in one case the operation was necessary.

The length of hospital stay was related to treatment required. The average hospital length of stay for patients who had successful hydrostatic reduction was 3.4 days, while for patients undergoing surgery was 7.7 days.

The values for Se, Sp, accuracy, PVPT and PVNT of clinical and ultrasonographic diagnosis obtained via Bayes's theorem are shown in Table 3.

Table 2. Occurrence of reccurences in relation to sex, time of onset and duration of symptoms before the hydrostatic reduction

Patients with Reccurences							
	Sex			No. of patients with reccurences, with regard to duration of symptoms before reduction			
	M	F	Total No	0-24h	25-48h	>48h	Total No
On the intervention day	3	2	**5**	3	1	1	**5**
Day after intervention	3	2	**5**	2	3	0	**5**
Total No	**6**	**4**	**10**	**5**	**4**	**1**	**10**

Table 3. Diagnostic value of clinical and ultrasonographic diagnosis obtained via Bayes' theorem

Bayes' theorem	Clinical diagnosis	Ultrasound
Sensitivity	86,8%	93,4%
Specificity	99,0%	99,4%
Accuracy	96,5%	97,5%
PVPT	95,6%	98,6%
PVNT	96,7%	97,0%

Discussion

In Autonomous Province of Vojvodina 15.2 cases of intussusception per 100 000 children is diagnosed annually, which is more than in other parts of Serbia,[7] but less than in other parts of the world. In Australia, an average of 29 patients per year are diagnosed with intussusception,[8] while in Tunisia the average is 27 cases per year.[2] It is still unclear which genetic and environmental factors have influence on the different frequency of intussusceptions in different parts of the world and among different races.[9] The peak age group of intussusception observed in the present study (7-12 months) is consistent with other studies.[7,9,10]

In the clinical presentation the most common symptoms were intermittent abdominal pain, vomiting and bloody stool. The results obtained in our study correlate with literature data,[2,11] however, many authors emphasize a significantly higher occurence of vomiting and bloody stool compared to intermittent abdominal pain.[3,9,12] Very often blood in the stool is revealed only after the rectal examination.[13] In our study rectal examination confirmed the red currant jelly stool in all cases where anamnestic data on its presence was obtained (42.10%), and in an additional nine cases (11.8%) with no history data.

Special attention was focused on evaluation of diagnostic value of clinical and ultrasonographic diagnosis. The results suggest that clinical diagnosis contributes strongly to adequate diagnosis of intussusception. As for the evaluation of diagnostic value of ultrasonographic diagnosis, our results are as follows: Se-93.4%, Sp-99.4%, the accuracy-97.5%. Other authors also state high sensitivity (98.0-100%) and specificity (88-100%)[14,15,16] and diagnostic accuracy of US of 100%.[11,15] In our series we found 1 false-positive case (ultrasound revealed intussuseption, but during the proccess of desinvagination saline solution smoothly passed through the ileocecal valve), and five false-negative cases (ultrasound indicated no intussusception, but children were returned to hospital within 48 hours).

There is a different frequency of intussusceptions in different seasons, with the largest peak during summer and winter, which coincides with the appearance of seasonal gastroenteritis and upper respiratory tract infections.[17] Viruses lead to a generalized reaction of lymphoid tissue, which shows its repercussions usually after 1-3 weeks after initial infection. The final effect is the reactive enlargement of Peyer's patches, which are becoming the leading point for the appearance of intussusceptions. The viruses often associated with this morbid state are the adenovirus, rotavirus, reovirus,[17] human herpesvirus 6, human herpesvirus 7, Epstein-Barr virus and cytomegalovirus.[2] In our study, the presence of a antecedent infection in the premorbid period was noted in 17 patients (22,36%) and there was no seasonal distribution of the appearance of invaginations.

The dominance of ileocecal forms was confirmed in our study, as in studies done in Tunisia[2] and Russia.[18] In Turkey,[12] Austria[19] and Australia[8] ileocolic form is dominant, while colocolic in-

tussusceptions, which are relatively rarely seen, have a slightly higher incidence in the countries of South Africa.[20] Intussusceptions of small bowel are a rarity in childhood, however, the study done in the Netherlands, which included 24 children, confirmed the presence of small bowel intussusception in 10 cases.[21] The reason why the ileocecal form of intussusception is most frequent in the infant period is the fact that at this early age there is a disproportion of the lumen of terminal ileum and the adjacent segment of colon, which is most prominent in the anatomical projection of ileocecal - Bauhin valve.[17]

In our research the head of the intussusceptum was usually localized in the area of the hepatic flexure (28.94%) and in the transverse colon (23.68%), which is consistent with the data we found in the literature.[22,23]

Current treatment of bowel intussusception can be conservative and operative. Three methods of nonsurgical treatment have been developed. Traditional fluoroscopically guided barium enema in recent decades has been replaced with alternative methods such as pneumatic reduction under fluoroscopy, and hydrostatic reduction under ultrasound control.[24] Pneumatic reduction, as a form of non-operative treatment, is widespread in China, Argentina, and in the countries of the United States and Western Europe. However, in our institution, this method has not found its place, while the hydrostatic reduction with barium, in the period covered by this study, has been completely replaced by hydrostatic saline reduction under ultrasound control. If conservative treatment is contraindicated or unsuccessful, open surgery is necessary.[25]

In our study, treatment of intussusceptions was conservative in most cases. Our reduction success rate of 82.43% is within the percentage range that can be found in numerous studies, ranging from 76-96%.[16,22,23] Surgical treatment was required in 15 patients (19.73%). Manual desinvagination was successful in all cases. During this procedure, an appendectomy was carried out in all patients. Some authors believe that the appendix acts as a reservoir for adenovirus, and as such represents a predisposing factor for intussusception and recurrences. In one study on 36 patients who had an appendectomy during the procedure, 3 patients presented with recurrence compared with 4 patients who did not have appendectomy.[26] The frequency of operating treatment is different in different studies and ranges from 4.5 to 53%,[10,11,19,20,26] but all agree that the shorter duration of symptoms and correct initial diagnosis are associated with higher success of conservative treatment and less frequent occurrence of complications.[11,14,20,26,27]

Like in other reported observations[23,28] our study confirmed the higher success rate of conservative treatment when the head of the intussusception is located in more proximal parts of the colon. When the head of intussusception was localized in the region of the cecum, the success rate of conservative treatment was 90.9%, while in the case of localization in the descending colon success rate was 50%.

The sex of the patients did not have any effect on the type of treatment. Most surgeries were performed in children under the age of 1 year (73.33%). Bratton et al. in their study stated that 56.2% of laparotomies were done in children under the age of 12 months.[10]

Idiopathic invagination was confirmed in 73 patients (96.05%), while in 3 cases (3.95%) specific pathological lead point was identified. According to literature, presence of the specific pathological lead point varies from 2 to 9%.[3] Blakelock and Beasley stated that the percentage of invagination with a specific lead point increases from 5% in children between 0-11 months to 60% in children between 5-14 years of age.[29]

According to the literature, after conservative treatment recurrences occur in 10-20% of cases and after operative treatment in 0-5% of cases. It is thought that the incidence of underlying organic abnormality is higher in patients with recurrences.[3] However, none of the ten patients who had recurrences in the present study had any underlying organic abnormalities.

Intestinal perforation has been reported as the most common potential complication of hydrostatic reduction of invaginations.[14,15] In our study, intestinal perforation occurred in 1 case (1.31%), as a complication of invagination itself, while complications during and after conservative and operative treatment were not reported. No mortality was observed in this study. In the world literature mortality was reported up to 4.2%.[30]

Conclusion

Clinical diagnosis with an accuracy of 96.5% and ultrasonographic diagnosis with an accuracy of 97.5% allow early diagnosis of intussusception, which significantly increases the success of non-operative treatment and reduces the possibility of complications. Conservative treatment provides a faster recovery, fewer days of hospital stay and significant cost savings. Considering the safety of ultrasonographic diagnosis and its repeatability, the ultrasonography is becoming a gold standard in diagnossis and mininally invasive treatment of intussusception in pediatric patients. Our experience suggest that sonographically guided hydrostatic reduction with saline enema is reliable, effective and safe technique and should be the treatment of choice for reduction of intussusception.

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The study of waiting line of receiving intensive care unit services in the hospitals

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Abstract

Background/Aims: One of the first steps in developing quality improvement programs for hospitals and reducing patients' waiting time is to understand the customer's expectations and then aligning the health care services with those expectations. The current study investigates the factors that cause waiting line of receiving intensive care unit services for the patients in the hospitals of Mazandaran province in 2011.

Methods: A cross-sectional questionnaire-base study was carried out among a randomly selected sample of 84 matrons, supervisors and ICU and CCU managers of 15 hospitals of the Mazandaran University of Medical Sciences, Iran. Using a Likert scale, respondents rated different factors that influence their waiting time in the hospital. The collected data was then analyzed using descriptive statistics, the average of standard deviation, frequency and frequency percentage, as well as statistical T test.

Results: Validity of the questionnaire was approved with a high Cronbach's alpha of 0.912. Average length of stay in ICU and CCU was 5.46 and 2.78 days, respectively. The analysis of factors affecting the long line of waiting showed that, in ICU, factors related to increasing needs for hospitalization averaged 4.2, ($p<0.002$) and factors related to equipment had a mean score of 4.2 ($p<0.001$); whereas in CCU, factors relating to medical personnel was 3.8 ($p<0.003$), and factors related to increased needs to hospitalization was 4.1 ($p<0.024$).

Conclusion: Hospitals of Mazandaran University of Medical Sciences face a lack of beds in their intensive care units. Besides, the increasing community needs, problems related to staffing, inadequate equipment and a lack of cooperation are the main factors that affect the patients' waiting time. Thus, increasing the number of beds is inevitable. This study suggests two main strategies as to how tackle the issue.

Key words: waiting line, hospital, ICU, CCU, Mazandaran

Introduction

One of the hot concepts attracting the attention of many scientists in the field of hospital management in the recent decades is the issue of clinical governance (1), which refers to systematic approaches enhance the quality of patient care in a health care system. Accordingly, in 1983, American national health service organization approved that all health service centers must use the comments of service recipients in their planning and take these comments into consideration in the evaluation of the training programs formulated for the personnel (2). ICU is an expensive unit with a fully functional approach for patients who have reversible conditions and require mechanical ventilation and other especial services (3). Intensive Care Unit (ICU) is a place where patients receive medical and nursing services and if this service is not timely received, there will be serious problems such as increased mortality and mean hospital and costs (4). A study conducted in Iran has shown that highest number of deaths in the intensive care units was reported in the timeline of first to fourth day of admission to the unit; whereas the lowest number of deaths was reported in the timeline of two weeks after admission. This indicates that all the diagnostic facilities should be provided in the first few days for patients in the intensive care units in order to minimize the mortality rate (5).

On the other hand, it is often seen that there is an inconsistency between the real expectations of the health care service recipients with the ones that

have been identified by the decision-makers and health care administrators. Such a gap stops health care managers to allocate their resources effectively to satisfy the expectations of their customers, hence resulting in a lower customer satisfaction (6). One reason for this gap could be the lack of direct communication with customers and a dearth of research about the patients' expectations.

Studies show that the average length of patients' stay at intensive care units in different parts of Iran is at least four days and at most 6.9 days. Singer and Little believe that the length of stay in intensive care units outside the country is two days (7). An explanation to the longer stay of patients in intensive care units in Iran could be the lower quality of nursing services offered to the patients which prolongs the treatment time. However if the length of stay is reduced, patients' cost will decrease as well as the bed occupancy time is reduced, while the number of active beds will increase and overall the productivity of unit will increase (8). Now, there are 172 ICU beds and 142 CCU beds in the University of Medical Sciences and health care of Mazandaran and 49 CCU beds and 54 ICU beds in the private sector and social security in the province. Yet, this number does not cover the population in need, considering that there are 30 patients waiting for the service every day. One solution to this problem is to increase the number of intensive care beds in short term but this doesn't seem rational and feasible given the limited resources. Thus the current study was conducted to identify factors affecting the long waiting time of ICU patients, in order to collect true and comprehensive information for managers and authorities based on which the hospital resources can be optimized.

Methods

A cross-sectional questionnaire-base study was carried out among a randomly selected sample of 84 matrons, supervisors and ICU and CCU managers from 15 hospitals of the Mazandaran University of Medical Sciences, Iran. Using a 5-point Likert scale from strongly agree to strongly disagree, respondents rated different factors that affect their waiting time in the hospital. The validity of the questionnaire was confirmed with a high Cronbach's alpha value of 0.912. The questionnaire contained several parts investigating the impacts of various factors on the waiting line of patients, namely: a) factors related to the role of medical personnel (nine questions), b) factors related to the role of nursing personnel (13 questions), c) factors related to equipment (11 questions), d) factors related to hospital infection (six questions), e) environmental factors (five questions), f) factor related to inter-unit lack of cooperation with the private sector (five questions), g) factors affecting the increase in the societal needs for intensive care services (six questions), and h) other factors (two questions). There were also five demographic questions in the questionnaire. The collected data was then analyzed using descriptive statistics, the average of standard deviation, frequency and frequency percentage, as well as statistical T test. To analyze the factors under study, the mean score for each factor was calculated. Then it was compared with the acceptable grade (3.5) and the difference significance was determined by T test.

Results

Bed occupancy day in the CCU units of 15 hospitals of the university in the year 1389 of Gregorian calendar (almost equivalent to the year 2011) was observed to be a total of 6916, whereas a total number of 2410 patients got discharged during that timeline. Hence, the average length of stay in the CCU section of the under study hospitals was 2.87 days.

Previous studies show that the hospitalization need in Iran is approximately 0.05 times for each person, which is about 50 times for every 1000 people (9). In our study, according to the center of IT management, the bed occupancy rate in the same year was 68%; therefore, the index of needed bed for each 1000 person of the population (3000000 people) was calculated as 1.1 beds. As a result, out of 3300 needed beds, a minimum of 165 and a maximum of 330 private beds are required.

As for the ICU units, the number of bed occupancy days in 2010 at 15 hospitals of the university was 16,123, whereas the total number of discharged patients in that year was 2953. So the average length of stay in the ICUs of the under study hospitals was 5.46 days. Besides, the bed occupancy

rate in 2010 in the hospitals of the university was 68% and the needed bed index for each 1000 person was equal to 1.1, therefore, the minimum and maximum number of beds needed for ICU was 165 and 330 beds, respectively.

Investigating the results of the study on the factors affecting waiting line showed that in ICU, factors related to equipment had a mean score of 4.2, which was more than the acceptable grade (3.5). This average difference was significant based on a one-way T test ($p<0.002$); therefore it can be claimed with 95% assurance that medical equipment affected the long line of waiting of the patients in need of intensive care services. Similarly, factors related to increasing the need for hospitalization also obtained a mean score of 4.2, which was more than the acceptable grade and this difference was significant based on one-way T test ($p<0.002$). In addition, factors related to medical personnel averaged 3.4, which was less than the acceptable grade and this difference was significant based on one-way T test ($p<0.038$). Therefore it can be concluded that at the 95% assurance level, medical personnel did not affect the long line of waiting.

Factors related to nursing personnel of the ICU averaged 2.94, which was less than the acceptable grade and this difference was significant based on T test ($p<0.001$). Factors related to hospital infection averaged 3.2 and factors related to other miscellaneous factors averaged 3.46, which were both less than the acceptable grade and this difference was significant too. Environmental factors and lack of cooperation of an inter-unit with the private sector averaged 3.98 and 4.3, respectively, which were significant based on statistical T test ($p<0.02$).

As for factors influencing length of stay in the CCU, it was observed that factors relating to medical personnel, nursing personnel, equipment, environmental factors outside the unit, lack of inter-unit cooperation, need for hospitalization, and other factors had mean scores of 3.8, 4.1, 3.92, 3.82, 3.73, 4.1, and 3.62 respectively which all were more than the acceptable grade and had a significant mean difference based on a one-way T test. Therefore, we can claim with 95% assurance that all the above factors affected the long waiting line of patients in need of CCU intensive care services. However, only for the factors related to hospital infection a mean score of 3.1 was obtained which was less than the acceptable grade. And given the fact that this difference was significant based on one-way T test ($p<0.032$), we concluded that at 95% assurance level, the hospital infection did not affect the long waiting line.

Conclusion

The current study was an attempt to assess the waiting line of receiving intensive care unit services in the hospitals in Mazandaran province and to identify the factors that influenced a long waiting time. Average length of stay in ICU and CCU was 5.46 and 2.78 days, respectively. Comparing these figures with those of previous studies, we would notice that in a study in the hospital of Towhid in Sanandaj, Iran, the average length of stay in ICU was four days (10), whereas this average was 4.23 days in the Baghiyatollah Hospital in Tehran (11). When it comes to the European countries, the average length of stay is much shorter and is only about two days (12). A similar study showed that if enough time is spent on the quality of nursing services, treatment time will decrease, as a consequence of which, on one hand the patient's expenditure will be less, and on the other hand, with the decrease in the bed occupancy time, the number of active beds in a definite time will increase resulting in a an overall enhanced productivity (13). The existence of the inductive request for hospitalization in the intensive care unit interest in keeping the bed and keeping recovered patients in the unit causes the length of stay to become long, and as a result increases the waiting period of applicants. Regarding the role of nursing personnel as a factor affecting the waiting line and quality of provided services, it is observed that in ICU, each nurse took care of more than one patient, whereas in CCU there was only one patient assigned per nurse. This is contradictory, since according to the standards, there should be one nurse for each patient in ICU and one nurse for two or three patients in CCU (14). A study showed that less direct care in the intensive care unit is seen in public hospitals compared to private ones, because nurses in public hospitals have to spend some time on asking for drugs, filing, photocopying, etc., and they don't have a secretary (15).

Another factor affecting waiting line of patients asking for especial care service is a lack of inter-unit cooperation with the private sector. Public hospitals are facing numerous problems for referring to the private sector. Poor economic situation of patients, insufficient coverage of insurance and failure to admit poor patients in critical condition by the private sector are among the factors that restrict patients' access to the private sector. Since the only mission and the *raison d'etre* for the existence of hospitals is to treat patients and promote health care, all hospitals are accountable for treating patients in critical condition, and the authorities should make laws for the private sector and emphasize its role in the health system. A study showed that 6180 out of 17440 patients hospitalized in the intensive care unit needed especial care of less than 10% (16). It seems that the existence of the inductive request for hospitalization in the intensive care unit, interest in keeping the bed and keeping recovered patients are among the serious factors that cause a long waiting line of the patients requiring especial care services. In the U.S. and Europe, convalescing patients or those patients who are suffering from a chronic disease are taken care of in non-hospital places in which suitable care is accessible (such as nursing houses, rehabilitation centers, places for convalescence, etc.) (17). Based on some estimations, Mazandaran University of Medical Sciences needs 330 ICU beds in order to offer efficient services and remove the waiting time of the patients requiring intensive care services regardless of the varying population of the province because of its tourist attractions. At present, there are 172 beds in the hospitals of the university (that is only half of the numbers required), and 142 CCU beds in these hospitals are for offering intensive care services. Moreover, a number of 350 beds are needed fully meet the needs of patients in CCU. In conclusion, it seems that the university should focus on two strategies in order to solve the current problem and adopt an optimum strategy. First, extra resources are to be added to increase the number of beds by 50%. Of course, this is a difficult and costly process, since each bed would cost about 85000 USD. Second, inter-unit cooperation with the private sector should be developed by adopting suitable measures and mechanisms. Only then the potential of the private sector could be used effectively, allowing the enhancement of intensive care services, a better coverage of services provided to patients and decreasing the patients' waiting line.

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Study on the influence factors of neonatal CRP

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Abstract

Objective: To study Influencing Factors on C-reactive protein in neonates.

Methods: The neonatal blood samples were collected and simultaneously tested C-reactive protein, blood routine, hepatic function, biochemistry when neonates were admission. There were 220 cases of neonatal that CRP was greater than 8 mg/L in 3196 cases. Mann Whitney U test, Pearson Correlation and multiple linear regression were used for statistical analysis.

Results: The preliminary screening results by Mann Whitney U test and Pearson Correlation shows: mean rank: neonatal septicemia (Yes:138.32; No:107.86, U=1381.0, p=0.046), NRDS (Yes:66.44, No:112.16, U=495.5, p=0.046). Pearson Correlation results shows that there are likely to correlation among CRP and HB, HCT, TBIL, DBIL, GLU, r=-0.149, -0.143, -0.164, 0.246, 0.316, respectively, $p<0.05$. Stepwise regression analysis is further used, dependent variable: CRP, Covariates: neonatal septicemia, NRDS, HB, HCT, TBIL, DBIL, GLU, only DBIL and GLU into regression equation, standardized partial regression coefficient are 0.477,0.311, 95% confidence interval (0.608,2.265), (0.588,9.445); p =0.001, 0.028, respectively. The model has statistical significance (F=9.298, P=0.001), R^2=0.341, goodness of fit is relatively low.

Conclusion: CRP is positive correlated with DBIL and GLU. Furthermore, DBIL has more positive effect on CRP than GLU.

Key words: C- reactive protein, direct bilirubin, glucose, neonates

Introduction

CRP was discovered as a substance in the sera of patients with pneumococcal pneumonia which reacted with polysaccharide C of Streptococcus pneumonia by Tillett WS and Francis in Hospital of the Rockefeller Institute for Medical Research. The circulating CRP was synthesized and secreted predominantly by hepatocytes in response to pro-inflammatory cytokines such as tumor necrosis factor α (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6). Some organs and system away from the inflammation in the inflammatory process would occur some changes. It was an important defense molecule in the body [1]. Accumulating evidence showed that: C-reactive protein is not only an inflammatory marker but also a positive relation between plasma CRP and the risk of coronary heart disease.CRP levels predicts future cardiovascular events independently of coronary artery disease (CAD) severity and correlates with number of angiographically complex coronary artery stenosis in patients with acute coronary syndromes without ST-segment elevation (ACS). CRP levels are a marker of atheromatous plaque vulnerability and CAD activity [2]. The present study may provide an important insight into the link between systemic and coronary levels of inflammation, which are also associated with vulnerable coronary morphology in the setting of acute coronary syndrome [3]. C-reactive protein level is a stronger predictor of hypertension [4]. C-reactive protein is an independent predictor of risk for the development of diabetes in the West of Scotland Coronary Prevention Study and low-grade inflammation are important in the pathogenesis of type 2 diabetes [5]. CRP has already generally utilized in clinical. But due to particularity in neonatal physiological and pathophysiological aspects, it is not entirely clear about influencing factors on C-reactive protein in neonates. This article is about on 220 cases of newborn that CRP is greater than 8 mg/L, at the same time to combine with other laboratory checks in admission hospital, Study reported below.

Methods

Two years, admitted 3196 cases of neonatal clinical data, each neonatal case of hospitalization were collected blood sample at the same time check: blood routine count, CRP, liver function, biochemical, electrolyte checks. CRP increased> 8mg/ml were 220 cases in 3196 cases. Diagnostic criteria for neonatal diseases used Practical of Neonatology [6].To analysis the neonatal admission diagnosis and the admission examination, the results were as follows:

Clinical diagnosis

220 cases of elevated CRP: male 135 cases, female 85 cases; gestational age 30-41 weeks; Average weight 3.099 ± 0.702kg. Diagnosis: neonatal hypoglycemia 14 cases, hemolytic disease of newborn 20 cases, newborn respiratory distress syndrome (NRDS) 8 cases, preterm low birth weight 50 cases, newborn pneumonia 151 cases, intracranial hemorrhage of the newborn 13 cases, swallowing syndrome 8 cases, newborn hypoxic ischemic encephalopathy (HIE) 29 cases, newborn non-physiological hyperbilirubinemia 81 cases, asphyxia of newborn 20 cases, congenital malformation 5 cases, neonatal septicemia 19 cases. Mechanical ventilation 19 cases, ventilation in the shortest time was 1 day, maximum of 15 days. All of the newborns were cured and discharged.

Maternal conditions

The maternal condition in 220 cases of newborns elevated CRP were as follows: cesarean section 91 cases, spontaneous delivery 129 cases, intrauterine embarrassment 45 cases, amniotic fluid contamination 62 cases, duration of pregnancy complicating upper respiratory tract infection 4 cases, pregnancy hypertension syndrome 10 cases, gestational diabetes 5 cases, hepatitis B with HBsAg (+),HBeAg(+),HBcAb(+) 7 cases, pregnancy syphilis 2 cases, cervical erosion 3 cases, severe eclampsia 2 cases, pregnancy period complicating fever 4 cases, premature rupture of membranes 44 cases, oligohydramnios 11 cases, polyhydramnios 2 cases.

Laboratory methods

ORION Company for the semi-automatic device TURBOXPLUS, immune turbidimetry CRP Assay kit are bought from the ORION Company, SYSMEX Corporation production XT-2000i of automatic blood cell Analyzer, Germany produced by Roche COBAS INTEGRA 400 plus automatic biochemical Analyzer.

Data management and statistical analysis

All data were analyzed using the SPSS16.0 software. Mann Whitney U test, correlation with Pearson Correlation, multiple linear regression analysis were used for statistical analysis .p –value of 0.05 or lower was considered significant.

Results

The preliminary screening results by Mann Whitney U test and correlation analysis of simple (Pearson Correlation) indicated that CRP were significant in neonatal septicemia group and NRDS group. Pearson correlation results showed that there were possible correlations among CRP and HB, HCT, TBIL, DBIL, GLU.

Stepwise regression analysis was further used, dependent variable: CRP, Covariates: neonatal septicemia, NRDS, HB, HCT, TBIL, DBIL, GLU. As the HB and HCT have a high degree of correlation (r=0.975, P=0.000), to avoid collinearity in multiple linear regression analysis, we selected either HB or HCT respectively to enter multiple linear regression analysis. The result was consonance (table 3).

Only DBIL and GLU into regression equation, CRP was positive correlated with DBIL and GLU, furthermore, DBIL had more positive effect on CRP than GLU by standardized partial regression coefficients. The model had statistical significance ($F=9.298, P=0.001$), $R^2=0.341$, goodness of fit was relatively low .Other important influential factors need to be detected.

Discussion

The serum C-reactive protein (CRP) is a major human acute phase protein. In the fetal period, it mainly is synthesized in hepatocytes following inflammatory stimuli, and not through the placenta. Microcontent forms are found in serum after birth. Circulating CRP is present in only trace amounts in healthy individuals, and is hardly detectable by the standard clinical tests, which typically

Table 1. Mann-Whitney U Test on CRP results in 220 cases in different diseases

disease	mean rank of CRP	control	mean rank of CRP	U	P
neonatal septicemia Yes	138.32	No	107.87	1381.0	0.046#
preterm low birth weight Yes	114.80	No	109.24	4035.0	0.587
newborn pneumonia Yes	111.9	No	107.43	4998.0	0.629
neonatal hypoglycemia Yes	115.79	No	110.14	1368.0	0.748
hemolytic disease of newborn Yes	102.60	No	111.29	1842.0	0.560
NRDS Yes	66.44	No	112.16	495.50	0.046#
newborn non-physiological Hyperbilirubinemia Yes	100.14	No	116.54	4790.0	0.065
intracranial hemorrhage of the newborn Yes	97.15	No	111.34	1172.0	0.435
HIE Yes	113.24	No	109.51	2661.0	0.767
asphyxia of newborn Yes	121.86	No	108.39	1578.0	0.385
amniotic fluid contamination Yes	112.56	No	109.69	4770.0	0.764
premature rupture of membranes Yes	119.11	No	108.35	3493.0	0.315

 # P<0.05

Table 2. The Pearson correlations among CRP and Main indicators of Hepatic function, blood routine and biochemical

	WBC	N	L	Plat	Hct	Hb	ALT	TBIL	DBIL	ALB	GLU
r	-0.007	0.049	-0.064	-0.027	-0.143	-0.149	0.109	-0.164	0.246	-0.174	0.316
p	0.915	0.470	0.346	0.688	0.034#	0.027#	0.146	0.026#	0.001#	0.072	0.031#
n	220	219	218	220	219	220	181	184	183	108	47

(#:P<0.05); WBC (×10⁹/L), N (%), L (%), Plat (×10⁹/L), Hct (%), HB (g/L), ALT (U/L), TBIL (μmol/L), DBIL (μmol/L), ALB (g/L), GLU (mmol/L)

Table 3. Multiple linear regression analysis results

Model	Unstandardized Coefficients		Standardized Coefficients	t	P	95%Confidence Interval for B	
	B	SE	Beta			Lower Bound	Upper Bound
Constant	-12.788	12.040		-1.062	0.295	-37.206	11.630
DBIL	1.436	0.408	0.477	3.517	0.001	0.608	2.265
GLU	5.017	2.184	0.311	2.297	0.028	0.588	9.445

have a lower detection limit of 3–8 mg/L. The serum concentration of CRP can rapidly increase up to 1000-fold or more after severe inflammatory stimuli or (and) the state of stress in a few hours or within 1 ~ 2 d, then decrease rapidly after pathogenetic condition remission, often as an early indicator of bacterial infection [7].This study shows that: the difference that CRP levels in infants whether suffering from neonatal pneumonia group is no significance.CRP changes with indicators of inflammatory response to WBC and N are not associated, neither with Plat changes. The reasons may be due to: CRP changes are ahead of the change in body temperature, peripheral white blood cell count, and CRP is not affected by gender, age, anaemia, high blood globulin and pregnancy, which consistent with our research results. The indicator that most commonly used in diagnosis of bacterial infection is white blood cell count and classification, its role is limited, many factors affect the white blood cells, Physiological fluctuation, range up to 30%~50%, together with a wide range of normal white blood cells in newborns, some white blood cells in newborn with low base, WBC mild rise does not exceed the normal range limit. Another part of newborns with bacterial infections, white blood cell count and classification count index changes are not significant, and cannot provide valuable information. As a standard of acute reaction protein, separate

elevated CRP is insufficient for the specificity of diagnosis of neonatal infection [8].To study whether concentrations of procalcitonin in the blood of neonates with nosocomial infections depend on the type of pathogen. A. Kordek found infections with Gram-positive (chiefly coagulase-negative staphylococci) and Gram-negative bacteria are accompanied by elevated concentrations of procalcitonin. In the case of Gram-positive bacteria, other laboratory signs of infection studied by them (concentration of C-reactive protein, white blood cell count, immature-to-total neutrophil ratio) are not discriminatory, confirming the diagnostic usefulness of procalcitonin measurements in nosocomial infections of the neonate with Gram-negative or Gram-positive bacteria [9] .Seventy nine pediatric patients with sepsis are studied, tumor necrosis factor-a (TNF-a) levels are significantly raised in patients with sepsis. TNF-a levels are raised significantly in culture positive cases in general and in Gram negative infections in particular. Serum TNF-alpha is a more sensitive marker for different categories of sepsis compared to CRP and microbiology culture [10] .Pneumonia is the major cause of mortality and morbidity in children worldwide. Procalcitonin (PCT) and C-reactive protein (CRP) are used in developed countries to differentiate between viral and bacterial causes of pneumonia. But in Africa, Presence of malaria parasites and high HIV incidence should be taken into consideration, either for clinical or epidemiological purposes, if using PCT or CRP to differentiate viral from invasive bacterial pneumonia in malaria-endemic areas. None of the two markers can predict invasive bacterial pneumonia mortality [11] .In our study, CRP increased in neonatal septicemia group is significance. Neonatal clinical condition changes quickly, meticulous clinical observation and timely dynamic measurement of inflammatory indicators are necessary.

Bilirubin is a kind of iron-containing porphyrin decomposition product in the aging of red blood cells. It exists in bilirubin-serum protein complexes form and transport and has been considered to have cytotoxic. As early as a century ago, people discovered that bilirubin had antioxidant, but its role of endogenous antioxidant was respected until recent years.Serum bilirubin is within the body of a natural physiological antioxidant. Bilirubin can effectively capture and remove oxygen free radicals, both direct bilirubin and indirect bilirubin are effective antioxidants. Serum direct bilirubin and indirect bilirubin levels reduction results in decreased antioxidant activity in vivo [12] .In 1994, Schwertner et al [13] for the first time found that either univariate analysis or Multivariate analysis, serum bilirubin concentration and coronary atherosclerosis (Coronary heart disease, CHD) level are significantly negatively correlated. And treatment by multiple regression analysis found that bilirubin decreased 50%, CHD incidence increased 47%.To make low serum bilirubin may be a new risk factor for CHD, physiological concentrations of bilirubin has the ability to prevent the peroxidation of LDL cholesterol, and the albumin bind bilirubin has antioxidant activity. That 1 mol direct bilirubin may counteract 2 mol peroxylradicals. In this study, CRP are associated with TBIL and DBIL, but only DBIL and GLU into the regression equation, CRP is positive correlated with DBIL and GLU, furthermore, DBIL has more positive effect on CRP than GLU . The reason may be that the body of high CRP indicate higher metabolism, augmentation oxidation activity in vivo. Inevitably lead to enhanced antioxidant activity in vivo, DBIL increased. However, the specific mechanisms and through which signaling pathways interact required further study.

Maternal type 1 diabetes increases the foetal plasma LDL cholesterol and CRP concentration and thus might predispose the offspring to development of atherosclerosis [14]. Small increases in CRP predict the likelihood of developing cardiovascular events both in diabetic and nondiabetic populations. In addition, in apparently healthy subjects, increased levels of CRP predict the risk of developing type 2-diabetes. There are some evidences that CRP, besides its predictive role in determining cardiovascular risk, may represent an active participant in atherogenesis [15]. So, CRP is an early diabetic vascular disease monitoring indicators. There are reports that blood glucose and CRP are increased in cases of SIRS and MODS. Pathogenetic condition is more severe, blood glucose and CRP elevated more obvious, more difficult to restore to normal [16] .This study shows a positive correlation of CRP and GLU. The reason may be the body in the stress response situation,

CRP increase. Body under a high metabolism, appears nervous, endocrine disorders, inducing catecholamine hormones, glucagon, glucocorticoids plenty release. Norepinephrine and epinephrine can promote glucagon secretion. Glucocorticoids can promote increased gluconeogenesis and accelerate glycogen decomposition. With stress situations a general decline in tissue sensitivity to insulin, so blood sugar rise. Also prompt the body under stress situation causes metabolic disorders, clinical should be actively corrected.

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Vitamin E and Carnitine suplementation effects on blood glucose levels in young rats submitted to exhaustive exercise stress

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Abstract

Background: In this study we evaluated the effects of carnitine and vitamin E supplementation on blood glucose levels in young rats submitted to exhaustive exercise stress.

Methods: Wistar rats were divided into four groups: 1) control group; 2) exercise stress group; 3) exercise stress + Vitamin E and; 4) exercise stress + carnitine group. Rats from the group 3 and 4 were treated with gavage administration of 1 mL of Vitamin E (5mg/kg) and carnitine (5mg/kg) for seven consecutive days. Animals from groups 2, 3 and 4 were submitted to a bout of swimming exhaustive exercise stress. We analyzed blood glucose levels after exercise stress.

Results: Blood glucose levels after exercise stress were significantly increased in the groups treated with Vitamine E and carnitine (control group: 98.7±9mg/dL vs. stress group: 84.2±11 mg/dL vs. carnitine + stress group: 147.4±15 mg/dL vs. vintamin E + stress: 158.3±7 mg/dL; $p<0.0001$).

Conclusion: Vitamin E and carnitine supplementation attenuate the hypoglycemia induced by exercise in young rats submitted to exhaustive exercise stress.

Key words: Carnitine; Vitamin E; Exercise; Stress.

Introduction

Exhaustive exercise stress increases the whole body oxygen consumption up to 20 fold, which then increases electron leakage from the mitochondrial transport system and disturbs the intracellular pro-oxidant and antioxidant homeostasis [1]. Exercise stress, especially for sedentary individuals can generate various imbalances in the body among reactive oxygen species and antioxidant system [1]. Furthermore, it increases cellular oxygen consumption in mitochondria to generate energy metabolism and ATP synthesis, whose consumption increases due to the intensity and duration of effort [1].

Supplementations are a non-pharmacological therapy that has been received attention in the literature. Around 45% of people who practice physical activity use some type of dietetic supplementation in order to keep a good health [2]. Carnitine is a quaternary ammonium compound biosynthesized from the amino acids lysine and methionine [3]. It has potentially protective effects against mitochondrial toxic agents. Another supplement is vitamin E (a-tocopherol), which seems to be a very important agent in providing protection against oxidation of cellular lipids by free radicals that are potentially damaging byproducts of cellular metabolism [4].

Although exercise stress was already shown to consume glycogen in old rats [1], no previous study investigated the effects of supplementation on rats submitted to exhaustive exercise stress. Thus, this investigation was undertaken to evaluate the effects of carnitine and vitamin E supplementation on blood glucose levels in young rats submitted to exhaustive exercise stress.

Method

Thirty-two just weaned male Wistar rats weighing an average of 95.5 g were used. The animals were bred at the Central Animal House of the Ribeirao Preto Campus of the University of São Paulo. The animals were kept in plastic cages (a maximum of 4 rats per cage) in a room with controlled

temperature (24–28ºC) and luminosity (a 12 h light:12 h dark cycle) with free access to water and balanced food rations. The animals were kept in accordance to the guidelines of the Committee on Care and Use of Laboratory Animals of the National Research Council of the National Institutes of Health.

Animals were randomized into four groups: 1) the control group (n=8), in which rats were treated with gavage administration of 1 mL of water for seven consecutive days; 2) exercise stress group (n=8), in which rats were treated with gavage administration of 1 mL of water for seven consecutive days and submitted to exhaustive exercise stress; 3) exercise stress + carnitine group (n=8), in which rats were treated with gavage administration of 1 mL of carnitine (5mg/kg) for seven consecutive days and submitted to exhaustive exercise stress and; 4) exercise stress + vitamin E group (n=8), in which rats were treated with gavage administration of 1 mL of Vitamin E (5mg/kg) for seven consecutive days and submitted to exhaustive exercise stress.

Groups submitted to exhaustive exercise stress were submitted at the last day of the experiment (7^{th}) to one bout of swimming exercise stress until exhaustion. They were submitted to exercise consisting of swimming in a glass tank (100 cm long, 50 cm wide, 80 cm deep) containing water maintained at 32ºC, when the animal stop swimming it was removed from the water, since it corresponds to a exhaustive situation [5]. The depth of the tank prevented the animals from resting their tails on the bottom of the tank while swimming. Swimming was selected because muscle trauma caused by prolonged running, exercise-stimulated electric shock, and plyometric contractions could be avoided. These factors alone could induce oxidative stress [6].

Blood was obtained from a small knick in the tail and measured with the kit Labtest GLICOSE PAP Liquiform®.

Data are reported as mean ± standard error of the mean (SEM). In order to evaluate the normality of the distribution we applied the Kolmorogov-Smirnov normality test. Statistical significance was assessed by analysis of variance (two way ANOVA), followed by Dunn post hoc test. Differences were considered significant when the probability of a Type I error was lower than 5% ($p < 0.05$).

Results

We observed that blood glucose level was increased in the groups treated with carnitine and vitamin E submitted to exercise stress compared to the control and stress groups (Figure 1).

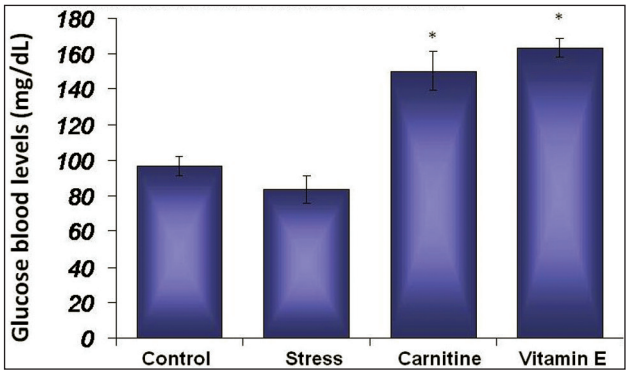

*Figure 1. Blood glucose levels in control (control), exercise stress (stress), exercise stress carnitine (carnitine) and exercise stress vitamin E (vitamin E) groups. *p<0.005: Different of stress and control groups.*

Discussion

In this study we aimed to evaluate the effects of carnitine and vitamin E supplementation by gavage on blood glucose levels in young rats submitted to exhaustive exercise stress. As a main finding, carnitine and vitamin E pretreatment attenuated the responses caused by exhaustive exercise stress regarding glucose consumption, since it attenuated the hypoglycemic condition.

Based on our investigation, as expected, blood glucose levels were reduced in the group not treated and submitted to exhaustive exercise stress. Previous studies also demonstrated that different type of stress increases glycogen consumption [7-14]. This is a behavior proposed by Selye more than 60 years ago [15]. It is explained by the fact that oxidative phosphorylation promotes glycogenolysis acceleration in response to catecholamine release caused by a stress condition [16], which lead to a lower concentration of glucose in the plasma, such as we found in our study.

According to our results, carnitine supplementation attenuated blood glucose levels reduction after exhaustive exercise stress. Carnitine is a widely used conditionally essential nutrient added to a range of functional food products including

weight loss formulations, infant formula milk, and sports bars and drinks. Carnitine is widely recognized as a key factor involved in the regulation and transport of activated fatty acids into mitochondria for oxidation [17]. A recent investigation evidenced that oral carnitine supplementation (3 g/day) for 2 weeks appears to have an impact upon glucose homeostasis and insulin release in healthy lean and overweight/obese males during an oral glucose tolerance test [18]. Mingrone [19] published a review on carnitine in type 2 diabetes, in which he concluded that carnitine was effective in improving insulin-mediated glucose disposal. In addition, Rahbar et al [20] have observed lowering of fasting glucose following 12 weeks of carnitine supplementation in patients with type 2 diabetes. Power et al [21] have subsequently also confirmed these observations in a mouse model and suggest that carnitine could be used as an adjunctive therapy in diabetes. On the other hand, lacks in the literature data regarding the effects of carnitine supplement on hypoglycemic situations.

Our findings indicate that vitamin E supplementation attenuated hypoglycemic condition occurred by exhaustive exercise stress in just weaned Wistar rats. Vitamins, as well as minerals and trace elements, have become of great interest in the world of sports because of their supposed role in enhancing performance. Most water soluble vitamins and vitamin E are involved in mitochondrial energy metabolism, yet the influence of vitamin supplementation on mitochondrial metabolism is largely unknown [22]. Many studies indicated that vitamin E treatment attenuated the hyperglycemic status [23, 24]. However, no study evaluated the effects of vitamin E treatment on hypoglycemic-induced rats. We believe that vitamin E was able to attenuate hypoglycemia induced by exercise stress due to its antioxidant property [25].

One may wonder if vitamin E and carnitine supplementation attenuated the decrease in plasma glucose levels or actually increased blood glucose levels. We believe that the last hypothesis is not plausible, since vitamin E [26] and carnitine [19] are used in diabetes treatment. Therefore, they could not increase blood glucose levels.

The data found in our study is clinically relevant. Because blood glucose levels are a very important issue recently investigated [27- Exhaustive exercise is observed in inactive people submitted to high physical exercise intensity. We believe that these data are important to develop futures therapies aiming to preserve hypoglycemia-induced by exhaustive exercise stress. These findings may possibly open new perspectives for more research and may benefit experimental and clinical investigations. Moreover, the efficacy and safety of vitamin E and carnitine are important to strength the relevance of those supplements to people who are not used to practice exercise.

In conclusion, carnitine and vitamin E supplementation attenuated hypoglycemia caused by exhaustive exercise stress in rats. Our findings strength the importance of carnitine and vitamin E supplementation in exercise stress situations.

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Nurses' and paediatricians' knowledge about infant sleeping positions and the risk of sudden infant death syndrome in Turkey

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Abstract

Objective: The purpose of this article is to determine nurses' and paediatricians' knowledge regarding the sleeping positions and environment of infants.

Methods: This descriptive and cross-sectional study was conducted at 18 randomly selected hospitals in eight different cities in Turkey. There were 1,156 participants in the study (252 physicians and 904 nurses). The data were collected by means of a questionnaire form developed by the investigators. Data analysis included percentage and chi-square analyses.

Results: Among the nurses, 74.1% were between the ages of 21 and 35, 32.0% had a bachelor's degree, 65.0% had job experience of six years or more. Among the paediatricians, 69.0% were between the ages of 21 and 35; 42.5% had job experience of six years or more. 88.8% of the nurses said that the mother should share same room with the infant but in a separate bed. Over two-thirds of the nurses said that a pillow should not be used when an infant was asleep, and 98.0% would not cover an infant's face. 86.5% of the paediatricians said that the mother could share same room with the infant but in a separate bed. 76.2% of the paediatricians said that they would not use a pillow when the infant were asleep, and 97.2% would not cover an infant's face. Most nurses and physicians responded that infants of 0–6 months of age slept on their sides **during** the daytime, in the nighttime, when left alone in a room, and after feeding.

Conclusions: The results showed that physicians and nurses were not sufficiently knowledgeable about infant sleeping positions; however, they had sufficient knowledge about the risk factors for sudden infant death syndrome. The education of both nurses and physicians working in pediatric wards about the risk factors of SIDS may decrease SIDS deaths in Turkey.

Key words: nurse; paediatrician; knowledge; infant sleeping position; sudden infant death syndrome; prevention risk factors; Turkey

Introduction

Sudden infant death syndrome is the sudden death of an infant under 1 year of age which remains unexplained after a thorough case investigation, including the performance of a complete autopsy, examination of the death scene and a review of the clinical history [1].

Despite declines in prevalence during the past two decades, SIDS continues to be one of the leading causes of infant mortality in the post-neonatal period [2,3]. More recently, the highest SIDS rates (≥ 0.5/1000 live births) are in New Zealand and the United States. The lowest rates (≤0.2/1000) are in Japan and the Netherlands [4]. Unfortunately, SIDS prevalence of Turkish infants is still unknown since autopsy cannot be performed widely.

SIDS is a complex, multifactorial disorder, the cause of which is still not fully understood. Behavioral risk factors identified in epidemiological

studies include prone and side sleeping positions, sharing a bed with an infant, using a pillow, covering infants' faces, smoke exposure, soft bedding, and overheating [5-9]. Studies indicated that the side-lying position was twice as risky as the supine sleeping position; infants in the side sleeping position might turn to the prone sleeping position [10-12]. In 2005, the AAP Task Force on the SIDS issued updated guidelines for healthy sleep practices for newborn infants that include several new or re-emphasized recommendations. In the updated guidelines, positioning infants on their side for sleep is no longer an accepted alternative to supine sleeping. In 2005, the AAP reaffirmed the recommendation to place all healthy infants to sleep in the supine position [13].

Physicians and nurses are a significant resource of knowledge for parents about infant sleep safety and SIDS risk decrease, and excessive effective in about to parental decisions [14]. In a study by Willinger and colleagues, a physician's recommendation of the supine position was the powerfully affect on the parental prefer of sleeping position, resulting in more than a threefold increase in the possibility that the infant would sleep supine and a fourfold decline in the likelihood of prone sleeping [14]. Nevertheless, previous study has indicated that just two-thirds of physicians and one-third of family physicians surveyed in Washington, DC, and North Carolina were aware of the AAP recommendation that infants be placed in the supine position for sleeping [15]. In a different research of family physicians, just 62% indicated that they routinely suggested supine sleeping for infants, but 21% generally or always dissuaded supine sleeping [16]. There are limited data on SIDS from developing and middle-income countries [9, 17-19]. The current study is one of the few extensive SIDS studies performed in Turkey. Therefore, educating health professionals on the risk factors for SIDS is important for prevention. Little is known about the knowledge and practice of nurses and paediatricians in relation to infant sleeping positions and SIDS. Similarly, there are few studies concerning the knowledge and attitudes of parents and health professionals about SIDS in Turkey [20-22]. Nurses and paediatricians play a very important role in parental education in various fields such as health centers, maternal child health centers, hospitals and kindergarten. To effectively plan for nurses' and paediatricians education and roles in national programs for SIDS risk factor reduction in Turkey, the current state of Turkish nurses' and paediatricians knowledge of SIDS risk factor reduction, their attitudes towards this issue, their current practice behaviors related to SIDS risk reduction need to be investigated.

The goal of this study was to determine nurses' and paediatricians' knowledge regarding the sleeping positions and environment of infants in Turkey. We posed the following research questions: In each of these two groups (a) What is the knowledge regarding SIDS risk factors? (b) What is the knowledge regarding infant sleep position?

Methods

Study Design, Setting and Sample

This descriptive study was conducted at randomly selected eight different cities (Istanbul, Izmir, Mersin, Antalya, Denizli, Sivas, Aydın, and Erzurum) in Turkey. The data were collected between February and December 2008.

Research population was created all the children's nurses and paediatricians in 18 hospitals in Turkey. Universe of the study consist of 1756 nurses and 885 paediatricians in eight cities that were randomly selected in Turkey. The volunteer sample consisted of 904 nurse and 252 paediatrician respondents, representing 51% of the total nurses and 28% of the total paediatricians.

Questionnaire Form

The data were collected by means of a questionnaire form developed by the investigators. The questionnaire was designed on the basis of earlier research literature concerning the sleeping positions of infants [2, 3, 7, 12, 18, 23]. The questionnaire consisted of 15 questions in two sections. Five questions were about the nurses' and paediatricians' sociodemographic characteristics such as gender, age, education, and years of work experience and 10 questions were directed at obtaining the paediatricians' and nurses' knowledge about sleeping positions for infants between 0 and 6 months of age and the risk factors for sudden

infant death syndrome. The questions included: "Which sleep position is best for an infant during the daytime, the nighttime, when left alone in a room, or after feeding?"; "Do you recommend the use of a pillow for an infant?"; "Do you recommend covering the infant's head or face with bedding?"; "Do you recommend mother and infant sleeping in the same bed?"; "Do you recommend mother and infant sleeping in the same room?"; "Do you recommend mother and infant sleeping in the same room but separate beds?".

The questionnaire was pre-tested for clarity of the items by 25 nurses and 25 paediatricians who worked at an affiliated hospital that was not a site for our study. The questions considered unclear were revised.

Data Collection Procedures

All member of the research team was responsible for the distribution of the questionnaires. The questionnaires were completed as self-reporting. For the 18 hospital in Turkey, the research team member went to each hospital unit in the morning for a period of 1 day for each hospital, distributed the questionnaires to each individual, explained the purpose of the research, and provided instructions according to the pre-defined protocol noted below. Instructions were as follows: "If you decide to participate in this study, please complete this questionnaire independently and answer all the questions. If you do not know the correct answer, guess. Please do not check reference materials or ask other staff members for an answer. The research team member will return to your work unit near the end of your shift. If you have chosen to complete the questionnaire, you can return it to the research team member at that time. Submitting your completed questionnaire to the research team member constitutes consent for participation in this study." The nurses and paediatricians completed the questionnaires during their work shift. The research team member then located each individual, checked the questionnaire for completion, and asked the participant to respond to any unanswered items. Each nurse and paediatrician completed the questionnaire approximately in 15–20 min.

Ethical Considerations

The institutional review board of the university reviewed and approved the conduct of this study. The nurses and paediatricians were informed about aim of the study. Information about anonymity, confidentiality and consent was included in the explanation, and written permission was obtained. Participation in this study was voluntary.

Statistical Analysis

Statistical analyses were performed using SPSS statistical software (SPSS Inc., Chicago, IL, USA) for Windows (version 13). Data analysis included percentage and chi-square analyses. A level of $p < 0.05$ was considered statistically significant.

Results

The demographic features of the nurses and paediatricians are shown in Table 1. Among the nurses, 74.1% were between the ages of 21 and 35, 32.0% had a bachelor's degree, 65.0% had job experience of six years or more, 24.2% worked in the general pediatric unit. Over half (52.8%) of the nurses were working in the state hospital, and nearly equal numbers of the participating nurses were from the Marmara region (53.2%) and from Istanbul (53.2%), Turkey. Among the paediatricians, 69.0% were between the ages of 21 and 35; 42.5% had job experience of six years or more; 31.0% of the paediatricians were worked in the general pediatric unit (Table 1).

We determined that 88.1% of the nurses said that the mother should not share the same bed with the infant, whereas, 87.6% of the nurses said the mother could share the same room with the infant. However, 88.8% of the nurses said that the mother should share same room with the infant but in a separate bed. Over two-thirds (68.0%) of the nurses said that a pillow should not be used when an infant was asleep, and 98.0% would not cover an infant's face. We also determined that 86.9% of the paediatricians said that the mother should not share the same bed with the infant, and 86.9% said that the mother could share the same room with the infant, 86.5% said that the mother could share same room with the infant but in a separate bed. However,

Table 1. Demographic characteristics of the nurses and paediatricians

Variable	Nurses	Physicians
	N %	N %
Age (years)		
< 20	34 3.8	10 4.0
21–35	670 74.1	174 69.0
> 36	200 22.1	68 27.0
Education level		
Associate's degree	342 29.6	
Bachelor's degree	370 32.0	
Vocational health high school	191 16.5	
Graduate degree		252 21.9
Working experience (years)		
0–1	113 12.5	42 16.7
2–5	203 22.5	103 40.9
> 6	588 65.0	107 42.5
Employment unit		
Neonatal intensive care unit	210 23.2	37 14.7
Pediatric intensive care unit	68 7.5	13 5.2
Infant unit	169 18.7	59 23.4
General pediatric unit	219 24.2	78 31.0
Pediatric emergency unit	72 8.0	18 7.1
Delivery room newborn unit	129 14.3	27 10.7
Pediatric polyclinic	37 4.1	20 7.9
Employment institution		
University hospital	398 44.0	101 40.1
State hospital	477 52.8	141 56.0
Private hospital	29 3.2	10 4.0
Region of employment		
Mediterranean	148 16.4	44 17.5
Aegean	203 22.5	50 19.9
Marmara	481 53.2	133 52.8 25 9.9
East Anatolia	72 7.9	

76.2% of the paediatricians said that they would not use a pillow when the infant were asleep, and 97.2% would not cover an infant's face (Table 2).

We further determined that 63.6% of the nurses recommended placing infants in the side position during the daytime, and 74.1% recommended the side position at night. When the infant is left alone in a room, 76.4% of the nurses recommended leaving infants in the side position. After feeding, 82.2% of the nurses recommended leaving infants in the side position. Finally, we determined that 46.4% of the paediatricians recommended placing infants in the side position during the daytime, and 44.0% recommended placing infants in the side position at night. When the infant is left alone in a room, 48.8% of the paediatricians recommended leaving the infant in the side position. After feeding, 70.6% of the paediatricians recommended leaving infants in the side position (Table 3).

Discussion

This study was the most extensive SIDS study performed in Turkey. In our study, one of the most important findings suggests that most of the nurses and paediatricians were aware of SIDS and both lacked sufficient knowledge about which sleeping position is preferable to prevent SIDS.

The American Academy of Pediatrics, the United Kingdom Department of Health, and the German Pediatric Association recommend that infants in the first year should not sleep separate from the

Table 2. Nurses' and paediatricians' knowledge about the conditions of infant sleep patterns related to sudden infant death syndrome

Variable	Nurse N %	Paediatrician N %	$x^{2\text{-value}}$ p-value
Pillow use			
Yes	289 32.0	60 23.8	6.23
No	615 68.0	192 76.2	0.01
Covering of the head or face with bedding			
Yes	18 2.0	7 2.8	0.58
No	886 98.0	245 97.2	0.45*
Sleeping in the same bed with mother			
Yes	108 11.9	33 13.1	0.24
No	796 88.1	219 86.9	0.66*
Sleeping in the same room with mother			
Yes	112 12.4	33 13.1	0.09
No	792 87.6	219 86.9	0.77*
Sleeping in the same room but separate bed with mother			
Yes	803 88.8	218 86.5	1.03
No	101 11.2	34 13.5	0.32*

**NS: Nonsignificant*

Table 3. Nurses' (N = 904) and paediatricians' (N = 252) knowledge about placing infants in sleep positions

Variable	Nurse N %	Paediatrician N %	$x^{2\text{-value}}$ p-value
Daytime position			
Supine position	163 18.0	86 34.1	
Prone position	79 8.7	29 11.5	35.64
Side position	575 63.6	117 46.4	<0.001
Supine and side position	87 9.6	20 7.9	
Nighttime position			
Supine position	138 15.3	110 43,7	
Prone position	49 5.4	21 8.3	103.75
Side position	670 74.1	111 44.0	<0.001
Supine, prone and side position	47 5.2	10 4.0	
Infant's position when left alone in a room			
Supine position	145 16.0	97 38.5	77.28
Prone position	37 4.1	22 8.7	<0.001
Side position	691 76.4	123 48.8	
Supine, prone and side position	31 3.4	10 4.0	
Infant's position after feeding			
Supine position	58 6.4	39 15.5	23.70
Prone position	74 8.2	26 10.3	<0.001
Side position	743 82.2	178 70.6	
Supine, prone and side position	29 3.2	9 3.6	

parents but in the parental bedroom in their own crib [24 -26]. This study tends to support this recommendation. We observed that a majority of the nurses and paediatricians recommended sleeping in the same room but separate bed with mother. In Turkey, generally mothers sleep their baby in the same room but separate bed. This is a normal cultural practice.

Our results show that the majority of Turkish nursing professionals and paediatricians in Turkey

were knowledgeable about most of the common SIDS risk factors. Pillow use and cover an infant's face is the other risk factors for SIDS [27]. In our study, nurses and paediatricians did not recommended using pillow and covering infant's faces. Prone and side sleeping are the most important risk factors for SIDS [5, 8]. A pilot study performed in Istanbul, Turkey, including seven hospitals and 134 paediatricians, found that 95.5% of the medical doctors define SIDS correctly, but only 75.9% of them recommended a certain sleeping position to mothers [28]. Yıkılkan et al. (2011) found that 83% of the health professionals selected side position as the safest sleeping position [20]. In our study, only 16.0% of the nurses and 38.5% of the paediatricians preferred the supine position when the infant is left alone in a room.

In our study, most of the nurses and paediatricians recommended the side-lying position for infants daytime, nighttime, when left alone in a room, after feeding. There were significant differences between nurses and paediatricians knowledge about infant sleep positions in the daytime, nighttime, when left alone in a room, and after feeding. In our study, the nurses and the paediatricians preferred the side sleeping position for infants due to fear of aspiration and poor sleep quality. Previously conducted studies have shown that reasons nurses do not recommend the supine position during sleep include fear of aspiration and poor sleep quality [29, 30]. However, it was shown in other studies that the supine infant sleeping position does not cause a risk of aspiration [31]. In our study, nurses and paediatricians have wrong knowledge about infant sleeping position. This is a risk for SIDS in Turkey. A retrospective study in Great Britain found that many infants who had been found prone at death were originally placed in the side-lying position, highlighting the instability of side-lying position [32]. In our study, nurses' and paediatricians' did not recommend the AAP recommendations for SIDS. This is consistent with the findings of others [29, 33, 34]. AAP guidelines reinforce the call for healthcare professionals in hospitals to implement recommendations for supine sleep well before an anticipated hospital discharge [13]. In Turkey, there aren't any written guidelines on sleep position for infants at the hospitals. Although policy plays an important role in compliance, conflicting messages may be given to parents if nurses and paediatricians are not convinced of the rationale. Consistent with the findings of others [34], this survey documented that the unstable side-lying sleep position was recommended by nurses and paediatricians to parents for use after hospital discharge. This is especially alarming, given the escalated risk of SIDS in side sleeping infants.

Although our study is one of the few extensive SIDS studies performed in Turkey, it has some limitations. One of them is that this study was not conducted an observational design. We asked nurses and paediatricians what they suggest for parent about infant sleep position. Perhaps nurses' and paediatricians' expression may not reflect the exact applications of them. Therefore, we suggested that this topic will be investigated with as observational designed studies. Another limitation is that questionnaires were given nurses and paediatricians and received back same day. Nurses and paediatricians may be talked each other and influenced each other expression. For reduce this limitation we said nurses and paediatricians that "No communicate each other in this regard during answering of questionnaire.

Conclusion

Nurses and paediatricians lack knowledge about which sleeping position should be recommended to prevent SIDS. Thus, nurses and paediatricians should be educated concerning the correct sleeping position and factors associated with SIDS. Nurses who have more communication with the families should also be aware of factors associated with SIDS. Nurses can play an important role in educating the public about the link between SIDS and infant positioning during sleep. SIDS and associated factors should be part of the curriculum in nursing and medical schools and nurses taking care of infants might benefit from postgraduate nursing education.

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Challenges & opportunities facing the pharmaceutical industry in Iran: A qualitative approach

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Abstract

Objective: This study aims to identify the most influential organisational key factors affecting the pharmaceutical drugs distribution system in Iran. The challenges and solutions will be reviewed and analysed.

Study design: This study was based on qualitative study methods. Participant selection criteria were defined and purposeful sampling method was used and continued with snow ball sampling. A total of 20 (67%) of the most senior managers from national pharmaceutical distribution companies in Iran were interviewed. Semi-structured interviews based on four in-depth interviews as well as a review of studies of the pharmaceutical distribution system of developed countries were used in the design. Framework analysis was used to analyse the qualitative results.

Results: Six factors were identified as key influential factors in the pharmaceutical drugs distribution system: pharmaceutical distribution policymaking, pharmaceutical distribution planning, drugs distribution structure, drugs distribution process, drugs distribution monitoring and the evaluation of drugs distribution. There is not a systematic supervision of regulatory rules. The pharmaceutical drugs distribution system in Iran does not have any targeted planning to deal with matters such as internet commerce and the shortage of products needed to deal with accidental injuries. The pharmaceutical drugs distribution structure in Iran is based on a traditional and inefficient structure that needs to be modified. In addition, matters such as the trafficking/smuggling of pharmaceutical products have not been exactly quantified.

Conclusion: In order to increase the pharmaceutical drugs distribution system's efficiency and to reduce supply chain costs in an effective manner, fundamental changes must take place. For these changes to be effective the Provincial Pharmaceutical Drugs Agency which is an additional body in the Iranian pharmaceutical drugs distribution system, must be considered/involved. Furthermore, attention must be paid to planning and integrated policymaking to set up chain pharmacies and to internet commerce in Iran.

Key words: Pharmaceutical Drugs Distribution- Framework Analysis- Iran

Introduction

A 50% growth in the drugs consumption market in the past five years in the world and the spread of these products and the variety of these products in the global consumer market has lead to a need for improvement in distribution methods in order to make it easier for consumers to access these products (1).

In recent years, with the growth of global health products market; supply chain management has been one of the fields that have affected this area (2). This branch of commercial knowledge has benefited greatly from advances in technology; particularly the expansion of electronic commerce (the internet) has experienced considerable changes which has facilitated and improved the process of health/pharmaceutical products distribution in the developed countries (3). This has created the right conditions for setting up a new system for the distribution of pharmaceutical products. As a result the pharmaceutical drug distribution system in the developed countries which has a close

relationship with human health issues is considered vitally important has undergone a considerable evolution. The use of radio location techniques or systems to identify market needs and track products from the production stage to the consumer is one of the major developments that have several application/uses in the field of pharmaceutical products distribution(4). According to recent years' conditions and the growth in the pharmaceutical drugs' production internationally, several methods including centralised distribution methods which were mostly used in countries whose distribution system were nationalised as well as decentralised and network distribution systems where the focus was on the private sector and large pharmaceutical companies were used in studying and evaluating drugs distribution systems (5).

Bearing in mind the changes in consumption patterns, the economic growth and the population growth in Iran, the $3,000,000,000 pharmaceutical market is expanding (6). In 2009-2010 the import of these products alone increased by 25% compared to the previous year (7). The lack of patterns, standards and suitable structures in the field of wholesale and retail pharmaceutical products has created turmoil in several areas such as the denial of suitable access for everyone, availability of trafficked and non-standard products, heterogeneous and unregulated pricing structures, increased wastage, etc….have come to light in the gamut(8).

In terms of both quality and quantity the lack of a suitable retail structure in the pharmaceutical products sector, undefined regulations in this and other retail sectors, lack of clarity in categorising products, unclear storage and sales rules, lack of a suitable/appropriate relationship between the distribution companies (chain) and the retail sector and the inactivity (or the absence) of trade organisations in organising and managing trade relations in a unified manner are among structural difficulties the retail rector struggles with.

Even though over the past two years the structure of private drug distribution companies have been established by the Department of Health, this sector's inexperience and the lack of procedural coordination in the private & public distribution sectors and the lack of coordination between these sectors' procedures and the retail sector has lead to distribution difficulties in this field.

Bearing in mind the above points, change of priorities and the supervisory management system's approach to supply, distribution, access and consumption of pharmaceutical drugs (healthcare products, medical equipment and food supplements) the Fourth Development Plan has prioritized these goals in the drugs and food sector(9). However, despite this and taking into consideration the increasing production and importation of pharmaceutical products (categories); after the Iranian Revolution the Iranian pharmaceutical industry/sector has not witnessed significant progress. According to experts, current conditions will not be able to cater for the country's growing needs in this field.

Even though one of the most important aspects of healthcare service provision is the accessibility and availability of the necessary drugs to treat patients, this aim will not be achievable unless the different elements of the drugs distribution system have been designed and defined in a way that improves distribution costs so that patients have access to drugs needed for their treatment (10).

To achieve this aim it is necessary that the planning at different levels from drugs production to importation to different levels of distribution as well as well defined levels of distribution is designed to ease the establishment of professional relationships. The country's unique and specific economic and social features/conditions as well as the existing conditions within the national pharmaceutical production and import programme will have to be compatible to achieve this aim. In various parts of the world within a short period of time since the beginning of the 1990s, the pharmaceutical industry's growth accelerated; the distribution category also underwent several changes(1).

The creation of wholesale pharmaceutical companies in the 1990s and the formation of multinational drugs distribution corporations towards the end of the 20th century and finally the formation of specialised distribution companies in recent years in the macro and upstream distribution sector and the changes in the retail drugs sector and the formation of chain pharmacies have meant distribution methods have changed from manual order placement to electronic. All in all this shows that the drugs distribution systems in various countries have undergone several stages and have evolved. This evolution

has been dependent on the changes/progress in the economic conditions and the growth of the drugs distribution systems in these countries(11-13).

It is obvious that to determine/design a suitable pattern/structure for the drug distribution of a country, it is initially necessary to identify the current situation and its compatibility to society's current needs and desires. If the situation does not meet the current or future needs of the country, other countries' experiences that have experienced similar conditions and have been successful in this area must be used as role models to design a new drugs distribution system. This must be done by taking into consideration the country's current economic and cultural constraints. Therefore, by studying the current drugs distribution system in Iran this research paper seeks to outline and review the difficulties and challenges and offer suggestions to improve the system.

Materials & methods

The pharmaceutical drugs distribution system in Iran consists of a number of national drugs distribution companies which are considered to be the main players. Hence, all the companies that were active in the drugs distribution system had the opportunity (qualified) to participate in the study.

The aim of this study was to interview all the senior managers of these distribution companies. Accordingly 30 interviews should have taken place. Official invitations were forwarded to the national distribution companies' senior managers and the necessary coordination to carry out the interviews was accomplished. The semi-structured interviews were designed using initial in-depth interviews as well as on the pioneering drug distribution systems of the US and European countries (15-16). The interview questionnaire was reviewed several times by the research group. Eventually the group succeeded in interviewing 20 individuals. One of the research members carried out all their interviews of senior managers in their place of employment. On average each interview lasted between 60-90 minutes and where it was necessary supplementary (follow up) interviews were also conducted. All the interviews were recorded and implemented. In the results section letter P is used to indicate that the interviewee is being quoted.

Framework analysis (stages) method was used to analyse the data. This method involved the following five stages: familiarity, identifying a subject framework, indexing, tabulation (drawing tables) and graphical representation and interpretation. This method was dedicated to analysing the qualitative results of policymaking studies.

At the start of the process, the content of the interviews were designed and planned. The initial theme framework was designed and based on research literature (15-16), guide lines for interview questions and subject guidelines. Members of the research group held several meetings to discuss the framework. By reviewing the interviews again and reviewing the introductory (familiarity) stage, this framework was reviewed. The various data relating to the interviews was indexed depending on the subject (theme) using one or more coding process. This code was again and again reviewed and corrected by three members of the research group and finally was discussed in a meeting attended by all the members. In relation to each theme the interviewees' views were compared using analytical tables. The relationship between themes and subthemes were identified and analysed. Wherever it was necessary reference was made to the implementation interviews and if needed information was added to the analytical tables. The next stage was to interpret the themes using a process similar to the one used in the indexing process (17). The theme framework within the analytical process was repeatedly reviewed and elevated (18). The initial framework consisted of four themes which increased to six themes during the analysis process.

Results and Discussion

Based on in depth interviews and studies relating to the US and European pharmaceutical distribution systems, the analytical framework shown in table 1 was obtained which is a suitable tool for studying the Iranian pharmaceutical distribution system. This tool consists of six main themes and 21 sub-themes.

Table 1. Key themes and sub-themes used in evaluating the pharmaceutical drugs distribution system in Iran

Themes	Sub-themes
distribution policy implementation	Regulatory requirements of pharmaceutical products, research & development (R&D) in the pharmaceutical industry, legal supervision of the pharmaceutical system, private sector's participation in the drugs distribution system and internet commerce(trading)
Pharmaceutical drugs planning	Technological solutions to drugs distribution, disaster management and the drugs distribution system, product shortages in the supply chain, consumers and the electronic commerce
Drugs distribution structure	Pharmaceutical products supply chain, wholesale distribution, wholesalers' role in pharmaceutical products, direct distribution approach, and pharmacy chains
Drugs distribution process	National drugs distribution, provincial Distribution chains, interaction between pharmaceutical producers, wholesalers and pharmacies in the drugs distribution system
Drugs distribution control	Protecting the supply chain and combating the trafficking of pharmaceutical products
Evaluating drugs distribution	The of the pharmacy market and the pharmaceutical industry and evaluating annual operation of drugs distribution companies

Theme 1: Pharmaceutical distribution policy implementation

The drug distribution in Iran has gone through several acute stages.

"before the Revolution the pharmaceutical drug distribution system was an open one based on branded products. The multinational companies had many active sales representatives in a healthy, large and thriving market." (P12). "from our point of view we did not have a progressive or advanced distribution system. It was a macro system where the producer or the sole importer was involved in the distribution process" (P2). The changes that took place in the Iranian drug distribution system after the Revolution were concentrated on two areas: 1- the nationalisation of the pharmaceutical industries and 2- the implementation of the generic plan (19). "The emphasis or focus on generic brands was approved by organisations such as the WHO because they preferred/recommended getting away from branded products with their extensive/huge advertising campaigns" (P14).

Encouraging the newly renamed nationalised pharmaceutical producers to make progress to urgently increase production and to meet country's needs during the imposed war was an effective policy. Setting up new pharmaceutical production facilities was a major policy step towards pharmaceutical drugs self-sufficiency. Out of more that 170 companies who are currently active in the production of pharmaceutical products, more than 70% were set up after the Revolution. (19). "All of a sudden a 4,000 pharmaceutical product list dropped to 590 which meant pharmaceutical marketing collapsed" (P16). Interviewees believed this situation was beneficial to the Iranian pharmaceutical industries. "due to the conditions resulting from the imposed war and the sanctions the circumstances proved to be very helpful" (P9). Despite this, the continuation of the generic programme or system after the war had many criticisms. " the generic system improves access and purchase level but lowers quality; each system (branded or generic) has its advantages and disadvantages. There has to be a balance between the two systems". (P7). Among other subjects that were discussed, the interviewees pointed to the quality of drugs offered for sale. "among priorities in health policymaking, sometimes a high price is paid for tiny amount of quality. Quality is very important but not to a point that it is used as a manipulative pricing tool. For new drugs spending Quality Adjusted Life Years (QALY) and DALY (Disability Adjusted Life Years) indices must be used". (P4).

Furthermore, from the supervision and legislation point of view our country is facing many challenges. "The current pharmaceutical legisla-

tion dates back to 1955/56, the only amendment came into effect in 1988/89; and it was a very minor amendment. The pharmaceutical regulations were introduced in 1988/89. There has not been any new pharmaceutical legislation or regulation since 1988/89'' (P11). ''There is a need to change the structure and legislations, the commissions and in general a review to adapt to current requirements and needs is necessary'' (P2).The lack of human resources in carrying out or enforcing regulatory supervision was also another difficulty facing the pharmaceutical drugs system (19). ''bearing in mind the pharmaceutical activity volume that exists, there is a need for experienced experts in regulatory supervision'' (P17). To overcome this difficulty ''international organisations suggest two methods: either employing specialist human resources or by coordinating and cooperating with several other countries to set up an organisation such as the FDA (Federal Drugs Administration) to carry out the regulatory supervision responsibility'' (P1).

The private pharmaceutical sector's growth in recent years has been so considerable that at least two pharmaceutical holding companies, several national distribution companies and a noticeable number of production units that are dependent on the private sector are currently active in this field (19). The interviewees' stated opinion was: ''the individual or organisation carrying out the task is not very important, what is important that the task is carried out. If the private sector is charged with carrying out the task, the government will have to play the supervisory role. Whatever happens, the role of the healthcare system does not change'' (P16).

Until 2001/2002 there were only five main pharmaceutical distributors. Currently with the addition of 30 private pharmaceutical distributors, these 30 companies have managed to gain 20% of the market share with difficulty. The five main established distributors still manage to control 75-80% of the market'' (P3).

Theme 2: Pharmaceutical drugs distribution planning

Due to the complicated pharmaceutical products supply chain there are reasons that mean change or disorder in one specific area leads to product shortage. (15)

One of the main difficulties/faults of the Iranian pharmaceutical system concerned the products shortages. By boosting national production, by technology transfer and the use of pharmaceutical knowledge programme this problem has been resolved up to a point (19). From the interviewees point of view the pharmaceutical shortages discussion'' always drains/detracts energy from the pharmaceutical system. Senior managers, middle managers, experts and drugs importers (company owners) are always struggling with this challenge to eliminate it'' (P8).

According to interviewees, among other problems affecting the drug distribution planning is the absence of a codified plan in confronting drug shortages in dealing with natural disaster incidents'' the experiences in dealing with the earthquakes in Bam and Khorramabad show that we have been very slow. Even four years ago that we were thinking about setting up a specific drug distribution system to deal with emergencies, nothing was done'' (P7). ''it is not always necessary to physically enact the plan. There is a need for a logical system. We need an organisation that can manage disasters, that uses resources efficiently and ensures medicines and supplies reach the injured. There is not a planned response in place'' (P9).

Theme 3: Drugs distribution structure

Drug distribution in Iran follows two different routes: 1- national drugs distribution, any company that obtains a national distribution licence is authorised to cover the entire country. 2- Provincial or local distribution whereby a company is authorised to cover specified areas. (19) ''national distribution is currently halted/blocked; there are logical reasons for the stoppage. Firstly distribution policies must move towards a provincial system and secondly the task or responsibility should be transferred from the Ministry of Health's central headquarters in Tehran to medical sciences universities all over the country'' (P11).

''we must ensure that drugs reach the consumer at the lowest possible cost, in the shortest possible time and by using the healthiest method. To the patient it does not make a difference which company offers or provides the medicines and it should not matter to the Health Ministry either. What is important is that the cost is as low as possible. The

ownership of the drugs is determined by or dependent upon government economic policies'' (P13).

''Currently provincial distribution has no advantage in the drug distribution system because national distribution companies use provincial depots to carry out the same duties with even better quality than provincial distribution'' (P19).

''in my opinion this task was created without adequate planning. In other words, before creating provincial distribution if we had calculated the drug distribution access time and compared it with the current system; if the access time had improved then we could have claimed that the provincial distribution system was effective. It appears that other than creating an intermediary, no other objective has been achieved'' (P20).

In addition, among other problems with the provincial distribution system is that it causes a lack of clarity in the country's pharmaceutical drugs consumption: ''in reality the proportion of the drugs that are distributed through the provincial system are not mentioned in the pharmaceutical statistics'' (P9).

A further problem with the national drug distribution structure relates to single (non-repeat) prescriptions drugs: ''in practice the provincial distribution and single prescription which were not part of the main pharmaceutical system combined to circumvent the national drug distribution system. Currently this is the situation affecting our system and in my opinion it is one of the challenges facing the pharmaceutical system'' (P15). However, within the pharmaceutical drugs system it is of considerable importance to be able to supply pharmacies with higher quality pharmaceutical drugs at the lower possible cost within the shortest possible time (16). ''the healthcare professional should be able to access the distribution system and in a logical way should be able prescribe the medication to patients in a timely manner. The distribution methods used should be the responsibility of the Health Ministry. What is important is that quality drugs should reach patients on time'' (P18).

Theme 4: Drugs distribution process

The supply chain path shows that drugs R&D and production is the pharmaceutical companies' responsibility who then forward these products to health professionals to prescribe them to end users, the patients. Different players intervene in the process to play different roles. However, the main attention is concentrated on producers, wholesalers and retailers of pharmaceutical products (16).

According to the traditional distribution structure, pharmaceutical products are produced by pharmaceutical companies and through wholesalers are supplied to pharmacies where they are stored until needed by patients and sold to them. The nature of the pharmaceutical products distribution system is important because such a system can influence the speed of patients' access to medicines and the cost of these drugs (15).

According to interviewees, the Iranian medicine distribution system has deviated from its usual process:

''With the involvement of single item prescription distribution and the provincial distribution the pharmaceutical system has become more complicated, but it used be simpler whereby the pharmaceutical producer or importer would supply the medicines to distributors and they in turn would supply pharmacies. Now the provincial distribution has joined the system as well as the single item prescription. In some provinces or states the purchasing authority buys from both producers and single item prescription distributors. Single item prescription distributors have the right to sell to distributors as well as pharmacies directly, for this reason the two systems have overlapped'' (P16).

In addition to this, the pharmaceutical drug importers have become an additional intermediate level or middleman within the pharmaceutical distribution system: ''as soon as drugs enter the country the pharmaceutical distributors get hold of the drugs and supply the country's distribution system. It would better if the pharmaceutical products importers and distributors combined'' (P6).

Pharmacies form the last point within the supply chain before pharmaceutical products reach patients. Pharmacies purchase products from wholesalers, sometimes directly from producers. Then they will take on the responsibility for storage and distribution to patients. Pharmacies must be able to keep adequate supplies of medicines and other pharmaceutical products and be able to provide relevant information to patients (16).

It is also necessary to establish pharmacy supply chains. In addition to reducing the country's

drug distribution system costs this will also mean that patients will have access to higher quality drugs (15). " instead of having 20 drug distribution depots employing 20 sales representatives to supply 20 pharmacies, it would be much more logical to combine and to administer these to form one company" (P16).

Theme 5: Monitoring (controlling) Drugs distribution

Counterfeit pharmaceutical products are products which are produced and distributed by companies and individuals who are not authorised or licensed to produce these products. As these products may contain too much, too little or no active ingredients or may contain poisonous ingredients, in many cases these products would be harmful to human health. These products are considered as global threats (15).

The trafficking of pharmaceutical products affects every country in the world. According to the World Health Organisation (WHO) more than 5% of the drugs in the global market are counterfeit, and this is not a problem that is not limited to the developing countries (16). For some reasons this matter is not taken seriously in Iran: "there are companies that supply urgent medical single item prescription products to patients which may contain imported medicines at the discretion of doctors" (P2).

Theme 6: Evaluating drugs distribution

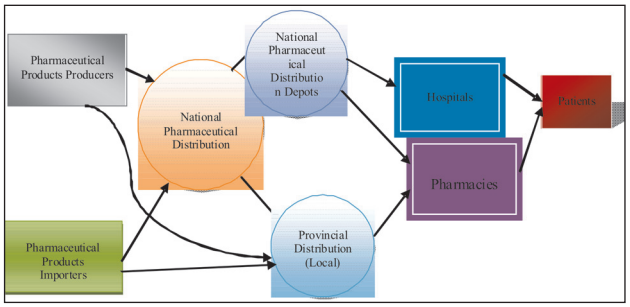
Drugs distribution in Iran does not follow a suitable process and it needs an overhaul: "some of these changes will only gradually come into effect with the replacement of individuals who think and act traditionally with fresh personnel. Just as we were forced to adapt to the use of new technology, we will slowly adopt modern and efficient management systems and methods" (P17).

"the next debate concerns the saturation of the market. When the market becomes saturated, thinking will be forced to move towards quality; that is the time that product quality will become an important priority" (P19). "over the next two years I do not see any hope for change, the situation will get worse. Unregulated activity and the lack of clarity and slowing of processes will hinder progress" (P4).

Conclusion

The discussions about intensification of pharmaceutical industry will continue, but there is not any form/consent that their products are necessary. Success in the pharmaceutical industry depends on or originates from constant demand for advanced healthcare.

Provincial distributions are currently viewed as a problem in our drugs distribution system and have caused the provincial drugs distribution process to be carried out through two channels of both national and provincial distributions. This problem has reduced coordination and increased drugs distribution costs.



Graph 1. An overview of the pharmaceutical products distribution process in Iran

As it was shown in graph 1, in the Iranian pharmaceutical products distribution structure provincial distribution in parallel with national distribution are responsible for pharmaceutical products distribution. This approach has lead to a lack of coordination in producing statistical reports as well as an increase in pharmaceutical system's running costs.

As the results of this research have shown, creating pharmacy support/supply chains in the country can lead to improvements in the final levels. Pharmacy support chains as well as reducing storage costs for pharmacies considerably can also lead to improvements in the drugs distribution process for pharmacies. In addition, pharmacy support chains will also improve pharmaceutical drugs storage processes in accordance with (GDP) & (GSP) standards.

1. Goods Distribution Products (GDP)
2. Goods Supply Products (GSP)

The results of this research suggest that the Iranian pharmaceutical products distribution system

needs fundamental reforms; in relation to GSC (Goods Supply Chain) at the provincial level this point must receive serious attention. Furthermore, codified planning must be in place to deal with drug shortages in emergency disaster situations. The experience of pioneering countries in this field can be an appropriate model to use in planning for natural disasters or other emergencies.

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Correlation of tumour suppressor gene p53 expression with pathohistological tumour characteristics

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Abstract

Colon carcinoma is one of the most common malignant tumours and the second cause of cancer deaths in developed countries.

The objective of research is to investigate the p53 expression in colorectal cancer and compare the expression levels of p53 with histopathological characteristics of tumours (intra and peritumoural lymphocytic infiltrate, stromal fibrosis - desmoplasia, lymphatic and vascular invasion, perineural invasion and necrosis), followed by detection and identification of p53 expression levels as an important prognostic factor of the further course, outcome and the data for the selection of appropriate therapy.

Research was implemented as a prospective, clinical and experimental study. We used a postoperative material obtained by resection of colorectal cancer from 63 patients of both sexes.

From tumours that had poorly expressed lymphocytic response, in 9 samples p53expression was detected. The results of this part of the study showed that 11 tumours with poorly expressed, 16 with moderately expressed and 3 with a pronounced desmoplastic reaction were p53 positive. 15 tumours with poorly expressed, 16 with moderate and 17 with severe necrosis had p53 expression. Expression of p53 was documented in 25 tumours without signs of invasion, and 5 tumours with invasion of blood vessels present were p53 positive. From tumours that had invaded lymphatic vessels 1 was p53 positive and 29 tumours with invasion of lymphatics present was p53 positive. In tumours with signs of perineural invasion 18 were p53 positive. In 12 tumours where perineural invasion was not verified, 18 were p53 positive.

Positive p53 status was present in 52.4% of tumours. Expression of p53 was absent in 47.6% of the tumours and does not correlate with the pathohistological tumour characteristics. Expression levels of p53 do not have a diagnostic, predictive and prognostic potential, while its importance is undeniable in the understanding of oncogenesis.

Key words: colorectal cancer, pathological characteristics, p53 correlation

Introduction

Colon carcinoma is one of the most common malignant tumours and the second cause of cancer deaths in developed countries (1).

Processes of division, differentiation and cell death are strictly controlled, and a disorder in the regulation of any of them gives rise to clones of cells that independently and inappropriately breed and produce tumour mass. Onset of tumour is a complex process involving many genetic and molecular mechanisms. Oncogenesis is the result of accumulation of disorder in the structure and function of genes regulating cell proliferation mechanisms, reparation of DNA molecule or programmed cell death. These genes are: oncogenes, tumour suppressor genes, genes that are the matrix for the synthesis of the reparatory system enzymes, as well as genes that control apoptosis (2).

The main role of tumour suppressor genes is to stop the cell cycle, in order to repair defects in

the structure of DNA molecule (3). Mutation and inactivation of tumour suppressor genes results in uncontrolled cell division and block of programmed cell death-apoptosis. They are inherited recessively and their expression occurs after inactivation of both alleles.

p53 is the most common mutated gene in cancers, localized on chromosome 17, encodes p53 transcription factor that regulates cell cycle through activation of transcription of genes that stop the cycle in the G1 phase (when the gene is damaged) and activates apoptosis under certain conditions (4). Genes activated by p53 transcription factor are WAF1 (cell cycle control), MDM2 (inhibits expression of p53), GADD45 (DNA repair control), Bax (apoptosis control) cyclin G, while inhibiting myc and bcl-2.

The basic functions of p53 are participation in the reparation of DNA molecules (correcting errors in the duplication of genetic material) as well as controlling the cell cycle, proliferation and differentiation. Also, when it comes to the accumulation of genetic errors, p53 allows apoptosis, which is why it is known as „guardian of the cell genome".

The data obtained as a result of various clinical and basic studies suggest that damage or mutation of p53 leads to gene amplification of p53 and loss of control of cell cycle and apoptosis. The level of these changes has reflected the degree of unfavourable prognosis in patients, the very reason that tumours with over-expression of p53 showed resistance to radiation and most chemotherapeutics (5).

The objective of this study was to determine the possible correlation between the morphological parameters and the expression levels of p53 and identification of possible prognostic significance of this correlation. In accordance with the basic objective the following specific tasks have been set:

1. Examination of p53 expression at the operational material-resectioned segments from patients with colorectal carcinoma.
2. Correlation between p53 expression and histopathological characteristics of tumours (intra and peritumoural lymphocytic infiltrate, stromal fibrosis – desmoplasia, lymphatic and vascular invasion, perineural invasion and necrosis) Detection and identification of p53 tumour suppressor gene expression levels as an important prognostic factor for further progress and outcome of disease and the data for the choice of suitable, optimal, target, individual anti-tumour therapy.

Material and methods

The study was implemented as a prospective, clinical and experimental study. We used a postoperative material obtained by resection of the colorectal tumours of 63 patients of both sexes, from the Surgical clinic of Clinical Centre in Kragujevac. In order to obtain as much relevant histopathological data, the routine haematoxylin - eosin (HE) and immunohistochemical methods were performed at the Centre for the pathological-anatomical diagnosis of Clinical Centre "Kragujevac" in Kragujevac.

Routine HE method was used for histological diagnosis of tumours, and pathologic analysis that included, in addition to standard, other prognostic and predictive parameters. The histopathological report showed the following data: the pathological stage of the disease - pTNM classification based on the degree of local tumour expansion, the presence of metastases in regional lymph nodes and data on distant metastases, the presence of intra and peritumoural lymphocytic infiltrates, stromal fibrosis – desmoplasia, lymphatic, vascular and perineural invasion, necrosis and information on the macroscopic manifestation of the tumour.

Colorectal cancer is predominantly adenocarcinoma derived from of the glandular epithelium of the mucous membranes; it grows slowly and in later stages gives metastases. Spreads in two ways: by direct infiltration of the mucous membranes or through metastasis. Metastatic spread may be lymphatic, haematogenous (invasion of submucosa venous vessels, resulting in poor prognosis) and perineural.

Intratumoral peritumoural lymphocytic infiltrate is the result of the host's immune response and is considered a favourable prognostic parameter (6).

Stromal reaction is manifested in the form of stromal fibrosis or desmoplasia. Expressed desmoplastic reaction is the indicator of higher tumour aggressiveness (7). Recent research has shown that the enzymes that carry out degradation of the extracellular matrix, one of the main mechanisms of cancerogenic invasion and metastasis, are originating from stromal cells (8).

In the routine processing of preparations, tissue samples were fixed in 4% neutral buffer formalin solution, in 24 hours, at room temperature. Upon completion of fixation, they were dehydrated by conducting an alcohols series of increasing concentration (70%, 96% and 100%), coloured in xylol and embedded in paraffin. Tissue sections, 4 μm thick, were cut with microtomes *Leica SM 2000R* and *Leica Reinhart Austria*.

After deparaffinization in xylol and hydration in decreasing order of alcohol, sections were stained with *Haematoxylin* according to *Mayer*, coloured in the 2% solution of eosin, then dehydrated, coloured and mounted on a plate with *Canada* balsam (9-11).

Immunohistochemical methods were used to identify the expression of antigen in colorectal cancer resectate. The procedure for immunohistochemical staining included the unmasking of antigens, blocking of endogenous peroxidase, incubation of preparation with primary antiserum and the procedure of immunohistochemical methods - LSAB + - HRP (12). For detection of p53 murine monoclonal antibody was applied (DAKO p53 DO-7 monoclonal mouse clone, 1:200) and highly sensitive specific streptavidin - biotin immunohistochemical method (LSAB + / HRP, DAKO, Denmark), in which the streptavidin is labelled with peroxidase and as a chromogen 1,3 – diaminobenzidine was used . As a general solvent of antiserum and rinsing solution between the different steps in the immunohistochemical staining procedure 0.1 M phosphate buffer pH 7.4 was used. Cell nuclei were stained with *Mayer's* haematoxylin.

Cut off is the selected threshold value to distinguish positive and negative expression of r53. Cut off in this study to assess positivity was > 30% (score of overexpression if more than 30% tumour cells showed immunoreactivity for p53). Scoring system is based on determination of the percentage of immunoreactive nuclei of tumour cells as well as the intensity of immunoreactive staining. Adding points for the percentage of immunoreactivity and intensity gives the total, maximum possible points for the evaluation of expression (table 1).

Immunohistochemical staining was carried out with the control of quality and specifics of staining, using positive and negative controls according to the propositions of UK NEQAS (UK National External Quality Assessment for immunocytochemistry). For statistical data processing SPSS software package and methods of descriptive statistics were used (frequencies, percentages, median, and percentiles). Testing according to two descriptive variables was carried out using Chi-square test and Fisher test. Investigation of the effect of several variables on a binary variable was performed using binary logistic regression multivariant.

Results

Nuclear expression of p53 was present in 33/63, i.e. at 52.4% (grade of positivity for more than 30% tumour cells showing immunoreactivity for p53). In 30/63 i.e. 47.6% had no expression of p53 (figure 1).

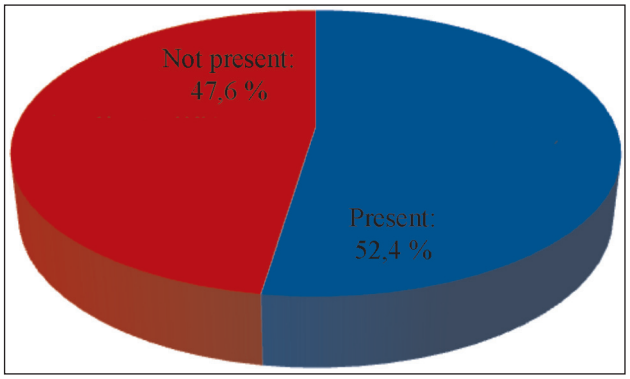

Figure 1. Expression of p53

Lymphocytic host's response to the presence of tumour was moderately expressed in 27/63, i.e. 42.9%, emphasized in 13/63, 20.6% (including

Table 1. Total possible maximum points for the assessment of expression

% immunoreactive nuclei	intensity of immunoreactive staining
0=< 5% stained nuclei	**0** = no nuclei stained
1= 5 do 30% stained nuclei	**1** = poor intensity of nuclei staining
2= 30 do 50% stained nuclei	**2** = moderate intensity of nuclei staining
3= 50 do 70% stained nuclei	**3** = very intensive staining
4= 70 do 90% stained nuclei	
5> 90% stained nuclei	

Crohn-like reaction, lymphoid aggregates with germinal centres in the invasive edge), and poorly expressed response in 23/63, i.e. 36.5%. In 40/63, i.e. 63.5% lymphocytic infiltrate was moderate and pronounced (table 2).

Table 2. Correlation of intratumoral lymphocytic infiltration and p53 expression

Lymphocytic infiltration	Frequency	Percentage (%)
Poorly expressed	**23**	36,5
Moderately expressed	**27**	42,9
High	**13**	20,6
Total	**63**	**100,0**

From tumours that had poorly expressed lymphocytic response in 9 samples p53 expression was present, while in 14 expression of p53 was negative. 21 tumours with moderate and prominent lymphocyte infiltrate had p53 expression and 19 were p53 negative.

Stromal fibrosis - desmoplasia in most tumours (28/63, 44.4%) was poorly expressed, in 26/63, i.e. 41.3% moderately expressed and emphasized in only 9 / 63, i.e. 14.3% (table 3**).**

Table 3. Correlation of desmoplastic reaction and expression of p53

Desmoplastic reaction	Frequency	Percentage (%)
Poorly expressed	28	44,4
Moderately expressed	26	41,3
High	9	14,3
Total	**63**	**100,0**

The results of this work showed that 11 tumours with poorly expressed desmoplastic reaction were p53 positive, 16 with moderate and 3 with highly expressed. 17 tumours with low expression, 10 moderate - marked and 6 with high desmoplastic reactions were p53 negative.

In 23/63, i.e. 36.5% necrosis was moderately expressed, while in 20/63, i.e.31.7% had weak or pronounced degree of necrosis (table 4).

Table 4. Correlation between p53 expression and necrosis

Necrosis	Frequency	Percentage (%)
Poorly expressed	20	31,7
Moderately expressed	23	36,5
High	20	31,7
Total	**63**	**100,0**

From the analyzed samples in this study, 15 tumours with poorly expressed, 16 with moderate and 17 with pronounced necrosis had an expression of p53. Five tumours with poorly expressed, 7 with moderate and 3 with pronounced necrosis were p53 negative.

Invasion of blood vessels was histologically verified in 51/63, i.e. 81.0% of tumours, while in 12/63, i.e. 19% extramural and intramural invasion of venous vessels was observed (Table 5).

Table 5. Correlation of invasion of lymphatic vessels and expression of p53

Blood vessel invasion	Frequency	Percentage (%)
Not present	51	81,0
Present	12	19,0
Total	**63**	**100,0**

26 tumours with no invasion signs of extramural venous vessels had a negative p53 expression, while 25 tumours without signs of invasion had p53 expression. 7 tumours with the present invasion of blood vessels were negative r53 and 5 were p53 positive.

Invasion of lymphatic vessels was present in 60/63, i.e. 95.2% of tumours, and absent in only 3 / 63, i.e. 4.8% of tumours (table 6).

Table 6. Correlation of perineural invasion and expression of p53

Invasion of lymphatic vessels	Frequency	Percentage (%)
Not present	3	4,8
Present	60	95,2
Total	**63**	**100,0**

From tumours that did not have an invasion of lymphatic vessels 2 were p53 negative and 1 was p53 positive. 31 tumours with invasion of lymphatics present were p53 negative and 29 were p53 positive.

Perineural invasion was present in 40/63, i.e. 63.5% of tumours, and absent in 23/63, i.e. 36.5% of tumours (table 7).

Table 7. Correlation of blood vessel invasion and expression of p53

Perineural invasion	Frequency	Percentage (%)
Not present	23	36,5
Present	40	63,5
Total	**63**	**100,0**

In tumours where the signs of perineural invasion were present, 22 were p53 negative and p53 positive 18. In 11 tumours where perineural invasion was not verified, there was no expression of p53, in 12 there was a positive expression of p53 (figure 2, 3, 4)

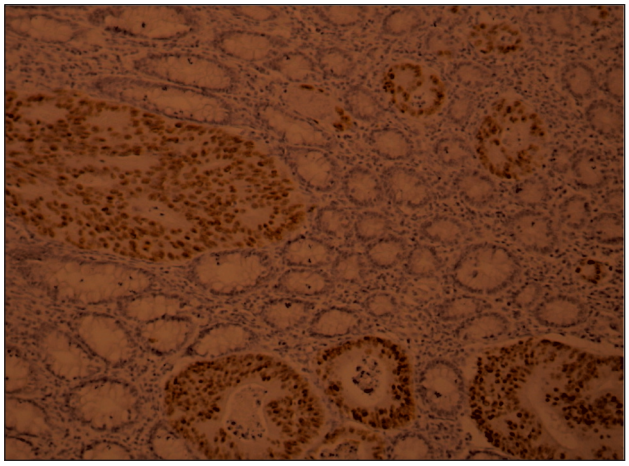

Figure 2. p53 - the internal negative control (IHH, x 100)

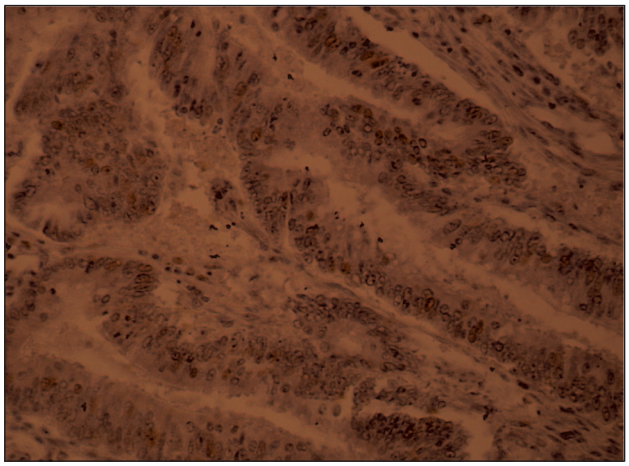

Figure 3. Tumour cells nuclei showed immunoreactivity of p53 to 30% (IHH, x 100)

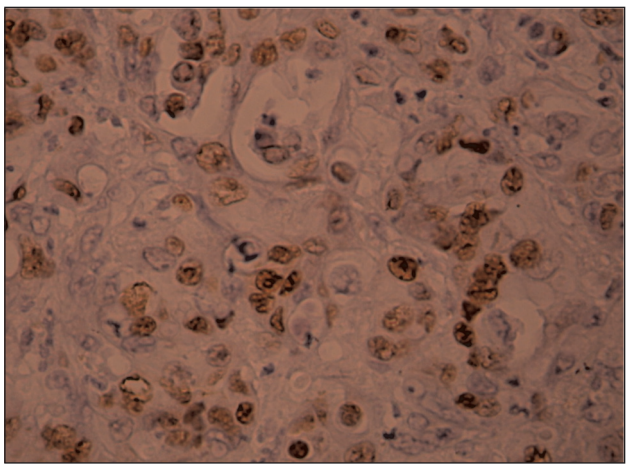

Figure 4. Tumour cells nuclei showed immunoreactivity of p53 over 30% IHH, x 400)

Discussion

Colorectal cancer (CRC) is one of the most common causes of morbidity and mortality in both western world and our region. Classifications and established prognostic parameters, which are today used in the treatment of CRC, still only partially provide information about the course and outcome of this disease, hence there is a need to improve existing and identify new diagnostic and prognostic markers. In this regard it is especially important to identify molecular markers that would provide insight into the potential behaviour or aggressiveness of the tumour (13-15). Since the current clinical and morphologic parameters (histological type of tumour, degree of differentiation, tumour stage, nodal status, invasion of vascular structures and surgical margins) still retain their dominant role in diagnostic procedures, molecular profiling would complement them, mostly in terms of recognizing the response on the therapy (genetic changes), or in terms of application in improving the screening of high-risk categories to allow for timely and successful treatment (16).

According to the literature, CRC originates from a series of mutations going through the adenoma-carcinoma sequence. APC (tumour suppressor) mutates first, which gives dysplasia, then K-Ras (oncogene) when anaplasia occurs and p53 mutations gives already altered tissue the malignant feature. CRC cancerogenesis and development include changes in several genes (APC, c-myc, K-Ras, b-catenin, SMAD4). The cumulative effects play a bigger role in carcinogenesis than the order of changes in these genes (17, 18). Using molecular markers can help determine the risk of developing invasive cancer from premalignant lesions (adenomas). Taking that into account, genetic therapy should target multiple genes involved in carcinogenesis. According to the same data, these tumours are characterized by genetic instability and loss of normal karyotype (17, 18). Other authors also suggest its importance in the progression of genetic defects (19).

Today, p53 mutation is the most common proven mutation in breast cancer, esophageal and small cell lung cancer (20, 21). p53 is the basis for Lane's functional model of "molecular policeman". Wild-type (normal form of p53) is a transcriptional regu-

lator of cell cycle's G1 phase (22). When DNA is damaged p53 is activated and, through p21, inhibits cyclin-dependent kinases and subsequent phosphorylation of proteins required for entry into S phase. This pause in the G1 phase allows the repair of DNA damage or the onset of apoptosis and prevents proliferation of mutated cells (23). Mutations of p53 result in accumulation of p53 protein, which leads to increased proliferation, loss of apoptosis, chromosomal instability and disruption of differentiation (24). On the other hand, p53-induced cell death may prevent the expression of bcl-2 protooncogene that inhibits apoptosis (25). All of the above literature data indicate that most of CRC occurs through a gradual process of a series of genetic and phenotypic changes i.e. hyperplasia, adenoma, carcinoma and metastasis.

According to the results from the available literature, invasion of lymphatic vessels is a negative prognostic parameter, while extramural venous invasion is an independent factor of an unfavourable prognosis and a predictor of increased risk of hepatic metastases (26-28).

Immunohistochemistry is an important diagnostic tool to assess the presence or absence of molecular tumour markers, determine their prognostic and predictive value and possible integration into clinical practice. Immunohistochemistry is a simple and affordable way to confirm the expression of p53, but the results cannot be trusted because methods of detection and analysis of the results (*cut off*) are not standardized).

Lymphocytic host response to the tumour presence was moderately expressed in 42.9% samples of total samples. Distinct lymphocyte response was found in the 20.6% samples of the total number of analyzed CRC (including *Crohn-like* reaction, lymphoid aggregates with germinal centres in the invasive edge), while poor response was observed in 36.5% of the total samples. In total, moderate or prominent lymphocytic infiltrate was present in 63.5% of the total number of analyzed CRC. On the other hand, stromal fibrosis – desmoplasia in most tumours (44.4%) was poorly expressed in 41.3% moderately expressed and emphasized in only 14.3%. Necrosis in 36.5% was moderately expressed, while in 31.7% was low, and high.

The results of this classification are considered very important prognostic parameters. According to data from the literature, both intratumoral and peritumoural lymphocytic infiltrate is the result of mobilization of the immune response and is considered a favourable prognostic parameter, particularly lymphoid follicles on the edge of invasive tumours (*Crohn-like*) (29). As already presented in contemporary literature, stromal reaction that is characterized by increased formation of dense, collagen stroma – desmoplasia, is the indicator of greater tumour aggressiveness (30). Stroma is a reservoir of growth factors on tumour cell enzyme matrix - metalloproteinase for degradation of extracellular matrix and favouring tumour invasion (7). On the other hand, the results of some studies have shown that secondary changes in tumour in regards to necrosis is the result of reduced oxygen flow, elimination of metabolic products, the effects of immune response and antineoplastic drugs (6, 8, 31, 32).

Invasion of blood vessels was not histologically verified in 81% of tumours, while in 19% an invasion of extramural and intramural venous vessels was present.

Invasion of lymphatic vessels was present in 95.2% of tumours, and absent in 4.8% of the tumours. Perineural invasion was present in 63.5% of tumours, and absent in 36.5% of tumours. The results are in agreement with results of many studies on the invasion of blood vessels, lymphatic vessels and perineural invasion in colorectal cancers that can be found in literature (7, 9, 31, 32).

The results of this study showed that nuclear expression of p53 was present in 33 cases or 52.4% of the total, with a rating of positivity evaluated as p53 expression in more than 30% of tumour cells. In 30 samples, or 47.6% of the total number of analyzed CRC there was no p53 expression. The data are consistent with data from the literature on the expression of p53 markers in colorectal cancer, according to which the normal p53 expression in all carcinomas is 45-70%, while the expression of this marker in colorectal carcinomas is 42-67% (33, 34).

In several multivariate analyses it was shown that lymphatic invasion is an adverse prognostic factor (35, 36, 37).

In numerous studies, it was determined that extramural venous invasion is an independent factor of unfavourable prognosis and increased risk of hepatic metastases (3, 36, 38,39). The significance of intramural venous invasion is less clear, but its

presence should be noted. As recommended by the College of American Pathologists, it is necessary to take at least three (optimum 5) samples of tumour tissue in the area of deepest tumour invasion, in order to reduce the false negative results (i.e., absence of extramural venous invasion) (40).

The results of various studies suggest that, in regards to prognosis, it is not sufficient to follow only the expression of p53, but it is necessary to monitor the expression of other tumour markers, whose behaviour can also lead to better therapeutic approaches for the treatment of malignant tumours (41-44).

Expression of p53 is independent of histopathological characteristics of tumours (intra and peritumoural lymphocytic infiltrate, stromal fibrosis – desmoplasia, lymphatic and vascular invasion, perineural invasion, invasive tumour edge formula and necrosis), i.e. there is no correlation between p53 expression and pathological characteristics of tumour, which would serve as a prognostic factor in the further course of illness.

Conclusion

Expression of p53 was present in 52, 5% of the tumours and does not correlate with the histopathological characteristics of tumours.

From all the foregoing it could be concluded that in previous studies the role of p53 as an important prognostic indicator has not been proven. Evaluation of the genes and molecular profiling can help identify groups of patients with overexpression of p53, which might imply a particular therapeutic intervention and an important therapeutic target for screening purposes.

Expression level of p53 does not have a diagnostic, predictive and prognostic potential, while its importance is undeniable in the understanding of oncogenesis.

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Congenital pulmonary hypoplasia can be associated with mature mediastinal teratoma

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Abstract

Both pulmonary hypoplasia and mediastinal teratoma are very uncommon conditions in the neonatal period. We performed a postmortem and pathological examination after a term neonate with a huge right superior mediastinal mass died because of severe aggravating respiratory difficulty immediately after birth. We found that the baby's respiratory failure was due to congenital pulmonary hypoplasia, and the right superior mediastinal mass observed by X-ray was a huge mature mediastinal teratoma. Therefore, neonatologists should consider the possibility of congenital lung maldevelopment in infants with serious respiratory difficulties that occur soon after birth, while a shadow manifesting as a large thymus gland by X-ray may indicate a type of mediastinal tumor.

Key words: Teratoma, Mediastinal tumors, Pulmonary hypoplasia, Congenital, Neonates

Introduction

Both pulmonary hypoplasia and mediastinal teratoma are uncommon diseases in the neonatal period. Pulmonary hypoplasia is a developmental abnormality of the lung. The most common site of neonatal teratomas is the sacrococcygeal region, while those located in the thoracic cavity are rare, especially when they are co-existing, and therefore, it is very difficult to make an accurate diagnosis clinically. We encountered a full-term neonate with acute respiratory distress that occurred shortly after birth, and we finally diagnosed the neonate with congenital pulmonary hypoplasia associated with a huge mature mediastinal teratoma.

Case presentation

A male infant, with a birth weight of 2.70 kg, was born by cesarean delivery with a history of preterm rupture of the membranes for 24 hours to a 25-year-old primigravida at 41 weeks gestation. The baby was normal during the antenatal period and at birth, without fetal distress and birth asphyxia, but severe aggravating dyspnea accompanied by cyanosis immediately occurred within 1 hour after birth. The mother was routinely examined during pregnancy and no abnormalities were found, and there was no history of exposure to radioactive substances and drugs. The parents were not close relatives and there was no history of family hereditary diseases. Physical examination findings on admission were as follows: temperature, 36.5°C; respiratory rate, 64/min; pulse rate, 140/min; and arterial blood pressure, 55/39 mmHg. The baby had a clear consciousness accompanied by severe respiratory distress, grunting respiration, retractions during inspiration, and cyanosis around the mouth, nose and extremities. Reduced breathing sounds were heard in both lungs and grade II-III/VI heart systolic murmurs were heard over the precordium, but his primary reflex was normal. Main laboratory findings were as follows. Arterial blood gas analysis showed that the pH was 6.9, partial pressure of carbon dioxide($PaCO_2$) was 145 mmHg, oxygen partial pressure (PaO_2) was 16 mmHg, HCO_3^- was 28.4 mmol/L, base excess (BE) was -4.5 mmol/L and the oxygen tension/ fraction of inspired oxygen ratio (PaO_2/FiO_2) was 123 mmHg. Blood routine results showed that the white blood cell count was 33.8×10^9/L, hematocrit was 0.34, lymphocyte was 0.34, the ratio of neutrophils was 0.6, hemoglobin was 112 g/L, platelets were 178×10^{12}/L, and the C-reaction protein (CRP) level was 1.0 mg/L. Chest

X-ray findings included hypoexpansion and diffuse, fine granular densities and air bronchograms. A large shadow was observed in the upper right chest (Figure 1). Echocardiographic findings were as follows: (1) patent ductus arteriosus (PDA); (2) atrial septal defect (ASD); (3) significantly elevated pulmonary pressure, which was 75 mmHg accompanied by high-speed reflux of the tricuspid valve and right-to-left shunting of blood through the PDA and ASD; and (4) right ventricular hypertrophy. Clinical diagnosis on admission was neonatal pneumonia, neonatal respiratory failure, persistent fetal circulation (PFC), acute respiratory failure, congenital heart disease, neonatal anemia, and a huge thymus gland. Treatment methods after admission included mechanical ventilation, inhaled nitric oxide (i-NO), supplementation of exogenous surfactant, and intravenous injection of magnesium sulfate and other therapies. However, the condition of the infant deteriorated and he finally died on the 4th day of life because of multiple organ system failure (MOSF), including renal failure, shock, and hyperkalemia.

The baby's parents gave consent for postmortem and pathological examination and the study protocol was approved by the institutional research ethics committee. The main findings were as follows (Figures 2-8). (1) Pulmonary hypoplasia was found and both lungs were not completely subdivided into lung lobes. (2) Congenital heart malformations, atrial septal defect (ASD, 8 mm in diameter) with patent ductus arteriosus (PDA, 5 mm in diameter), enlargement in the right atrium and ventricle, and right ventricular hypertrophy were observed. (3) A mediastinal mature teratoma was observed, which involved Gley's glands, and pancreatic, adrenal, neural, ganglionic, striated muscle, vascular and lymphatic tissues. The thymus gland was replaced by tumor tissues and no thymus gland tissue was found under a microscope. (4) We found partial atelectasis and air sac collapse, while others parts of the air sacs showed cystoid extensions. (5) The right adrenal was displaced to the inferior right kidney.

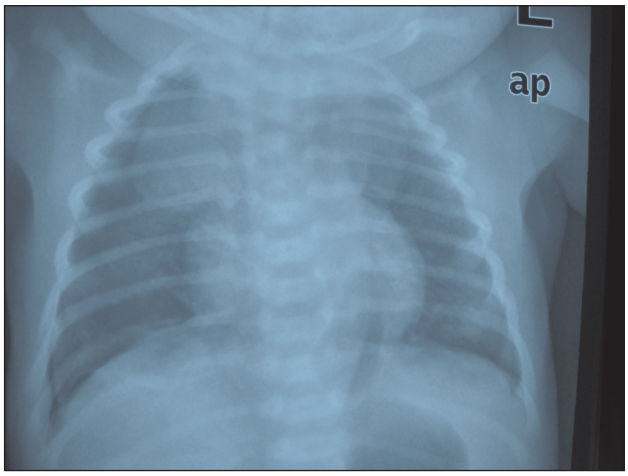

Figure 1. Chest x-ray showed a large-shadow large-shadow in the upper- right mediastinum.

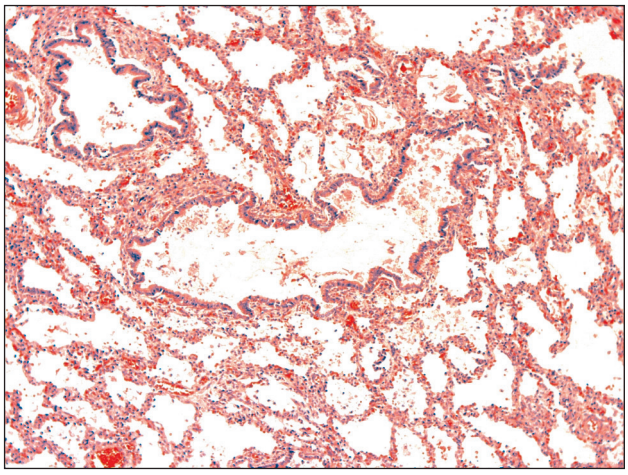

Figure 2. Pathological examination showed cystic expansion in pulmonary alveoli and bronchia (HE×100)

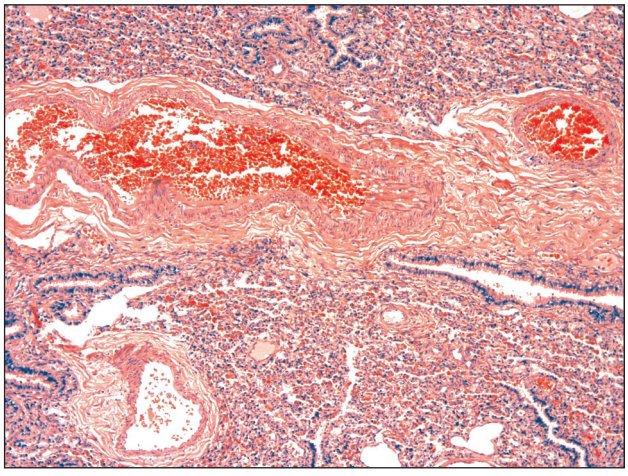

Figure 3. Pathological examination showed tortuous in pulmonary arteriolar and decreased in pulmonary veins (HE×100)

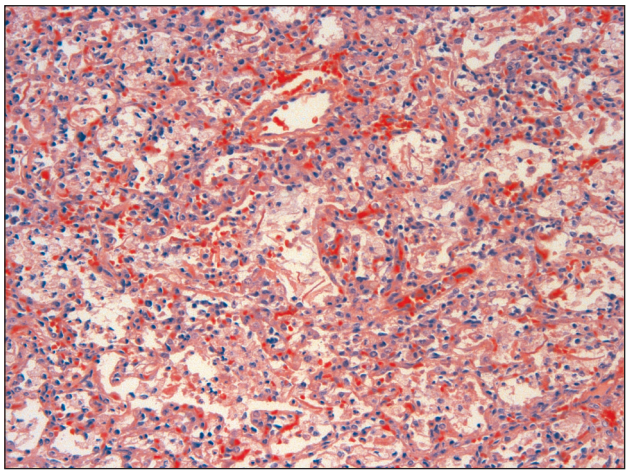

Figure 4. Pathological examination showed hypoplasia in pulmonary alveoli (HE×100)

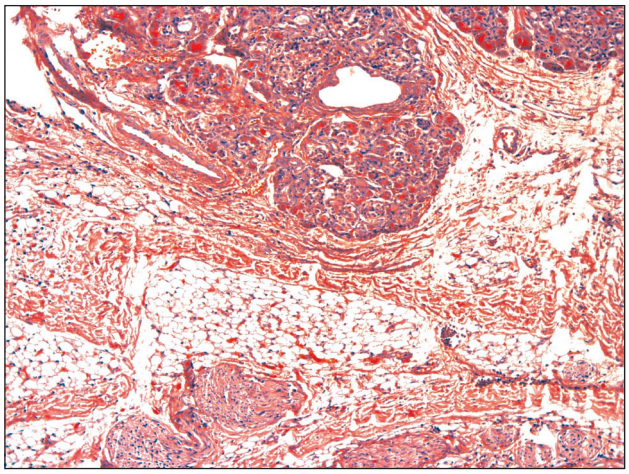

Figure 5. Pancreatic and disorganized nervous tis tissues in neoplasm (HE×100)

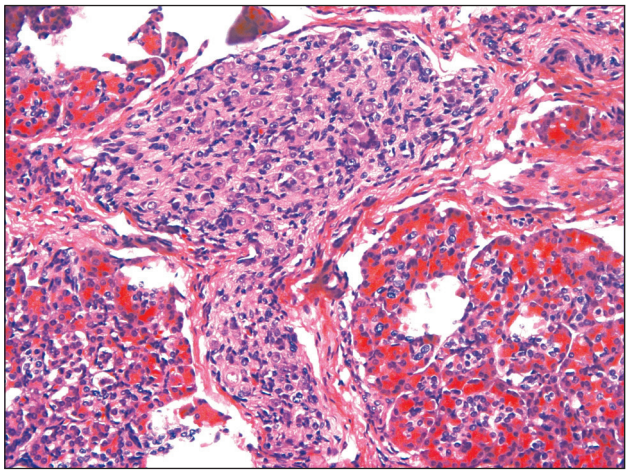

Figure 6. Nerve ganglion in neoplasm (HE×100)

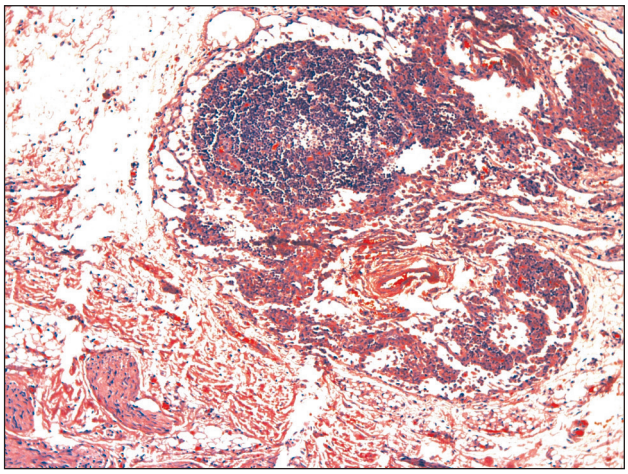

Figure 7. Lymphatic tissue in neoplasm (HE×100)

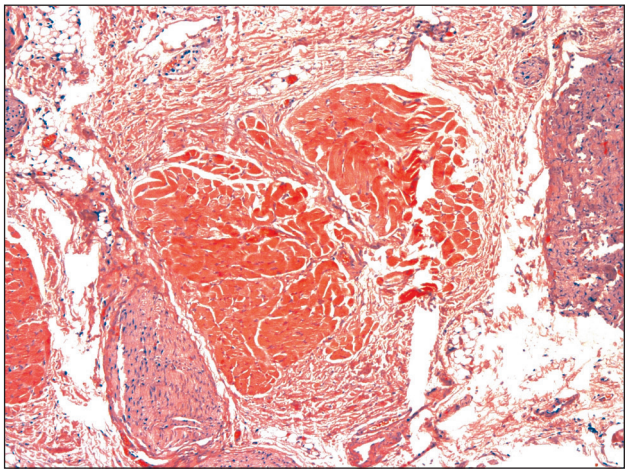

Figure 8. Striated muscles in neoplasm (HE×100)

Discussion

The patient was administrated to our NICU because of progressive respiratory difficulty after birth, and was diagnosed with RDS, and PPHN clinically. He was given a series of affirmative treatments but finally died. A postmortem and pathological examination found pulmonary dysplasia, and a large shadow in the upper right mediastinum observed by chest X-ray was mediastinal teratoma.

Pulmonary hypoplasia is a part of the spectrum of malformations characterized by incomplete development of lung tissue, including a decrease in the number of alveoli, cells, and airways, eventually resulting in decreased size and weight of the lungs. Pulmonary hypoplasia is a rare disease, and its incidence ranges from 9–11 per 10,000 live births and 14 per 10,000 births [1], but it is a common cause of neonatal death [2]. It is believed that there are 2 types of pulmonary hypoplasia: primary and secondary.

However, primary pulmonary hypoplasia is rarer and most are associated with other maternal or fetal abnormalities. It is generally agreed that prolonged rupture of the membranes and oligohydramnios is the main cause of pulmonary hypoplasia [3]. Yang et al [4] reported that 15.7% of live birth fetuses have premature rupture of the membranes and 62.5% of them die afterwards. Another important cause of pulmonary hypoplasia is congenital diaphragmatic hernia, which is often associated with pulmonary hypoplasia [5,6]. However, as found in the current case, pulmonary hypoplasia caused by a huge mature mediastinal teratoma is rarely observed, possibly because most of the thoracic cavity is occupied by the large mature mediastinal teratoma, and therefore, development of the lung is significantly restricted. Teratoma is an uncommon germ cell tumor in the neonatal period and is commonly seen in male adults, and most of them belong to benign masses [7,8,9]. In our case, a chest X-ray showed a large mass in the right superoanterior mediastinum and was considered as a huge thymus gland until it was confirmed as a teratoma by postmortem and pathological examination, this is a worthy cause lessons. The teratoma tissue in our patient was implicated in the pancreas, adrenal, Gley's glands, neural and ganglionic tissues, striated muscle, and vascular and lymphatic tissues.

We searched in Medline and the Highwire Stanford network station from January, 1753 to May, 2011, and only found 8 neonates with acute respiratory failure caused by intrathoracic masses [10,11], 5 had congenital cystic adenomatoid malformations (CCAM), 2 had a mediastinal teratoma, and 1 had a pneumatocele. Among them, 2 neonates with large CCAMs presented with severe respiratory distress immediately after birth because of pulmonary hypoplasia. In summary, we found that the pulmonary hypoplasia of our patient was closely associated with the huge mature mediastinal teratoma. We consider that the possibility of congenital lung maldevelopment in infants with serious respiratory difficulties soon after birth should be considered, while a shadow appearing as a large thymus gland by X-ray may be a type of mediastinal tumor.

Acknowledgments

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Effect of socioeconomic factors on Gastroenteritis during summer among children between 1 - 72 months

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Abstract

Aim: Our aim is to determine the association between social factors and acute gastroenteritis occurred during summer, among children aged between 1 and 72 months and provide help to normal growth of children and contribute to taking preventive measures.

Material and Method: It is a cross-sectional prospective case control study which was carried out between 2005 and 2006 June to August. 450 children with acute gastroenteritis that admitted to Ministry of Health Ankara Education and Research Hospital were recruited. Control group was constituted with 200 children that did not have acute gastroenteritis in the last one month. A questionnaire was filled out face to face with mothers. The data were analized by SPSS (Statistical Program for Social Sciences), version 12.

Results: The mean age was 31.8±20.9 months in patient group, and 31.4±21.4 months in control group. Children with acute gastroenteritis had higher rates of incomplete vaccination. Children in patient group (67.3%) had higher rates of living in shanty than controls (45.5%) (p=0.0001). The duration of using vitamin supplementation was lower in the patient group.

Conclusion: The rate of acute gastroenteritis increases with the lack of ORS knowledge, incomplete vaccination, inadequate vitamin intake and low socioeconomic status. Washing hands before preparing meal decreases the rate occurance in diarrhea.

Key words: diarrhea; socioeconomic factors

Introduction

Children constitute one of the most susceptible groups to environmental deterioration and harmful factors. Health is a state of full welfare from a physical, mental and social perspective, and it is affected by the environmental factors (1). The potential risk caused by certain environmental factors causes various health problems. Since children contact with the soil more frequently and often take their hands to their mouths especially in the first couple of months, they are affected more by the unhealthy conditions and harmful substances (2).

At the Fourth Ministerial Conference on Environment and Health, which was held in Hungary Budapest by the World Health Organization (WHO), the main topic was "Child and Environmental Health", and it was emphasized that child and environmental health constitute the basis for the accomplishment of sustainable developments targets by the countries (3).

Communicable diseases are still the most important cause of death in childhood around the world. The diarrheal diseases are one of the most common disease groups among communicable diseases (4). Despite the improvements in the mortality rates, they cause 2.5 million deaths every year in children under the age of 5 in the developing countries and regions (5).

Diarrheal diseases are important not only because they cause acute dehydration and death but also because they cause malnutrition, growth arrest and improper drug use (6). Consecutive diarrhea attacks are the most important cause for both malnutrition and the disruption in the growth and development processes (4). When analyzed with a view to social background, it is seen that the communities with

high mortality and morbidity rates for diarrheal diseases have low education and socioeconomic levels, little environmental awareness, and insufficient infrastructure facilities (6).

The causes leading to diarrhea are closely connected to the health status of the community. The infections, which occur as a result of the misinformation of mothers on nutrition and mothers' inattention for hygiene conditions, are the primary causes of diarrheas (7).

Feeding the baby only by breast milk in the first six months, then breastfeeding until two years old, giving proper additional foods, not using feeding bottles or pacifiers, ensuring food, water and hand hygiene, ensuring sewage services and ensuring full vaccination protect children from diarrheal diseases (8,9).

In our country, diarrhea ranks in the fifth place among the causes of death for the children of 0-4 age group, and currently diarrhea morbidity is high and the application of oral fluid treatment (OFT) has not reached the targets (6).

Material and method

This study is a prospective case-control study planned with a cross-section pattern. The study covered 450 children of 1-72 months that applied to the Ministry of Health's Ankara Training and Education Hospital Child clinic with diarrhea between the dates of 1- June-August 2005 and June-August 2006. The control group covered 200 children of 1-72 months that did not have diarrhea at least in the last one month. The prepared questionnaire form was filled by the same physicians who conducted the face-to-face interviews with the mothers.

The questionnaire form asked questions about: the child's age and gender, the education status of the parents, the ages of the parents, the mother's knowledge of OFT, the socioeconomic level, the vaccination status, the type of residence, the vitamin intake, the water sources, the duration of breastfeeding, the intake of cow's milk, the mother's use of toilet paper, the mother's hand washing after the toilet use, the mother's hand washing before preparing the food, the frequency of house guests per week, the mother's work status, and the number of the household members.

The definition of diarrhea, as accepted by the WHO, was taken as the passage of three or more liquid stools per day (24 hours), or more frequently than is normal for the babies fed with breast milk (10). The daily number of stool was asked, and the children with three or more were included in the study. The children that took antibiotics in the last two weeks and the children with another systemic disease with diarrhea were excluded. The rating of dehydration was made by the physician in line with the WHO criteria (11). The mothers that prepared the mixture of sugar-salt at home in the case of diarrhea were asked about how they prepared this liquid, and the correct answer was accepted as "Adding two tablespoons of sugar, one teaspoon of salt, one teaspoon of carbonate to five glasses of water " (10). Any kind of food other than breast milk was accepted as additional food. The vaccination status of the children in the defined age group was evaluated according to their vaccination cards. The mothers were asked about any vaccines that were not stated in the card. When the child did not have a vaccination card, a series of questions were asked to the mother in order to detect the vaccination status of the child in terms of each vaccine. The mothers were asked to state the dose number of the vaccine for the diphtheria-pertussis-tetanus and oral polio virus vaccines (12).

The data obtained were coded and evaluated by using SPSS (Statistical Program for Social Sciences) version 12. The statistical significance of the data was evaluated by using the Pearson Chi-Square test and Mann-Whitney U.

Results

The average age of the phenomena included in the study was 31.8±20.9 months, and it was 31.4±21.4 months for the control group; in this respect there was not a statistically significant difference between the phenomena and the control group ($p>0.05$). The diarrhea status was more frequent in the children of 7-24 months (44.4%) in the patient group (Table 1).

There was not a statistically significant difference between the child's gender and the diarrhea status ($p>0.05$).

Some characteristics of the 650 mothers studied are indicated in Table 2.

Table 1. Distribution of age in patient and control groups

Group		Children's Age (in months)				Total
		≤6	7-24	25-48	49-72	
Patients	n	62	200	119	69	450
	%	13.8	44.4	26.4	15.4	100
Control	n	21	58	64	28.5	200
	%	10.5	29	32	126	100

Table 2. Some characteristics of mothers

	Patient (n:450)	%	Control (n:200)	%
Age				
<20	27	6	8	35
21-30	308	68.4	114	422
31-40	103	22.9	64	167
>40	12	2.7	14	26
Educational Status				
İlleterat	20	4.4	22	11
Primary School	315	70	116	58
Higher secondary	108	24	28	14
College and University	7	1.6	34	17
Profession				
House Wife	425	94.4	161	82.1
Working	25	5.6	35	17.9

Table 3. Comparrison of level of knowledge about oral fluid treatment and mother's educational status

Mother's Educational Status		Knowledge About Oral Fluid Treatment		Total
		Present	Absent	
İlleterat	n	3	39	42
	%	7.1	92.9	100
Primary School Graduate	n	88	343	431
	%	20.4	79.6	100
Higher Secondary School Graduate	n	19	117	136
	%	14	86	100
Collage or University Graduate	n	30	11	41
	%	73.2	26.8	100

As the mother's education level rises, the ratio of knowing the OFT use increases (p=0.0001) (Table 3). The income level was lower in the patient group, and it was found that diarrhea ratio decreased as the income level rose (p=0.04) (Table 4). The two groups were found to be different in terms of their living environments, and it was found that the patient groups had a higher ratio of living in the slums than the control group (p=0.0001). The ratio of using tap water was found to be significantly higher for the diarrhea group (p=0.0001). While not statistically evaluated, the ratio of using water from wells was 1.3% in the patient group, while there was no use of water from wells in the control group. As the number of people living in the same household rises, the diarrhea ratio increases (p=0.0001). Regarding the frequency of house guests per week, the ratio of having 4-5 house guests per week was 37.3% in the patient group and 24% in the control group; the frequency of house guests per week in the patient group was found to be significantly higher (p=0.0001).

Table 4. Distribution of socioeconomic status and their characteristics of the groups

Monthly income (in Turkish Liras)	Patients (n)	%	Control (n)	%
488	186	41,3	75	37,5
489-1000	190	42,2	75	37,5
>1000	74	16,4	50	25
Dwelling type				
Flat	147	32,7	109	54,5
Slum House	303	67,3	91	45,5
Water Supply				
Fountain	351	82,7	89	45,5
Carboy	72	11,3	86	43,9
Others	27	6	21	10,7
Number of people living in the same house				
≤3	1	0,2	44	22
4-5	105	23,3	122	61
6-7	146	32,4	28	14
>7	98	44	6	3
Number of visitors (weekly)				
≤1	60	13,3	39	19,5
2-3	80	17,8	98	49
4-5	168	37,3	48	24
6-7	118	26,2	11	5,5
≥8	24	5,3	4	2

Table 5. Ortalama anne sütü ve inek sütü kullanım özellikleri

	Patients			Control Group		
	n	Mean Values (month)	Standart Deviation	n	Mean Values (Month)	Standart Deviation
Mean values in starting feeding with cow's milk	335	8,8	5,4	158	12,2	6,1
Duration of breastfeeding	450	11,4	7,8	200	14,5	6,9

Table 6. Vaccination and vitamin supplement usage in the groups

		Patients		Control Group	
		n	%	n	%
Vaccination	Complete	389	86,4	195	97,5
	Incomplete	61	13,6	5	2,5
Duration of vitamin supplement usage	Not used	192	42,7	27	13,5
	1-12 months	205	45,5	95	47,5
	≥12 months	53	11,8	78	39,5

The ratio of mothers' hand washing before preparing the food was found to be significantly higher in the control group (p=0.0001). While the status of mothers' hand washing after the toilet use was higher in the control group, this was not found to be statistically significant (p>0.05). The ratio of mothers' use of toilet paper was found to be significantly higher in the control group (p=0.0001).

The average period of receiving breast milk was 11.4±7.8 months in the patient group and 14.5±6.9 months in the control group. The duration of breastfeeding was found to be significantly lower in the patient group in comparison to the control group (p=0.0001) (Table 5).

The ratio of starting cow's milk after 12 months was 27.1% in the patient group and 35% in

the control group; significant difference was found between the groups when they were compared in terms of the average period of transition to cow's milk, and the transition to cow's milk was earlier in the patient group (p=0.0001).

Significant difference was found between the patient group and control group in terms of full vaccination rates, and the full vaccination rate was found to be lower in the patient group (p=0.0001) (Table 6).

When the groups were compared in terms of vitamin preparations intake durations, the ratio of the ones without the intake was 42.7% in the patient group and 13.5% in the control group; and the ratio of intake ≥12 was 11.8% in the patient group and 39% in the control group. The ratio of the ones without vitamin preparation intake was found to be significantly higher in the patient group (p=0.0001).

Discussion

The main purpose of protecting child health is to prevent the occurrence of any diseases. This can only be achieved through the improvement of the environmental conditions and the full implementation of personal hygiene rules especially for diarrhea.

Currently one of every three deaths is the death of a child under the age of five. Not only the quantity of the child mortality but also the quality of child life matter. It is an important problem to have children who manage to survive but have to spend their years with bad health and growth arrest conditions, who cannot fully develop their mental and physical potentials, who cannot fully contribute to their families and communities in the future (13,14).

Socioeconomic status is considered to be a risk factor setting the background for diarrhea. Mother's education status is a variable related to the socioeconomic status, and it is also the leading factor defining the baby's health. When the mother is educated she understands the messages related to health education better. As the number of education years of the mother increases, both diarrhea prevalence and diarrhea-specific infant mortality rate decrease (15). In their study Nguyen et al. found that the ratio of mothers' with college education was 35.1% in the diarrhea group and 51.4% in the control group, and concluded that diarrhea was more common in the group where mothers were younger and had low education level (11). In our study, both groups were from the same socioeconomic level and the ratio of mothers with college and higher education was low. For this reason, we think that there is no difference between mothers' education level and diarrhea in this study.

Poverty is not just an economic term, however the current literature uses daily income per capita as the measure of poverty (16). The poverty of children is almost always related to the poverty of the family (17). Belek et al. conducted a study in Antalya and informed that the father's status as a wage-earner, salaried worker, or unemployed increased diarrhea by 4.5 times, and the low level of income per capita increased it by 5 times (18). In our study, the ratio of the ones with income below 488 (41.3) YTL was 41.3% in the patient group and 37.5% in the control group, and it was found that diarrhea cases decreased significantly as the income level rose. Nguyen et al. informed that diarrhea prevalence had a downward trend in childhood as the income level rose (11). In order to mitigate or eliminate poverty's impact on children, attention should be paid to the health training of mothers, the state should provide unconditional and free economic assistance to all children particularly to the ones coming from families with irregular income, healthcare law should be made so as to provide health insurance for all children, and the resources allocated to health and education should be increased (17).

It was informed that the babies living in the slums have 1.7 times more diarrhea (15). In our study it was found that 67.3% of the patient group and 45.5% of the control group lived in the slums. The patient group had a significantly higher ratio of living in the slums when compared to the control group. We think that this is an expectable result of the unfavorable living and hygiene conditions of the slums.

There is not enough information on the level of contamination of the water sources and the development made. Also there is not an effective supervision program in implementation for preventing pollution. Any spring water without a preservation zone around can easily be contaminated (19). Özaltın et al. found that the ratio of giving

tap water without any processing to children was 75% (14). In our study, the sources of water that the children drank were asked and 82.7% of the patient group were using tap water. This ratio was 45.4% in the control group. The use of bottled water was 11.3% in the patient group and 43.9% in the control group. The ratio of tap water use was higher in the patient group.

In their study Özaltın et al. found that 80.5% of the study subjects had city water in their houses (20). In our study everybody had city water at home**.** The city water is expected to be in compliance with the standards for drinking water and all public is expected to use the city water as the drinking water. Özkan et al. conducted a study in Gölbaşı district, and while 92.2% of the households in the study area used the city water as the drinking water, 55.1% of them stated that using city water as the drinking water was not right (5). This data makes us think that the public does not consider the city water to be safe for drinking. The patient group had a significantly high ratio of drinking tap water. In addition to the water distribution system, water gets contaminated in the process of storage at home, and this is considered to be an important health risk especially for children (21). Even the water, which is found to contain enough chlorine after being taken from the tap, might be contaminated in a very close place, or enough time might not have passed for chlorine to take effect. It is necessary to teach the simple boiling method, personal chlorination and other disinfection methods to the individuals and to make them understand importance of those methods (19).

Bozkurt et al. did not find a difference in terms of the number of people living in the same household between the patient group and the control group (22). Gascon et al. observed that as the number of people living in the household increases the ratio of diarrhea in children gets higher compared to the control group (23). In our study, similarly an increase was found in diarrhea prevalence as the number of people living in the household increased. As the number of people living in the household and the number of house guests increased in the patient group, the ratio of diarrhea in children increased. The reasons affecting this situation might be the failure to comply hygiene conditions, transmission from one individual to another, and reduction in the time and care spared for the child(23,11).

Frequent hand washing, following hygiene rules while preparing food and the use of clean water can be used to prevent diarrhea. It is very essential to wash hands with plenty of water and soap before preparing the child's food, after toilet, after changing the diapers and right before feeding the child (24,25). It was found that diarrhea morbidity can be reduced by 35% just by making people adopt hand washing behavior (15). Luby et al. found that the diarrhea cases decreased by 25% with regular visits, by giving training on hand washing with soap in their study area (26). Kotch et al. (in nurseries) found that diarrhea ratios were reduced by paying attention to hand washing and to the hygiene of the equipments used in child care (27). In our study, the ratio of mothers' hand washing before preparing the food was 61.3% in the patient group, and this was higher than the ratio stated in Nguyen's similar work (18.7%) (11). It was found that the control group has a significantly higher ratio of mothers regularly using toilet paper. Mothers play a significant role in breaking or forming the contamination chain at home, and they should be informed sufficiently through the trainings to be held on this topic (11).

Breastfeeding is one of the most important factors contributing to the regular growth of the children. Breast milk contains all the nutrients that a baby needs in the first 4-6 months of life. UNICEF and WHO recommend that babies are fed only with breast milk in the first 6 months after birth (without any other solid or liquid food or water), and that the solid and mash additions should be started starting from the seventh month (28). While breastfeeding is a common practice in our country it is not enough to limit the feeding behavior with only breast milk (29). In our study the ratio of the children that received breast milk in the first 6 months was 18.4% in the patient group and 8% in the control group. In their study Nguyen et al. informed those figures as 22.3% in the patient group and 36.4% in the control group(11). In our study the average duration of breastfeeding was 11.4 months in the patient group while it was 14.5 in the control group. 34% of the patient group and 27% of the control group were still receiving breast milk as the study continued. The ratio of diarr-

hea was significantly low in the children that received breast milk. The children that receive breast milk have diarrhea less because of the lesser possibility of being exposed to contaminated food and drinks and because the antibodies and the other non-specific substances in the breast milk are protective against diarrhea and breast milk increases the intestinal micro flora preventing the formation of enteric pathogens (15). In addition to the protective effect of the breast milk, Cullu stated that another factor increasing the diarrhea prevalence in children fed with feeding bottle was that the food sources were not clear enough(30). According to the results of 2003 Population and Health Survey in Turkey, the average breastfeeding duration for all children was 14 months, which was two months longer than what it was in 1998 (28). The average breastfeeding duration in the control group was consistent with this study. The average breastfeeding duration was found as 9.8 months in Erkuran's study (31). In our study both groups had better breastfeeding ratios compared to the values found by Erkuran. In our country while the breastfeeding ratio is high in the first months, the duration of starting additional food and giving breast milk is short. While serious works have been carried out for this throughout the country the desired level could not be achieved yet. For this reason, we would like to emphasize that it is necessary to continue and expedite those works, to focus more on the regions with low socioeconomic level especially like the ones we serve and to make use of all communication tools for this.

The use of cow's milk as an equivalent of breast milk in the first year of life is not recommended because it increases the kidney solid burden due to excess protein and minerals in it, it is an allergen, it has a low content of iron and it creates gastrointestinal bleeding at the micro/macro level. The protein content of the cow's milk is three times more than the recommended amount and its sodium content is 50% above the safe level (32). In his work, Erkuran found that the group with low socioeconomic status and low education level started cow's milk before the 12th month and consequently the diarrhea prevalence was more in those children (31). When the groups are compared in terms of the average period of passing to cow's milk, it was seen that the patient group's passing to cow's milk happened earlier. The people should be evaluated with their living conditions and social environment and the training for child nutrition should cover all individuals related with the topics.

In the period when the study was conducted, a child that was in the age limits of the study should have had one dose of BCG vaccine (2nd month), four doses of diphtheria, pertussis, tetanus and live poliomyelitis vaccines (2nd, 3rd, 4th and 18th month), three doses of hepatitis B vaccine (3rd, 4th and 9th month) and one dose of measles vaccine (9th month) to be considered as fully vaccinated according to the Vaccine Schedule of the Ministry of Health (12). Inn their study Bilir et al. informed that 3.9% of the children had no vaccines, 29.6% had missing vaccines and 66.5% was fully vaccinated (33). According to the 2003 Turkey data of the State Statistics Institute, the ratio of the fully vaccinated children until the age of one was 48%, the ratio of the ones never vaccinated was 4.4%; and the ratio of the fully vaccinated children between the 12-23 months was 54.2%, the ratio of the ones never vaccinated was 2.8%, and the ratio of the ones with missing vaccines was 43% (12). In our study, the ratio of full vaccination according to age was 86.4% in the patient group and 97.5% in the control group; the ratio of the children with missing vaccines was 13.6% in the patient group and 2.5% in the control group. Differently from the other works, both groups did not have any children that had no vaccinations.

It is recommended to give small and frequent meals (at least six meals a day) to the child during diarrhea and to feed one extra meal for two weeks after diarrhea. It is recommended to use vitamin and mineral mixture for an intake of supportive folate, vitamin A, zinc (it reduces the severity and duration of diarrhea and decreases the diarrhea prevalence in the following months), magnesium and copper (minimum amount is twice of the daily recommended daily intake) every day (6,34). Our study also compared the vitamin preparation intake durations of the groups before diarrhea and the ratio of the children that did not take vitamins was found to be 42.7% in the patient group and 13.5% in the control group. The studies indicate that attention should be paid to nutrition during diarrhea and that the vitamin preparation support is

important. As far as we know, the literature does not contain any studies on the vitamin preparation intake in the pre-diarrhea period. Further studies are required on this topic.

Conclusion

As a result, this study consisted of phenomena that were in the low-income level group and that had higher ratios of living in the slums and using tap water. It is important for families to observe the hygiene rules at home and to improve the environmental factors at home in order for them to break the domestic infection chain. We think that the people responsible for the child care should be given the necessary trainings on this.

It is also important that mothers wash their hands before preparing the food and have the habits of using toilet paper and hand washing after using the toilet for breaking the domestic infection chain. As the number of individuals living in the household increases the possibility of the child getting diarrhea rises, and this might be caused by the failure to comply with hygiene rules and the increased interpersonal transmission.

We think that the mothers that have the most important role in the raising, care and training of the children or the caregivers should be given trainings particularly on cow's milk, breast milk, starting additional foods and vaccination; and also the relevant institutions and people should perform their tasks with respect to the improvement of the social living environment.

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Association between household characteristics and sensitization to house dust mite in childhood asthma

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Abstract

Objective: asthma is a chronic inflammatory airway disease. The development of asthma and allergy appears to be the results of gene-environment interaction. Potential environmental risk factors such as allergens and life style pattern may trigger respiratory symptoms. Evidence of increased asthma and allergic response among urban versus rural children has been reported. The aim of this study was to investigate the association between household characteristics in childhood asthma, who have positive skin prick test (SPT) to mite and to compare the results with those of the patients who have negative SPT.

Method: The study population consist 150 asthmatic children aged 1-14 years attended to Dr Sheikh hospital in Mashhad, between Januay 2008 and December 2009.

Results: Out of 150 children with asthma, 28 (18.7%) had positive SPT to mites.

All of the patients with positive SPT to mites lived in urban areas.

Conclusion: We found significant relationship between mite skin test positivity and living in urban area (P=0.043), which suggests living in urban areas as a potential risk factor for mite sensitivity in childhood asthma.

Keyword: Household characteristics, Mites, sensitization, Child, asthma

Introduction

Asthma is a common chronic disorder, which is characterized by airway inflammation and bronchial hyper-responsiveness to various stimuli [1]. There has been an increase in prevalence of asthma over the last 30 years, despite progress in understanding of pathogenesis and improved treatment [1].

The occurrence of asthma depends both on genetic predisposition and exposure to environmental factors [2]. Changes in environment and life styles are the most important factors for high incidence of allergic diseases [3, 4, 5]. There is growing evidence that exposure to allergens and irritants in the residential areas are particularly important [6]. Mites, which are the most allergens in dust of houses, are the major indoor allergens in asthmatic patients [3-5].

The prevalence of asthma has increased in many developed countries, which may be due to several factors, including increased exposure to house dust mite allergens [7].

The aim of this study to investigate the association between household characteristics (type and age of dwelling, urban or rural living area, damp homes) and childhood asthma, who have positive SPT to house dust mite and to compare the results with those of the patients who have negative skin test.

Material and Methods

Mashhad University of medical sciences written consent form was obtained from all patients participating in the study. The study population consist of one hundred fifty (91 boys, 59 girls) asthmatic children aged 1-14 years (mean 7.18 ± 3.41) attended the pediatric allergy clinic of Dr. Sheikh Children hospital in Mashhad (North east of Iran), for SPT. The study was conducted in Mashhad (southeast of Iran) between August 2008 and December 2009.

Inclusion criteria were as follow;

1. Age 1-14
2. asthma disease
3. patient consent

And out exclusion criteria included;

1. Age < 1 year
2. Age > 14year
3. If control positive was Negative

We performed all skin prick tests according to standard procedures, using purified allergen extracts. Positive and negative controls were histamine (10 mg/ml) and normal salin, respectively. A reaction was deemed positive if the resulting wheal was at least 3mm by 3mm.

The test wheal had to be at least three millimeters larger than the negative control in both diameters to be deemed positive. Information about home characteristics including type and damp dwelling, and urban or rural living areas were assessed by a questionnaire. Our patients were categorized into two groups according the results of their SPT to mite. Those with positive results were categorized as group I and patients who had negative skin prick test to mite as group II (Table 1).

Table 1. Result of SPT to mite

Group I		Group II
Positive		Negative
No	28	122
%	18/7	81/3

Statistical analysis

Data were analyzed by SPSS software Ver 11.5 using Chi-square test. Also P<0.05 was considered statistically significant.

Result

Out of 150 children with asthma, 133 (88.7%) lived in urban area, 61 (40.7%) lived in apartment, 85 (56.7%) lived in homes older than 10 years, 101 (67.3%) lived in homes which had history of dampness (Table 2). Out of 150 children with asthma, 28 (18.7%) had positive SPT to mites (Group I). Of 28 patients with positive SPT to mites, 15 (53.6%) were boys and 13 (46.4%) were girls. All of the patients of the Group I lived in urban areas.

12 (42.9%) patients of the Group I lived in apartment and 16 (57.1%) in home having a basement, and 16 (57.1%) lived in homes older than 10 years. Twelve (42.9%) patients of the Group I lived in homes which had history of dampness (Table 3). We didn't find any relationship between mite skin prick test positivity and home dampness, age of the buildings, and number of floors. We found significant relationship between mite skin test positivity and living in urban areas (P=0.043)

Table 2. Home characteristic in whole of the patients

		Frequency	Percent
Site	Urban	133	88.7
	Rural	17	11.3
Type of home	Apartment	61	40.7
	House	89	59.3
Age of dwelling	>10 y	65	43.3
	≤10 y	85	56.7
Home dampness	+	49	37.7
	-	101	67.3

Table 3. Home characteristics in Group II

		Frequency	Percent
Site	Urban	28	100%
	Rural	0	0
Type of home	Apartment	12	42.9%
	House (Flat)	16	57.1%
Age of dwelling	>10 y	16	57.1%
	≤10 y	12	42.9%
Dampness	+	16	57.1%
	-	12	42.9%

Discussion

The incidence of bronchial asthma has been reported to be increasing in urban than rural patients [8]. There are a number of studies which clearly demonstrated that asthma mortality and morbidity are worse in urban centers than the other areas [9]. The role of indoor allergens in explaining the urban-rural difference is complex. Allergens such as house dust mites have an ideal environment to proliferate in most houses in urban areas. Thus the dose of allergens is much higher in the urban compared to the rural environments. The level of exposure to house dust mite is also different in the urban compare to the rural areas. Reducing exposure to house hold dust inhalant has been proposed as one strategy to reduce asthma. Children with asthma who live in the inner-city are exposed to multiple allergen especially house dust mite in their homes. Reduction in these triggers of asthma has been difficult to achieve [10].

Considerable variation within and between different homes has shown that factors such as age of home, floor level, and humidity influence the growth conditions of mites [11]. Specific features of urban and rural lifestyle may constitute distinct risk factors but may also coexist within certain socioeconomic levels. Children of rural environments are at lower risk for asthma and aeroallergen sensitization. The protective effect has been associated with close contact with large animals, but the genetic factors also play a contributory role [12].

Our data confirm previous reports, for example in Jimma, atopy was a strong risk factor for asthma in urban jimma. In the rural areas, skin sensitivity to mixed threshing was only slightly less common than urban jimma, whereas sensitivity to mite was significantly more common [13].

In Korea, Lee MH et all showed that sensitization rate to citrus red mite between the urban and rural children were difference [14]. In Germany, Musken H and et al have established that skin test sensitivity to storage mites was higher in rural than in city dwellers [15].

On the hand, Lourenco et al in Portugal observed that sensitization profiles were not different between the urban and rural patients; however allergic rhinitis prevalence was higher in urban patients [16]. House dust mites, have an ideal environment to proliferate in most houses in urban areas. Thus the dose of allergens is much higher in the urban compared to the rural environments. The level of exposure to house dust mite is also different in the urban compare to the rural areas. Reducing exposure to household dust inhalant has been proposed as one strategy to reduce asthma. Considerable variation within and between home, floor level and humidity influence the growth conditions of mites. Specific feature of urban and rural lifestyle may constitute risk factors but may also coexist within certain socioeconomic levels. Children of rural environments are at lower risk for asthma and aeroallergen sensitization. The protective effect has been associated with close contact with large contribulatory role. The result of our study was limited by small sample size.

Conclusion

The present study indicates significant difference in hose-dust mite sensitivity among the rural and urban childhood asthmatic of Khorasan (southeast of Iran).

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T4 glottic carcinoma: Oncological results and survival rate

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Abstract

Objectives/Background: The best course of action in the case of T4 glottic carcinoma is chosen for each individual case. The aim of this study was to evaluate the potential prognostic factors and influence of postoperative and radical radiotherapy on the survival rate of patients suffering from T4 glottic carcinoma and to analyze the most appropriate conservative treatment for these patients.

Methods: Study Design: A retrospective study (1995-2000) enrolled 63 patients with squamocellular glottic cancer in T4N1M0 stage, monitored for 5 years, divided into two groups: 30 postoperatively irradiated patients and 33 radically irradiated patients. Analysed variables were: age, sex, total therapeutical dose, number of fractions, dose per fraction and type of radiotherapeutical treatment. Standard therapeutical fractionation regimens were used, with daily sessions of 2-3 Gy, five times a week. Radiotherapy consisted of mega-voltage 10 MEV X-ray therapy. Log Rank test, Kaplan-Meier survival study, t- test, Pearson X2 – test and Cox regression were used in order to select the factors with independent effect.

Results: Multivariate analysis demonstrated that none of the predictors, not even the type of radiation therapy, were statistically significant, with independent influence on survival.

Conclusion: There is no significant difference in survival of patients with T4 glottic carcinoma among postoperatively and radically irradiated patients. Our results imply that the optimal radiotherapeutic modality for these patients is a total therapeutical dose no less than 65 Gy and daily fractionation with dose no less than 2,51Gy.

Key words: T4 glottic cancer, prognostic factors, radical radiotherapy, postoperative radiotherapy, survival

Introduction

Many studies have indicated that the therapy protocols in the case of T4 glottic carcinoma are applied flexibly, and that the best course of action is chosen for each individual case. At the same time, in addition to any objective findings, other non-medical factors also affect the choice of therapeutic treatment.

Many therapeutic procedures are used in T4 glottic carcinoma therapy, including different surgery methods, radical radiotherapy, chemotherapy, a combination of radiological-surgical therapy and concomitant chemoradiotherapy [1-7].

It is still the case in the clinical treatment of T4 glottic carcinoma that combined surgical-radiological therapy (postoperative radiotherapy) and radical radiotherapy are utilized most frequently. Surgical treatment usually means using different methods, such as conservative-functional and palliative surgery [3,8,9].

The aim of any kind of postoperative radiotherapy is achieving locoregional control of the malign illness, accompanied by an acceptable level of complications that may occur during the course of therapy, while radical radiotherapy is traditionally reserved only for patients who will undergo a complete laryngectomy or are generally of poor health and therefore are not good candidates for more extensive surgery. Radical radiotherapy is indicated also in the case of inoperable carcinoma in the T4 stages [5,9,10].

There are many controversial reports regarding the influence that the choice of therapy can have on the increased survival rate of the patients suffering from T4N1M0 glottic carcinoma.

The aim of this study was to evaluate the potential prognostic factors and influence of postoperative and radical radiotherapy on the survival rate of patients suffering from T4 glottic carcinoma and to analyze the most appropriate conservative treatment for these patients.

Materials and methods

The patients

A total of 63 patients suffering from squamocellular glottic carcinoma, stage T4N1M0, that underwent radiotherapy at the Oncology Clinic of the Faculty of Medicine in Niš from September the 1st, 1995 until September the 1st, 2000, were included in the study. The clinical T stage was defined according to the TNM system, on the basis of the UICC criteria [11].

Megavoltage therapy using 10 MeV X-rays was used as part of the radiotherapy treatment. All of the patients received treatment in the same manner, by utilizing the technique of two separate parallel planes (5x5 do 5x7cm). They all underwent daily fractionation, with daily session of 2-3Gy per fraction, five times a week.

All patients included in the study signed writen permision for therapeutical intervention and appropriate institutional research oversight committee from the Medical faculty in Nis gave permision for study realisation. The patients were divided into two groups: a group of patients who underwent postoperative radiotherapy and a group of patients who underwent radical radiation therapy.

The patients that underwent postoperative radiation therapy

This group numbered a total of 30 patients. A complete laryngectomy was performed on a total of 28 patients (93.3%), either separately, or combined with pharyngectomy or the concomitant removal of the base of the tongue, in accordance to how the cancer was spreading. Only one patient had a subtotal laryngectomy (3.3%) and one (3.3%) had a hemilaryngectomy. A radical dissection of the neck had to be performed on 8 of the patients, while a complete laryngectomy and a functional dissection on both sides had to be carried out on another 8 patients.

There was only one female patient in this group (3.3%). The youngest patient was 38, and the oldest 79 (the median was 60 years of age). The total therapeutic dose per patient was 42 - 66Gy (the median for the group was 60Gy). The number of fractions per patient was 16–28 (a median of 24). The therapeutic dose was 2-3Gy per fraction (median of 2.5Gy).

The patients who underwent radical radiation therapy

This group consists of 33 patients. There were 3 women (9.1%). The youngest patient was 39, and the oldest was 79 (the median was 65). The overall number of therapeutic doses per patient was 42-127Gy (the median was 67Gy). The number of fractions per patient was 20–34 (the median was 28), and the therapeutic dose per fraction was 2-3Gy (the median was 2.39Gy).

The patients were monitored over a period of 5 years, following radical or postoperative radiotherapy. The study did not encompass patients who could no longer be found or patients who had died from other illnesses before the end of the five-year period following radiation.

Statistical analysis

An analysis of the predictor variables was carried out first, along with an analysis of their frequency among patients who underwent different forms of therapy: radical or postoperative radiation therapy. An analysis of the survival rate was carried out over a five-year period, followed by an analysis of the survival rate of the subjects in relation to the predictors.

A regression analysis was used to study the influence of each of the monitored factors on the survival rate of these patients. The factors that exhibited their statistically significant influence on the survival rate in the univariate analysis were added to the multivariate Cox model. The Kaplan-Meier survival analysis was used to present the results,

and Log-Rank test to determine the statistical significance of the length of the survival period. In order to compare the parametric numeric features of observation, the t-test was used. The Pearson χ^2-test was used to compare the differences in the frequency.

Results

The analysis of the predictors

There were no significant differences in age and gender between subjects with different therapeutic procedures (Table 1).

The total dose was significantly lower and dose of radiation per fraction was higher in the group of patients who underwent postoperative radiation compared to radical radiation therapy. The patients who underwent radical radiation therapy received a larger number of fractions during their radiation therapy (Table 2).

The analysis of the survival rate in relation to the predictors

Among the subjects with T4 glottic carcinoma, the survival rate after one year was 57.14%, while at the end of the 62-months' period, the survival rate was 9.52% (Table 3).

There was no significant difference in the survival rate related to sex (median survival for males 14 months vs. 8 months for females), but there was significant difference in the rate of survival according to age (Log-Rank test; p=0.018) (Table 3).

There was no statistically significant difference in the survival rate of the patients suffering from T4 glottic carcinoma in relation to the chosen therapeutic treatment between the groups: either postoperative radiation therapy or radical radiation therapy (Log-Rank test; p=0,643). The five-year survival rate for the subjects who underwent postoperative radiation therapy was 10%. The survival median for this group of subjects was 14 months ($CI_{95\%}$ 9, 72 - 18, 28). In the group of subjects who underwent radical radiation therapy, the survival

Table 1. Patients' characteristics

Monitored factors		Subjects with different therapeutic procedures		Value p
		Postoperative radiation therapy	Radical radiation therapy	
Age groups – T4 stage	Under 45	2 (6.7%)	3 (9.1%)	p=0.280
	Between 45-60	15 (50%)	10 (30.3%)	
	Over 60	13 (43.3%)	20 (60.6%)	
Sex – T4 stage	Male	29 (96.7%)	30 (90,9%)	p=0.343
	Female	1 (3.3%)	3 (9,1%)	

Data are presented as numbers (%)

Table 2. Treatment characteristics

Monitored factors		Subjects with different therapeutic treatment		p
		Postoperative radiation therapy	Radical radiation therapy	
Total dose - T4 stage	45-50Gy	5 (17.2%)	3 (10.3%)	p=0.002
	50.1-57.5Gy	6 (20.7%)	1 (3.4%)	
	57.6-65Gy	15 (51.7%)	9 (31%)	
	Over 65Gy	3 (10.3%)	16 (55.2%)	
Number of fractions- T4 stage	16-20	5 (17.2%)	4 (12.9%)	p=0.002
	21-25	14 (48.3%)	1 (3.2%)	
	26-30	10 (34.5%)	16 (51.6%)	
	Over 30	0 (0%)	10 (32.3%)	
Dose per fraction- T4 stage	2-2.25Gy	2 (6.7%)	11 (33.3%)	p=0.026
	2.26-2.5Gy	22 (73.3%)	19 (57.6%)	
	2.51-3Gy	6 (20%)	3 (9.1%)	

Data are presented as numbers (%)

Table 3. The survival rate of the subjects with T4 glottic carcinoma

		1yr	2 yr	3yr	4yr	5yr	Value p
Total survival		57,14%	25,40%	17,46%	11,11%	9,52%	/
Sex	**Male**	57,63%	25,42%	16,95%	11,86%	10,17%	0,542
	Female	50,00%	25,00%	25,00%	0,00%	0,00%	
Age	**Under 45**	20,00%	0,00%	0,00%	0,00%	0,00%	1vs2=0,006*
	Between 45-60	68,00%	32,00%	24,00%	20,00%	16,00%	1vs3=0,034*
	Over 60	54,55%	24,24%	15,15%	6,06%	6,06%	2vs3=0,212
Type of therapy	**Postoperative radiation therapy**	60,00%	30,00%	20,00%	13,33%	10,00%	0,643
	Radical radiation therapy	54,55%	21,21%	15,15%	9,09%	9,09%	
Total dose	**45-50**	50,00%	25,00%	0,00%	0,00%	0,00%	1vs2=0,973
	50,1-57,5	57,14%	0,00%	0,00%	0,00%	0,00%	1vs3=0,135
	57,6-65	58,33%	33,33%	25,00%	20,80%	16,67%	1vs4=0,068
	Over 65	73,68%	31,58%	26,32%	10,53%	10,53%	2vs3=0,442 2vs4=0,237 3vs4=0,758
Number of fractions	**16-20**	33,33%	11,11%	0,00%	0,00%	0,00%	1vs2=0,011*
	21-25	60,00%	40,00%	26,67%	20,00%	13,33%	1vs3=0,023*
	26-30	65,38%	30,77%	23,08%	11,54%	11,54%	1vs4=0,126 2vs3=0,656
	Over 30	70,00%	10,00%	10,00%	10,00%	10,00%	2vs4=0,568 3vs4=0,920
Dose per fraction	**2-2,25**	61,54%	0,00%	0,00%	0,00%	0,00%	1vs2=0,184
	2,26-2,5	56,10%	34,15%	24,39%	17,07%	14,63%	1vs3=0,385
	2,51-3	55,56%	22,22%	11,11%	0,00%	0,00%	2vs3=0,320

**Statistically significant difference,*

rate after five years was 9, 09%. The patients who underwent radical radiation therapy had a survival median of also 14 months ($CI_{95\%}$ 6, 15 - 21, 85) (Table 3 and Figure 1).

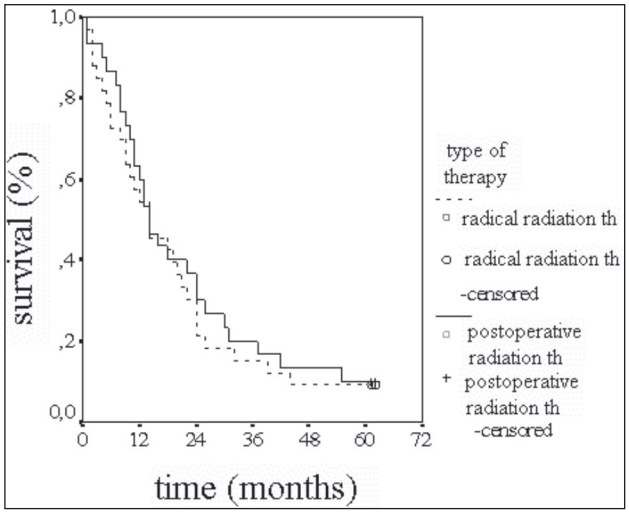

Figure 1. The survival rate of the subjects with T4 glottic carcinoma and different therapeutic procedures

No statistically significant interrelation was noted between the rate of survival of the subjects and the total dose of radiation for the group with T4 glottic carcinoma. A statistically significant difference in the survival rate was noted between the subjects who received different amounts of radiation fractions (Log-Rank test; p=0,049). The poorest survival rate was in the group with the smallest number of fractions. (Table 3).

The radiation dose per fraction has no statistically significant influence on the rate of survival of subjects with T4 glottic carcinoma.

None of the analysed factors stood out as significant, or had an independent influence on the further course of the illness or the survival rate of the patients (Table 4).

Table 4. The Cox regression analysis of the survival rate of the subjects with T4 glottic carcinoma

Monitored factors	exp (B)=RR	Value p
Sex	1,362	p=0,553
Age	0,967	p=0,886
Total radiation dose	0,778	p=0,076
Number of fractions	0,831	p=0,256
Dose per fraction	0,891	p=0,640
Type of therapy	1,128	p=0,651

Univariant Cox regression analysis, RR-Relative risk

Discussion

Radical radiotherapy should allow a complete and permanent remission of the malign illnesses. In classic tumor fractionation, literature data suggest the optimal daily doses of 2 - 3Gy, weekly doses of 8 - 10Gy, and the total therapeutic doses range from 30 - 90Gy, depending on the type of tumor, its localization, size and biological properties (5,14). In our group of patients that underwent radical radiation therapy, the total therapeutic dose was 42 - 127Gy, with a median of 67Gy.

Postoperative radiotherapy is indicated in all cases with an expanded tumor with unclear resection edges, and is utilized usually 4-6 weeks after surgery [13-15]. The indications for postoperative radiation therapy include subglottic expansion, cartilage infiltration, perineural invasion, expansion of the primary tumor into the soft tissue of the neck, multiple positive lymph nodes of the neck and expansion of the tumor outside the scope of the lymph node [3,13-15]. In the data that we gathered, in the group of patients that underwent postoperative radiation therapy, the greatest number of patients (93.33%) underwent complete laryngectomy, either independently or in combination with a radical dissection of the neck or functional dissection on both sides of the neck. The total therapeutic dose during postoperative radiation, for these patients, was from 42 to 66Gy, with a median of 60Gy.

For all of the subjects with T4N1M0 glottic carcinoma, the five-year survival rate was 9.52% (median 14 months). Our results differ from the average data found in literature where a five-year rate of survival was 25-52%, irrespective of the choice of treatment [10,12,16]. This discrepancy can, in part, be accounted for by our limited radiotherapeutic capacities (waiting lists), which extend the waiting period prior to the start of any kind of treatment. As a result, a great number of patients actually start therapy palliatively. At the same time, what must not be overlooked is that the presence of metastases in the neck decreases the survival rate by 40-50% [4].

The following factors play an important role in local control of glottic carcinoma: age, sex, histological structure of the tumor and its edges, stage, size, total therapeutic dose, dose per fraction and duration of the therapeutic treatment. As less significant factors, we can single out smoking, diabetes, alcohol consumption and dietary habits [17-19].

We found no statistically significant difference in age between the patients who underwent postoperative radiation therapy and those who underwent radical radiation therapy. Glottic carcinoma is more frequent among the elderly, and usually occurs after the age of 40. Nevertheless, if it occurs among younger people, it takes a more aggressive form [20,21]. The evidence gathered in our study support this claim, considering the fact that none of our patients under 45 lived longer than 14 months, and the median for these subjects was only 8 months. The subjects aged 45-60 had the best rate of survival, with a survival median of 18 months.

There were no significant difference in survival period of the subjects in relation to sex, even though it has often been emphasized that sex is an important prognostic factor and that women usually have a better prognosis both in terms of local control and survival [22,23]. Glottic carcinoma in European countries occurs 7-22 times more frequently among men than women which can also be seen in our study. This can be accounted for by the effects of certain hormonal factors or continued irritation. It is assumed that men who work in industry suffer from chronic laryngitis and throat irritation more often than women and chronic inflammatory changes are usually accompanied by dysplasia and metaplasia of the epithelium [20,24].

No statistically significant interdependence of the rate of survival and the total therapeutic dose of radiation was noted, but the longest period of survival with a median of 21 months was calculated for the subjects with a total therapeutic dose of over 65Gy. .In regards to the total therapeutic dose

for local control and survival, many heated debates can be found in much of the literature on the subject, and there is even a suggestion that with the increase in the total therapeutic dose, the risk of a laryngeal edema also increases (5,23-28).

Even though we did not find that the dose of radiation had a statistically significant influence on the rate of survival of the subjects with T4 glottic carcinoma, we found that the subjects who received doses of 2.51-3Gy per fraction had the best survival rate. Our results support the claims of the so far small number of researchers who have suggested that a greater dose per fraction gives better rates of survival, and that the total therapeutic dose is less important in this respect [12,14,28].

We found no statistically significant difference in the survival rate when comparing patients who underwent postoperative radiation therapy and those who underwent radical radiation therapy. The survival median for the patients from both groups was 14 months. Nevertheless, it is important to point out that in our working conditions, it is usually the elderly patients, those with an advanced tumor, and who are generally in poor health and have other concomitant illnesses, who are sent to radical radiotherapy, which is supported by the fact that more than half of the patients who underwent this kind of procedure (60, 6%) were over the age of 60.

Our retrospective study has shown that a similar percentage of patients who survive glottic carcinoma can be reached both with postoperative and radical radiation therapy, which has been documented in the Cox regression analysis, in which none of the studied factors, including the type of radiotherapy treatment, was singled out as being significant, nor having an independent influence on the rate of survival of the patients with T4N1Mo glottic carcinoma. That there are no significant differences in the rate of survival of patients with advanced glottic carcinoma who underwent postoperative radiation therapy and those who underwent radical radiation therapy has also been argued by other authors (29,30-31,32). Spector at al. 2004. also showed that the type of therapy (surgical, radiation (postoperative or radical)) is not a significant factor which influences the survival rate of the patients with T4 stage glottic carcinoma [9].

Conclusion

The type of radiation therapy (postoperative or radical) is not a significant factor which influences the survival rate of the patients with T4N1MO glottic carcinoma.

The optimum radiotherapeutic method for these patients is a total therapeutic dose which is no less than 65Gy and a daily fractionation with a dose of no less than 2.51Gy.

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Paternity after microscopic inguinal surgery of varicocele in infertile males: A 5-years follow up

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Abstract

Objectives: Infertility affects about 15% of couples. One of the most common causes of male infertility is varicocele. In this study, the live birth rate after microscopic inguinal varicocelectomy and some related factors were studied in Northeast of Iran.

Design and patients: In this cross-sectional study, 976 infertile males who underwent microscopic inguinal varicocelectomy (2004-2009) in an academic hospital were studied and 264 were randomly selected. Female factors were ruled out. Data regarding age, varicocele grade and live birth rate were recruited and entered into SPSS-14 software; T-test and $\chi 2$ were used to analyze the variables.

Results: The mean (±SD) age was 29.09 (±4.80) years, 139 (52.7%) reported to have a successful result after a mean (±SD) duration of 21.74 (±6.24) months. Unilateral varicocelectomy had significantly more positive results (58.8%) than bilateral (20.9%) but the relationship with grade was not significant. Primary type had 54.5% live birth v.s. 31.8% in secondary type (P-value<0.05). The mean duration between operation and live birth was significantly different in primary and secondary type (P-value<0.05).

Conclusions: Surgery of primary infertility could reveal to a higher live birth rate in a much shorter duration; also unilateral varicoceles are better responders to the surgery.

Key words: Varicocele, unilateral, infertility, live birth rate.

Introduction

Infertility is an important health issue which about 15% of couples in reproductive age should cope with it. Male factors are involved in about 40 to 50% of these cases. One of the most causes of male infertility is varicocele, which is defined as a dilatation in pampiniform venous plexus surrounding the testis (1, 2). Upon world health organization (WHO) studies, varicocele is reported as a cause of infertility in 35-50% of primary infertility and 81% of secondary infertility (2, 3). Its prevalence is 8-20% in the general population (4). Also some studies indicate the familial trait of this disease so that clinical varicocele is more common in first degree relatives, particularly among brothers (3). It has been said that the spontaneous pregnancy rate after varicocele repair varies from 16% to 55.2% (2).

There are kinds of conflict in different studies regards the benefit of varicocele repair on reproductive outcome and chance of conception in infertile couples and variable pregnancy rate. Cayan et al reviewed and compared the results of similar studies about the succeed rate after various methods of repairing the varicocele between 1980-2008, and concluded a higher rate of spontaneous pregnancy and lower recurrence and complications after the microscopic surgery compared to the conventional techniques (2).

In this study, the live birth rate after microscopic inguinal varicocelectomy and the relationship with the degree of varicocele were studied in a 5-year follow-up in Northeast of Iran.

Patients and Methods

In this cross-sectional study, medical records of all patients (N=976) who underwent varicocelectomy by a urology specialist (2004-2009) in an academic hospital in Gorgan, Northeast of Iran were studied.

Patients were included from infertile couples whose the only cause of infertility after different exams was varicocele. Infertility in these patients was defined as "1 year of unwanted non-conception with unprotected intercourse in the fertile phase of the menstrual cycles" (5).

Patients who underwent inguinal microsurgical varicocelectomy after at least seven months from the surgery time were included. Spouses had been examined for polycystic ovary, hormonal tests, such as prolactin, thyroid function tests, FSH-LH, Salpyngography and laparoscopic evaluation to rule out female factors. Single patients and those who had other indications for varicocelectomy were excluded.

On the other hand, patients were classified into 2 groups: 1-primary infertility if he had no history of prior paternity, 2-secondary infertility if he had previously fathered a child with his current partner or a previous partner (6).

Testis and scrotal ultrasonography were done for all and varicocele grade was classified as followings: grade 1- palpable or visible only on Valsalva maneuver (straining); grade 2- palpable but not visible when standing upright at room temperature; and grade 3- visible when standing upright at room temperature (7). Spermograms were performed by computer assisted assay method twice. To increase the accuracy, all of these examinations were performed by a certain radiologist and laboratory.

Surgical procedure was microscopic inguinal varicocelectomy. All information related to age at the time of surgery, time of marriage and infertility duration, varicocele grade, ultrasound reports, physical examination results and spermatogram before and after the surgery were extracted.

Then patients were called and asked about the occurrence of pregnancy and live birth. Patient selection was randomly upon medical records code and if patients were not accessible, another patient was replaced (N=264).

Data were entered into SPSS-14 software and T-tests and $\chi 2$ were used to analyze the variables. P-value less than 0.05 was considered significant.

Results

The mean (±SD) age of patients was 29.09 (±4.80) years. Among these 264 cases, 139 (52.7%) had reported a successful result and live birth occurred after a mean (±SD) duration of 21.74 (±6.24) months (10-45 months).

Mean (±SD) age was not significantly different between patients who had positive results (ie; revealed to live birth after the surgery), and whom with negative results (ie; no fertility after varicocele repair) (28.40 ±4.06 years versus 29.86 ± 5.42 years) (P-value>0.05).

Unilateral varicocelectomy had significantly more positive results (58.8%) than the bilateral surgery group (20.9%); live births occurred in people with unilateral varicocele 2.8-folds more than patients with bilateral varicocele (P-value<0.05).

As shown in table 2, outcome of the surgery had no significant relationship with varicocele grade. Positive surgery results were seen in 58.3% of patients with grade I, 50% of grade II and 54.2% of grade III (P-value>0.05).

Primary and secondary infertility was seen in 242 and 22 patients, respectively. The primary type had 54.5% live birth after varicocelectomy while it was 31.8% in secondary type (P-value<0.05).

Table 1. The frequency of live birth after inguinal varicocelectomy according to unilateral and bilateral involvement

Surgery Result / Side	Positive		Negative		Total	
	No.	٪	No.	٪	No.	٪
Unilateral	130	58.8	91	41.2	221	100
Bilateral	9	20.9	34	79.1	43	100
Total	139	52.7	125	47.3	264	100

Table 2. Live birth rate after varicocelectomy in different varicocele grades

Surgery Result / Varicocele Grade	Positive		Negative		Total	
	No.	٪	No.	٪	No.	٪
I	7	58.3	5	41.7	12	100
II	49	50	49	50	98	100
III	83	54.2	70	45.8	153	100
Total	139	52.7	125	47.3	264	100

Table 3. Live birth after varicocelectomy in primary and secondary infertility patients

Surgery Results / Type of varicocele	Positive		Negative		Total	
	No.	٪	No.	٪	No.	٪
Primary	132	54.5	110	45.5	242	100
Secondary	7	31.8	15	68.2	22	100
Total	139	52.7	125	47.3	264	100

However, the mean duration between operation and time of live birth was 21 (±6.13) months in primary and 28.28 (±4.82) months in secondary type, this difference was statistically significant (P-value<0.05).

Patients' age was not significantly effective on the duration between operation and time of successful fertility (P-value>0.05).

Discussion

Present study showed 52.7% live birth after the microsurgical inguinal repair of varicocele in a population of infertile men, aged 29.09 (±4.80) years.

In another study from North of Iran, pregnancy rate after inguinal microscopic surgery has been reported 36% which was lower than our study (8). This rate was 20.2-55% in different studies (2-5).

It could be explained by the different definition of success rate in various studies. We considered a "live birth rate" as the outcome and most of the others named it just as improved "semen quality" and "pregnancy rate" (2-5, 7-8). It means that we apply a more concise definition for the successful result of varicocele repair.

On the other hand, age of male patients and female factors like advanced age of female partner are among the related effective factors which are discussed in other papers (9), and could cause the different success rate.

Although, results of the present study showed that the mean age of patients with positive results were lower than patients who had negative results, but this difference was not statistically significant. Some studies showed the same results (10), others showed no significant improvement in spermatograms of patients over 30 years-old after 1 year follow up (11).

But in this study, patients' age was not significantly effective on the duration between operation and time of successful fertility (P-value>0.05).

Unilateral varicocelectomy had significantly more positive results (58.8%) than the bilateral surgery group (20.9%) (P-value<0.05). This was not similar to most of the other studies. Scherr and Goldstein prospectively followed a total of 91 patients in USA, 65 bilateral and 26 unilateral left repairs. Bilateral varicocelectomy revealed significantly greater improvement in post-operative seminal parameters compared to the unilateral repair (12).

In another study in Canada, data of 369 consecutive varicocelectomies performed for male factor infertility showed a significantly greater improvement in sperm quality (motility) and male fertility potential in bilateral varicocelectomy (clinically palpable bilateral varicoceles) than unilateral one (13). In an Egyptian report, postoperative paternity was significantly higher in patients with bilateral varicocele (54.5%) diagnosed in ultrasonography of the testes (14).

Maybe this discrepancy is related to some or all of the following factors:

1. Sperm quality (motility) and seminal parameters are the main post-operative measurements in other studies, not the rate of live birth.
2. Clinical or ultrasonography diagnosis of varicocele could play a role in this differences.
3. The most important thing is that our sample size in the group of Bilateral varicocele (N=9) was very low and it couldn't be discussed accurately. Further studies with larger sample size are needed.

Present results showed that a successful result (live birth) occurred after 21.74 (±6.24) months (range from 10- 45 months). Cayan et al in Turkey infertile males, showed an overall spontaneous pregnancy rate of 36.6% achieved after varicocelectomy with a mean time to conception of 7 months (range 1 to 19) (4). Maybe longer time is

needed to paternity and more patience should be offered to these patients.

Positive surgery results were seen in 58.3% of patients with grade I, 50% of grade II and 54.2% of grade III (P-value>0.05). Varicocele grade had no significant effect on the result of surgery. This result was similar to the other studies (15-16). Albeit cases with grade I were only 7 and not enough to be compared to other grades.

The primary type had 54.5% fertility rate and live birth after varicocelectomy while it was 31.8% in secondary type (P-value<0.05). However, the mean duration between operation and time of live birth was 21 (±6.13) months in primary and 28.28 (±4.82) months in secondary type, this difference was statistically significant (P-value<0.05).

Walsh et al (2009) reported that although in secondary type infertility, cases are older with older partners compared to primarily infertile men, but they have significantly better sperm concentrations with a history of fathering a child (6). This difference should be further evaluated in a prospective study.

Conclusions

According to the present results, primary infertility could revealed to a higher live birth rate in a much shorter duration; also unilateral varicoceles are better responders to the surgery.

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A case of malignant acanthosis nigricans with gastric cancer and literature review

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Abstract

Acanthosis nigricans(AN) is a skin disorder characterized by focal or diffuse pruritic hyperpigmentation and hyperkeratosis of the skin with dermal papillomatosis. Malignant acanthosis nigricans(MAN) is rare and usually a paraneoplastic syndrome with which gastrointestinal adenocarcinoma is commonly associated. Here we report a case with tripe palms, progressive pruritic dark discoloration, excessive keratosis with dermal papillomatosis and gastric adenocarcinoma along with a review of the published literature.

Key words: acanthosis nigricans; malignant; gastric adenocarcinoma

Introduction

AN is a skin disorder characterized by focal or diffuse pruritic hyperpigmentation and hyperkeratosis of the skin with dermal papillomatosis. MAN is rare and usually a paraneoplastic syndrome with which gastrointestinal adenocarcinoma is commonly associated. The pathogenesis of MAN remains unknown. A role of growth factors such as fibroblast growth factor(FGF), transforming growth factor-α (TGF-α), melanocyte stimulating hormone α (MSH-α), and insulin like growth factor 1 (IGF-1) has been discussed[1,2]. Treatment of MAN is often unsatisfactory, therpies for coexisted tumor are reported to improve the skin symptom, but the degree of improvement varies. Here we report a case with tripe palms, progressive pruritic dark discoloration, excessive keratosis with dermal papillomatosis and gastric adenocarcinoma along with a review of the published literature.

Case report

A 72-year-old Chinese Han man presented to our hospital with progressive pruritic darking discoloration and excessive keratosis of the trunk and face over 2 years, appetite and weight loss for 4 months. He had been diagnosed and treated as dermatitis without amelioration. Thus he was transferred to our hospital. The patient had a history of hypertention and type 2 diabetes. There was no history of hematemesis, melena, hemoptysis, cough or dyspnea.

Physical datas on admission showed pallor, but no jaundice. Dermatological examination revealed diffuse skin darking discoloration and thickening with excessive keratosis, popular papillomas and warty nodules were also appeared , especially on the face, neck, low back, knee joint and both legs (Figure 1). Velvety plaques of both palms were shown(Figure 2a). Mild oral papillomatosis, thickened and furrowed tongue were also appeared(Figure 2b).

Figure 1. Skin darking discoloration and thickening with excessive keratosison, and papilloma

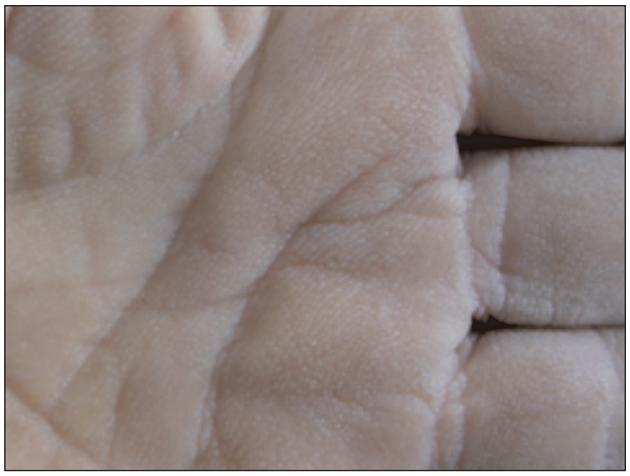

Figure 2-a. Tripe palm

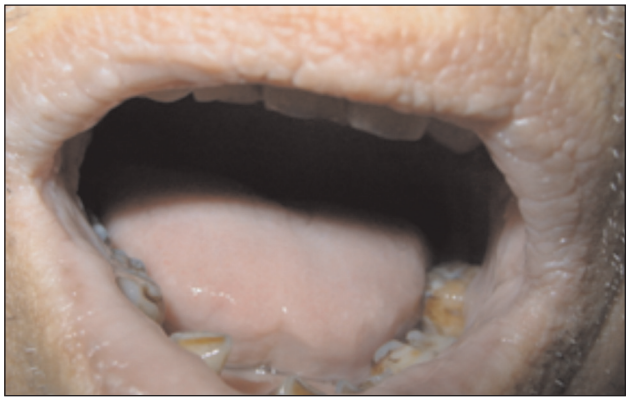

Figure 2-b. Mild upper lip papillomatosis and thickened tongue

Laboratory data showed hemoglobin was 67g/L, fecal occult blood was positve, liver function, renal function tests tumor marker levels (CEA, carcinoma antigen CA199) were normal. So we further to investigate the gastrointestinal tract. Ultrasonic revealed big ulcer in the preventriculus and gastric fundus region with several enlarged lymph glands in abdominal and retroperitoneal area. Gastroscopy was performed and manifested gastric fundus huge ulcer with preventriculus invaded. Histopathological examination of tissue specimen showed mucocellular adenocarcinoma. On the same time, a skin biopsy specimen taken from his leg revealed increased dermal pigmentation, hyperkeratosis and mild acanthosis with dermal papillomatosis, which improved AN. the final diagnosis were MAN, gastric adenocarcinoma with retroperitoneal metastasis, T2DM. Retinoids was used , but with mild improvement. It's so pity that the patient give up further treatment and discharged from hospital.

Discussion

There are 2 forms of AN: benign and malignant forms. AN is usually related to benign conditions, especially in those congenital, obesity, endocrinopathies (such as insulin resistance, hypophyseal tumors), erythema nodosum, or produced by medications (sex hormones, nicotinic acid), while the skin disorder is always mild and rarely involving the oral mucosa[1;3]. Lesions in MAN is always severe, diffuse and oral mucosa involved. MAN is rare and usually a paraneoplastic syndrome with which gastrointestinal adenocarcinoma is commonly associated[3-5]. It may precede the diagnosis of the tumor. So it is necessary to exclude the presence of malignant diseases. MAN can occurs before (17.6%), in the course of (61.3%)or after (22%) tumors, most coexists with adenocarcinomas of the abdominal organs (70–90%), mainy gastric cancer (55–61%) [4;6]. Nonepithelial tumors such as sarcomas or lymphomas are rarely coexisted[2]. The pathogenesis of MAN remains unclear. The role of growth factors such as fibroblast growth factor, transforming growth factor-α (TGF-α), melanocyte stimulating hormone α, epidermal growth factor-α (EGF-α) and insulin like growth factor 1 (IGF-1) has been discussed, playing an important role in the pathogenesis of hyperplasia and hyperpigmentation observed in MAN. Torley D, et al showed that activation of IGF1, FGF and EGF receptors may lead to excessive skin proliferation[7]. Yasutoshi Hida, et al presented two cases of MAN coexistent with gastric cancer, and in both cases, the epidermis showed strong expression of FGFR3 spread throughout the acanthotic lesions, revealed activation of FGFR3 to have some relevance to the development of MAN [8]. Haase et al. demonstrated that ERK, a mitogen-activated protein kinase (MAPK), was also activated in the lesions of MAN patients[9]. Treatment of MAN is often unsatisfactory, therpies for coexisted tumor are reported to improve the skin symptom, but the degree of improvement varies. Retinoids, cyproheptadine, etretinate, PUVA (psoralen + UVA treatment) are used in the treatment of paraneoplastic syndrome. Swineford SL and Drucker CR. presented a case of florid papillomatosis associated with gastric adenocarcinoma and treated with oral retinoids re-

sulting in significant clinical improvement[10]. But in our case, retinoids had little improvement without therpy for the coexisted tumor.

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Validity and reliability study for the self-efficacy scale

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Abstract

Aim: The aim of this methodological study was to analyze the validity and reliability of the Turkish adaptation of the Self-Efficacy Scale originally developed by Lechner, de Vries, and Offermans.

Methods: The adapted scaled was administered to 92 women, grouped according to age and educational status. The data was collected using a socio-demographic data form and a seven item modified Self-Efficacy Scale.

Results: Cronbach's Alpha coeffient was .84, indicating high internal consistency in responses. Both the validity and reliability of the modified Self-Efficacy Scale were found to be high.

Conclusions: We propose that this scale can be used in the evaluation of self-efficacy perception in Turkish society. Self-efficacy scores may be predictive of participation in early diagnosis screening programs. Moreover, this scale could be used to help design programs and develop strategies to increase early detection behaviors like breast self-examination, mammography, and Pap smears.

Key words: self-efficacy, breast and cervical cancer, early detection, Turkish women

Introduction

Breast and cervical cancer are two of the most common and fatal diseases of women worldwide. With an incidence of 34.73 cases per hundred thousand, breast cancer ranks first among all the cancer types observed in Turkish women[1], while cervical cancer ranks ninth with an incidence of 4.5 cases per hundred thousand[2].

Mammography and self-examination of the breast are invaluable for early detection of breast cancer, while regular Pap smears are recommended for the early detection of cervical cancer. Participation of women in these screening tests significantly impacts the mortality and morbidity of these disease[3, 4]. It is vital, therefore, that health practitioners, especially public health nurses, are aware of those factors that are predictive of participation in these screening tests.

Perception of self-efficacy is one of the major cognitive perception factors for initiating and maintaining changes in behavior, including behaviors that promote good health. The Self-Efficacy concept was first introduced by psychologist Albert Bandura in 1997 within the scope of "Cognitive Behavior Change"[5]. Self-efficacy theory is based on a social cognitive theory that attempts to predict and explain behavior using concepts such as self-efficacy expectation, result expectation, and impulse[6]. Bandura defined self-efficacy as "the judgment of the individual related to his achievement of a certain performance level"[7].

According to Bandura, if an individual believes he can achieve a specific result, then this individual will exhibit the essential behaviors required to achieve the result. In this sense, self-efficacy perception plays an important role in determining the kinds of activities that the individual will do or avoid. As the self-efficacy expectation increases, the efforts become stronger and more persistent[7].

Self-efficacy has been used in many theories, such as the Theory of Planned Behavior and the Integrated Behavioral Model[8]. In recent years, beginning with Champion's Health Belief Model and Pender's Health Promotion Model, self-efficacy perception has emerged as an important determinant in the initiation and maintenance of behaviors linked to improving health[8, 9, 10]. Individuals avoid early diagnosis behaviors as a direct result of low self-efficacy[8, 10, 11]. Research on the relationship between breast cancer screening and self-efficacy revealed a strong positive relationship between self-examination of the breast and self-efficacy; indeed, self-efficacy was the strongest determinant of self-examination of the breast[12]. Moreover, several studies have shown that

high self-efficacy is evident in patients participating in mammography screening[3, 1].

A study examining the participation of Korean women in Pap smear tests found a positive relationship between participation and levels of self-efficacy[14]. Fang et al. (2007) also detected a positive relation between self-efficacy and Pap smear screening behavior, while Hogenmiller et al. (2007) concluded that self-efficacy is the primary determining factor in Pap smear screenings. Egbert and Parrott (2001) demonstrated a negative relationship between cancer screening restraints and self-efficacy, and a positive one between early detection awareness and self-efficacy.

In a study conducted using a transtheoretical model, Lechner et al. (1997) used the Self-Efficacy Scale and found that self-efficacy perception was lower in women at the pre-thinking stage of behavior compared to women at other stages[18]. Evaluation of an individuals' self-efficacy perception, as related to behaviors for the early diagnosis of breast and cervical cancers, could lead to enhanced survival.

Since the construct of self-efficacy is a function of both the behavior in question and the situational contexts in which the behavior takes place and may differ from one population to another. Therefore, self-efficacy scales need to be developed for different populations because their situational contexts may differ. Suitable assessment tools will be helpful for any attempt to increase self-efficacy. Knowledge of the self-efficacy level of individuals will aid in the development of strategies aim at increasing participation in early detection behaviors like regular breast self-examination, mammography, and Pap smears.

Objectives

The aim of this research is to evaluate the validity and reliability of a modified Self Efficacy Scale[17] in order to assess self-efficacy perception of breast and cervical cancer diagnosis in Turkish women.

Methods

Design: It is a methodological study.

Sample: There are 7 items in the modified Self-Efficacy Scale. For each item in scale studies, it is recommended that 10 people be included [19]. For that reason, the sample number was determined to be at least 70. A total of 92 women living in the Narlidere District of Turkey formed the sampling group for this research. Data related to the age and educational status of the women was obtained from district nursing heads. Stratification was made in the selection of women according to age and education status. Women to be included in the stratification were determined using the non-probability method.

Instruments: These data were collected using a socio-demographic data form and a seven item modified Self-Efficacy Scale.

Socio-Demographic Properties Information Form: The 'Socio-Demographic Properties Information Form' consisted of 4 questions on age, educational status, marital status, and income level.

Self-Efficacy Scale: The scale, the early diagnosis of breast cancer in their behavior to measure the perceptions of women's self-efficacy was developed in 1997 by Lechner et al. However, the author of the scale reported that can be used to measure the perceptions of women's self-efficacy of behavior for the early diagnosis of breast cancer and cervical cancer at the same time. The scale assesses the relationship between self-efficacy of women and the early detection of breast and cervical cancer [17, 18]. It is a Likert-type scale. In this scale, different conditions were introduced to participants and they were asked whether they would like to participate under those specific conditions. Points between -3 (definitely no) and +3 (definitely yes) were given as a response to the general query "Would you consider participating in the screening if...?" The total score could range from -21 to +21. A high score was indicative of greater self-efficacy perception related to the specific behaviors (participation in tests for breast and cervical cancer). Cronbach's Alpha reliability coefficient of the scale was .90.

Application of Data Collection Tools: The data was collected by researchers during face-to-face interviews. Women were asked to answer the questions of scale considering the behavior of both breast and cervical cancer screening.

Data analysis: The SPSS v.11 program was used for statistical analysis of the data. Expert opinions were obtained for content and scope validity. The Kendall good compatibility coeffici-

ent was used to evaluate the agreement between expert opinions. Cronbach's Alpha coefficient was used for internal consistency of the scale and Pearson correlation analysis was used for test-retest reliability. Pearson correlation analysis was also used for item-total point analysis. Results used for data analysis are presented in Table 1.

Table 1. Statistical Methods Used in the Validity and Reliability Analysis of The Modified Self Efficacy Scale

Validity Study	
Language Validity Content/scope validity (expert opinion) Content/Scope validity	Translation from English into Turkish Back translation from Turkish into English Kendal W Analysis
Reliability Study	
Item-Total Point Analysis	Pearson Correlation Analysis
Scale internal consistency	Cronbach's Alpha Coefficient
Invariance of scale against time Evaluation of the relationship between mean test-retest points	Pearson Correlation Analysis
Comparison of mean test-retest points	T Test in Dependent Groups

Language Validity: For the language validity of the Self-Efficacy Scale, five people, including a linguist and four nursing lecturers, translated the scale from its original English into Turkish. Another expert who was competent in Turkish and English languages translated the scale back to english. The original and the Turkish translation of the scale were compared by the researchers and the final form of the Turkish version was completed.

Ethical Dimension of the Study: In order to conduct the study, permission was sought via e-mail from the ethical committee of the Nurse College of Dokuz Eylul University and from the principle developer (Lechner) to use and modify the Self-Efficacy Scale. In order to increase the validity and reliability of the scale, permission was also obtained from Izmir Narlidere Municipality. People were informed of the research purpose and asked whether they volunteered to participate or not. Verbal consent was obtained from participants.

Results

The mean age of the women participating in the study was 49.35 ± 16.54 years (range, 20 to 84). Of this group, 21.7% of the women were illiterate, 5.4% literate, 41.3% received primary education, 31.6% received secondary and higher education, 85.9% were married, and 57.6% of subjects studied, income and expense are equal to each other.

Validity

The assessment points of 10 experts were compared using Kendall W analysis. No significant differences were detected (Kendall W= .149; p= .177), indicating relative agreement between experts.

Reliability

We performed item analysis and evaluated internal consistency for the seven items included in the Self-Efficacy Scale using Cronbach's Alpha reliability measure. Table 3 shows the item-total point correlations of the scale. Item-total point correlations varied between .672 and .763, and were determined to be statistically significant (p= .000). Cronbach's Alpha value of the scale, which is the reliability coefficient of internal consistency, was .84 (Table 3). Table 4 presents the results of test-retest analysis of the Self-Efficacy Scale. To assess test-retest reliability, the scale was reapplied to the same 79 participating subjects after 15 days. The reliability, as quantified by the test-retest coefficient, was found to be .936 (p = .000). Table 4 shows the results of test-retest mean score analysis. On the first application, the mean score was 5.87, and 6.30 on retest. This difference was statistically insignificant.

Discussion

Evaluation of the validity of Self-Efficacy Scale

The many subtypes of validity that have been defined are all measures of the degree to which the quantity to be assessed was actually assessed. The most preferred domains of validity for any scale is content/scope validity and structural validity [20]. The fact that a panel of experts came to the same conclusions after evaluating the suitability and comprehensibility of the items was accepted as an indicator of content validity [21]. In this study, scope validity of the scale was evaluated using the Ken-

Table 2. Evaluation of expert views on the content validity of the modified Self-Efficacy Scale (n=10)

Self-Efficacy Scale For mammography and pap smear test	Lowest-Highest Point	Mean of Item Points	Kendall good compatibility coefficient
Would you participate in screenings if the screening centre was far away?	7-10	9.30±1.05	W= .149 p= .177
Would you participate in screenings if screenings were painful?	7-10	9.40±1.07	
Would you participate in screenings if screenings were paid?	9-10	9.90±0.31	
Would you participate in screenings if you had any doubts about screenings?	5-10	9.00±1.63	
Would you participate in screenings if other women did not want to participate?	8-10	9.10±0.87	
Would you participate in screenings if screening took a lot of time for you?	8-10	9.30±0.94	
Would you participate in screenings if the time of screening was not suitable for you?	7-10	9.60±0.96	

Table 3. Item-total point correlation of the modified Self-Efficacy Scale

Item No	Item-Total Point Correlation		Cronbach's Alpha Level of the Scale
	r	p	
1	.698	.000	.844
2	.672	.000	
3	.676	.000	
4	.763	.000	
5	.699	.000	
6	.714	.000	
7	.792	.000	

Table 4. Comparison of mean test and retest scores, test-retest reliability on the modified Self-Efficacy Scale

Scale	Scale Point		t	p	Correlation of Test-Retest Point	
	First Application X ± SS	Second Application X ± SS				
Self-Efficacy Scale	5.87 ± 12.00	6.30 ± 13.07	.83	.49	.936	.000

dal W compatibility test. As a result of the test, it was determined that there was consensus between experts and that the statements included in the scale were suitable for Turkish women and a true representation of the construct that we wanted to assess (self-efficacy).

Evaluation of the reliability of Self-Efficacy Scale

Item analysis refers to the relationship between the value of each item and the total value of items in the assessment tool. It is used in the selection of items by determining to what extent the items forming the assessment tool are related to the assessment tool as a whole. For this, a correlation coefficient must be evaluated[22]. It can also be theorized that correlation coefficients are not sufficiently reliable and that items can be removed from the scale[20]. The correlation coefficient obtained from each item indicates the connection of that item with the assessed theoretical value. If the value of the item is high, the said item is sufficient for assessing the relevant behavior. It was recommended that an acceptable coefficient be greater than .25 in the item selection, and that the items with very low correlation value should be removed from the assessment tool without further consideration to other analysis results[22].

For item analysis, .67 was accepted as the limit value for item-total point correlation, the scale va-

ried between .67 and .79 for the items included. It was determined that the total points of all the items included in the scale showed sufficient correlation, and that the item reliabilities of the scale were high. Item-total point analysis is accepted as an indicator of internal validity as well as an indicator of internal reliability, and further indicated that the scale reflects overall structural validity [23].

Reliability refers to the consistency between several independent assessments of the same variable. Reaching the same results by following the same process and using the same criteria shows that coincidental results are less likely. Reliability is determined with a correlation coefficient (r) and it is accepted that reliability is high when the value approaches one [20]. The criteria reflecting the reliability of a scale is "internal consistency". Cronbach's Alpha coefficient is used in order to evaluate the internal consistency in a Likert-type scale [24]. This coefficient is the assessment of the internal consistency and homogeneity of the items included in the scale [24, 25]. The higher the Cronbach's Alpha coefficient, the more consistent the items included in scale are [26]. Therefore, the obtained values indicate that the homogeneity of the scale is at a sufficient level. When Cronbach's Alpha Coefficient is less than .40, it is unreliable; between .40-.56. the test is said to have low reliability; between .60-.79, the test is is fairly reliable, and between .80-1.00, as for our test, it is highly reliable [22].

In this study, Cronbach's Alpha coefficient of the modified Self-Efficacy Scale was .84, so we regard the results as having high reliability. Cronbach's Alpha coefficient of the original scale was .90, so translation did not aversely affect reliability.

While there have been reports testing the validity of the Self-Efficacy Scale using similar scales, no previous study has tested the reliability of the Self-Efficacy Scale when translated into another language. In their study, Tung et al. (2008) used the scale developed by Lechner et al. in 1997 in order to assess the self-efficacy perception for the early diagnosis of cervical cancer. They adapted the scale to 0-100 and found its Cronbach's Alpha to be .93.

According to Table 4, coefficients between Self-Efficacy Scale items and test-retest were found to be .936 and a statistically significant relationship was detected. Another indicator of the reliability of our modified Self-Efficacy Scale was that the difference between the test and the retest was insignificant. This demonstrates the invariance of the assessment tool, and indicates that the reliability of the scale for the Turkish population is high (Table 4).

Conclusions

Our modified Self-Efficacy Scale (originally developed by Lechner et al., 1997) had high reliability and validity. Indeed, it was as reliable and valid as other modified versions of the same test. For this reason, we propose that the scale can be used in the evaluation of self-efficacy perception within Turkish society for the early diagnosis of breast and cervical cancer.

Self-efficacy appears to predict behaviors that lead to the early diagnosis of breast and cervical cancer. Clinicians and researchers can use this scale to identify perceived self-efficacy and to design programs that encourgage tests for early detection like breast self-examination, mammography, and Pap smears.

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Audiological diagnosis of hearing loss in individuals exposed to industrial noise

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Abstract

Introduction Noise has direct harmful effects on hearing, leads to hearing loss and disables communication.To prevent disability, certain measures must be taken, audiological selection of susceptible individuals.

Objective Our aim was to show the clinical usefulness of supraliminal tests (Tone Decay Test, Reflex Decay Test) on workers exposed to industrial noise.

Method Research method involved 50 workers who were exposed to industrial noise their entire working life (experimental group) and the same number of unexposed workers (control group). Both groups were conducted by non-invasive diagnostic methods: medical history, ENT examination and audiological testing (liminal tonal audiometry, audiometry and tympanometry supraliminal with registration of stapedial reflexes), before the start of working hours – exposure to industrial noise.

Results There was a statistically significant difference (p = 0.024) correlated to pathological audiogram according to the length of service in the group exposed to noise above 20 years (48%). Pathological audiogram is dominant in both groups in age from 41-50 years with 45%, so that correlated with length of service over 20 years, we see statistically significant differences. Sensorineural hearing lossis dominating in the experimental group with the fall of hearing of 41-60dB (34%), while in the control group 72% has normal hearing. Cochlear damage is found in 90.5% of the experimental and control 100% damage grupe. Both sided hearing impairment is present at 84% of the experimental and 75% of the control group. The presence of skotoma 4KHz in the experimental group with SN hearing loss was 90.5%, Tone Decay Test was positive in 32% of the experimental and 4% of the control group - a sign of retrocochlear lesion or hypersensitive hearing. Fatigue acoustic reflex (Reflex Decay Test), an indicator in forecasting impact of noise on hearing represented a 100% in the experimental group and 75% in the control group of patients with hearing impairment.

Conclusion Audiological tests should be introduced into clinical practice during periodic examinations of workers exposed to industrial noise to prevent disability.

Key words: noise, sensorineural hearing, supraliminal tests

Introduction

Hearing impairment

Hearing impairment is one of the most serious handicap in the field of human communication. Normal hearing requires anatomical integrity and functional adaptation of all parts of the auditory system: the outer, middle and inner ear, cochlear nerve and central auditory pathways. Damage to any part of the auditory analyzer leads to a decrease in hearing. Hearing impairment of various degrees are called hearing loss,and if the damage is so great that residual hearing may not be used even with hearing amplifier, or there isn't any residual hearing, we're talking about deaf. Human organ of hearing registers frequency sound waves in capacities of 16 000 to 20 000 Hz.

Industrial noise

Any unwanted sound is noise. Significant medical, economic and social problem is the noise in a working environment that includes sound from the operation of machinery or equipment in production and the noise coming from the environment (devices for ventilation or air conditioning, neighboring organizations, traffic, etc.). Besides direct harmful effects on the organ of hearing, noise caused by functional changes in the CNS, the heart,

blood vessels, digestive tract indirectly reduce productivity at work, leading to increased number of errors and injuries at work, so the draft regulations on the and permitted values of noise levels in industry are technical, medical, legal, social and even political issue (1).

Mechanisms of protection against noise

Mechanisms of protection against noise can be: physiological (physiological changes characteristic of the middle ear and neurological phenomena of adaptation and fatigue), technical (standards of its noise, use of protective equipment) and social - legal (legal norms and regulations - in our country are using the international standards of the International Organization for Standardization (ISO)). The noise, introduced as an irritating factor in the body of man a vicious circle, there is a mobilization of protective - adjustable factors by type of organism adaptation syndrome the role of the regulatory system of the hypothalamus - pituitary - adrenal axis (2,3), which long acting noise leads to the exhaustion of this system , which results in functional and organic changes in various organs and systems. Heaviness of hearing loss developed by acute sound trauma(a very loud sound),or chronic acoustic trauma (long acting noise) depends on the damage of individual cells of perceptive hearing organ (Corti's organ), with the existence of individual hypersensitivity to noise can lead to rapid occurence of hearing loss even under conditions that other people relatively well tolerate (4,5).

Protective measures

In order to prevent premature disability, protective measures must be taken that are related to the use of protective devices and audiologic selection of susceptible individuals prior to employment, while the periodic systematic audiological examinations must work towards the protection of high-risk exposed group. In clinical otolaringological practice in Serbia periodical inspections are mainly carried out with the superficial imprecise drafting and interpretation of findings (approximate air conductivity without recording the bone conduction) without conducting specific supraliminal tests auditory whose implementation would certainly help the early detection of susceptible individuals and thereby contribute to reducing the degree of disability.

Objective

Aim of this study was to show the usefulness in the clinical, audiological practice of supraliminal specific tests (Tone Decay Test, Reflex Decay Test) in workers exposed to industrial noise and for monitoring and prognosis initial hearing loss and susceptible individuals with the aim of preventing disability.

Method

Information about respondents

The study included 50 workers of the industrial plant - weaving, selected randomly, equal gender representation of different age and length of service, the same profession without changing workplace - whole lifetime, exposed to industrial noise (hereinafter referred to as the experimental group). The control group consisted of 50 patients, administrators same characteristic which in the course of employment were not exposed to industrial noise (hereinafter referred to as the control group).

In the study we used data from service safety at work about examination values of noise in this drive, and microclimate conditions (temperature, humidity), and for which the intensity of sound pressure at all measured locations exceed the standards allowed values. According to data services safety workers of this plant are protectors (muffs) in operation.

For more efficient data collection, we used a prepared form which contains all data of the respondent. Audiological treatment was performed before business hours or before the eight-hour exposure to noise in the "deaf room". Otolaryngology analysis covers the subjects of both groups and includes the following: medical history, otolaryngologic examination, pure tone audiometry and recruitment test supraliminal (Tone Decay Test), and tympanometry with acoustic reflex testing (Reflex Decay Test).

Criteria from exclusion from the study: hearing impairment caused by acoustic trauma and blast, ototoxic drugs, congenital anomalies of ear, Meniere's disease, patients with diabetes and subjects who had sensorineural hearing loss prior to employment.

Instruments

Supraliminal tonal audiometry tests were performed on the device Diagnostic Audiometer AD 229 (Diatec, Interacoustics, Denmark) and Impendance Audiometer AT 235 (Diatec, Interacoustics, Denmark). To assess the severity of hearing impairment compared to the results of tonal liminal audiometry we used seven common frequency for testing of hearing by air (128, 256, 512, 1024, 2048, 4096 and 8192 Hz) and five frequencies for testing through the bone (256, 512 , 1024, 2048 and 4096 Hz), and in order to avoid false positive results (cross-hearing) was conducted properly kept jamming, which is not tested (masking). Tonal audiometry has enabled diagnosis of conductive and sensorineural hearing loss (6,7,8). Comparison of hearing threshold, monitoring for sudden fall of hearing loss (scotoma) at 4000 Hz, about acoustic causes of the diseases as an etiological factor of hearing loss and need for protection of hearing. were tested and compared sensorineural hearing loss in both groups of respondents, quantitatively and qualitatively (by weight, shape, symmetry, position of the lesion).

Examination in depth of the auditory field was presented by supraliminal audiometry (supraliminal - above the threshold of hearing) in order to determine the localization of damage (cochlear or retrocochlear) in the moment when tonal audiometry shows that damage is sensorineural. We have determined the value of special audio test - Tone Decay Test (auditory fatigue phenomen) for early screening of susceptible individuals (4).

Device for timpanometric testing registered cochlear-stapedial reflex which enabled testing its afferent parts: cochlear receptors and cochlear nerve. At n. vestibulocochlearis lesions reflex threshold was very high or the reflex was completely losted. In cases where the reflex was present it showed extreme fatigue, rapid decline in amplitude at a constant stimulation (Acoustic Reflex Decay Test). We have assessed the value of the data obtained by testing the presence, threshold, and fatigue of acoustic reflex - Reflex Decay Test with aim to predict the impacts of noise on hearing in the prevention of deafness (9).

Results

As a result of ambient technology process, the distribution of respondents by gender indicates the dominance of females in the experimental group as a result of the technological process environment. The difference is not statisticaly significant so the sex in this study has no influence on the parameters of auditory tests.

Examination of demographic characteristics showed that the average age of the patients in both groups (45% of respondents) is in the range of 41 to 50 years and did not have statisticaly significant differences in this parameter study.

Correlation analysis of data showes statistical significance of differences (p = 0.024), the length of service, so in the group exposed to noise dominates the length of service over 20 years at 19 (38%) subjects (Table 1).

Based on the findings of tonal audiometry showed statistically significant difference (p = 0.023) compared experimental and control groups, the presence of pathological audiograms in 24 (48%) experimental group (Table 2).

Comparative review of the findings of pathological audiograms and length of service in the experimental group indicates that the abnormal

Table 1. Length of service of respondents - exposure to noise

			length of service (years)					Total
			1-5	6-10	11-15	16-20	20+	
Group	E - group	Count	2	6	11	12	19	50
		% within group	4.0%	12.0%	22.0%	24.0%	38.0%	100.0%
	K - group	Count	4	11	15	9	11	50
		% within group	8.0%	22.0%	30.0%	18.0%	22.0%	100.0%
Total		Count	6	17	26	21	30	100
		% within group	6.0%	17.0%	26.0%	21.0%	30.0%	100.0%

E –experimental group - exposed to noise; K –control group – was not exposed to noise

audiogram present in 24 (48%) subjects with work histories over 20 years, with the observed satististicaly significant difference (p = 0.024).

Assessment of hearing loss (in decibels - dB), is the most common in the range of 41 - 60 dB in 17 (34%) subjects of experimental group, and the control group 4 (8%) for the same values of characteristics (Table 3). Statistical treatment of the value of comparative findings showed a significant difference (p = 0.002).

Tonal audiometry which was administered in each subject before the start of working hours, we observed a highly statistically significant difference (p = 0.003) in diagnosing damage to the sensorineural loss 21 (42%) in the experimental group than in the control group 6 (12%) (Table 4).

Because of the importance of sensorineural hearing loss for this research, it has been done distribution into retrocochlear and cochlear, and statistical analysis of data didn't found significant differences; representation of cochlear damage of 19 (90.5%) in the experimental group and 100% in the control group.

Representation of sensitivity kept at high pitch, descending type of audiogram with a sudden drop in hearing 4KHz in both groups does not indica-

Table 2. Normal and abnormal audiogram respondents

			audiogram		Total
			normal	abnormal	
group	E - group	Count	26	24	50
		% within group	52.0%	48.0%	100.0%
	K - group	Count	37	13	50
		% within group	74.0%	26.0%	100.0%
Total		Count	63	37	100
		% within group	63.0%	37.0%	100.0%

E –experimental group (exposed to noise); K –control group (not exposed to noise)

Table 3. Level of hearing loss in subjects

			hearing loss in dB				Total
			<20	20-40	41-60	61-80	
group	E - group	Count	23	7	17	3	50
		% within group	46.0%	14.0%	34.0%	6.0%	100.0%
	K - group	Count	36	9	4	1	50
		% within group	72.0%	18.0%	8.0%	2.0%	100.0%
Total		Count	59	16	21	4	100
		% within group	59.0%	16.0%	21.0%	4.0%	100.0%

E –experimental group (exposed to noise); K – control group (not exposed to noise); dB - decibel

Table 4. The ratio of conductive and sensorineural hearing loss

			KO i SN hearing loss			Total
			normal	KO	SN	
group	E - group	Count	23	6	21	50
		% within group	46.0%	12.0%	42.0%	100.0%
	K - group	Count	36	8	6	50
		% within group	72.0%	16.0%	12.0%	100.0%
Total		Count	59	14	27	100
		% within group	59.0%	14.0%	27.0%	100.0%

E –experimental group (exposed to noise); K –control group (not exposed to noise);
KO – conductive hearing loss; SN – sensorineural hearing loss

te a statistically significant difference (p = 0.059) and is present at 19 (90.5%) subjects of experimental group.

Tone Decay Test, test fatigue hearing provides important information on the recovery time necessary ie. the time needed for hearing threshold to return its original value, it's positive at 16 (32%) the experimental and at 2 (4%) control group, comparative statistical analysis of data both groups show there was no significant difference.

As in all patients tympanometric finding is orderly, and acoustic reflex induced above the threshold of hearing in patients with sensorineural hearing loss experimental group 89% and in the control group 100%, no statistical analysis found significant differences. In examining the fatigue (the appearance of recruitment) acoustic reflex, as important indicators in forecasting impact of noise on the hearing, there was a statistically significant difference (p = 0.03). Fatigue acoustic reflex as an absolute indicator of the prognosis impact of noise on the hearing is present in the experimental group with 100%, while the incidence in the control group is 75% subjects.

Discussion

Time of a serious threat to human life and work of increasing intensity of noise and vibration that is growing exponentially, is the present time, when the noise penetrates all aspects of human life and follows the man, not only at work, but during the holidays and even at night during the sleep. Time for rest and recovery of hearing has become increasingly shorter, which is fundamental to the function and hearing loss and thus for all other effects of noise on organizam. Industry revolution brought great development of machinery, causing as an unwanted byproduct steady increase of noise. New technologies and the application of protective devices have not shown the desired results since it is still in the world in half of the job noise levels above the maximum permitted level and even in developed countries, third of affected workers do not work all the time wearing protective equipment, so the noise as a factor of influence on modern man has great social and economic consequences (6,7).

Harmful effects of noise (acoustic energy) on the hearing as a sensory organ of the receiving sound waves directly can lead to various degrees of hearing loss which further could result in aggravation or disable communications.

The research was carried out assessment of hearing loss at people who are exposed to industrial noise. Hearing loss is more common at patients who were in the course of many years of service exposed to continuous industrial noise during the eight-hour working time. It was noted that with more years of increasing incidence of hearing loss, so we can conclude that the length of service ie. prolonged exposure to industrial direct impact on the occurrence of frequent hearing loss.

According to our research the most common hearing loss of 41-60 dB when it comes to severe hearing impairment on subjects who were exposed to industrial noise. We observed that the hearing loss usually with predominance sensorineural damage, ie. cochlear damage in the experimental group. Sensorineural hearing loss in the cochlear type are asymmetric which indicates the location of noise sources in relation to the closer ear during several hours and several years of exposure to noise at work (6,7).

The presence of skotoma 4KHz as a sign of sensitivity to high tones can be seen in a large percentage - 90.5% of the examinees and an indicator of fatigue damage and the need to protect your hearing. Specific audiological tests that can be used to prevent possible hearing handicap at exposed persons have recently pushed the use of new, modern methods - brain stem evoked potentials (BERA). We must not forget that these expensive machines are mainly in large malls that are inefficient and expensive for early screening during periodic examinations of workers. Therefore, we emphasize the clinical significance of tests to determine supraliminl recruitment because we need a simple audiological testing apparatus and of course knowledge of pathology audiological tests. Auditory fatigue and adaptation based on survey size and intensity of occurrence of auditory fatigue in the presence of various intensities sounds as speed recovery. Auditory fatigue is an important retrocochlear phenomenon and the initial prognosis of hearing impairment on subjects exposed to industrial noise. Fast fatigue and poor adaptation indicate greater chances of hearing impairment in the future if the effect of sound agent

continues as these tests gives an early advantage in the prevention of disability.

Significant for this study because of its practicality, feasibility in light audiological diagnosis is Tone Decay Test, hearing fatigue test that provides information on the required recovery time, the time needed to restore hearing to the original value. Fatigue hearing is positive in a significant number of the examinees (95.65%), which demonstrates a lesion or hypersensitive hearing the sound stimulation.

Acoustic, stapedial reflex in response m. stapedius to a sound stimulus supra-speech intensity. Is an integral part of impendanometric tests, performed on the same device after tympanometry and an inseparable part of the findings of impendanometric. So far, the most frequently monitored parameters of acoustic reflex are: threshold amplitude, output and reflex curve and fatigue reflex. Many authors are dealing with this problem (3,7) performing detailed analysis of these parameters in workers exposed to extensive industrial noise action of known physical characteristics (that lasted) to determine which changes have occurred in these parameters with those of workers, to what extent and under what conditions. Acoustic reflex, as a noninvasive method of short-term, objective, and easy to use does not require the cooperation of workers, which gives objective results obtained and erroneous assessments impressions and subjective reactions of employees are avoided. Test results of our work is largely coincide with these authors which provides this audiological testing important role in early screening for hearing loss of exposed to industrial noise, in order to prevent permanent disability (6,7).

Significant place in the diagnosis of hearing loss at individuals exposed to industrial noise has a test pad (fatigue) acoustic reflex (acoustic reflex decay test) that allows testing of the integrity cochleovestibular nerve, objective approach that does not depend on the extent and possibilities of cooperation with the respondent. Positive results indicate the sensitivity of the organs for hearing the sound at increased stimulation and can be taken as an absolute indicator in forecasting impact of noise on the hearing (10). In our study was positive in 100% of the examinees with hearing loss.

A simple application of the above-mentioned auditory tests, their significance in diagnosis and topodiagnostic hearing loss, early screening for hearing impairment in people exposed to noise determine their practical significance. Faster fatigue and poor adaptation suggests a greater possibility of hearing impairment in the future if the effects of harmful agents continues. Because of existence of individual hypersensitivity to noise, which can lead to rapid emergence of hearing loss, even under conditions that other people well tolerated, measures with the aim of preventing premature disability must be taken. Periodic systematic examinations of persons exposed to industrial noise, with better handling and audiologic supraliminal application tests (Tone Decay Test and Acoustic Refex Decay Test) can significantly contribute to the prevention of disability especially when it comes to developing countries with limited possibilities of modern diagnostics. According to the estimates (for 2008) of the World Health Organization (8,1) the number of people with hearing damage greater than 45dB HL was about 288 million people while the number of people with hearing impairment above 25 dB HL was 664 million.

Timely and accurate diagnosis of certain diseases associated with appropriate treatment greatly increases the chances for successful treatment and prevent severe pathology of the disease. Early diagnosis of hearing loss (early detection of pathological processes) contribute to the adequate treatment prevent serious consequences such as deafness and speech distortion.

The problems that arise in the field of early detection and diagnosis of hearing disorders, in exercise of the profession in areas with high noise levels, are important because they are progressing at a slower pace, they depend of personal sensitivity and they have progressive character.The risk of hearing impairment of exposure to noise of 80 dB at 5 %, at the noise of 85 dB is 15% and at the noise of 95 dB intensity is 25% exposed persons. Large number of cofactors increases the risk: age, diabetes, neurodegenerative diseases, hypotension / hypertension, ototoxic drugs etc. (10). Early detection and diagnosis of hearing loss are therefore of great usage as medical, economic and social problem, so the health care system should enable cost-effective, easy to perform and the general working population available test to assess the quality of hearing. This concept test is the screening

test that is aimed to show individuals possible problem with the hearing without the ambition to provide quality testing of hearing loss. Damage to some of the methods for assessing the quality of hearing could be used as a screening test available to the general working population, it must meet the criteria of the health profession without being achievable within the existing technology solutions, including economic pay off. Doing supraliminal screening tests for early diagnosis and treatment of patients can be a reality for both medical professionals and patients. While there are some problems (lack of information, disorganized medical, legal and economic regulations) advantage of this form of screening is a multifaced, promote prevention and prevent hearing impairment. Development of new diagnostic screening procedures necessary to implement the multidisciplinary approach to medical requirements agreed with the technological capabilities, taking into account the economic moment.

Conclusion

Sensorineural hearing loss is a significant entity whose diagnosis, especially differential diagnosis requires a complex diagnostic procedure. Exact determining the etiology and hearing lesion is the only proper approach to the prevention of disability, which gives the best results when it's timely conduct. Reserach of these specific audiological tests, has no absolute value for the diagnosis but it can be set only on the basis of the entire medical history, clinical features and comparisons of other researches. Tonal liminal audiometry, often performed incompletely in the periodic examinations of workers exposed to industrial noise, with no bone conduction and at several frequencies, will provide the right diagnosis, at least in the 21st century. A limited number of sophisticated equipment such as BERA , a small number of trained professionals and economic. Shutting this diagnostic method for mass application to screening susceptible individuals are no excuse for the failures of the work that undoubtedly lead to disability. Therefore, audiologic supraliminal tests should be introduced into clinical audiological practice to enable timely diagnosis set during the periodic review of the vulnerable working population, and taking measures in order to prevent the occurence of hearing loss and deafness as significant contribution to economic and social policy of the country.

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Attitude of health information system managers and officials of the hospitals regarding the role of information technology in reengineering the business procedures: A qualitative study

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Abstract

introduction: In the current era, concepts such as innovation, speed, service and quality would be more considered. Consequently, paying attention to business process reengineering (BPR) is necessary, using modern information technology in organizations. With regard to the growing trend of global competitions, hospitals have also approached BPR for success and increase of their efficiency and effectiveness. In this study, the relationship between reengineering projects and information technology (IT) and the role of that in running BPR programs in hospitals have been considered, along with explaining concept of reengineering and the importance of its applying to medical organizations and hospitals.

Method: This study has been conducted as cross-sectional descriptive and thematic qualitative analysis to measure the usage level of IT for implementing BPR programs at selected hospitals in Shiraz University of Medical Sciences, by using library information and internet searching as well as semi structured interviews and focus groups.

Findings: Findings show that executive managers of hospitals should insist on their attempt to implement BPR programs in order that they can achieve cost reduction, the effective use of resources, patient satisfaction and so on. It is right that information technology gives companies capability to carry out the business process reengineering, but the real power of IT is that it enables organizations to break the old rules and to use the new ways. Yet, one of the important problems of IT is the increase expenditures related to that as the biggest enabler of BPR.

Conclusion: With regard to the importance of BPR implementation in hospitals as well as the powerful role of IT in this field, it would be suggested that studies in the field of IT expenditures would be conducted, along with accurate implementation of these programs.

Key words: Business process reengineering, Information technology, hospital.

Introduction

In the era when technology is quickly changing and the production lifecycle is shorter than always, the current methods of increasing production, meaning to rationalize process and automation, cannot fulfill organizations' demand. Especially, heavy investments in information technology have had disappointed outcomes, mainly due to companies' tendency to use technology for mechanizing the old solutions, because the acceleration in processes cannot resolve significant executive shortages and deficiencies of process (1-2).

On the other hand, for accessing to new decade mottos as the title of innovation and originality, speed, service and quality, it is time that we restart the task instead of modifying and ordering traditional and old processes, in fields of software and har-

dware. In fact, reengineering is the special method of using mind and business reviewing. Re-planning or reengineering is the method of innovation and restoration. It is the method that organization products continuously examine the accuracy(3).

In other words, reengineering processes is the method for re-planning business processes as well as organization evolution that some of these attempts are successful and some are faced failure surely(4-5). However, reengineering is a new concept that is defined by Hammer and Champy as: essential reviewing and fundamental reengineering of processes in order to achieving the extraordinary progresses at effectiveness criteria such as expenditure, quality, service and speed(6). Also reengineering, by other definition, is a planned change for redesigning a business process in order to achieving the best attempts in terms of quality, the speed of customer service and cost that is typically empowered by information technology(7).

According to the recent definition, information technology plays a decisive role in business reengineering. In other words, modern information technology is considered as a part of any attempt to re-plan because it allows organizations to carry out the task of business process reengineering. But, just using computer to resolve current business problem do not lead to redesigning it. On the contrary, the misuse of technology can prevent from all work improvements in redesigning, because of strengthening the old ways of thinking and old behavioral patterns(4).

With regard to what was said and considering the growing trend of global competitions, many organizations such as health organizations and especially hospitals have approached growing trends such as total quality management and business process reengineering for their success, increase of efficiency and effectiveness.

In this regard, the evidences show that environmental design and the process of health services were more focused on the clinical effectiveness and technical performance in 80s. But, in 90s, this focus included upgrading service quality to patient as a customer, along with clinical components. However, the healthcare purchasing method has been slowly turned from payment model by the customer into third-party payments by insurance companies and reimbursement programs. Therefore, it seems, in such atmosphere, reengineering presents an approach to resolving problem, with emphasis on re-planning business processes to achieve impressive progress in cost, quality, service and speed criteria(5).

Furthermore, other evidences show that the implementation of reengineering process in hospitals has been successful in recent decade(8). However, it is necessary to say that studies related to information technology for current healthcare is in the position where commercial organizations were almost 30 years ago. One of the reasons is the changing methods of insurance companies from reimbursement of costs spent for patient care in hospitals into separated reimbursement systems. Hence, in this regard, hospitals try to be active within the scope of each patient's financial ability that is very similar to commercial activities of organizations which try to operate in agree with budget of each project (9).

According to what was said, in this study- with regard to multiple motivations that are for reengineering in organizations, especially hospitals and with regard to important role of managers and information technology experts in implementing and establishing this system-has been discussed to express managers' views and health information system officials of hospitals which are under the cover of Shiraz University of Medical Sciences regarding the new concept of reengineering and its importance in hospitals, the relationship of reengineering projects with information technology and the role of information technology in implementing reengineering programs on various business, especially hospitals.

Method

The current study has been conducted through thematic analysis and by qualitative method. Participants in this study were 8 of the hospital health information system's officials and 6 of managers of hospitals under the cover of Shiraz University of Medical Sciences in Shiraz, Iran.

Mentioned individuals were selected by Purposive sampling method as within that researcher selects individuals who can give the best answers to the research questions based on his aim for more benefit samples (10). Therefore, with regard to aim of study, desired sample included individuals

who had the most information(11) about establishing information technology system in hospitals and influence of that on reengineering processes.

Considering the sampling was continued up to data saturation and repetition, 8 of health information system's officials of hospitals were profoundly interviewed as semi structured finally and 6 of managers participated in two sessions of focus group.

For interviews, topic guide had been already provided, but because all of interviews were done as a semi structured and without clear boundaries, the partnership level of participants was acceptable.

Time of individual interview sessions and group discussion had been already predicted and had been coordinated with desired individuals and during this coordination individuals were ensured that data confidentiality and their words would be completely kept and all individuals were interviewed fully consciously and voluntarily and after getting verbal agreement.

However, to interview, a quiet place and away from the individuals' workplace was possibly tried to be predicted for this task that the client's entrance and exit and phone ringing would not distract and disturb the meeting. The duration of each individual interview was averagely between 30 to 40 minutes with Standard deviation of 6 minutes and the average time of 100 for session groups with standard deviation 10 minutes.

In each session, after asking permission of individuals, interviews were recorded by the cell phone and saved on separate files. At the end of each interview, all recorded issues were written down and after typing and arranging, findings were confirmed by them, to ensure compliance with interviewees' words. After ensuring data accuracy, all provided texts were reviewed several times and texts were broken down into main themes and subthemes and then were coded with Microsoft office word as the usual software.

Findings

Findings obtained through analysis of individual interviews and group sessions with participants were leaded to expressing 8 main themes (table 1) that obtained themes are discussed as follows:

Knowledge about the reengineering concept: Results obtained from interviews show that attention to definition and terms of use and the implementation of the reengineering in hospitals are very significant and as long as this process is not known, the necessity of using IT for implementing and establishing this process cannot be considered.

In this regard, participants were expressed statements from their points of view regarding reengineering definition. "*Generally, reengineering means starting from a white paper, rethinking and redesigning the processes which organization makes a value by them, does a business or removes an operation*" [P_2] .

The necessity of reengineering in hospitals: Most participants in the interviews (13 people/93% of individuals) had this idea that hospitals are required to check their processes and to redesign them due to the cost increase of health services and especially hospital diagnostic services and the necessity of determination of competitive prices.

One of the participants states in this regard which *"the most variable factor is technology in healthcare industry and, the methodology of service presentation will be altered with any changes in technology For example, the process of gastroenteritis surgery has been greatly changed with introducing endoscopy or the use of new technology always makes new capabilities to do business in health industrial and consequently it increases competitive pressure and the need for improvement of business processes will be required*" [P_3].

In this regard, by summarizing participants' opinions, it seems that important factors which hospitals are forced to use reengineering concepts are as follows:

1. Delivery of services to foreign clients with appropriate quality
2. Decreasing bottlenecks of domestic clients with quality service improvement
3. The improvement of the financial performance with decreasing expenses
4. The improvement of clinical performance
5. Reducing time-consuming processes of service providing
6. The selection of positive experiences in foreign health organizations
7. The pressure to make regular and stable conditions
8. To maintain competitiveness with other health organizations

Table 1. Attitude of health information system managers and officials of the hospitals regarding the role of information technology in reengineering the business procedures

Main themes	Sub themes
Knowledge about the reengineering concept	-
The necessity of reengineering in hospitals	1. Delivery of services to foreign clients with appropriate quality 2. Decreasing bottlenecks of domestic clients with quality service improvement 3. The improvement of the financial performance with decreasing expenses 4. The improvement of clinical performance 5. Reducing time-consuming processes of service providing 6. The selection of positive experiences in foreign health organizations 7. The pressure to make regular and stable conditions 8. To maintain competitiveness with other health organizations
Executive steps of reengineering in hospitals	1. Identifying the process or part of the hospital which needs to be changed 2. Determining aims of reengineering project 3. Defining the methodology 4. Standardizing the process and analyzing that 5. Developing solutions and checking possible alternatives 6. Implementing reengineering project
Using information technology for reengineering process	-
The different roles of IT in different reengineering steps	1. The role of IT as a starter or changing factor 2. The role of IT as a facilitator 3. The role of IT as a reinforcing system
The cost- effectiveness of IT in health section	-
IT practical experiences	-
The role of IT in successful reengineering implementation in hospitals	1. The perception and knowledge of executive factors of the necessity of reengineering processes 2. The commitment of the supreme manager of the organization to reengineering processes 3. The acceptance of redesigning processes from the bottom to the top of the chart 4. Directing reengineering processes from the top to the bottom of the organization 5. Using new tools such as the optimization in reengineering process 6. The appropriate use of information and communication technology and computers 7. continuous quality improvement as a prerequisite of reengineering 8. restructuring organization to support reengineering process

Executive steps of reengineering in hospitals: Since not only knowledge about need for implementing and establishing reengineering processes in hospitals is not enough but also attention to special steps for its establishing and implementing is essential, in the following interviews, people were asked to express their analysis of the reengineering implementation method in hospitals as certain steps. Even though interviewees express analysis and different opinions in this regard, in a general summary obtained from the analysis of interviewees' statements, for implementing reengineering process in hospitals can be imagined a process including 6 steps which are included:

1. Identifying the process or part of the hospital which needs to be changed
2. Determining aims of reengineering project
3. Defining the methodology
4. Standardizing the process and analyzing that
5. Developing solutions and checking possible alternatives
6. Implementing reengineering project

Using information technology for reengineering process: Most of participants (12 people/ 86%) believed that nowadays great advances are observed in using IT in various organizations. *"Nowadays, considerable advances in information technology and communications give staffs this opportunity in order to work from outside of their offices"* [P_9].

Furthermore, modern information technology provides the possibility of getting important benefits to organizations such as *"it leads to reducing cost and increasing the accuracy of information*

exchange, it decreases human mistakes during doing complicated and repetitive tasks, it result in decreasing the required time to do tasks and it leads to financial saving, it coordinates and merges activities simultaneously and finally it leads to improving access to information and increasing efficiency and organizational effectiveness" [P_{10}].

The different roles of IT in different reengineering steps: Findings obtained from interview sessions with hospital IT experts leads to presenting a proposal framework as a different role of IT, as follows:

1. The role of IT as a starter or changing factor that itself may leads to stimulate some needs and influences new demands.*"A new technology very often causes feel the need for other things; for example, computer scan invention may be due to the need for using different computer images"* [P_4]. However, as one of the participants also stated *"a technology may cause a problem at first, and then resolve it. This issue can be readily observed during establishing new computer systems in organization instead of manual systems"* [P_8].
2. The role of IT as a facilitator which means that the information technology is a tool to more facilitate doing tasks or to decrease their workload. *"...for instance, to facilitate the use of computer images, an image system should be able to cover image preparation actions, image creation, sending and receiving image and the management of image database"* [P_1].
3. The role of IT as a reinforcing system that indeed are supporting system for process or performance completion. *"In fact, this is the role of IT innovation which refers to how it works"* [P_4]. Here, in fact, IT has been designed to facilitate the steps of the special process and uses for better performance and more productivity as the reinforcement.

With regard to obtained findings from themes of *"using information technology in reengineering process"* and *"different roles in different reengineering steps"* and professional discussion with related experts, it seems that using information technology can have an important role in all steps of establishing reengineering process and all three mentioned roles will influence on establishing reengineering in hospitals, while using IT can bring significant benefits for organization.

The cost- effectiveness of IT in health section: Findings obtained from group interview sessions were indicated despite heavy investments which has been made for IT development in health management around the world. *" Many projects has been done in different countries for establishing hospital information system; for example, In South Africa, this plan has been spent nearly $ 30 million, but it was failed in executive steps or in England hospitals spend nearly £ 200 million for implementing IT per year, but it is not very effective"* [P_{10}] *"... It has been said that Audit Committees in the UK has even criticized the use of computer systems in NHS' hospitals"* [P_{12}] *"The discussion that has still been continuing in developing and developed countries is attention to the amount of money which is considered for investment in information technology, especially when little financial resources is allocated for investment in medical technology and purchasing medicine and medical equipment"* [P_{14}].

However, re-engineering may not be necessarily cheap and it is usually expensive in the early stages. *"The cost of assembling computer and installing a package service can be very expensive, but, with computerizing, it simultaneously decreases the process implementation, saves the manpower and helps strategic control and leads to savings and saving money in hospital"* [P_{11}].

But, on the other hand, findings indicated some of successful aspects in IT applications in hospitals which were mainly reported regarding telemedicine, electronic monitoring and reengineering processes. *"... India telemedicine projects that are implemented in partnership with private-governmental sector is one of the successful cases of IT application in health that here, of course, is not related to our discussion"* [P_{12}]. *"The model of electronic monitoring application that is based on activity based costing and is concentrated on user expenses in governmental hospitals is one of the other successful cases as well"* [P_{13}].

IT practical experiences: Findings indicated that IT has a vital role in reengineering success even though establishing this system covers the most part of expenses in order to the implementation of reengineering processes. One of the participants said, quoting informed sources *"in completed reengineering projects, IT alone includes the great part of expenses, meaning between 22% and 36% of to-*

tal real costs " [P_9]. Nevertheless the high cost of IT does not necessarily means the effective implementation of that and the majority problems of IT can cause costs related to it go higher that this point should be considered due to reengineering processes at the time of checking and estimating IT costs.

The role of IT in successful reengineering implementation in hospitals: Findings obtained from interview with hospital HIS managers and officials in this section had a great diversity that has been tried to mention the most important themes.

Two of participants totally believe that *"the design and the development of IT system can be very important for reengineering processes such as purchasing hospital supplies and inventory management"* [P_6 and P_{10}]. For complementing and confirming this point, one of managers believes that *"since the analysis of variable costs in hospitals indicates that the cost of hospital supplies such as consumable materials and disposable Supplies for medical, surgical and laboratory needs include nearly 90% of variable costs, it seems that reengineering procurement processes and inventory are necessary in our hospitals"* [P_9].

In a general summary of interviews, the factors that can lead to successful reengineering implementation in hospitals have been reported as follows:

1. The perception and knowledge of executive factors of the necessity of reengineering processes
2. The commitment of the supreme manager of the organization to reengineering processes
3. The acceptance of redesigning processes from the bottom to the top of the chart
4. Directing reengineering processes from the top to the bottom of the organization
5. Using new tools such as the optimization in reengineering process
6. The appropriate use of information and communication technology and computers
7. continuous quality improvement as a prerequisite of reengineering
8. restructuring organization to support reengineering process

Discussion and Conclusion

Business reengineering process creates the strength of facing tremendous changes. The main thought of reengineering is the thought of releasing from old and archaic principles and is also avoiding assumptions which have been ruled affairs because great achievements and improvements in performance cannot be accomplished by shortening and automating current processes; yet, old and archaic assumptions should be fought and archaic principles which have been caused low productivity more than anything else should be discard(2). Since systems providing health services as well as especially hospitals are faced with great changes in different areas, it is necessary that hospital executive managers continue their attempts to implement reengineering projects so that they can achieve costs decrease, the effective use of resources, the patient satisfaction, etc.

Hence, in this research, the attitudes of managers and officials of health information system of hospitals has been considered regarding the role of information technology in business reengineering processes so that the study on the current status and attitudes dominated hospitals which are under the cover of Shiraz University of Medical Sciences and their readiness for preparing the implementation of reengineering processes can be considered.

In this research that has been conducted as a qualitative one, 8 themes have been obtained within interviews with specialists that have been summarized under the headings as follows: the definition of reengineering in hospitals, predicted steps for implementing reengineering in hospitals, the use of information technology (IT) in reengineering process, the different roles of IT in different steps of reengineering, The cost effectiveness of IT in health section, practical and functional examples and samples of IT and the role of IT in successfully implementing the reengineering in hospitals.

Regarding cost effectiveness of reengineering in hospitals that has been one of the themes obtained from the current study, the results of other studies indicate that more than 50% of organization which had been completely implemented the reengineering projects, more than 40% of their running costs were spent on IT section, but though in other organizations, IT costs for implementing reengineering was average or low(12). Also in IT empowerment discussion that was one of the subthemes related to the different roles of IT in current study, studies indicate that 58% of organizations have considered IT as a vital role in empowering the redesigning of their main processes. Thus, 68% of organizations have consid-

ered IT process as a vital one to support reengineering in their organizations. In this regard, IT management has been considered as one of the 10 important and vital factors to implement reengineering programs and considered as 7th barrier of major barriers to implementing reengineering instead of technical deficiencies that are accompanied by weak IT management(13). In practice, more than 75% of the 30% of the best runner reengineering organizations, have considered IT as the most important factor for enabling and conducting reengineering programs that these organizations have had unexpected improvement, the considerable profit and revenue, and also the cost reduction as a result of reengineering(13). In other study, IT was considered as a necessary empowerment in 66% of the companies involved in reengineering project, but it was not considered as an important and influential factor for other 32.5% (14).

Another research regarding companies that have used IT for reengineering projects indicated that IT influences reengineering in 3 main areas including:

1. IT as an enabler that within it, many big companies that have been considered, have largely invested in IT as the enabler of reengineering programs such as D2D, XEROX, IBM, …
2. The use of IT for supporting business processes: Most studied companies believed that IT supports their business processes and can enable redesigning processes to access the functional objectives.
3. IT as a compulsion: This idea that has been expressed in some studies is called IT legacyor survivor systems which imposed redesigning efforts. Most of studied financial services companies were faced with big problems that were the result of the previous legacy systems and was retrospectively designed for supporting the organization products(15).

It seems that the results of this study is somewhat similar to subthemes obtained from current study which have considered 3 roles of starter, facilitator and enabler for IT in implementing reengineering processes. Some interviewees in the current study believed that designing and developing IT system are very important for reengineering processes such as purchasing hospital supplies and inventory management (P6 and P10). In this regard, the intervention study was conducted in the GCR cancer treatment hospital in west of India. In this hospital, at first, preparation task and tender implementation for all items of needed goods and retailer selection and rate determination of contracts were assigned to purchasing Committee that was included a list ,including 400 items for annual purchasing that made nearly 1200 purchase orders annually. After intervening and reengineering of the purchasing system, at first, all 2000 merchandise items were categorized as small groups that each of them was the subset of a larger group. For each small group was defined the product number, the purchase price and the purchase order number. Unlike the past, purchasing policy after reengineering required tender for each small group of items, not each of merchandise items. Also credit payment period was decreased from 3 months to 1 month and sellers chose the rates for each small group of items to fulfill hospital annual needs. This effort resulted in decreasing the number of sellers from 400 sellers (a few, average, large) to 75 average and large sellers. Finally, this committee saved 15-20% in favor of hospital supplies(16).On the other hand, IT gives organizations the ability to do the task of business reengineering processes. If organizations are going to be successful in the period of continuous technological change, it is necessary to gain the exploitation of technology as one of their main competencies.

Not only is the real power of technology that causes old processes work, but also it enables organizations in order to break the old rules and to create new ways for working which means that they should redesign. Also unlike automation, redesigning is regarding innovation; it is regarding the exploitation of last technological capabilities instead of familiar capabilities(4).

This point should be insisted that the IT application has the strongest influence on standardizing or removing process variables. IT also has a vital role in implementing reengineering and improving health system business processes such as HER or electronic health record that is an example of IT to facilitate the implementation of reengineering in hospitals. But, success in IT applications in governmental hospitals can be related to 2 main factors:

1. Emphasis on evaluating the costs and benefits
2. The ability of representing benefits to all beneficiaries for providing health services, including providers (government), experts (hospitals) and patients (citizens)(17).

It is true that IT works as the biggest reprograms enabler, but IT problems are because of increasing its related costs that these costs include the important part of renewed actual costs, the figure between 22% and 36% of the total costs of completing the

reengineering. Interestingly, in various researches has not been found any clear relationship between high costs of IT and the best performance in reengineering projects; that is the high cost of IT does not necessarily mean effective implementation(18). But, reengineering projects are not always successful. Nearly 25% of 300 reengineered programs did not achieve to their goals in North America and this amount regarding the industry would be nearly 70%. Actual profits of project was estimated less than what was expected, in cases such as servicing customer, process suitability, quality, cost reduction, competitiveness, technology and costs improvement. To surrender pressures for producing quick results, many managers who has implemented the reengineering ignored(6). With all these problems, why do organizations still try to implement the reengineering programs? Basically, they do not have any choices; when the dramatic improvements of business processes are frequently related to organizational survival and its success. Hence, hospitals have also attempted to improve their performances by different methods as 63% of North America hospitals have been involved in reengineering programs during this research(6). In developing countries like Iran which health expenditure per capita is not high and also health budget is being declined, reengineering can represent solutions to decreasing useless processes in subsets of governmental health centers.

In conclusion, it would be proposed that along with implementing the reengineering projects in different organizations and especially hospitals, special attention should be paid to the enabling role of IT in this regard and with forming a team consisting related experts, in addition to help to the successful implementation and achieving positive results, high cost of IT as well as factors preventing successful reengineering implementation would be controlled by accurate studies.

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Word-of-Mouth (WOM) as A Tool of Health Communication: A Case Study of Turkey

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Abstract

Word-of-mouth (WOM) strategy is a key area because many consumers in various sectors rely on the product experiences and advice of the competent people. In health care sector, WOM is also an important indicator as advertising tool. The main purpose of this study is to explain dimensions of health based WOM and relationships between the dimension and encouraging, discouraging, and satisfaction. Results of the study revealed three dimensions, which are "tie strength and relationship", "health knowledge and experience", and "similarity and preference awareness". The results of the study suggest that these WOM dimensions have significant effects on level of satisfaction, encouraging, and discouraging. The study has significant implications as to how well health marketing practitioners and managers implement WOM marketing strategies and advice dimensions of health practices.

Key words: Health, Health Care, Health Marketing, Word-of-Mouth, Health Communications.

Introduction

In the health care sector, there are several factors that affect who, why, and when consumers utilize health care services [1]. Consumers find word-of-mouth (WOM) as compelling source of information. In today, many of consumers in variety sectors receive information from different sources, such as physical surroundings, mass media, and other persons. Information from other persons about goods and services may come from sales personnel or from other consumers. In marketing, word-of-mouth (WOM) is an important strategy and normally used to describe advice from other consumers. The interactivity, speed, and lack of commercial bias of WOM make it a very effective source of information about prospective consumer choices, particularly with regard to services for which pre-purchase experience may be limited.

Despite WOM's re-emerging role in marketing communications and relatively sufficient number of books published on the subject; the academic researches and publications on WOM related to health sector are still limited. In this study, the researchers investigate the dimensions related to WOM on physician preferences and, satisfaction, positive and negative WOM behaviors.

Literature Review

The literature on direction of effects of WOM has two streams. These are positive and negative WOM [2,3]. In a study that compares positive and negative WOM, scholars report an interesting finding. The researchers found that number of people producing positive WOM is bigger than individuals who produce negative WOM, and the occurrence of positive as well as negative WOM in some instances is positively related to market share [4]. In consumer choice, WOM is often the dominant factor; for example, Keaveney [5] observes that positive WOM is the main source of information when people found a new service supplier. However, Bailey [6] indicates that individuals shape their attitudes on the basis of negative information. Coombs and Holladay [7] point to the amplifying effect of negative WOM, particularly occurring during and after a crisis situation. Based on the reasons discussed above and considering literature research, the researchers have come up with the following WOM dimensions that are believed to play a role in a success of a physician health service. These dimensions are as follows: Tie Strength and Relationship, Health Knowledge and Experience and Similarity and Preference Awareness.

Tie strength and relationship

The main one factor affecting WOM is the power of relationship between decision maker and

recommendation source. Recommendation sources used in consumer decision heuristics are usually studied under the rubric of WOM communication [8]. WOM recommendation sources can be categorized according to the closeness of the relationship between the decision maker and the recommendation source, or the "tie strength" [9]. The tie strength of a relationship is defined as strong if the source is someone who knows the decision maker personally. The tie strength of a relationship is defined as strong if the source is someone who knows the decision maker personally [8]. So, many of consumers rely on WOM to evaluate credence qualities of services [1], such as health, movie, education etc.

Health knowledge and experience

Many of consumers have an experience or familiarity about a good or service. In this manner, the concept of prior knowledge is defined in terms of the extent of these experiences or involvement [8]. The knowledge and experience on good or services has been widely researched [8,10,11] and commonly refers to information that is before external search occurs. Brucks [10] state that there have been significant relationships between prior knowledge and ability to process new information.

The tie strength of relationship between WOM source and receiver is related to knowledge and experience about a specific subject. If knowledge and experience of health services is high, the trustworthiness also will be high. According to Duhan et al. [8], the type and level of prior knowledge will be important indicators in terms of next consuming behavior. Nelson [12] argues experience dimension of WOM and suggests that the inclusion of experience qualities are necessary because people would give more personal recommendations (WOM) of products possessing experience qualities as they have tried them and can better explain the product to the next person [1].

Similarity and reference awareness

A rational customer often also considers how likely that the recommendation will succeed, that is, meet the purpose of the application of the recommendation. Therefore, not only do we need to observe the requirements of the customer, we also have to consider their preferences. One of the early studies on the effect of the positive and negative WOM on movie appreciations reports that negative WOM has a significant effect on movie preference [13].

Ranaweera and Prabhu's study [14] asserts that there is a positive correlation between satisfaction and WOM. Mittal and Lassar [15] find that satisfied customers outnumber dissatisfied customers by more than four to one in the health care and car repair services [4]. Three hypotheses were developed for empirical investigation of effects of WOM factors about in advising consumers to going a physician, encouraging or discouraging consumers after positive or negative WOM, and satisfaction after WOM, based on the review of literature, implication, and discussions. These hypotheses are:

H1: The dimensions related to word of mouth on health are positively associated with advising to go a physician.

H2: The dimensions related to word of mouth on health are positively associated with the level of satisfaction that a person gets from a physician.

H3: The dimensions related to word of mouth on health are positively associated with discouraging to go a physician after negative word-of-mouth.

Method

Research and questionnaire design

The questionnaire form developed for this study consists of three parts. The first part of the questionnaire contained 17 statements which are related to characteristics of WOM senders. Five point Likert Scale ("5" Very Important, "1" None Important) was used by respondents in responding to WOM statements about physicians. To generate statements that consisted of the domain of opinions about advice contents three focus groups were conducted to 34 health consumers. In addition to the focus groups interviews, statements used in this part were adapted from previous studies related to general and health dimension of WOM, [1,2,3,8] and were designed according to types and applications of advice strategies. Then, researchers generated a total 17 items. The second part of questionnaire included three single item measures relating to referring to encouraging going a physician, discouraging after

negative WOM and satisfaction after WOM. The participants were also asked to indicate their level of agreement on these four items on five-point Likert scale with 5 being "strongly agree" and 1 being "strongly disagree". The last part included demographic variables.

Sample

The sample of this study is comprised of people living in the province of Eskisehir, Turkey. The questionnaire was distributed by sixteen trained researchers. Questionnaires were answered by respondents in the researchers' presence. In lower educational groups and for groups of respondents who needed further explanations in filling out the questionnaires, researchers helped the respondents fill out the forms to a greater degree than they did for respondents with higher educational levels. Due to the importance and sensitivity of the issue, researchers first briefly explained the research purpose, and then gave the questionnaires to willing participants. The explanation and the filling out of the questionnaire took approximately 15 minutes. A total of 2000 questionnaires were distributed, 1680 of which were completely answered, resulting in a return rate of 84 percent.

Results

Characteristics of participants

According to the demographic results, %51.5 of the respondents were male and %48.5 of the respondents were female. % 34.1 of the respondents' income was between 501-1000, followed by who had lower than 500 USD with %34.1. Most of the respondents' ages were between 18-25 (36.4%), the other groups were 26-35 (%29.5) and 36-45 (16.7%). Approximately %26 of the participants were students, %13.3 of them were public officials, %11.2 of them housekeeper and %10 of them were workers.

Dimensions of health based WOM

The scale related to WOM contains a total of seventeen items, thus principal component factor analysis was used to sort out and classify these variables as well as to convert them into main factors. To apply factor analysis on items related WOM on health, it is necessary to test the Kaiser-Meyer Olkin (KMO) measure of sampling adequacy. For the attitude variables, Kaiser-Meyer Olkin (KMO) was 0.902, indicating that the sample was adequate for factor analysis [16]. The Bartlett Test for Sphericity (BTS) was 11267.904 ($p < .001$), indicating that the hypothesis variance and covariance matrix of variables as an identity matrix were rejected; therefore, factor analysis was appropriate. According to principal axis analysis, three factors (dimensions) had an Eigen value equal to or greater than 1.0 [16], explaining a total of 58.06 percent of the variance. The three dimensions were termed, respectively: "Tie Strength and Relationship", "Health Knowledge and Experience", and "Similarity and Preference Awareness". Reliability coefficients of 0.70 or higher are considered adequate [17]. For all 17 items, the alpha value was 0.88. Cronbach's alpha values of each dimension were above 0.70, indicating a satisfactory level of internal consistency among items in each construct (Table 1).

Table 2 features the results of correlation matrix, mean and standard deviation of the three dimensions. According to the results, it can be seen that relationship among three factors are statistically significant ($p < 01$). I can also be seen that the mean for health knowledge and experience (mean: 4.02) was higher than the means of the other factors.

Relationships between WOM dimension and dependent variables

In order to identify the relationships between the three dimensions in factor analysis and independent variables that comprise referring to encouraging going a physician, satisfaction after positive WOM, and discouraging after negative WOM, a multiple regression analysis was utilized. The results of the regression models indicated that the regression models were statistically significant. As shown in Table 3, the results of the regression models indicated that the regression models were statistically significant ($F = 31.93$; $p < 0.01$ and $F = 9.74$; $p < 0.01$), and 5% of the overall encouraging and 1% of the overall discouraging to go a physician were explained by the three dimensions of health based WOM. The regression coefficients indicated that the dimensions of 'similarity and preference Awareness' ($\beta = 0.19$; $p < 0.01$) and tie

Table 1. Factors and items on WOM

Factors and Items	Factor Loadings (β)	Mean	SD ±
Tie Strength and Relationship (Alpha:0.85)			
Referring person is close to me	.58	3.86	1.06
Referring person's level of trustworthiness	.59	3.47	1.17
Referring person is my body	.77	3.52	1.10
I know the referring person	.81	3.57	1.07
I have previous referral experiences with this person	.81	3.30	1.11
I have a social relations with referring person	.78	3.36	1.08
Referring person is in my social network	.63	3.03	1.24
Health Knowledge and Experience (Alpha:0.84)			
Referring person is a reliable source on health	.49	4.19	0.95
Referring person deals with health	.74	3.96	1.05
Referring person is a public official in medical services	.76	3.99	1.14
Referring person's body of knowledge level on health	.85	4.11	0.97
Referring person's health experiences	.72	3.89	1.03
Referring person closely follows developments in health sector	.76	3.96	0.99
Similarity and Preference Awareness (Alpha:0.79)			
Referring person knows well my attention	.81	3.86	1.03
Referring person values my usual health preference	.82	3.80	1.02
Referring person is similar with me	.58	2.99	1.21
Referring person know my health situation	.76	3.84	1.07
Factors' Eigenvalues: 5.99; 2.42; 1.46 % of factors' variance: 35,24; 14.23; 8.59 Cumulative % of variance 58.06			

strength and relationship (β = 0.11; p < 0.01) exerted the strongest influences on the overall encouraging behavior. In terms of the second regression model, the regression coefficients referred that the first dimension, termed tie strength and relationship (β = 0.09; p < 0.01) and the third dimension, termed similarity and preference awareness (β = 0.08; p < 0.01) exerted the strongest influences on the overall discouraging behavior.

Table 2. Correlation matrix and descriptive (mean, std. deviation)

Factors	TSR	HKE	SPA
Tie Strength and Relationship (TSR)	1.00		
Health Knowledge and Experience (HKE)	.35*	1.00	
Similarity and Preference Awareness (SPA)	.45*	.44*	1.00
Mean (SD: ±)	3.44 (0.81)	4.02 (0.76)	3.64 (0.85)
* p < 0.01			

The third regression model considered satisfaction after advice phenomenon as the outcome variable, and the three dimensions of WOM as predictor variables. The regression model was found to be statistically significant (F = 6.90; p < 0.01) with 6% of overall satisfaction after WOM explained by the three dimensions. The results of regression analysis indicated that the dimensions of tie strength and relationship (β = 0.17; p < 0.01), similarity and preference awareness (β = 0.13; p < 0.01), and health knowledge and experience (β = 0.07; p < 0.05) indicated statistically significant relationships with the overall satisfaction as outcome of physician services (Table 4).

Conclusion

This study developed a 17-item survey instrument to evaluate dimension of WOM related to health or physicians' services. The results show that dimension about health based WOM can be conceptualized and measure as a three-dimen-

Table 3. Regression results on encouraging to go a physician and discouraging after negative WOM

Factors	Dependent variables					
	Encouraging to go a physician			Discouraging to go a physician		
	Std. β	t	p	Std. β	t	p
TSR	0.11	4.46	0.00*	0.09	3.56	0.00*
HKE	0.10	3.97	0.00*	0.07	2.61	0.00*
SPA	0.19	7.79	0.00*	0.08	3.15	0.00*
Constant		264.70	0.00*		170.25	0.00*
	R^2=0.059 Adj. R^2=0.057 F= 31.93*			R^2=0.019 Adj. R^2=0.017 F= 9.74*		
* p < 0.01						

Table 4. Regression results on satisfaction after WOM

Factors	Dependent variable		
	Satisfaction after WOM		
	Std. β	t	p
TSR	0.17	7.01	0.00*
HKE	0.07	2.78	0.00*
SPA	0.13	5.14	0.00*
Constant		158.75	0.00*
	R^2=0.071 Adj. R^2=0.061 F= 6.903*		
* p < 0.01			

sional construct comprising 'tie strength and relationship', 'health knowledge and experience', and 'similarity and preference awareness'. These dimensions could be evaluated that advices or experimental recommendations have an important effect on perceived physician services quality. The scale exhibits ideal internal consistency and met rigorous conceptual and empirical criteria for validity. The results reveal that tie strength and relationship is the most important dimension of health related WOM followed by health knowledge and experience, and similarity and preference awareness. In compose of confidence, the level of tie with persons advising a product or services has a significant effect because of the product experiences or involvement.

The results of multiple regression analysis indicates that the aspect of similarity and preference awareness seems to exert the strongest influence on encouraging going a physician in comparison to other dimensions. The results also reveal that tie strength and relationship exert the strongest influence overall discouraging behavior. The third model of multiple regression reveal that all three dimensions related WOM are significantly correlated with overall satisfaction as outcome of service quality.

These results may be considered as a path for marketers of health services. Health services that the experience is real important are figured based on this kind of worm of mouth communication. What is thought for doctors and hospitals could me more important than any other industry. Main reason for this is that perceived risk in health services may result worse and make up for that negative result may be real difficult. So, it is not difficult to say that what people think can be influential on the others. Negative thoughts could increase the tendency for not benefiting related doctor or hospital. For this reason, patients will look some characteristics on the people who recommend a doctor or hospital to them. For example, having close relationships, knowledge level of the person and experience of the person could be important in evaluation of the information gathered by WOM.

Limitations of the study could be considered in two ways: the scope of the study and research sample. First limitation is about general recommendation related to the doctors. WOM may result differently under specialization. For example, perceptions of a pediatrician and a gynecologist can be different. Similarly, perceptions will different according to the importance of the sickness.

Irretrievableness of health services can be thought as a one-time service that patients will demand. Recommendations according to the diseases will be also different. It has been pointed out that sampling is the other limitation. Future research on health related WOM could be extended to include wider demographic base, both geographically and international-wise, to further explore the extent to which the findings are generalizable. The respondents in the study were limited to those who live in a single Turkish city.

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A case of pulmonary epithelioid haemangioendothelioma and short communications

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Introduction

Pulmonary epithelioid haemangioendothelioma (PEH) is a rare vascular tumor of low-grade malignancy. There were only approximately 120 cases reported in the worldwide. There were some commons in patients with PEH based on existing cases, but patients varied greatly in signs and symptoms, radiological findings, histological presentation and prognosis. Here we described a case of PEH in a 31-year-old woman.

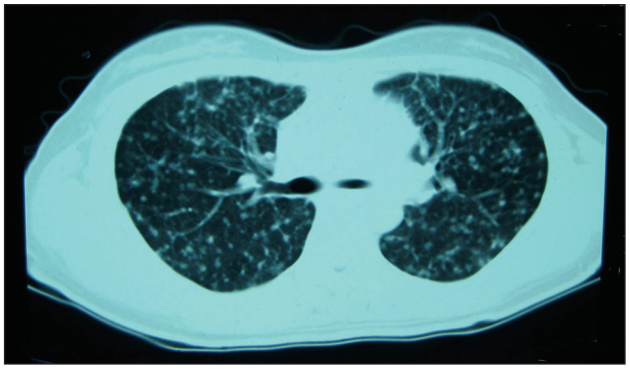
Key words: Chest computed tomography; pulmonary epithelioid haemangioendothelioma; Transbronchial lung biopsy; CD31

Case report

A 31-year-old woman was admitted to our hospital for shortness of breath and dry cough over the last 4 months. She was a housewife, with no smoking, occupational and family history. She had on special illness except infected with zoster virtue one year ago.

There was no fever, night sweat and hemoptysis when she firstly presented with dry cough and shortness of breath 4 months ago. Chest computed tomography (CT) scans showed innumerable small sized nodules with equal density in both lungs. There were no abnormally enlarged lymph nodes (Figure1a). Although both PPD test and sputum Mycobacterium tuberculosis test were negative, she was initially suspected with miliary tuberculosis and underwent normal anti-tuberculosis treatment for 2 months. The cough and shortness worsened over this period.

The breath sounds diminished at both lung bases when she came to our hospital. The other physical examination and laboratory findings were not significant. Chest computed tomography (CT) scans revealed that number and size of nodules in both lungs were increased compared with those in initial CT (Figure1b). Fibreoptic bronchoscopy was performed and did not reveal any airway abnormalities. CT-guided transthoracic needle aspiration biopsy and transbronchial lung biopsy both provide a definitive diagnosis. Pathological examination showed that some epithelium cells with moderately atypical nuclei (Figure2a). Immunochemistry results confirmed the diagnosis of PEH: positive for CD 31, CD 34 and Factor VIII, negative for AE1/AE3 and CK 18 (Figure2b, 2c, 2d, 2e, 2f).



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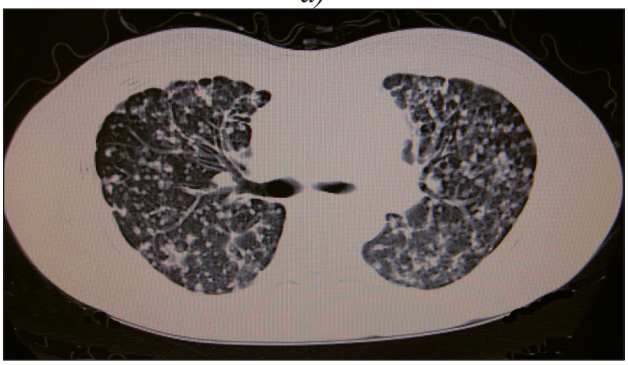

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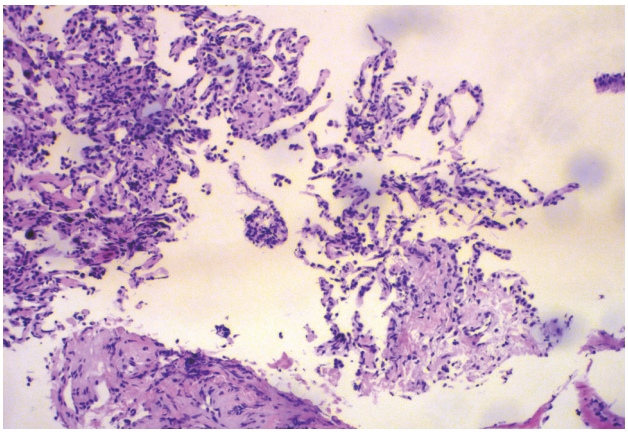
Figure. 1. Chest computed tomography scans: a) initial presentation: multiple bilateral small lung nodules; b) 2 months later presentation: nodules increased in number and size



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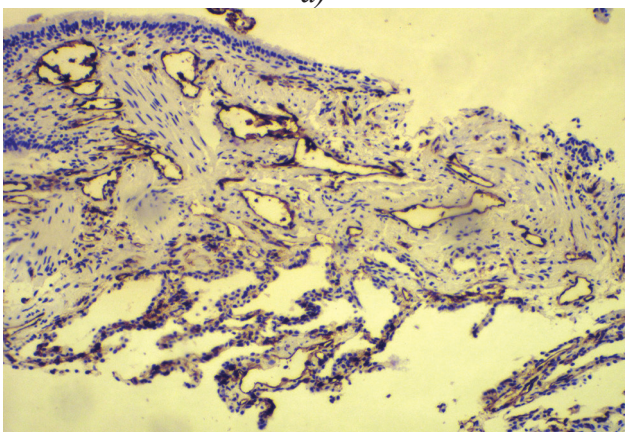

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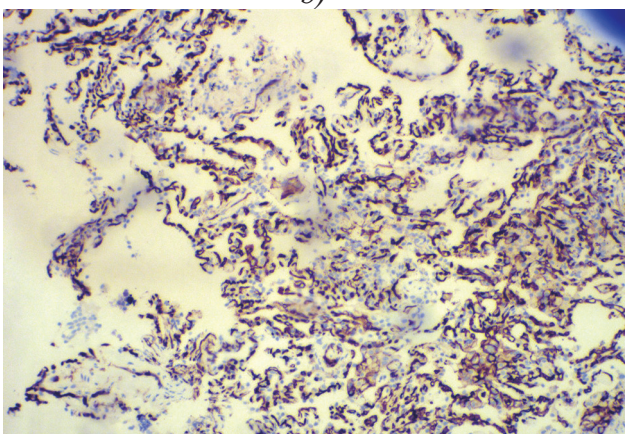

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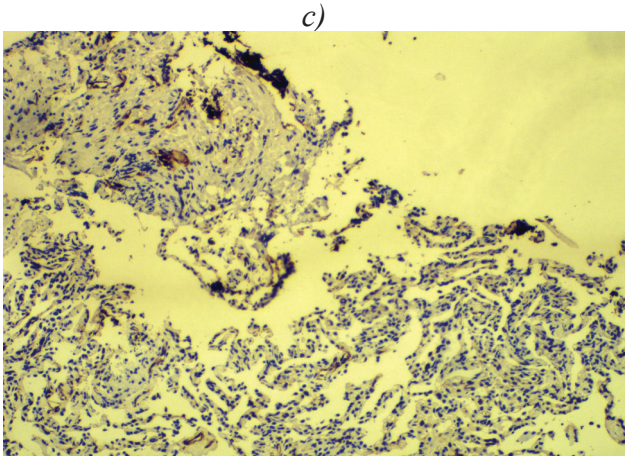

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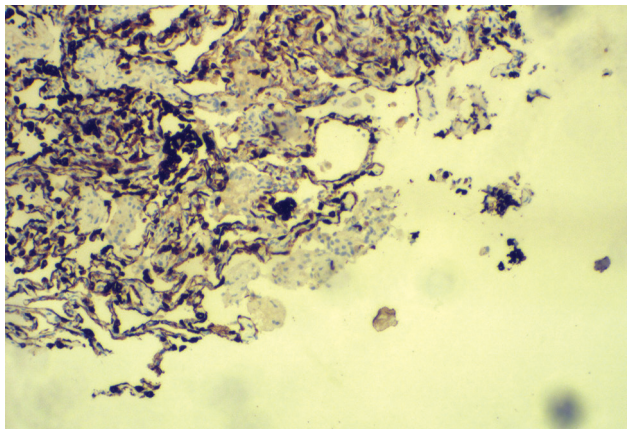

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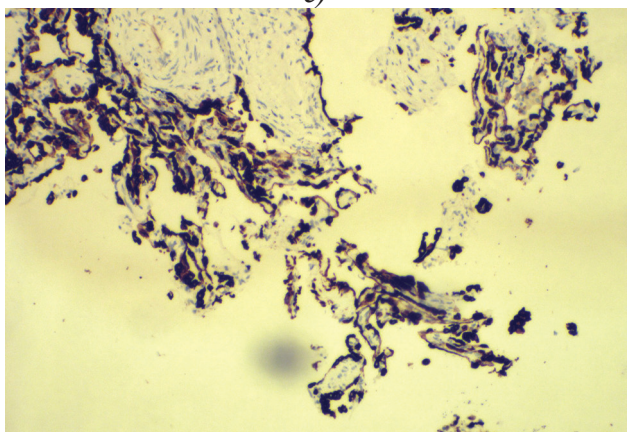

f)

Figure. 2. Histological and immunohistochemical staining of a histologic section. Histological presentations: (a) epithelioid like cells with moderate atypical nuclei; Cytoplasm of tumor cells demonstrating positive for (b) CD31, (c) CD34, and (d) Factor VIII . Tumor cells were negative for (e) cytokeratin AE1/AE3, (f) CK 18.

As this disease can be multifocal or metastasize, Computed tomography section of the liver and Bone scan were performed. There were not multiple nodules in liver, neither metastasis in bone. She refused to open lung biopsy when she learned the diagnosis. She also denied any therapy and discharge by herself.

Discussion

Dail et alfirstly described PEH in 1975, which was named as pulmonary intravascular bronchoalveolar tumor.[1] Electron microscopy and immunochemistry confirmed that tumor cells originated from endothelial cells.[2] It is a rare vascular tumor of low-grade malignancy. PEH is usually disco-

vered incidentally and most patients were asymptomatic. There were approximately 120 cases of PEH in literature currently, most of which were female, especially those in middle age.[3] There were no clinical symptoms and biomarkers specific for PHE. Although chest radiograph or CT could lend much insight into the diagnosis, final interpretation should be based on histological and immunohistochemical findings.

PEH is characteristic of bilateral multiple nodules ranging from 5 mm to 2 cm in diameter on CT, especially in lung bases. Approximately 20% of patients had ≥20 nodules (1). PEH was usually found in relation to small and medium-sized vessels and bronchi.[4] PEH may also present as a solitary lung mass, measuring up to 5 cm. Other atypical CT features have included diffuse glass ground opacity and irregular interstitial thickening.[5] Ross *et al* found that appoximately 9% of PEH patients had hilar adenopathy and 9% had a pleural effusion.[6] PEH presentation is often mistaken for metastatic carcinoma, or other diseases showed multiple pulmonary nodules, such as infection with pathogens, sarcoidosis, amyloid nodules, hamartomas, connective tissue diseases including vasculitides (Wegener's type) and tuberculosis. Histology and immunochemistry findings can make the discrimination.

Histology features of PEH are clusters of spindled epithelioid cells with large, irregular nuclei and nucleoli with a moderate amount of vacuolated cytoplasm. PEH cells are positive cells for CD31, CD34, and factor VIII antigen in immunochemistry, all of which reveal the vascular origin.[7] Boudousquie *et al* also described several clonal abnormalities in a patient with PHE, including a complex unbalanced translocation (7;22) involving multiple breakpoints, a Robertsonian t (14;14) and loss of the Y chromosome.[8] Histology and immunochemistry features are the keystone for the diagnosis of PHE.

To our knowledge, there is no effective treatment for PEH so far. When the number and size of PEH is limited, surgical resection appears to be the optimal option. Spontaneous regression of the tumor has been observed for up to 15 years after initial diagnosis.[9] There was also a case in which lung nodules regressed spontaneously after initial diagnosis, but PEH recurred with mediastinal metastasis 20 years later.[10] There were also reports about chemotherapy for PEH, in which six courses of carboplatin plus etoposide were made for a patient with PEH. It was observed that full remission occurred at 18-month follow-up.[11] There are also several case reports that PEH patients achieving partial or complete remission after treatment with interferon.[12-13] It is difficult to distinguish the spontaneous from chemotherapy-assisted remission based on limited case reports. Male, symptomatic patients, presence of cough, haemoptysis, chest pain, multiple unilateral nodules, pleural effusion, metastases to more than one site and lymph node metastases are poor prognostic factors. Symptomatic patients and presence of pleural effusion are independent predictors of survival in patients with PEH.[14] Much attention should be paid to PEH patients with above prognosis affecting factors.

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Karyometric analysis of goblet cells in patients with bronchial asthma and allergic rhinitis

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Abstract

Background: The most frequent allergic diseases are respiratory allergic diseases, with asthma and allergic rhinitis as the two most important clinical entities. Difficulties in their diagnostic differentiation are due to similarity in their pathophysiology, clinical manifestations, and therapy.

The study objective: The study objective was to quantify and compare nasal epithelium goblet cells nuclei characteristics in patients with bronchial asthma and allergic rhinitis.

Methods: The nasal mucosa cytology specimens were obtained by nasal smear from 20 asthma patients and 14 patients with rhinnitis. All samples were stained by hematoxylin-eosin method and examined using an Olympus BX50 microscope. Visual fields were randomly selected and digitalized. The following parameters were analysed: nuclear area, longest and shortest nuclear axis, ratio of longest axis to shortest axis, nuclear perimeter, nuclear roundness, nuclear density, and area profile on polygonal plane.

Results: The cytology samples showed a large number of goblet cells, neutrophils, a few plasma cells and eosinophils. All examined parameters showed significant difference between analysed groups. Average nuclear area of globet cells, longest and shortest axis lenghts, nuclear perimeter, nuclear density and area-polygon were larger; while longest axis to shortest axis ratio and nuclear roundness were smaller in patients with rhinitis allergica.

Conclusion: Our study showed that goblet cells karyometric parameters differ among patients with asthma and allergic rhinitis, which might be ascribed to the difference in activity of these cells. Karyometric examination of goblet cells could help in cases of diagnostic uncertainty between these diseases.

Key words: karyometry, bronchial asthma, rhinitis, goblet cells, allergy

Introduction

Allergic diseases represent major problem in modern society. Rhinitis, sinusitis, allergic dermatitis, asthma and other, lead to life quality deterioration and play an important role in the overall morbidity and mortality. Respiratory allergic diseases are the most frequent allergic diseases with two most important clinical entities of allergic rhinitis and bronchial asthma. During the last decades the prevalence of allergic diseases increased significantly especially in industrialized countries.[1-3]

Bronchial asthma is a chronic inflammatory disease of airways that involves interaction of many cell types and multiple mediators. This is a complex disorder, characterized by airway hyperresponsiveness, airflow obstruction, bronchial inflammation, recurrent attacks of breathlessness and wheezing, that vary in severity and frequency.[2,4] Factors leading to asthma development are not completely understood. Experts believe it mostly depends on combination of genetic predisposition and exposure to inhaled substances and particles. There are no clear recommendations on how to make an accurate diagnosis of asthma, as there is no gold standard definition.[2,5]

Rhinitis allergica is an inflammatory disease of nasal mucosa, usually classified into allergic and non-allergic rhinitis. Allergic rhinitis is caused by allergens such as pollen, dust, mold, food, medications, etc. It is characterized by shortness of breath,

nasal congestion, rhinorrhea, irritation in the nose, throat, eyes and ears. The symptoms are caused by an IgE-mediated immune response to a specific allergen, release of inflammatory mediators, $CD4^+$T lymphocytes activation, and mucosal infiltration with plasma cells, mast cells, and eosinophils.[6,7] The same inflammatory process can affect the mucosa of the nose, lower respiratory tract, sinuses and eustachian tube, thus causing frequent association with chronic diseases of these organs.[1,3,4]

Asthma and allergic rhinitis are associated with a significant increase in nasal mucus secretion by submucosal glands and goblet cells. Goblet cells are mucus secreting cells with basal nuclei, distributed throughout the surface of the respiratory epithelium.[8, 9] Difficulties in differentiating asthma from other respiratory allergic diseases lay in its not completely understood pathophysiology. Asthma is a syndrome with common symptoms and signs for different diseases, all of which cause reversible airway obstruction. There are differential difficulties especially in the presence of other allergic respiratory diseases, chronic obstructive pulmonary disease in patients with occasional episodes of breathlessness and wheezing. [2-5]

Considering that asthma development may be associated with presence of allergic rhinitis and other allergic diseases, the study objective was to quantify and compare nasal epithelium goblet cells nuclei characteristics in patients with bronchial asthma and allergic rhinitis.

Methods

The study was carried out at the Institute of Pathophysiology and Center for Biomedical Research, Faculty of Medicine University in Nis, and the Clinic for Pulmonary Diseases and Tuberculosis "Knez Selo" in Serbia.

The material consisted of nasal respiratory epithelium cytology specimens obtained by nasal smears from 34 patients, treated at the Clinic for Pulmonary Diseases and Tuberculosis. Twenty patients were diagnosed with bronchial asthma and fourteen with allergic rhinitis. Diagnosis of bronchial asthma was set according to medical history and physical examination. The patients had episodic symptoms of airways obstruction, at least partially reversible (more than one wheeze, breathlessness, cough, etc.). Spirometry is performed in all patients and alternative diagnoses were excluded.[4,5] Sixteen asthma patients had at least one positive skin prick test to an allergen. Diagnosis of allergic rhinitis was set after carefully taken medical history and physical examination (nasal symptoms: congestion, rhinorhea, sneezing, itching, etc.). Also, other potential diseases were excluded. These patients had different allergies, determined with more than one positive skin test to an allergen, or specific immunoglobulin (Ig)E assays.[3,10]

By that time, majority of patients used anti-inflammatory therapy, oral or inhaled corticosteroids, inhalatory β2-adrenergic agonists and theophylline preparations. Exclusion criteria for both groups were inhaled or oral steroid use, or a history of a respiratory tract infection, in the previous 3 weeks, or a reported tobacco use within the past 5 years. Bronchodilators were withheld for 8h before pulmonary function testing and collecting of nasal smears. The study was approved by Institutional Ethic board and all patients signed informed consent.

Three series of cytology specimens were taken from each patient by a nasal smear. Fixation of the samples was done immediately, with equal volumes mixture of 96% ethanol and ether. Fixation process lasted 3-5 minutes. The samples were stored at refrigerator (2-5^{0}C), till the moment of staining. All samples were stained using hematoxylin and eosin method under the same conditions. Thereafter, they were covered by Canada balsam and a cover slip.

The samples were examined using an Olympus BX50 microscope with objective magnifying power of 10x40x2. Microscope images were digitalized by Sony CCD-IRIS/RGB camera, with 2x magnification lens. The digital signal was cached using the Olympus Micro Image 128 Capture Kit v.3.2. We used the Olympus Micro Image optical co. (europe) GmbH software v.4.0 for Windows 95/NT/98, for computer image processing.

Five to ten randomly selected microscopic visual fields in each sample were digitalized and analyzed. The images were assessed for cell composition and morphology. Average values of goblet cells' karyometric parameters were calculated (3 – 5 goblet cells per visual field). Visual separation of the nuclei was performed labeling manually the nuclear membranes on the computer image. In consideration were taken only nuclei that were in focus.

Overlapped, deformed and damaged nuclei were not analyzed.

The following karyometric parameters were assessed:

1. nuclear area (NA, μm^2),
2. longest nuclear axis (LNA, μm),
3. shortest nuclear axis (SNA, μm),
4. ratio of longest axis to shortest axis (ASPEKT),
5. nuclear perimeter (NP, μm),
6. nuclear roundness (NR),
7. nuclear density (ND), as a microphotometric parameter,
8. area profile on polygonal plane (area-polygon) (μm^2).

Values for these parameters were calculated using the above mentioned software according to established mathematical patterns. The parameters were statistically analyzed with descriptive (average, standard deviation) and analytical tests (Student t test, Xi2 test), by SPSS 11.0. program.

Results

The total of 34 patients with bronchial asthma (n=20) and allergic rhinitis (n=14) were examined. The patients were between 18 and 35 years old and their characteristics are given in Table 1. Statistical analysis showed no significant difference in the incidence of diseases by sex.

Microscopic examination of the cytology samples disclosed a large number of goblet cells, neutrophils, a few plasma cells, and very few eosinophils (Figure 1).

Results of karyometric analysis are shown in Table 2. All examined parameters showed significant difference between analyzed groups. Average nuclear area of goblet cells, longest and shortest axis lengths, nuclear perimeter, nuclear density and area-polygon were larger, while ratio of longest axis to shortest axis and nuclear roundness were smaller in patients with allergic rhinitis (Table 2).

There was no significant correlation between the patients' age and analyzed karyometric parameters.

Table 1. Characteristics of examined patients

Characteristic	Asthma bronchiale	Rhinitis allergica
Females (n / %)	9/45	7/50
Males (n / %)	11/55	7/50
Age (year)	*24.8±8.18*	*23.4±4.8*
Disease duration (year)	*6.4±3.1*	*4.2±2.5*
Therapy (n / %)		
oral corticosteroids	4/20	0/0
inhaled corticosteroids	10/50	6/42.8
inhalatory β2-adrenergic agonists	8/40	4/28.6
theophylline preparations	8/40	0/0
without therapy	7/35	6/42.8

Data are presented as n/% or mean±SD, NS for all parameters

Table 2. Goblet cells karyometric parameters

Karyometric parameter	Asthma bronchiale	Rhinitis allergica	p
NA (μm^2)	60.34±10.92	97.27±24.9	0.001
LNA (μm)	92.92±15.18	133.77±15.32	0.001
SNA (μm)	10.12±1.25	12.01±1.64	0.001
ASPECT	1.34±0.23	1.18±0.10	0.001
NP (μm)	28.17±2.58	35.12±4.84	0.001
NR	1.09±0.05	1.05±0.03	0.01
ND	7.61±0.96	10.18±1.42	0.001
Area-polygon (μm^2)	58.24±10.67	94.57±24.61	0.001

Data are presented as mean±SD

NA - nuclear area, LNA - longest nuclear axis, SNA - shortest nuclear axis, ASPEKT -ratio of longest axis to shortest axis, NP - nuclear perimeter, NR - nuclear roundness, ND - nuclear density.

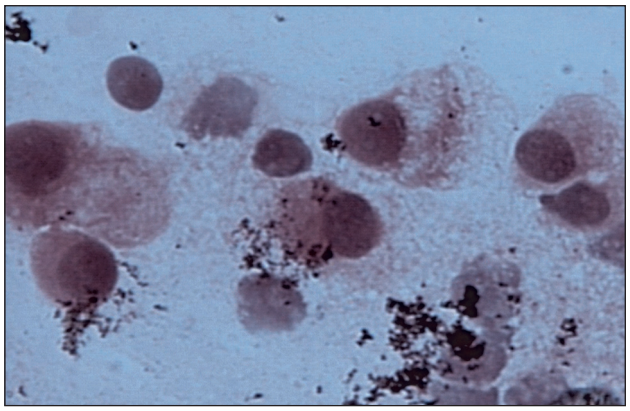

Figure 1. Microscopic view of nasal smear cytology sample. Large number of goblet cells, neutrophils and a few plasma cells. Hematoxylin and eosin staining. Olympus BX 50 microscope, 10x40x2.

Discussion

Characteristics of mucous membranes epithelium in bronchial asthma are its proliferation, goblet cells hyperplasia, submucosal mucus glands hypertrophy, increased smooth muscle mass, increased vascular permeability, and thus wall thickening.[8,11] Airway wall in asthma is infiltrated mostly with $CD4^+$T lymphocytes and eosinophils, while mast cells, macrophages, plasma cells and neutrophils can be variably increased.[8]

Similarly, the pathogenic mechanisms and symptoms of allergic rhinitis result from a complex allergen-driven mucosal inflammation caused by interaction of resident and infiltrating inflammatory cells and a number of vasoactive and proinflammatory mediators. Nasal polyps, plasma leakage and congestion of venous sinusoids are also common findings.[5] Number of goblet cells does not differ in patients with allergic rhinitis and normal subjects, and enhancement in mucus discharge is ascribe to a nonhyperplastic increase of goblet cells functional activity.[9]

According to these facts, we presumed that nasal mucosa smears would reveal increased number of inflammatory and goblet cells, that would be used for karyometric analysis. Microscopic examination of the obtained cytology speciements showed a large number of goblet cells and neutrophils, and a few plasma cells and eosinophils. Eosinophilic airway infiltration is a key characteristic of asthma and has important role in the disease pathogenesis. The reason for this might be the existence of a defect in eosinophilic apoptosis and delayed apoptosis.[8,12] In our cytology samples, rare mainly apoptotic eosinophils were found, with irregular cell and nuclear shape. Since corticosteroid therapy leads to normalization and acceleration of eosinophil apoptosis, these findings indicate an adequate therapeutic application of cortico-preparations in these patients.[4,12,13]

The total size of goblet cells nuclei was significantly higher in patients with allergic rhinitis. This was confirmed by the larger area of the nuclear profiles (sections), and significantly larger longest and shortest nuclear diameters. The logical consequence of these features is significantly larger perimeter of the nuclear sections in patients with allergic rhinitis compared to asthmatics. Possible reason for the larger nuclei size is perhaps hyperactivity of these cells.

Nuclear shape was analyzed by longest and shortest axis relations, as a degree of circularity (a perfectly circular shape has a roundness value of 1, other values indicate irregular shapes). Nuclei of goblet cells in allergic rhinitis showed greater similarities between the values of the largest and smallest diameter, as opposed to nuclei in asthmatics, which indicates more regular circular cross-section of nuclei in allergic rhinitis. Comparing the values of circularity, in accordance with previous, significantly more regular circular shape of nuclei was demonstrated in rhinitis. This might be consistent with the fact that cells with increased synthetic activity show more circular nuclear shape. Also, in several other studies, mitotic cell index was found to correlate with mean nuclear roundness, mean nuclear ellipse or tumors size.[14,15]

The mean value of optical nuclear density represents a measure of their coloration with basic colors. Hematoxylin stains the cell nucleus and other acidic structures blue, as the cell RNA detection correlates with basophilic staining of ribosome. Thus, it can be concluded that goblet cells nuclei in patients with rhinitis had higher amount of nucleic acids in relation to the cell nuclei of asthmatics. This might be another evidence of goblet cells higher metabolic activity in allergic rhinitis.

All measurements of nuclei size and optical density confirm the assumption of significant difference in the activity of goblet cells in allergic

rhinitis and asthma. This might in cases of diagnostic dilemma be a useful indicator.

In airway inflammation a number of goblet cells mostly increase as mucous metaplasia and goblet cell hyperplasia, rather than its hypertrophy. In healthy individuals less than 5% of airway epithelial cells are goblet cells, while in asthma up to 25% of cells may have goblet cells phenotype.[11,16] This metaplasia serves as a host protective function in response to airway damage. During chronic airway diseases the damage persist, promoting mucus metaplasia, mucous gland hypertrophy, and mucus hypersecretion.[10,17,18]

Epidemiological studies show coexistence of asthma and allergic rhinitis in many patients.[19,20] For some researchers there is no question if this is actually a united airway disease, based on interaction and association between upper and lower respiratory tract.[3-5] The same inflammatory cells and mechanisms are involved in pathophysiology of the diseases. Furthermore, allergic rhinitis is considered to be an independent risk factor for asthma development.[5,21,22] It may aggravate asthma, be a comorbid condition, or complicate its diagnosis.[4,5] Both diseases are additionally linked by common therapeutic approaches.[22,23] Presently, there are WHO recommendations that symptoms of rhinitis should be sought in asthmatic patients and vice versa.[10,20]

However, there are noticeable differences between the diseases. Inflammation has a central role in asthma pathophysiology, while rhinitis is usually associated with inflammation, and some of its forms, such as vasomotor or atrophic rhinitis, are not predominantly inflammatory.[3,4] Also, although nasal inflammation resembles bronchial inflammation, specific remodeling features present in asthma are lacking in rhinitis.[20]

A careful medical history, physical examination, pulmonary function and other tests are needed to ensure the correct diagnosis of allergic condition.[4] There are no many studies considering and comparing karyometric parameters of goblet cells in these two diseases. However, our patient study group is relatively small and a larger number of patients should be examined in order to confirm our findings.

Our study showed that goblet cells karyometric parameters differ among patients with bronchial asthma and allergic rhinitis. There was a great difference in size, coloration and shape of goblet cells nuclei, which might be ascribed to the difference in activity of these cells. Cytology examination of nasal mucosa and goblet cells karyometric analysis could help in cases of diagnostic uncertainty between these diseases.

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Determining the knowledge and behavior of the individuals about earthquake preparedness at home in Turkey

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Abstract

Aim: This study was conducted as descriptive for the purpose of determining the knowledge and behaviors of the individuals about earthquake preparedness at home.

Materials and methods: The population of the study was composed of individuals living in the neighborhoods that receive service from a Family Health Center in the city of Erzurum, and the study was conducted between the dates of 17.09.2010 and 04.01.2011. With stratified sampling method, 301 people formed the sample. The data were collected using the questionnaire which was composed of questions about the knowledge and behavior of the individual about earthquake preparedness at home as well as questions about demographic features, and which was developed by the researcher. The data are evaluated using percentage.

Conclusion: it was determined that even though individuals' knowledge level about earthquake preparedness is good, they don't convert this knowledge into behavior and they are not ready for an earthquake.

Key words: Earthquake, knowledge, behavior, preparedness

Introduction

Turkey is located on the Northern Anatolia Fault line, which constantly creates an earthquake threat. According to the experts, Turkey is in the third place in respect of seismic activities. In Turkey, there are in average 10 quakes higher than 2.0 according to Richter scale everyday [1]. These data reveal the importance of being prepared for an earthquake since a major one can happen at any moment in Turkey.

According to the map of Earthquake Zones, 95% of our population is facing the threat of earthquake, since 92% of our country is within the earthquake zones. In average 1,003 of our citizens die because of an earthquake every year and 7,904 buildings collapse [2-4].

When it is considered that earthquakes are natural disasters that can't be prevented, the importance of the precautions and preparations that should be done before the earthquake in order to minimize the loss of life and property is revealed. And this is only possible by all the organizations to do their part in the subject of earthquake preparedness, and the public to have the necessary knowledge about the precautions that should be taken and preparations that should be done and to convert this knowledge into behavior [5-7].

It is necessary to know the earthquake expectation about the region you are living in, to take out an earthquake insurance, to ask for an engineer to check the earthquake resistance of your house, to prepare an emergency situation plan that can be applied in case of an earthquake, to record the important phone numbers that would be beneficial to use in emergency cases after the earthquake, to determine the spaces that can be secure or insecure during the earthquake in all the rooms of your house, to make a family plan to turn off the natural gas, water valve and electric switchgear in order deactivate them during the earthquake, to fix the furniture or heavy items to their places, to determine an alternative outdoor meeting place and communication style for a possible earthquake that can happen when family members are not at home, to perform an earthquake drill as a family, to keep a fire extinguisher at home, to prepare an earthquake bag including light, battery, radio, whistle, water, dry food, required drugs, blanket, money, important documents etc. and to keep this bag in an easily accessible place to ensure that you can take the bag and leave the house quickly dur-

ing an earthquake, to attend to a first aid training course, to prepare a first aid kit and to check the ingredients of the kit periodically in respect of expiration dates and hygiene [5-12].

This study was conducted as descriptive for the purpose of determining the knowledge and behaviors of the individuals about earthquake preparedness at home.

Materials and methods

This study was conducted as a descriptive research. The study was conducted in the neighborhoods of Erzurum that Yenişehir Family Health Center provides service to, between the dates of 17.03.2010 - 04.06.2010.

Population of the study was composed of 16744 houses in 9 neighborhoods. By calculating the study sample from the 16774 houses that compose the population using the statistical formula that is applied when the population number is known, the sample size was calculated as 375.5 houses. The number of houses that should be taken from each neighborhood was determined with stratified sampling method by taking the population density as the basis. From the sample size determined for each neighborhood, the houses that the questionnaire will be applied were determined using random sampling method. After subtracting the questionnaire forms of those who are not willing to participate to the study and those who made marking mistakes, the number of questionnaire forms that were evaluated remained as 301. From each house, two adults over the age of 18 participated to the study. The questionnaire form was applied by the researches during face-to-face interviews.

For the collection of the study data, a questionnaire form, which is composed of 9 questions that determine the individuals' demographic features and 32 questions that determine their knowledge level in respect of earthquake preparedness at home (odd questions) and that determine whether this knowledge is converted into behavior or not (even questions), was used.

The questionnaire form was prepared by the researchers after reviewing the literature about the subject. After making the required corrections based on the results of the pre-application, the questionnaire form took its final form. Before starting the questionnaire application, all the individuals were informed about the purpose and content of the study and their voluntary participation to the study was ensured. The required written permit was taken from the Family Health Center located in the place that the study was conducted. The data obtained from this study was evaluated with percentage.

Results

It is observered that 64.8% of the individuals are female, 52.2% are high school graduates, 27.2% are married, 65.8% are self-employed, 55.1% perceived his/her economical status as an moderate amount, and 61.8% had living in the apatment. The mean age was 25.93 years (Table1).

Table 1. Sociodemographic features of the individuals

Sociodemographic features		n	%
Sex	Male	106	35.2
	Female	195	64.8
Education	Primary School	33	11
	High School	157	52.2
	University	111	36.9
Marital status	Married	82	27.2
	Single	219	72.8
Occupation	Officer	67	22.3
	Worker	11	3.7
	Self-employed	198	65.8
	Housewife	19	6.3
	Retired	6	2
Children status	Have	71	23.6
	None	230	76.4
İncome status	Low income	91	30.2
	Moderate income	166	55.1
	Hihg income	44	14.6
Housing Type	Family house	115	38.2
	Apartment	186	61.8
Ownership status	The host	188	62.5
	Tenant	113	37.5
Age mean	25.93		

Majority of the individuals within the scope of the study know that it is necessary to be aware of the possible earthquake expectation in their region and it was obvious that majority of these individuals are aware. It was determined that even

though individuals know that they should ask for an engineer to check their houses for earthquake resistance and take out an earthquake insurance, majority of these individuals didn't do these. Similarly, even though majority know the necessity of making an emergency situation plan that will be followed in case of an earthquake with the family members and the necessity of recording the important phone numbers that can be beneficial during emergency situations following the earthquake, it was determined that majority of them didn't do these. And it was found that even though the individuals know they should determine the safe/unsafe spaces in each room of the house for use during an earthquake, majority didn't determine these spaces. Similarly, it was seen that even though majority of the individuals know the necessity of making a plan for turning off natural gas, water valve and electric switchgear in order to deactivate them during the earthquake and the necessity of having a fire extinguisher at home, they didn't convert this knowledge into behavior. It was seen that 79.6% of the individuals know the need of determining the objects that can cause serious injuries, intoxication and death when they fall, however 58.5% didn't determine these objects. Again even though the majority of the individuals know that it is necessary to determine an alternative outdoor meeting place and communication style to be used in case of an earthquake, they didn't determine these either. 80.1% of the individuals know that they should perform an earthquake drill as a family; however 86% didn't perform such a drill. It was determined that majority of the individuals know that they should prepare an earthquake bag for earthquake preparedness purposes and that they should keep this bag in an easily accessible place to ensure that they can take the bag and leave the house quickly during an earthquake, however majority of them didn't prepare such a bag. While the percentage of the individuals that know the necessity of attending to a first aid training program is 83.1%, the percentage of those who didn't attend is 83.1%. Again, it was determined that even though majority of the individuals know that they should have a first aid kit and that they should check its contents regularly, they don't have a first aid kit (Table 2).

Discussion

Erzurum face to face with earthquake danger because it was in second degree earthquake zone and the majority of were cut by active faults developed on alluvial fans[13]. In addition, Erzurum has been subject to destructive earthquakes on a large number of due to be installed at the intersection of faults[2,14]. For this reason, information and behavioral conditions of people living in the local earthquake preparedness must be sufficient. However, according to the results of this study, although individuals have enough knowledge about earthquake preparation to protect against earthquake damage was not taking adequate precautions (Table 2). In various conducted studies in Turkey, it was found that public makes preparations like reinforcing their houses and making insurances in rates changing between 2% and 30%[15-17]. In the provinces of eastern anatolian region of Turkey has been observed to be low insurance rates. To be insured against earthquake in Erzurum rates varied between 8% and 12% is observed[18]. Similarly to other studies in Turkey; it was showed that even though education levels and knowledge are positive, some of the earthquake preparedness behaviors such as taking out an earthquake insurance, ensuring that the house is earthquake resistant, reinforcing the house if required, fixing the furniture to their places, an alternative outdoor meeting place and communication style, earthquake/first aid bag, attend a first aid course are not performed[19,20].Dinleyin There are various obstacles against the knowledge to be converted into action. For example, even though an individual wants to take precautions and be prepared for a disaster, the individual may not do that since the economical status doesn't allow that or it is not possible to access precautions. In conversion of attitude to action, the frequency of other risks in the environment and their dimensions are also important. If an individual is everyday under the risk of dying from a traffic accident, a stray bullet, a collapsing building; that individual can underestimate the earthquake risk and the daily concerns can have the priority[21].

In our study, the facts that the earthquake preparedness knowledge level to be high and behavior status to be low show that knowledge cannot be converted into behavior (Table2). And in a study conducted in Istanbul, only 19% of the partici-

Table 2. Knowledge and Behavior Concerning Earthquake Preparedness

Knowledge and Behavior Concerning Earthquake Preparedness	Yes		No	
	n	%	n	%
1. Do you know that it is necessary to be aware of the possible earthquake expectation in their region?	239	79.4	62	20.6
2. Do you have knowledge?	170	56.3	131	43.5
3. Do you now take out an earthquake insurance?	264	87.7	37	12.3
4. Have you undergone?	51	16.9	250	83.1
5. Do you know that they should ask for an engineer to check their houses for earthquake resistance?	253	84.1	48	15.9
6. They get your check?	65	21.6	236	78.4
7. Do you know the necessity of making an emergency situation plan that will be followed in case of an earthquake with the family members?	266	88.4	35	11.6
8. Did you?	76	25.2	225	74.8
9. Do you know the necessity of recording the important phone numbers that can be beneficial during emergency situations following the earthquake?	243	80.7	58	19.3
10. Have you saved?	107	35.5	194	64.5
11. Do you know they should determine the safe/unsafe spaces in each room of the house for use during an earthquake?	244	81.1	57	18.9
12. Have you identified?	94	31.2	207	68.8
13. Do you know the necessity of making a plan for turning off natural gas, water valve and electric switchgear in order to deactivate them during the earthquake and the necessity of having a fire extinguisher at home?	243	80.7	58	19.3
14. Did you?	99	32.9	202	67.1
15. Do you know the need of determining the objects that can cause serious injuries, intoxication and death when they fall?	239	79.4	62	20.6
16. Have you found instead of ??	125	41.5	176	58.5
17. Do you know that it is necessary to determine an alternative outdoor meeting place and communication style to be used in case of an earthquake?	193	64.1	108	35.9
18. Have you identified?	59	19.6	242	80.4
19. Do you know that they should perform an earthquake drill as a family?	241	80.1	60	19.9
20. Did you?	42	14	259	86
21. Do you know that you can keep the home fire extinguisher?	250	83.1	51	16.9
22. Do you contains?	43	14.3	258	85.7
23. Do you know that they should prepare an earthquake bag for earthquake preparedness purposes?	264	87.7	37	12.3
24. Are you prepared?	50	16.6	251	83.4
25. Do you know that they can take the bag and leave the house quickly during an earthquake?	262	87	39	13
26. Do you?	49	16.3	252	83.7
27. Do you know you should attend a first aid course?	250	83.1	51	16.9
28. Have you participated?	66	21.9	235	78.1
29. Do you know that they should have a first aid kit?	279	92.7	22	7.3
30. Do you have your?	108	35.9	193	64.1
31. Do you know that they should check first aid kits contents regularly?	254	84.4	47	15.6
32. Have you checked?	90	29.9	211	70.1

pants stated that they made the necessary preparations[22]. However, knowledge is not enough. Even the fact that Turkey is a country in an earthquake zone facing big and destructive earthquakes is not enough to change the behaviors and the necessary lessons to be taken. In order to minimize the loses and damages that can occur in residential areas during an earthquake, preparation to earthquake disaster and taking/applying measures to minimize the losses are important[23]. Having a family emergency/earthquake plan or being prepared to a possible earthquake as a family is required and essential for survival during such an event and continuing life for a specific period of time after the earthquake. In Europe and America, earthquake preparedness family plans are made for before, during and after earthquake actions, the awareness of the public is raised, and the families are warned about taking the necessary precautions. After earthquakes that cause major life and property losses in the last years, the importance of this subject is emphasized on the basis of government, institutions and organizations and public in Turkey, and the public is started to be warned for preparations that should be done[24]. Earthquake preparedness plan should be memorized with practices that will be performed before an earthquake. And this is only possible with earthquake drills performed as a family. By ensuring that the plan is updated and remembered in this manner, the individuals will have the chance to fully comprehend their roles and duties during a possible earthquake situation and evaluate the conditions, in other words they will be ready. Repeating these drills every year, in fact repeating these two times per year is recommended[25, 26]. To facilitate these drills and to prepare the individuals to real conditions; it would be beneficial to establish cooperation between authorities, media, disciplines and organizations[25, 27].

In conclusion, it was determined that even though individuals' knowledge level about earthquake preparedness is good, they can't convert this knowledge into behavior and they are not ready for an earthquake. The behaviors should be changed with long term training programs. For this purpose, it is required to ensure that public training programs are widespread, long term, and resource and public organizations that will encourage behavior change are formed.

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A case of sarcoidosis associated with lung cancer

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Abstract

A 65-year-old woman presented at the First Affiliated Hospital of Zhejiang University with chest pain and cough. She had been diagnosed with sarcoidosis 4 years ago. Two years after the initial diagnosis and treatment, she presented with multiple facial subcutaneous nodules, which were pathologically diagnosed as sarcoidosis after biopsy at another hospital. The aforementioned symptom recurred on September 22, 2009, and computed tomography of the chest performed at the time revealed lymphadenectasis at both the hila of the lungs and at the mediastinum, in addition to the appearance of nodular lesions at the apex of upper lobe of the left lung, which was indicative of lung cancer. Radical resection of the cancer was performed on October 26, 2009. The results of postoperative pathological examinations showed evidence of posterior segment adenocarcinoma at the apex of the upper lobe of the left lung as well as granulomatous inflammation (on inspection of the lymph nodes), thereby confirming the diagnosis of sarcoidosis. The patient underwent postoperative chemotherapy and has since been maintained in a stable condition.

Key word: sarcoidosis, lung cancer, diagnosis

Introduction

Sarcoidosis is a systemic granulomatous disorder characterized by hilar and mediastinal lymphadenopathy, as well as pulmonary, skin, and eye lesions. Although both sarcoidosis and lung cancer are frequently encountered conditions, their simultaneous occurrence in a patient is rare. We describe a case of lung cancer presenting with sarcoidosis.

Case report

This study was approved by the institutional review board of the First Affiliated Hospital, College Of Medicine, Zhejiang University (Hangzhou, China) and written informed consent was obtained from every participant. The patient, a 65-year-old woman who had been experiencing episodes of cough and chest pain for 4 years, was admitted to the First Affiliated Hospital of Zhejiang University on September 30, 2009, because she had been experiencing these symptoms for 8 days.

Approximately 4 years before the time of presentation, the patient developed cough without any apparent cause; she also experienced left upper chest pain. She did not show fever, chest distress, night sweats, and sputum formation. Computed tomography (CT) of the chest performed at that time showed lymphadenectasis at both the hila of the lungs and at the mediastinum. The patient was diagnosed with sarcoidosis and was treated as an inpatient at the First Affiliated Hospital of Zhejiang University. After treatment with prednisone, the lesions were visibly reduced. However, 2 years later, the symptoms recurred, i.e., multiple facial subcutaneous nodules of varying sizes appeared, and after biopsy of the subcutaneous nodules at a different hospital, the condition was again diagnosed as sarcoidosis. Recently, the aforementioned symptom recurred on September 22, 2009, with once hemoptysis of fresh color yet. CT of the chest performed on September 29, 2009, showed lymphadenectasis at both the hila of the lungs and at the mediastinum (Figure 1) and a nodular lesion at the apex of the upper lobe of the left lung (Figure 2). The patient had no dust exposure or smoking history and had received both a hysterectomy and an appendectomy. Physical examination performed on admission showed the following results: body temperature, 37.2°C; pulse rate, 92 beats per minute; breathing rate, 18 breaths per minute; blood pressure, 129/82 mmHg; multiple visible facial subcutaneous nodules with no festering, irritation, or enlargement in systemic superficial lymph nodes; no lung sounds on chest percussion; slightly heavy breathing on auscultation; and no dry or wet rale. Furthermore, no abnormalities were detected

on cardiac and abdominal examinations. Auxiliary examinations revealed no abnormalities in routine blood, urine, and stool tests; coagulation function test; and 4 preoperative tests, complete biochemical test, tumor marker; tuberculosis antibody, purified protein derivative tests, and tests for the determination of erythrocyte sedimentation rate and C-reactive protein level. In the B-ultrasonic examination, no abnormality was found in the liver, gallbladder, pancreas, spleen, kidney, or adrenal gland. The electrocardiogram was normal, and positron emission tomography (PET)/CT indicated that the small nodule at the upper lobe of the left lung had an increased fluorodeoxyglucose metabolism, which suggested that the lobe might be either lung cancer or sarcoidosis, most likely the former. The likelihood of the nodules being a cancer was high, but no extra-pulmonary metastasis was found. The patient refused to undergo pneumocentesis and fiberoptic bronchoscopic examination and requested surgical treatment; therefore, she was transferred to the department of cerebral surgery for further treatment. Radical lung cancer surgery was carried out on October 26, 2009. Analysis of the intraoperative frozen section suggested adenocarcinoma. Postoperative pathologic results confirmed posterior segment adenocarcinoma at the apex of the upper lobe of the left lung (Figure 3) and granulomatous inflammation (Figure 4), which was detected during inspection of the lymph nodes. Taking the medical history into consideration, we diagnosed the lymphadenopathy as sarcoidosis. The patient received postoperative chemotherapy and has remained in a stable condition since then. I have obtained written consent from the Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University and have obtained written consent from the patient.

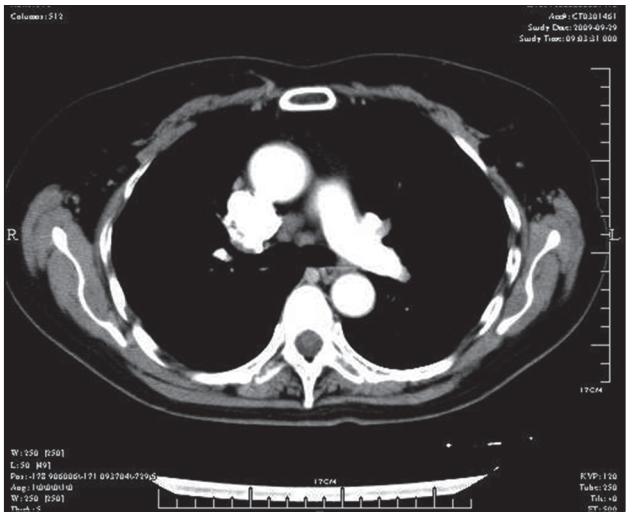

Figure 1. Enlarged mediastinal lymph nodes

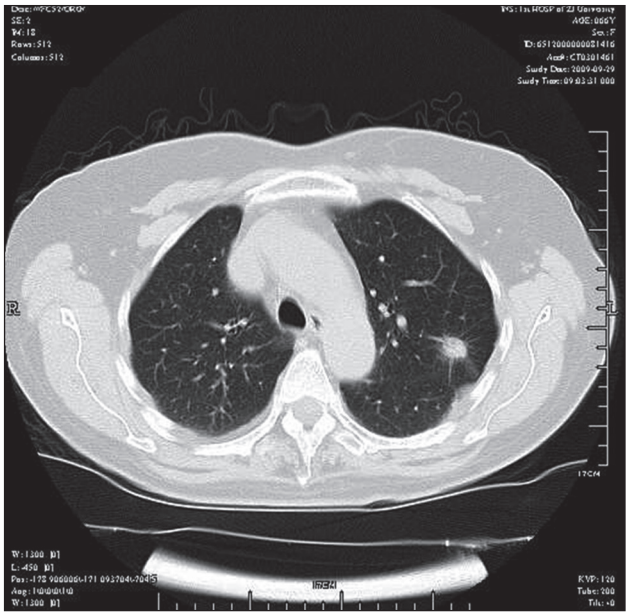

Figure 2. Nodular lesion at the apex of the upper lobe of the left lung

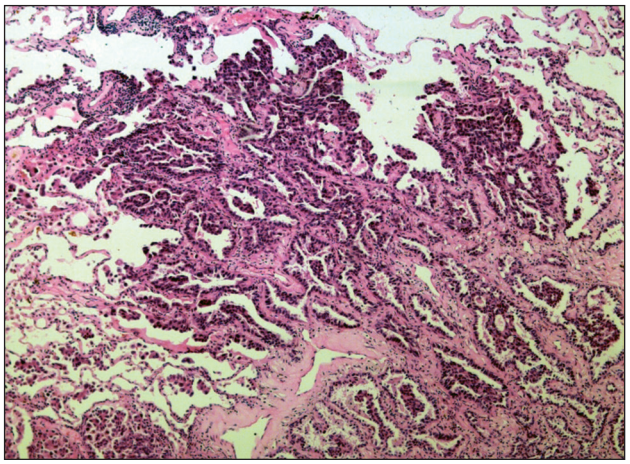

Figure 3. Lung tumor: an adenocarcinoma cell carcinoma was found

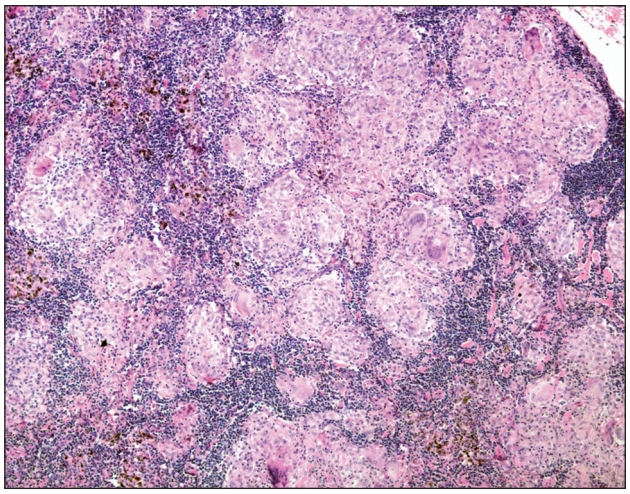

Figure 4. Lymph node: a noncaseating epithelioid cell granuloma with no metastasis was observed. Hematoxylin-eosin staining, original magnification, ×400

Discussion

Sarcoidosis is a multisystemic disorder of unknown cause characterized by the formation of noncaseating epithelioid cell granulomas[1]. Although sarcoidosis can involve any organ, it affects the lungs in 90% of the patients[1]. The typical imaging characteristic is a bilateral symmetrical hilar enlargement. Enlargement of the hilar and mediastinal lymph nodes are the earliest and most common pathological changes, and mainly appear in the right windpipe borderline group and aorta–pulmonary artery group. The progress of sarcoidosis, as diagnosed on the basis of chest radiographs, is divided into 4 stages[2]: stage I, bihilar adenopathy alone; stage II, adenopathy with infiltrates; stage III, infiltrates alone; stage IV, fibrosis. The subtle clinical manifestation of sarcoidosis and the variance in its pathological changes are some other characteristics of this disease. The diagnosis of sarcoidosis still lacks validation by specific and sensitive laboratory testing methods[3], and accurate diagnosis requires lymph node and tissue biopsy. Lung cancer is also a common clinical disease, but lung cancer and sarcoidosis are rarely observed simultaneously in the same patient. According to the literature, patients with sarcoidosis appear to be at an increased risk of cancer, particularly cancers of the lung, stomach, small intestine, and liver, as well as melanoma and nonmelanoma skin cancer, non-Hodgkin's lymphoma, and leukemia[4]. In this case, the patient was diagnosed with sarcoidosis over 4 years prior to the discovery of the cancer, and hormone therapy showed positive effects while controlling the symptoms. Following treatment, the lymph nodes at both the hila of the lungs and the mediastinum showed an obvious reduction in size. However, the illness re-emerged after discontinuation of the hormone treatment. Two years later, the patient displayed extrapulmonary symptoms of sarcoidosis (facial subcutaneous nodules), a diagnosis which was supported by the biopsy. The symptoms recurred 8 days prior to admission. CT re-examination showed new lesions at the posterior segment of the apex of upper lobe of the left lung. From a clinical perspective, the new lesions can be considered as a manifestation of the sarcoidosis infiltrating the lung or as new tumors in the lung. On the basis of the appearance of the new nodules, it can be stated that the edge of the lesion was not smooth with excrescences and that lung cancer was suspected, but these findings cannot be confirmed at this point. However, the results of the PET/CT examination further strengthened the likelihood that the new lesion was a cancer. In this situation, lung puncture and fiberoptic bronchoscopic examination or operation can be used as direct methods to verify the nature of the new lesion. After consideration, the patient refused other relevant invasive operations and requested surgery. The pathology results following the surgery confirmed upper adenocarcinoma at the posterior segment of the apex of the upper lobe of the left lung. The lymph node pathology confirmed the sarcoidosis, which suggested that in this case, the sarcoidosis coexisted with lung cancer, and that the lung cancer had not metastasized to the lymph nodes. At present, the mechanism underlying the coexistence of sarcoidosis and lung cancer is unclear. This may have happened because of the immune response to tumor tissue secretion, which may be spread by the lymphatic system. Patients with asymptomatic sarcoidosis may be more prone to lung cancer as well as to the coexistence of malignant tumors and sarcoidosis. This case suggests that sarcoidosis can co-exist with lung cancer several years after the diagnosis of sarcoidosis, and when a new lesion appears in the lung, the possibility of disease progression, particularly lung cancer, should be taken into consideration. Under

these conditions, PET/CT as a new non-invasive operative inspection method provides us with a powerful tool to make the diagnosis. In addition, this case also suggests that, in clinical evaluations, we need to periodically re-examine patients with sarcoidosis to observe disease progression and identify any complications as soon as possible in order to avoid delayed diagnosis.

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"Subcutaneous tissue of obese children may be too thick for injection solutions to reach intramuscular tissue"

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Abstract

Background: It is very important to measure the subcutaneous tissue thickness of the obese children and choose the appropriate needle length to reach the muscle layer.

Objective: The aim of this study is to measure the subcutaneous tissue thickness of the obese children at the major injection sites (deltoid, vastus lateralis and gluteal area) with ultrasound (US) and to determine the most appropriate needle length for intramuscular injections.

Study Design: A total 74 healthy overweight (n=14) and obese children (n=60) from Gulhane Military Medical Academy participated in this study between April to November 2009. Thickness of subcutaneous tissue was measured by radiologist with ultrasound probe on major injection sites for children.

Results: A statistically significant positive correlation was found between weight groups and subcutaneous tissue thicknesses in the all injection sites; the higher the weight group (BMI ≥95), the thicker the subcutaneous tissue. Although a statistically significant positive correlation was found between age groups and subcutaneous tissue thicknesses, there was no correlation between sex and subcutaneous tissue thickness.

Conclusion: To reach the muscle (perpendicular) a nurse should asses both the age and injection site together while choosing the appropriate needle length in overweight and obese children.

Key words: child nursing, intramuscular injection, needle length, obese children, subcutaneous tissue

Introduction

For most childhood vaccines, intramuscular injections are recommended. If the medications or vaccines are designed to be absorbed from muscle but injected to subcutaneous layer they will be ineffective [1] . Because poor vascularity may result in slow mobilization and processing of antigens, injecting a vaccine into the layer of subcutaneous fat is a cause of vaccine failure. In addition, superficial administration leads to an increased incidence of local reactions such as irritation, inflammation, granuloma formation, and necrosis[2,3] .

Depending on the injection site, differences in peak plasma concentrations can occur[4]. There is no universal agreement regarding the best intramuscular (IM) injection site for children. The preferred site for infants up to 12 to 18 months is the vastus lateralis. After this ages deltoid muscle is used for IM injections because it is associated with less pain and fewer and milder adverse reactions. Deltoid muscle can be used for small volumes of fluid in children as young as 18 months of age. It is generally recommended to use the gluteal muscles as an injection site only after a toddler has been walking for about 1 year. In older children dorsogluteal muscle with large muscle mass can

tolerate greater volume of fluid. Gluteal muscles have been used for intramuscular injections in childhood [1,5,6].

Besides injection sites, injection technique and needle length are also crucial for ensuring proper delivery. Tubiana-Rufi et al.[7] found that frequency of intramuscular injections with skinfolding was 86% with the 12.7-mm needles (88% in the arm region and 84% in the thigh region) and 38% with the 8-mm needles (48% in the arm region and 28% in the thigh region). For all intramuscular injections, the needle should be long enough to reach the muscle and prevent vaccine or medication from seeping into subcutaneous tissue. Wong et al[1], recommends ½ (12.7 mm) to 1 ½ inches (38.1mm) needle length for dorsogluteal site. Recommendations from the United States Centers for Disease Control and Prevention (CDC) [8] for other sites are outlined in Table 1.

Injection technique necessitates choosing the appropriate needle size and appropriate site of injection for each person on the basis of the size of the muscle [2,9]. Appropriate needle length depends on age and body mass. Accidental subcutaneous injections are not uncommon in obese population [2]. Zaybak et al. [2], found that intramuscular injections administered at the dorsogluteal site in 98 % of women and 37 % of men, and at the ventrogluteal site in 97 % of women and 57 % of men, would not reach the muscles of obese adults. Since the prevalance of childhood obesity has been increasing in developing countries as well as developed countries [10,11], it is still a major concern of uncertainty whether recommended standard needle length is able to achieve drug delivery into muscle in obese children. Obesity along with the too short needle length increases the incidence of local reactions. If the depth of fat is so great that the needle cannot reach the muscular layer, the average absorption of the drug in the population will be lower and the patient may not develop an adequate therapeutic response[2,3]. Although there are some studies about needle length for intra muscular injections in obese adults there is a little information about obese children in the literature. Hence, information about subcutaneous tissue thickness and determining the optimal needle length is essential for effective intramuscular injection in obese children.

Methodology

Objective

The aims of the study were to describe the subcutaneous tissue thickness of the obese children at the major injection sites (deltoid, vastus lateralis and gluteal area) with ultrasound (US) and to determine the most appropriate needle length for intramuscular injections according to sex and body mass index (BMI).

Design

Descriptive study design was used and the study carried out between April and November 2009.

Participants

A total 74 healthy children (35 boys and 39 girls) from a pediatric endocrinology outpatient clinic of a university hospital participated in this study. Juvenile obesity is defined as a BMI > 95th percentile. The participants were classified by percentiles into two groups: Overweight (85 – 95 percentiles) =14 children (18.90 %) and Obese (95 + percentiles) = 60 children (81.10 %).

Measurements

Weight and height measurements were performed by one pediatric endocrinologist in the pediatric endocrinology outpatient clinic using the same scales. 7.5 mHz linear-array transducer (Sonoline Elegra System™, Erlangen Germany) was used by two experienced radiologist to measure

Table 1. Intramuscular Vaccination-Delivery Recommendations From the CDC Pink Book (CDC 2009[8]

Age Group	Injection Site	Needle Length, in (mm)	Injection Technique
Newborn (first 28 d)	Anterolateral thigh muscle	5⁄8 (15.90)	90° to skin and spread skin if necessary
Infant (1–12 mo)	Anterolateral thigh muscle	1 (25.40)	
Toddler (1–2 y)	Anterolateral thigh muscle	1–11⁄4 (25.40–31.75)	
	Deltoid muscle of the arm	5⁄8–1 (15.90–25.40)	
Children (3–18 y)	Deltoid muscle of the arm	5⁄8–1 (15.90–25.40)	
	Anterolateral thigh muscle	1–11⁄4 (25.40–31.75)	

the thickness of subcutaneous tissue. Distance from skin surface to the muscular fascia accepted as subcutaneous (SCT) thickness. Unpressured measurements of deltoid, vastus lateralis and gluteal site were performed. Applying the gel to skin surface to increase the contact surface and to transmit the sound wave, an US probe has been touched to skin for unpressured measurements.

Data were collected in Gulhane Military Medical Academy Pediatric Endocrinology Outpatient Clinic. Children who have any illness affecting the tissue thickness except obesity were excluded. Demographics and weight and height measurements of the participants were obtained by researcher and the thickness of subcutaneous tissue was measured by an experienced radiologist. The thickness of subcutaneous tissue was measured at the following three sites in each child:

(1) Deltoid muscle (located acromion process; upper third of muscle that begins about two fingerbreaths below acromion but is above axilla);
(2) Antero-lateral thigh-vastus lateralis (located in the middle one third of dividing vertical distance between greater trochanter and knee joints into thirds);
(3) Dorsogluteal site (located lateral in the superior of imaginary line between greater trochanter and posterior superior iliac spine).

Body mass index was calculated as individual's body weight divided by the square of his height and grouped into two groups classified as overweight representing 85 – 95 percentiles and obese representing ≥95 percentiles.

Ethical Consideration

Institutional Review Board Approval and written informed consent of obese children and their families were obtained.

Data Analysis

Appropriate sample size was calculated with G* Power Ver. 3.0.10 (Franza Faul, Universität Kiel, Germany) and for the 90 % power, it was determined that 80 children should be involved in the study. But two children who have problem affecting tissue thickness without obesity and four children under the 85th percentiles were excluded. The *Shapiro-Wilk* test for appropriateness to normal distribution for measurement values was applied. Descriptive statistics for qualitative variables has been shown as number and percentages and for quantitative variables has been shown as mean±standart deviation and median. Comparison between two groups (e.g. gender), were analyzed using student's t test, and for nonparametric data by Mann-Whitney U test. Comparisons among multiple groups (e.g. age groups, classification of obesity) were analyzed using one-way ANOVA and Bonferroni post-hoc test, in values which are not to fit the normal distribution Kruskal-Wallis variance analysis and as a post-hoc test, Bonferroni correction Mann-Whitney U test were used. For the purpose of examining the relationship between participants' characteristics and the subcutaneous tissue thickness of all injection sites, Spearman Rank Correlation Test was used. P-values of ≤ 0.05 were considered statistically significant.

Results

Seventy-four participants (35 boys, 39 girls) whose BMI was more than 17.30 kg/m^2 (range17.30 – 37.19) were recruited for study. The demographics of the participants are summarized in Table 2. Their mean weight was 62.04 kg (range 32 – 105) and their mean age was 11.07 (range 5 – 18). The number under the 9 years old was 24, between10–12 years old 27 and over the 13 years old 23. Sixty children (81.10 %) were obese and fourteen children (18.90 %) were overweight.

Median values of subcutaneous tissue thicknesses at the deltoid, vastus lateralis and dorsogluteal sites were 11.00, 20.00 and 41.80 mm for girls and 11.00, 23.00 and 44.60 mm for boys respectively. There was no statistically significant difference among measuring sites by sex (Table 3).

There was no statistically significant difference among measuring sites by age except in dorsogluteal site. The subcutaneous tissue thickness in children over the 13 years old was statistically significantly higher than that of children under 13 years old at dorsogluteal site (p= 0.007) (Table 3).

Median values of subcutaneous tissue thicknesses at the deltoid, vastus lateralis and dorsogluteal muscle were 9.10, 15.95 and 35.30 mm for overweights and 11.60, 21.60 and 44.50 mm obe-

Table 2. Participant demographics (n=74)

Variables	Mean (SD)	Min – Max
Age (year)	11.07 ± 2.77	5.00 – 18.00
Height (cm)	152.00 ± 14.00	110.00 –177.00
Weight (kg)	62.04 ± 16.45	32.00 –105.00
BMI	26.47 ± 3.68	17.30 – 37.19
Sex	**n**	**%**
Male	35	47.30
Female	39	52.70
Age Groups		
≤ 9	24	32.40
10 –12	27	36.50
≥13	23	31.10
Weight groups (by percentiles)		
Overweight (85 – 95)	14	18.90
Obese (≥95)	60	81.10

Table 3. Mean and median subcutaneous tissue thickness by sex, age and weight groups

Parameter	Measuring sites					
	Deltoid		Vastus Lateralis		Dorsogluteal	
	$\bar{x}$ ±SD	Median	$\bar{x}$ ±SD	Median	$\bar{x}$ ±SD	Median
Sex						
Female(n=39)	11.20 ± 2.30	11.00	21.36 ± 6.93	20.00	42.08 ± 10.69	41.80
Male (n=35)	11.88 ± 3.23	11.00	21.66 ± 6.71	23.00	43.36 ± 11.13	44.60
Statistics	Z=0.688		Z=0.319		t=0.505	
p	0.491		0.749		0.615	
Age Groups						
≤ 9 y (n=24)	11.43±2.83	10.65	19.39±5.73	17.75	39.03±7.50	38.80
10 – 12 y (n=27)	11.37±2.21	11.30	21.16±5.56	20.60	41.09±9.80	41.80
13 + y (n=23)	11.80±3.37	11.00	24.12±8.34	27.00	48.36±12.90	49.00
Statistics	X^2=0.202		X^2=4.690		F=5.384	
p	0.904		0.096		0.007	
Weight Groups						
Overweight(n=14)	9.65±2.36	9.10	16.10±4.69	15.95	36.64±7.52	35.30
Obese (n=60)	11.96±2.70	11.60	22.76±6.60	21.60	44.09±11.06	44.50
Statistics	Z =2.895		Z =3.776		Z =2.685	
p	0.004		<0.001		0.007	

Table 3a. Dorsogluteal pairwise comparisons with Bonferroni corrections by age groups

Injection Sites	Age Groups		Mean Difference (I-J)	p
	(I)	(J)		
Dorsogluteal Site	≤ 9	10 – 12	-2.06	1.000
		13 +	-9.33	**0.008**
	10 – 12	13 +	-7.26	**0.044**

Table 3b. Deltoid, vastus lateralis and dorsogluteal pairwise comparisons with Bonferroni corrections by weight groups

Injection Sites	Weight Groups		Mean Difference (I-J)	Z	p
	(I)	(J)			
Deltoid	Overweight	Obese	-18.45	-2.895	**0.004**
Vastus Lateralis	Overweight	Obese	-24.10	-3.776	**<0.001**
Dorsogluteal	Overweight	Obese	-17.13	-2.685	**0.007**

ses respectively. There was statistically significant difference among measuring sites by weight groups. It is presented in table 3a and 3b which age group and weight group was different.

According to weight groups, subcutaneous tissue thickness of obese and overweight's was statistically significantly different in entire measuring sites (Z=-2.895; p=0.004 for deltoid. Z=-3.776; p<0.001 for vastus lateralis and Z=-2.685; p=0.007 for dorsogluteal site).

The subcutaneous tissue thicknesses in boys were statistically significantly higher than that of girls at deltoid and dorsogluteal sites in ≤ 9 years old group (p= 0.030 for deltoid, p=0.043 for dorsogluteal).

There was no statistically significant difference between boys and girls at all sites in 10–12 years old group, notwithstanding subcutaneous tissue thickness in boys higher than that of girls in the same age group.

The subcutaneous tissue thickness in girls higher than that of boys at all sites in 13+ years old group, but only the differences between two sexes in this age group in deltoid and vastus lateralis were statistically significantly important (Table 4).

A statistically significant positive correlation was found between weight groups and subcutaneous tissue thickness in the all injection sites; the higher the weight group (BMI; ≥95), the thicker the subcutaneous tissue (p=0.004 for Deltoid, p<0.001 for Vastus Lateralis, p=0.007 for Dorsogluteal).

A statistically significant positive correlation was found between age groups and subcutaneous tissue thickness in the all injection sites except deltoid; the higher the age, the thicker the subcutaneous tissue (p =0.007). But there was no statistically significant correlation between sex and subcutaneous tissue thickness in the all injection sites.

Discussion

The present study showed that obese children in both gender (over 95th percentiles) had thicker subcutaneous tissue than overweight children (between 85 th.-95th percentiles).

According to gender differences only, subcutaneous tissue thickness was similar at all injection sites. Without gender differences, 13+ years old group showed statistically significant thicker dorsogluteal subcutaneous tissue thickness. Subcutaneous tissue of deltoid and dorsogluteal sites in boys at ≤ 9 years old tend to be thicker than those age-matched girls. Results of Hoffman et al. [12] who found prepubertal girls had greater buttock subcutaneous fat thickness than prepubertal boys were inconsistent with our results. Subcutaneous tissue thicknesses of both genders in 10-12 year olds were similar at all injection sites. Hoffman et al. also found no difference in thigh subcutaneous fat thickness between prepubertal girls and boys but pubertal girls had greater thigh subcutaneous fat thickness than pubertal boys. Shin and Kim[6] associated this result with testosterone level of males. Males and females have similar amounts of testosterone until puberty, and then testosterone levels increase much more dramatically in males, as does muscle mass. While testosterone increases muscle mass, it doesn't affect the subcutenous tissue thickness[6,13] . In the present study, girls in 13+ years old had thicker subcutaneous tissue than

Table 4. Differences between subcutaneous tissue thickness by sex and age groups

Measuring Site	Age (years)	Girls n=39		Boys n=35		Z/t	p
		$\bar{x}$ ±SD	Median (mm)	$\bar{x}$ ±SD	Median (mm)		
Deltoid	≤ 9	10.29±2.15	10.00	13.14±3.05	13.00	-2.182	**0.030**
	10 – 12	10.74±1.91	10.40	11.83±2.55	11.30	-1.441	0.152
	13 +	13.31±1.93	14.00	10.40±3.70	10.00	-2.429	**0.013**
Vastus Lateralis	≤ 9	17.92±3.86	17.40	21.24±7.99	17.50	-0.269	0.815
	10 – 12	19.89±4.92	18.00	22.88±5.88	24.60	-1.466	0.152
	13 +	28.96±8.60	29.80	21.63±6.49	23.45	-2.271	**0.023**
Dorsogluteal*	≤ 9	36.46±6.64	36.50	42.96±7.22	44.50	2.142*	**0.043**
	10 – 12	40.36±9.87	40.60	42.02±9.62	44.40	0.428*	0.673
	13 +	53.95±8.46	55.10	44.34±13.52	48.50	-1.743*	0.096

**t test was performed*

those age-matched boys but this was statistically significant only at the deltoid and vastus lateralis sites. These results were consistent of those of Shin and Kim [6] who found that boys over 14 years old had statistically significantly thinner subcutaneous tissue at all sites compared with girls.

Asayamal et al. [14] evaluated Waist-Hip circumferences Ratio (WHR) of obese and nonobese Japanese children ages ranging from 6-15 y in both boys and girls and found that WHR was higher in boys than in girls throughout pediatric ages, and decreased gradually in boys with age, while there were two sharp reductions at ages 10-13 y and 13-16 y in girls because of the marked increase in hip circumference at 13 y but a decrease in waist circumference from 13-17 y.

Moeller et al. [11] found that normal weight girls developed a gynoid body fat distribution with thicker fat layers on the legs whereas normal weight boys lose fat on their legs during puberty. But the obese juveniles of all age groups do not show the typical pubertal change in subcutaneous adipose tissue distribution. According to Moeller et al. [11] obese juveniles keep thick fat layers on their trunks, independently of age and/or pubertal stage. These results are inconsistent with our study.

It was evaluated that 5/8 inch (15.90mm) needle length recommended by CDC is appropriate for injections to deltoid muscle of all children over 85th percentile, in both gender and between the ages of 5-18 years. Sullivan[15] found that up to 61% of children getting intramuscular injections in the shoulder are probably receiving overpenetration injuries, because the recommended needles are longer than the average fat and muscle layer of the deltoid. In the present study, since only the subcutaneous tissue thickness was measured it wasn't evaluated whether overpenetration has occurred or not. But 1 inch (25.40 mm) needle length recommended by CDC should have been evaluated for the risk of over-penetration [utmost subcutaneous tissue thickness was 11.60 mm (min: 9.10 - max: 11.60)].

It was evaluated that 1 inch (25.40 mm) needle length recommended by CDC is appropriate for injections to vastus lateralis muscle of all children over 85th percentile, in both gender. But the subcutaneous tissue thickness of the vastus lateralis (27.00 mm) was more than the length of the needle; 1 inch (25.40 mm) in girls over the 13 years old and over the 85th percentile. It can be recommended that the needle length should be at least 1 ¼ inch (31.75 mm) to reach muscle layer.

Wong[1] recommended ½ (12.7 mm)-1 ½ inches (38.1mm) needle length for dorsogluteal injection sites. It was found in this study that dorsogluteal subcutaneous tissue thicknesses in overweights were 35.30 mm and in ≤ 9 years old girls was 36.50 mm. Except those groups the subcutaneous tissue thicknesses in other groups were over the recommended needle length. When the factors such as age and gender have been considered, it is evaluated that the recommended 1 ½ inches (38.1mm) needle length wasn't appropriate for all children over the 95th percentile and will not reach the muscle layer. Recommended needle length for obese children should be a minimum of 45 mm.

Conclusion

To reach the muscle (perpendicular) a nurse should asses the age, gender and injection site together while choosing the appropriate needle length in overweight and obese children. If there is no appropriate needle, alternative injection sites may be choosen. If alternative sites are not possible, the longer needles are needed and special needles should be produced by manufacturers for obese children.

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Correlation of p53 expression levels with the degree of histological differentiation histological stages of colorectal carcinomas

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Abstract

According to epidemiological data, colorectal cancer is the most common malignant tumor of the gastrointestinal tract and the second most common cause of death of patients with malignant diseases. The processes of division, differentiation and death of cells are strictly controlled and the disturbance in the regulation of any of them causes the creation of clone cell that independently, purposelessly multiplies and produce a tumor mass. The emergence of tumours is a complex process involving many genetic and molecular mechanisms. Cancerogenesis is the result of accumulation of disorder in materials and functions of genes that regulate the mechanisms of cell proliferation, DNA repair or programmed cell death. These genes are: oncogenes, tumor suppressor genes, genes that are the matrix for the synthesis of enzymes of reparatory system, as well as genes that control apoptosis.

Objective: The subject of research in this study was to determine the significance of correlation of clinical - morphological parameters and the level of expression of p53 in colorectal carcinomas. The hypothesis of the study is that there is a connection between the level of expression of proto-oncogenes with pathological stage and degree of histological differentiation of colon tumours.

Methodology: The research was done as a prospective, clinical - experimental study. Postoperative material obtained by resection of colorectal tumours from 63 patients of both sexes was used, from the Surgical Clinic of the Faculty of Medicine in Kragujevac. Immunohistochemical investigations were carried out in the department of pathology and forensics of CC "Kragujevac" in Kragujevac. In order to get relevant pathohistological data, routine hematoxylin - eosin (HE) method and immunohistochemical methods DAKO LSAB / HRP were used. Routine HE method was applied for pathohistological verification and analysis that included tumor prognostic and predictive parameters. Immunohistochemical highly sensitive and specific technique DAKO LSAB / HRP was applied to identify the expression of p53 in resected colorectal cancer samples. The statistical analysis applied to descriptive statistics, HI - square and Fisher's test, Mann-Whitney test, Kruskal - Wallis's test and binary logistic regression.

Results: The majority of tumours studied belonged to the well-differentiated tumours, glandular differentiation in the T3 stage. Nuclear expression of p53 was present in more than half of the tumours. Nuclear expression of p53 has not correlated with the degree of histological differentiation and pathological stage of tumor.

Discussion: of the obtained results was based on their comparison with existing literature data in this field. According to data mentioned in discussion chapter, contemporary literature still has conflicting data on the expression of p53 in the function of prognostic parameters in colorectal carcinoma, which is conditioned by the number of patients studied, selection and processing of samples, selection of immunohistochemical technique, usage of antibodies of different specificities, statistical analysis and interpretation of data.

Conclusion: derived from this study's results suggests that molecular markers that complete the clinical - pathological parameters are not so represented in colorectal carcinomas due to a lack of

quality prospective studies, undefined scoring system, the dose of subjectivity in the interpretation, which is reflected in practical - diagnostic use, and opens issues for further research.

Key words: colon, cancer, p53, immunohistochemistry.

Introduction

Colorectal carcinoma (CRC) is one of the most common causes of morbidity and mortality both in the western world and in our region. Classification and established prognostic parameters that are now used in the treatment of CRC still only provide partial information about the course and outcome of this disease, so there is a constant need for improving existing and identifying new diagnostic and prognostic markers. In this regard, it is particularly important to identify molecular markers that could provide insight into the potential behaviour or aggressiveness of tumours.[1,2,3] As existing clinical morphologic parameters (histological type of tumor, degree of differentiation, tumor stage, nodal status, invasion of vascular structures and surgical margins) still retain its dominant importance in the diagnostic procedures, molecular profiling would contribute to their completion, usually in terms of recognition of response to applied therapy (genetic change), or in terms of application in improving the screening programs of high-risk categories that would enable the timely and successful treatment.[4]

Gene p53 is the most frequent mutated gene found in tumours. It is localised in 17th chromosome and it codes p53 transcriptive factor which regulates cell cycle through activation of gene transcription, which stop it in the G1 phase and it also activates the self-destruction of cell – apoptosis, when necessary; it belongs to the group of tumour-suppressing genes.[5] Basic role of tumour suppressing gene is to stop the cell cycle with the objective of repairing the errors in the structure of DNA molecule.[6] Mutation and inactivation of tumour suppressing gene result in uncontrollable cell division and blockage of cell's self-destructing – apoptosis. They belong to a group of recessive oncogenes because their expressing starts after both alleles are deactivated.

The normal form, *wild* – type takes part in DNA molecule repair, controls the cell cycle, proliferation and differentiation and, under certain condition, triggers the apoptosis through inducement of expression of bcl – 2 gene family which involves antiapoptotic (bcl – 2, bcl – XL) and proapoptotic (Bad, bcl – 2 associated protein, x – Vax) proteins. Mutated p53 type looses the tumour suppressing ability or this ability is inactivated through interaction of p53 with other cellular proteins or viral oncoproteins (DNA – HPV viruses).[7]

Wild p53 is, in normal tissues, is expressed at a undetectable level, while the mutated form is expressed in over 50% of all tumours. The method and level of p53 expression are significant for monitoring of development and prognosis only if it is co-expressed with other tumour markers, except in terminal phases of illness when the success rate of any therapy, as well as the outcome, is almost completely known. Numerous studies lead to conclusion that it is not enough to monitor the expression of only p53, but also other tumour markers whose behaviour may point to better therapies when it comes to malignant diseases.[8]

Objective of work

The objective of this study was to detect and identify the level of expression of p53 in the tumor at the operational material – resected segments of patients with colorectal carcinoma, obtained at different colon localizations. Comparison of proto-oncogenes' expression levels with pathological tumor stage (pTNM) determined by macroscopic and microscopic examination of resected samples, regional lymph nodes and distant metastasis. Correlation of expression of proto-oncogenes and pathological stage as an important prognostic factor in the further course and outcome of disease.

Correlation of proto-oncogenes' expression levels with the degree of histological differentiation and histological grade of tumor. In broad terms, the aim of this study was to determine the possible correlation of clinical and morphologic parameters and expression levels of this tumor marker and identification of possible prognostic significance of that correlation.

Materials and method

The research has been done as a prospective, clinical – experimental study. Postoperative mate-

rial used is obtained from the resection of colorectal tumour from 63 patients of both sexes, from the Surgical Clinic of Medical Faculty in Kragujevac. Immunohistochemical analyses have been made at the Department of pathology and forensic medicine of KC 'Kragujevac' in Kragujevac.

The procedure of immunohistochemical staining has included the processes of de-masking the antigen, blocking the endogenic peroxidase, incubation of preparations with primary anti-serum and the implementation of immunohistochemical method – LSAB +- HRP, according to the standard protocol.[9] Monoclonal mouse's antibody (p53 DAKO DO-7 monoclonal mouse clone) diluted 1:200 was used for p53 detection. Cut off – selected value of the threshold for determining positive and negative expression of p53 was > then 30% (positive expression of more than 30% tumour cells show immunoreactivity on p53). Using the scoring system is based on determining the percentage of immunoreactive nucleuses of tumour cells as well as on determining the intensity of immunoreactive staining. Adding the points for the percentage of immunoreactivity and for the intensity gives the complete possible maximal score for the expression evaluation (Table 1).

Table 1. Total possible maximum score for the assessment of expression

% of immunoreactive nucleuses	The intensity of immunoreactive staining
0=< 5% of nucleic staining	0 = no staining of nucleus
1= 5 to 30% of stained nucleuses	1 = weak intensity of nucleus's staining
2= 30 to 50% of stained nucleuses	2 = mild intensity of nucleus's staining
3= 50 to 70% of stained nucleuses	3 = very intensive staining
4= 70 to 90% of stained nucleuses	
5> 90% of stained nucleuses	

Statistical methods

Mann – Whitney test was used for comparation of variable's averages of two populations. For the comparation of variable's averages of more populations Kruskal-Wallis test was used. Hi-square test and Fischer test were used for determining the connection of two descriptional variables. Researching the influence of more variables on binary variable was done with multivariate binary logistic regression.

Results

According to the degree of differentiation, well differentiated tumours were dominant (low-grade - well and moderately differentiated) 68.3%, while the percentage of poorly differentiated tumours (high-grade - poorly differentiated and non-differentiated) was 31.7%.

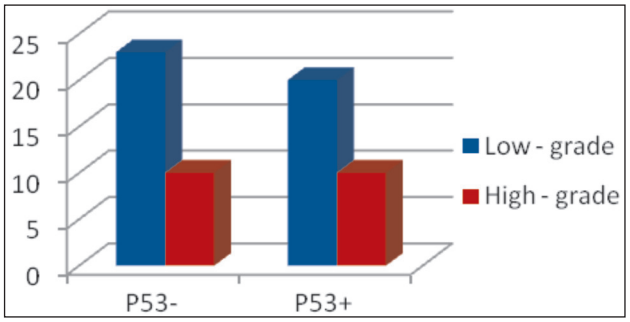

Figure 1. Diagram of the analysis of degree of differentiation and p53.

On the basis of local invasion of primary tumours, we have five stages. The largest number of tumours was in the T3 stage, i.e. 73%. Results of nodal status test are shown in tables 2 and 3. Results of examination of distant metastases are shown in table 4.

Table 2. Examination of nodal status

Nodal status	Incidence	Percentage (%)
Not present	34	54,0
Present in 1 to 3 ln	12	19,0
Present in more than 3 ln	17	27,0
Total	**63**	**100,0**

Table 3. Examination of nodal status

Nodal status	Incidence	Percentage (%)
Not present	34	54,0
Present	29	46,0
Total	**63**	**100,0**

Table 4. Examination of distant metastases

Distant metastases	Incidence	Percentage (%)
Not identified	56	88,9
Present	7	11,1
Total	**63**	**100,0**

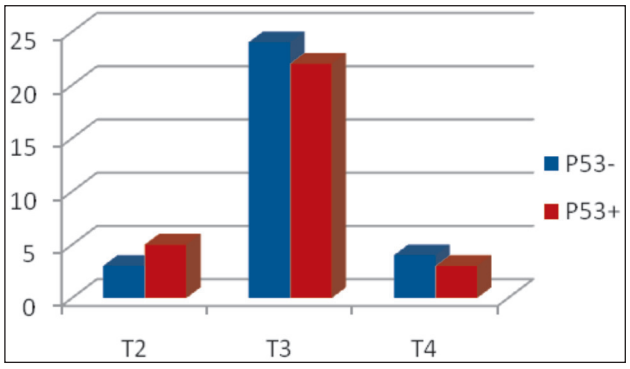

Figure 2. Diagram showing the analysis of tumor stage and p53

Nuclear expression of p53 was present in 52.4% (positivity score more than 30% tumor cells showing immunoreactivity to p53). In 47.6% there was no expression of p53. Results of statistical analysis in which the tumours' grade was compared with expression of p53, showed that the difference in percentage of this expression and the degree of differentiation was not statistically significant (p = 0.870). The difference in the score and the degree of differentiation was not statistically significant (p = 0.881). Results of the degree of differentiation and p53 examinations are shown in table 5. The degree of differentiation and p53 are independent (p = 0.881)

In well differentiated tumours, 20 were p53 positive while 23 tumor samples remained negative. Poorly differentiated tumours had an equal number of positive and p53 negative cases - 10. Statistical analysis of this segment showed how the difference in the percentage of expression and the stage was not statistically significant (p = 0.971). The difference in the score and the stage was not statistically significant (p = 0.804). Results of the correlation of tumor stage and p53 are shown in table 6. Stage and p53 are independent (p = 0.700).

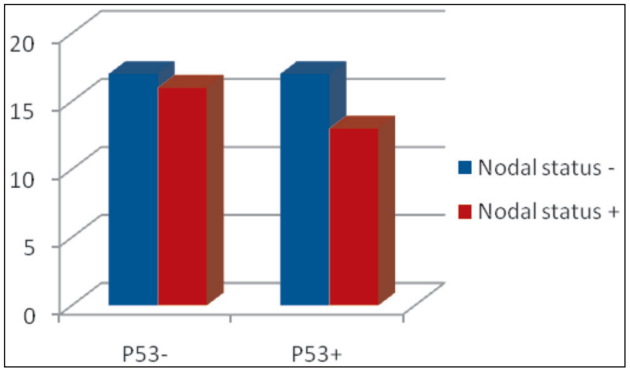

Figure 3. Diagram showing the analysis of metastasis in lymph nodes and expression of p53

In stage T3 tumours, 24 samples showed no expression of p53, whereas in 22 it was present. The T4 tumor stage had 3 samples with p53 overexpression and 4 were p53 negative. Three T2 stage tumours had no expression of p53, and it was present in 5 tumours.

In this segment of the study, the results of statistical analysis showed that the difference in the percentage expression of p53 and nodal status was

Table 5. Differentiation degree and p53

Histological grade	P53-	P53+	Percentage (%) -	Percentage (%) +
Low - grade	23	20	53.49	46.51
High - grade	10	10	50	50

Table 6. Tumour stage and p53

Stage (pT)	P53-	P53+	Percentage (%) -	Percentage (%) +
T2	3	5	37.5	62.5
T3	24	22	52.17	47.83
T4	4	3	57.14	42.86

Table 7. Metastases in lymph nodes and expression of p53

Metastases in lymph nodes	P53-	P53+	Percentage (%) -	Percentage (%) +
Nodal status -	17	17	50	50
Nodal status +	16	13	55.17	44.83

Table 8. Distant metastases and p53 expression

Distant metastases	P53-	P53+	Percentage (%) -	Percentage (%) +
Metastases not present	29	27	51.79	48.21
Metastases present	4	3	57.14	42.86

not statistically significant (p = 0.226). The difference in the score and nodal status was not statistically significant (p = 0.226). Nodal status and p53 are independent (p = 0.682).

In tumours in which metastases in regional lymph nodes were not found, 17 tumours were p53 positive, and in 17 there was no expression of p53. In the 16 tumours with the presence of metastatic deposits there was no p53 overexpression, while in 13 it was verified.

The results of this segment of the research showed that the difference in the percentage of p53 expression and metastasis was not statistically significant (p = 0.440), the difference in the score and metastasis was not statistically significant (p = 0.276). Metastases and P53 are independent (p = 1.000).

In tumours having distant metastases, 27 were p53 positive, whereas in 29 tumours without metastases the expression of p53 was not verified. In tumours having distant metastases 3 had p53 overexpression, while in 4 there was no p53 expression. Figures 5, 6 and 7 show immunohistochemical confirmation of p53 expression.

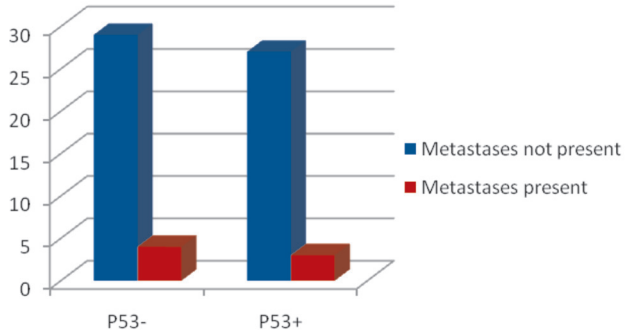

Figure 4. Diagrams showing the analysis of distant metastases and p53 expression

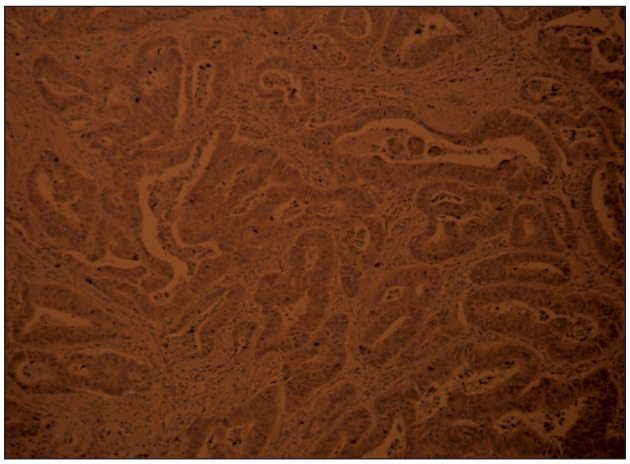

Figure 5. Nuclei of tumor cells do not show immunoreactivity to p53 (IHH, x 100)

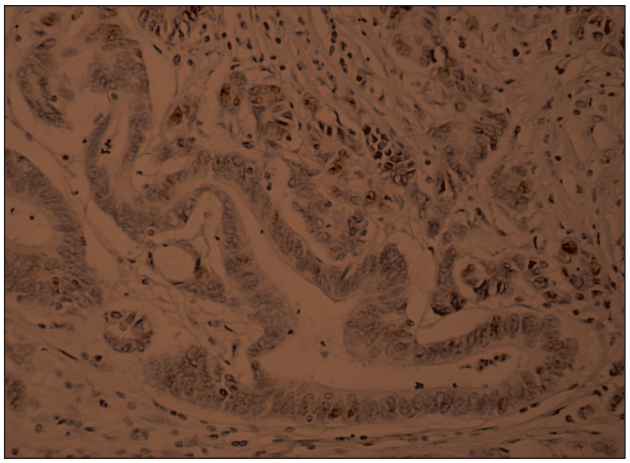

Figure 6. Nuclei of tumor cells showed p53 immunoreactivity up to 30% (IHH, x 200)

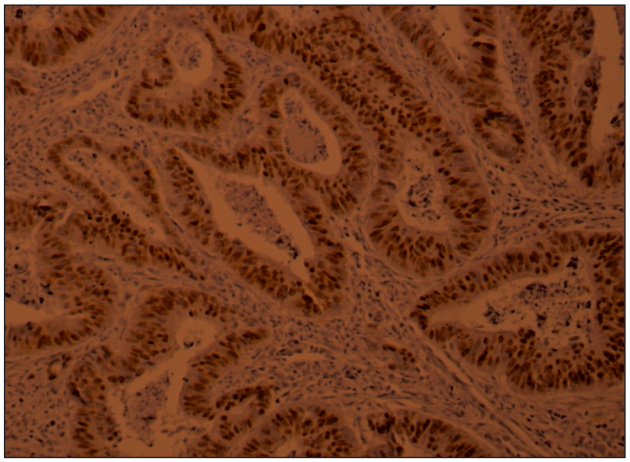

Figure 7. Nuclei of tumor cells showed p53 immunoreactivity over 30% (IHH, x 200)

Discussion

Results of this study have also shown that the nuclear expression of p53 was present in 33 cases or 52.4% of overall cases, and p53 expression was used as a positivity mark in more than 30% of tumour cells. In 30 samples (47.6%) of overall number of analyzed CRC there was no p53 expression. Acquired results are consistent with data in available literature regarding p53 marker expression at colorectal carcinoma, according to which the usual p53 expression in all carcinomas is 45 – 70%, while the expression of this marker in colorectal carcinoma is 42 – 67%.[10]

Today, p53 mutation is the most frequently proven mutation at breast, oesophagus and non-small cell lung carcinoma.[11] p53 is the base of Lane's functional model of 'molecular policeman'. Wild

type (normal type of p53) is the transcriptive regulator in G! Phase of cell cycle.[12] When DNA damage occurs, p53 is activated and through p21 inhibits cyclin-dependant kinases and subsequent phosphorylation of proteins needed for the S phase entry. This G1 phase pause allows the DNA error reparation of the induction of apoptosis and prevention of mutated cells' proliferation.[13] p53 mutations result in accumulation of p53 proteins which leads to higher proliferation, loss of apoptosis, chromosome instability and differentiation disruption.[14] On the other hand, p53 induced cell death can prevent bcl – 2 expression of proto-oncogene which inhibits the apoptosis.[15] All previously used literary information state that the majority of CRC starts through successive process of sequential genetic and phenotypic changes, meaning, through hyperplasia, adenoma, carcinoma and metastasis.

Some studies have presented the CRC cases in which the p53 expression was 76%, and in those the increased expression was linked with shorter survival period.[16] The others authors have shown that the expression level does not have a conection with biological behaviour, tumour stage, histological type, localisation, tumour size, presence of lymphatic node and venal invasion, perineural invasion, metastases in lymphatic nodes and outlying metastases (hepatic and peritoneal), all of which disputes the p53 significance.[17]Other studies made an assumption of gene therapy possibility, based on information that the growth of p53-transfected malignant cells is stopped, and the presence of mutant p53 gives way to a vaccine therapy, according to those.[18]

Wild p53 is expressed in normal tissues, but at an undetectable level. It is considered that mutated p53 is expressed in over 50% of all tumours, when it is possible to detect it, commonly through immunohistochemical means. As multimarker, whose level and way of expression is monitored in many tumours, it is used for monitoring its connection with the development of malignant diseases.[5,7]

Results of mentioned studies are somewhat contradictive, since it was known by now that tumourgenesis occurs only if both p53 alleles mutate, or are missing, meaning, while p53 is heterozygote – one normal p53 is preserved. Previously mentioned studies have shown that p53 represents the watchdog of cell functions which can lead two ways: in aoptosis, or uncontrollable cell division. But, in some studies was noted that there a hyper expression of *wild* p53 in the tumour, when p53 mutant is not expressed. In such cases, it is presumed that some other genetic pathway is activated and that it crosses over with *wild* p53's expression path, which is the case with mutated mdm-2, which now would not be able to inhibit the p53 expression.[19] The results of all mentioned studies suggest that the p53 expression, regarding the disease prognosis, can only be interpreted if p53 is coexpressed with other tumour markers. Direct correlation of p53 expression and prognosis is noted in the later stage of the disease, when any therapy is questionable, meaning, there is no significance in measuring the level of its expression.[20]

The results obtained by analyzing 63 CRC in this study, showed that according to the degree of differentiation, 43 samples, or 68.3% of the total number of samples belong to well-differentiated tumours (low-grade - well and moderately differentiated), while 20 samples, respectively, 31, 7% of the total number of samples belong to poorly differentiated tumours (high-grade - poorly differentiated and non-differentiated).

According to literature data, pathologic (pTNM) classification is based on two main pathohistological evaluation parameters of crucial prognostic significance: local, maximum depth tumor invasion and metastatic potential or the presence or absence of metastases in regional lymph nodes and distant metastasis.[21] It represents so far the only independent prognostic parameter in all published studies.[22]

The largest number of tumours examined was in T3 stage (73% of total CRC). As stage T3a-d were classified tumours that infiltrate muscle layer, subserosis, non-peritoneal pericolic or perirectal tissue from 5mm to more than 5 mm in depth. 12.7% was in T2 stage. Tumours were classified as T2 stage if infiltrated muscle layer but do not break through. 11.1% of the total number of analyzed CRC was in T4 stage. T4 stage tumours directly infiltrate other organs and structures penetrate visceral peritoneum. Only 1.6% of tumours were in T1 stage in which, according to standard classification protocol, includes tumours confined to sub-mucosae. Also, 1.6% of total samples analyzed haven't had invasion of lamina muscularis mucosae, which according to the criteria for the

classification suggests that the tumor was at the mucosal level (in situ - intraepithelial carcinoma). 98.8% of tumours were found in stage T2, T3, or T4 i.e. primary tumor has already infiltrated submucosa, other layers of the bowel wall until spreading to other organs and visceral peritoneum. [23]

Test results of CRC metastases analyzed in this study showed that in 54% of tumours had no histologically proven metastases, while in 46% of the total number of samples, metastatic deposits were present in regional lymph nodes. In 19% of the total number, metastases were present in 1 to 3 lymph nodes (rN1) and in 27% of the samples metastases have spread to 4 or more lymph nodes (pN2). 11.1% of the total number of analyzed tumours had verified histologically distant metastasis, i.e.in 88.9% they were not present or verification was not possible.

The results of this study showed that nuclear expression of p53 was present in 52.4% of the total number of cases, where positivity score was evaluated as p53 expression in more than 30% of tumor cells. In 47.6% of the total number of analyzed CRCs there was no expression of p53. The data are consistent with data from available literature on p53 expression markers in colorectal cancer, according to which the normal expression of p53 in all carcinoma was 45-70%, while the expression of this marker in colorectal carcinomas was 42-67%.[10]

According to some literature data, nuclear expression of p53 was present in 49.6% of tumours and has not correlated with pathological parameters: tumor stage, histological grade. Also, according to the same data, increased expression levels coincided with a shorter survival period, but only monitored in correlation with P21 and mDm2.[24] Inverse relationship of p53 expression and clinical-morphological parameters can be explained by different mechanisms of cancerogenesis.[25] Research of other authors which have included thirty studies (in twenty-four studies immunohistochemical methodology was applied) showed that the expression of p53 is the predictor of poor outcome. Paradoxically, twenty-four studies have found conflicting results.[26]

Comparing the level of expression of molecular markers (EGFR p53, c-MET) with clinical - morphological parameters (degree of differentiation, histological type, invasion of lymph and blood vessels, tumor localization, gender and age) in the search for biological marker, most studies provide unconvincing results. The reasons are inhomogeneous populations, limited sample, the conflicting histopathological and treatment protocols, the technical aspects (IHH), evaluation of results, the preoperative adjuvant or radiation therapy at the time of diagnosis. Expression of p53 may be an independent prognostic factor when there is no correlation with clinical and other settings even coexpression with other molecular markers-Bcl-2, Mdm2.[27]

Limited value of a molecular marker is not surprising because tumours express more proto-oncogenes, suppressor genes and onco – foetal antigens, of which each contributes to the progression and metastasis. Better understanding of tumor progression can be achieved only by monitoring through coexpression of more markers.[28]

Monitoring of p53 and MDM-2 coexpression showed that expression of a single marker is not related to the degree of differentiation, tumor stage and presence of metastases. In the same study, increased expression of p53 correlates with adenoma with the presence of moderate to severe degree of dysplasia, but not their size, although the percentage of expression is approximately 41%, which is consistent with previous studies. MDM-2 can lead to degradation of p53 and favouring the "wild form of p53". Mutations in p53 and K-Ras genes rarely co-exist, indicating the different ways of tumourgenesis.[29] The literature available data, some authors correlate coexpression of p53 and EGFR with poor prognosis and as indicator for disease recurrence. Multiple genetic changes and known molecular markers can provide a complete explanation for the obtained results of markers' coexpression.[30]

Immunohistochemistry is an important diagnostic tool to assess the presence or absence of molecular tumor markers, determine their prognostic and predictive value and possible integration into clinical practice. Molecular markers that complete the clinical - pathological parameters are not as prevalent in CRC because of the lack of quality prospective studies, undefined scoring systems, the dose of subjectivity in the interpretation, which is reflected in practical - diagnostic use.[31]

Differences in expression may be due to the use of antibodies of different specificities. Some of the studies whose results are presented in the

available literature allow access to data according to which in 33% of all colon tumours has no verified p53 mutation using DO-7 monoclonal antibody that has demonstrated clinical correlation in other clinical studies. Some authors have shown that the detection of p53 protein accumulation may not be consistent with the presence of mutations.[32] Although the expression of p53 correlates with deletions of chromosome 17p, facts of p53 as a prognostic indicator, based on immunohistochemistry, are very opposite, so that confirmation of protein expression of p53 mutations depends on the specific antibodies used. Other authors have produced antibody Pab240 that strictly selectively reacts only with the mutated form of p53.[33]

Many genetic forms do not result in expression but positivity may also occur in the absence of mutation. The literature data states that 80% of p53 overexpression derived from the discovery of mutated protein DO-7 anti-p53 and that there are non-mutational mechanisms that cause expression by sequestration of normal p53 protein from the virus transformed proteins.[34] Controversial prognostic significance of certain p53 genetic abnormalities is possible because of mutations within certain "conserved regions" that even neutralize the negative functional effects of other structural proteins.[56] Harbouring (removed - protected) mutations cause aggressive forms of cancer with a higher tendency to lymphogenic and hematogenic dissemination.[31,35]

Mutations in the type of point (missense-frame shift) can lead to loss of both alleles of p53 and the creation of undetectable p53 which may explain the increased expression in adenomas with low dysplasia in relation to the expression in adenomas with high dysplasia and in carcinoma. P53 gene point mutations result in the production of detectable protein with longer survival whose nuclear accumulation is detected immunohistochemically, which served as a means of identification of p53 mutations. Many studies say that the point mutations and crossbred deletions are responsible for the development of distant metastases and in lymph nodes. The position of point mutation and alleles' deletion are the "four hot" sites of p53 mutations. Wild type p53 in combination with viral and cellular oncoproteins may extend its half-life and increase the nuclear presentation which will be reflected in the expression. In such situations positive immunohistochemical reaction is possible without mutation, which supports the concept of accumulation of p53 caused by other mechanisms rather than mutation. In addition, increased detection of p53 protein in CRC with wild type p53 is possible in mutation of MDM-2 gene.[36,37]

Immunohistochemistry is a simple and accessible way to confirm the expression of p53, but the results cannot be trusted because methods of detection and analysis of the results are not standardized (*cut off*). A large number of authors had studied the expression levels with the selected cut off (more than 10% - the threshold value chosen to distinguish positive and negative expression of the sample), in groups that had from 94 to 995 patients and most of them came to the conclusion that there is no significant correlation between p53 expression and clinical - morphological parameters. Some authors have obtained the expression of p53 in 42% of tumours, immunohistochemically on frozen section preparations, without correlation with TNM stage of tumor, histological grade, and localization. Frequency of antibodies' immunoreactivity varies from 36 to 46% on frozen clips. [38,39]

Other studies done on preparations from paraffin blocks give discontinuity between expression and tumor stage, as opposed to the length of survival.[40] Using different antibodies, different methods of preparation affect the course of tissue staining as well as p53 protein epitopes to which antibodies are directed, because they may not survive fixation procedure. All studies agree on the frequency of expression of p53, but in order to achieve statistical significance between expression and clinical - pathological parameters more studies and approval are needed. Forty-six studies published in the period from 1995 to 2002 confirmed that the number of studied cases has an important role in the study and verification of p53 as prognostic marker.[41] DNA sequencing is more reliable method of detection of p53 mutations than IHH, where different expressions are often not in accordance with the clinical - pathologic manifestations of tumours. Other studies have shown that there is no correlation between histological type, degree of tumor differentiation, stage and localization. Highlighted poor immunoreactivity at p53 with signet - ring cell carcinoma.[42]

Conclusions

Expression of p53 is independent of pathological tumor stages (pTNM) regional lymph nodes and distant metastases, i.e., there is no correlation between p53 expression and pathological tumor stage, which would serve as a prognostic factor in the further course and outcome of disease.

Expression level of p53 does not correlate with the degree of histological differentiation and histological grade of tumor. Expression level of p53 does not have diagnostic, predictive and prognostic potential, while its importance is undeniable in the understanding of oncogenesis.

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Does Coronary Angiography Induce Clinically Relevant Changes in Thyroid Function Parameters of Euthyroid Patients After One Month?

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Abstract

Background: Diagnostic and therapeutic studies using contrast agents are currently used frequently. Conflicting results have been present regarding the effect of these agents on thyroid function.

Aim: The aim of this study was to evaluate the effect of contrast media administrated during coronary angiography on thyroid function parameters.

Methods and results: Thyroid function parameters of 50 consecutive patients who underwent elective coronary angiography were studied before entering the study and 1 month after the procedure. The baseline mean TSH, FT4 and FT3 values were in the normal range in all patients before the procedure. However, one month after the procedure, the mean values of all thyroid function parameters decreased significantly (-0.73 ± 1.65 mU/ml, p=0.003 for TSH; -0.28 ± 0.56 pmol/l, p=0.001 for FT3; -0.07 ± 0.20 pmol/l, p=0.024 for FT4).

Conclusion: Routine study of thyroid function tests in subjects with normal thyroid glands before coronary angiography is unnecessary.

Key words: contrast, euthyroid, function

Introduction

Excess free iodide in the blood (ingested or injected) may cause thyrotoxicosis in patients at risk. Iodinated contrast media contains small amounts of free iodide and may be significant for patients at risk. Contrast medium induced thyrotoxicosis is rare. There are many causes of thyrotoxicosis. However, the two main reasons are Graves' disease and hyperthyroidism on the basis of thyroid autonomy. Iodine-induced thyrotoxicosis belongs to the second group. As early as 1820, the correlation of clinical symptoms of hyperthyroidism and iodine contamination in subjects with goiter has been described (1). At the beginning of this century, Breuer (2) and Kocher (3) made further investigations concerning these facts. Today, it is an accepted theory that in subjects with pre-existing thyroid autonomy, iodine contamination can result in iodine-induced thyrotoxicosis. Iodine-induced thyrotoxicosis can also occur in areas with sufficient iodine intake (4) but patients from an iodine-deficient area are even more endangered, as recently reviewed by Stanbury *et al* (5). The inadvertent administration of iodine happens through various substances: iodine-containing drugs, disinfectants, antiseptics, and even contrast agents. Iodine-induced thyrotoxicosis has been described even in apparently normal thyroid glands (6). On account of these facts, it is quite usual (for example in cardiology departments) to examine the thyroid gland and take blood samples for thyroid hormone measurement before patients undergo coronary angiography.

In the present study, we aimed to investigate the effect of contrast media administrated during coronary angiography on thyroid function parameters.

Materials and Methods

Study population

This is a prospective and observational study. A total of 50 consecutive patients who underwent elective coronary angiography because of symptoms and/or abnormal stress tests in Yuksek Ihtisas Education and Research Hospital, Cardiology Clinic were included in this study. A fasting peripheral venous blood sample from all patients was obtained before entering the study and 1 month after the procedure. The subjects who had acute or chronic inflammatory diseases, peripheral artery disease, malignancies, renal, hepatic, and thyroid disea-

ses, immunologic diseases, cardiomyopathy, acute coronary syndromes in the last one month before hospitalization, severe valvular heart diseases, and patients taking thyroid effecting drugs such as amiodarone were excluded from the study. Selective coronary angiography of patients was carried out with various amounts of Ultravist-370 non-ionic opaque material (Bayer Schering Pharma AG). A written consent was obtained from all patients and our local ethical committee approved the study.

Laboratory data

Fasting peripheral venous blood samples were obtained from all patients in the study for the measurement of fasting plasma glucose, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, urea, creatinine, and complete blood count including hemoglobin, hematocrit, and platelet count. Blood samples were centrifuged and plasma was obtained. Fasting blood glucose, total cholesterol, HDL-cholesterol and triglyceride levels were measured by enzymatically by the auto analyzer (Hitachi 911, Japan). Plasma glucose was measured with the glucose oxidase technique. Measurement of LDL-cholesterol level was done through application of a formula as described by Friedewald et al. (7).

Baseline thyrotrophin (TSH), free thyroxine (FT4) and free triiodothyronine (FT3) were measured with a commercial kit E170 Roche Diagnostics before and 1 month after the procedure. For this kit, normal ranges of TSH, FT4 and FT3 are 0.27-4.2 mU/ml, 0.93-1.7 pmol/l and 2.0-4.4 pmol/l, respectively.

Statistical analysis

Data were analyzed with the SPSS software version 15.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were presented as mean ± SD and categorical variables as frequency and percentage. Student's t-test was used to compare normally distributed continuous variables. A two-tailed p-value of <0.05 was considered statistically significant.

Results

The demographic, clinical and laboratory characteristics of the study group were presented in table 1. The study population was composed of largely middle-aged men. The baseline mean TSH, FT4 and FT3 values were in the normal range in all patients before the procedure (Table 2). However, one month after the procedure, the mean values of all thyroid function parameters decreased significantly ($p<0.05$). In subgroup analysis of diabetics, such decrease was also seen and this decrement was not significantly different from the decrement of non-diabetics ($p>0.05$) (Table 3).

Table 1. Baseline characteristics

Characteristics	Mean ± SD
Age (years)	60.8 ± 14.1
Male sex	34 (68%)
BMI (kg/m2)	23.8 ± 3.5
Diabetes mellitus	13 (26%)
Systolic BP (mmHg)	117 ± 22
Diastolic BP (mmHg)	71 ± 10
Fasting blood glucose (mg/dl)	112 ± 31
Urea (mg/dl)	38.9 ± 9.6
Creatinine (mg/dl)	0.8 ± 0.3
Hemoglobin (g/dl)	14.4 ± 1.6
Hematocrit (%)	43.3 ± 4.9
Platelet (/mm3) x1000	245 ± 71
Total cholesterol (mg/dl)	174 ± 35
LDL cholesterol (mg/dl)	105 ± 33
HDL cholesterol (mg/dl)	41 ± 10
Triglyceride (mg/dl)	140 ± 84
Used opaque (ml)	106 ± 24

Discussion

In patients without risk factors, contrast medium-induced thyrotoxicosis is very rare. Thus, it is not necessary routinely to assess thyroid func-

Table 2. Hormone levels before and after the procedure and the mean differences

Test type	Before the procedure	After the procedure	Mean difference	P value
TSH (mU/ml)	2.24 ± 1.77	1.50 ± 0.82	-0.73 ± 1.65	0.003
FT3 (pmol/l)	3.24 ± 0.47	2.96 ± 0.31	-0.28 ± 0.56	0.001
FT4 (pmol/l)	1.29 ± 0.18	1.23 ± 0.17	-0.07 ± 0.20	0.024

Table 3. The mean differences of hormones in subgroup analysis of diabetics

Test type	Mean difference		P value
	Diabetes mellitus	No diabetes mellitus	
TSH (mU/ml)	-0.28 ± 0.92	-0.89 ± 1.83	0.254
FT3 (pmol/l)	-0.29 ± 0.53	-0.27 ± 0.58	0.906
FT4 (pmol/l)	-0.05 ± 0.22	-0.07 ± 0.20	0.694

tion or morphology before injection of contrast media. However, a small group of patients are at increased risk. Therefore radiologists should be aware of the potential effects on thyroid function associated with the administration of iodinated contrast media. The history and physical examination are important, and risk factors should always be evaluated.

Iodine is an essential agent for thyroid hormone synthesis. When increased amounts of the agent are administrated to subjects having normal thyroid gland, a transient decrease in thyroid hormone synthesis resulting reduced T4 and T3 levels occurs within normal range (8). A 200-ml contrast medium contains large amounts of free iodide equivalent to 45 times the daily intake. Normally, after administration of contrast medium, a small decrease in FT4 and FT3, and a small decrease followed by a rapid increase in TSH occur within normal ranges during first 3 weeks. Accordingly, a decrease was seen in FT4 and FT3 in our study. However, in contrast to normal response, a decrease was observed in TSH. All values were in normal range.

Most studies, investigate the risk of high iodine loads via x-ray contrast media to develop thyroid dysfunction. In order to evaluate the risk for development of thyroid dysfunction (a well known late onset phenomenon) most investigations were carried out some weeks after the application of the radiological diagnostic procedure (6, 9, 10). In patients living in endemic goiter regions, iodine induced thyrotoxicosis occurring several weeks after the iodine load is a well described danger (11). Little is known, about the short-term effects on thyroid function of coronary angiography in euthyroid patients.

In a study performed by Koroscil et al. no significant short-term change has been found in thyroid function parameters after administration of contrast agents in euthyroid patients (12).

Similarly, no significant changes of thyroid hormone levels have been observed on the 5th day following coronary angiography (13).

In contrast to these studies, Gartner et al. have demonstrated that mean TSH values have increased significantly 3-5 days after the iodine load within the normal range. However, FT4 and FT3 have remained unchanged demonstrating subclinical hypothyroidism (14).

These changes have interpreted as physiological adaptation to augmented iodine administration in another study (15).

Interestingly, in our study, all thyroid function parameters significantly decreased within the normal range. Speculatively, a central role of contrast medium on TSH in the brain can explain these decrements.

In conclusion, as a routine study of thyroid function tests in subjects with normal thyroid glands before coronary angiography is unnecessary.

Limitations

The major limitation of our study was an observational case-control study that some confounding factors might affect the results. Second, methodologically, neither urinary iodine excretion nor other thyroid parameters such as reverse-T3 were measured. In addition, thyroid ultrasonography was not performed before the study entry.

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Preoperative psychoprophylactic visiting alleviates maternal anxiety and stress and improves outcomes of Cesarean patients: a randomized, double-blind and controlled trial

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Abstract

Background: Antenatal psychological distress is a pivotal issue critically associated with postpartum health disorders in mothers and the progeny, of which pluses Cesarean section-induced anxiolytic and stressful responses may produce potential remarkable sequelae to maternal and infant well-beings. Preoperative psychological preparation is preferably suggested for alleviating psychological troubles to premedications, while its accurate effect in this context is not well defined. The aim of this study was to test the hypothesis that preoperative psychological visiting by trained expert theater nurses using specially designed psycho-leaflets could reduce prior Cesarean stress and anxiolytic levels, and improve maternal and infant outcomes.

Methods: After approval by the institutional review board and patient's consent, 146 parturients with American Society of Anesthesiologists (ASA) physical status class I or II were randomly allocated to a "psychological visiting" or "non-psychological visiting" group. The interventional information given by trained expert theater nurses mainly focused on dealing with the complications, inadequate anesthesia and postoperative analgesia, post-surgical rehabilitation, breathing and relaxation training, mental control, and postpartum care. The endpoints of the study included the scorings rated using patient self-rating anxiety scale (SAS) and depression scale (SDS), salivary cortisol, and maternal and infant outcomes. The association between maternal demographic variables and anxiety levels was assessed through multivariate logistic regression.

Results: The median visiting time of the psychological group was 53 min, but 21 min in the non-psychological group ($p = 0.008$), while preoperative psychoprophylactic visiting produced considerable effect on anxiolytic level alleviation and cortisol reduction, but not depressive level, in women undergoing Cesarean section than those without psychological intervention. Women received psychological intervention had an earlier onset of lactation, superior postoperative analgesia, less adverse events and shorter urinary indwelling catheterization than those of the comparison. No significant difference was observed in infant outcomes between both the groups. Maternal demographic data were strongly associated with the anxiolytic level.

Conclusions: These results indicate preoperative psychoprophylactic preparation for Cesarean patients alleviates maternal anxiolytic and stressful levels, improves maternal outcomes, and increases overall satisfaction with Cesarean experience.

Key words: Psychoprophlaxis, Cesarean section, Stress response, Anxiety, Corticosteroid, Antenatal education

Introduction

The level of stress is strongly associated with surrounding environments a man lying within (1, 2). A growing body of evidence indicates that a

tight relationship exists between antenatal stress responses and the development of postpartum short- or/and long-term health disorders in mothers and the progeny (3-7).Anxiety and depression are two major risk factors to adverse obstetric, fetal and neonatal outcomes that manifested and avidly related with prenatal stress state (8). Some 6-10% women even develop pathological fear of childbirth termed "tokophobia" that is of concern owing to potential remarkable sequelae to both the mother and her babies (9, 10), resulting in maternal request for Cesarean delivery (11). Nonetheless, Cesarean itself is also a distinct cause of maternal stress responses which closely depends upon anesthesia, surgical procedures and subsequent possible adverse complications (12, 13).

Antenatal education has been considered as an effective method relieving maternal psychological disturbance and facilitating their coping ability during childbirth (14). Besides, relaxation training exerts beneficial role in reducing anxiety and perceived stress in pregnant women (15). To date, clinical professionals preferred group education through which questions raised by patients can be discussed overallly to individual education that is prone to personalization, and the accurate role for general antenatal education remains largely unknown (16). Additionally, antepartum information of Cesarean section is far less for gravidas compared with those for vaginal delivery (17), and fear for childbirth can lead to an increase in Cesarean delivery (11), while the knowledge of how to alleviate these dreadful responses in parturients is devoid. Whether prenatal psychological visiting was effective or not in ameliorating preoperative psychological distress in Cesarean patients is yet to be guaranteed.

This study is designed to testify the role of psychological visiting by trained expert theater nurses using specially designed psycho-leaflets in reducing prior Cesarean stress responses, and anxiolytic and depressive levels, and in improving maternal outcomes.

Materials and Methods

Subjects and Ethics

A total of 146 parturients with American Society of Anesthesiologists (ASA) physical status class I or II who underwent selective Cesarean delivery were randomized after approval by the Hospital Ethics Examining Committee of Human Research, and the informed consent was obtained to each woman. This study was carried out from May to August 2010 at a tertiary teaching hospital in China. Women were eligible for the trial if they were Chinese-speaking with gestational age at least 36 weeks and uncomplicated singleton pregnancy.

Exclusion Criteria

Parturients were excluded from the study if one or more following excluding criteria were met: i) refusal for participation; ii) with cognitive dysfunction; iii) used or using centralling acting drugs; iv) with chronic pain; v) with existed psychiatric and psychological disorders; vi) multiple gestations; vii) emergency Caesarean section or parturients failed vaginal delivery with epidural analgesia; viii) allergic to opioids; ix) contraindications for performing neuraxial anesthesia; x) received informal information before or/and after randomization regarding the interventional contents would be given by the visiting nurses; xi) with concurrent diseases that would influence the psychological state of parturients such as hyperthyroidism.

Demographic Variables

The demographic data were collected as follows: age at delivery, height, body mass index (BMI), gestational age of the fetus, smoking status, educational and family economic status, history of psychological interview, nulliparous or multiparous status, pregnancy education, and maternal vital signs (blood pressure, heart rate, respiratory rate and oral temperature).

Randomization, Allocation and Mask

Parturients were enrolled in this study consecutively following their diagnoses for Cesarean delivery. Once the signed written consent was obtained from the eligible woman, she then was randomly assigned to either the non-psychological visiting group or the psychological visiting group by a completely random allocation in a single block. The random-number list was generated by means of the QuickCalcs[11] (GraphPad Software

1 Online Calculators for Scientists, available at http://www.graphpad.com/quickcalcs/RandMenu.cfm. Last accessed August 20, 2011.

Inc, La Jolla, San Diego, CA). The sealed opaque envelope containing the group assignment kept by the study supervisor was opened after obtaining informed consent. The health-care providers, data collectors, data-analyzing members, laboratory testing professionals, and parturients were masked to the group allocation except for the interventional visiting personnel.

Preoperative Visiting Educators

The visiting nursing educators were trained in a full-scale antenatal program concerning the interventional information and maneuver two weeks prior to the study begin. A total of ten nurses took part in this training program, and they were divided into two parts by a lot-drawing means with five members each part. One of the non-psychological nurses who withdrew due to changes in employment was replaced by another colleague who received a detailed introduction to the study and the interventional program as given to the other part members. The median age of the visiting nurses was 32 years (interquartile range, 27 to 36 years), and all of them had a mean of nine years experience in childbirth health care. One day before the initiation of the study, all educating nurses were called up for a workshop of the study methodology and the requirements for adhering to the study. During the trial, the workshop was organized again for all the visiting nurses every four weeks.

Study Protocol

Two preoperative interventional visiting programs were specially designed with identical format but not containing contents within the information leaflet displayed as Table 1. In the psychological visiting program, the contents were mainly focused on dealing with the complications of anesthesia and postoperative analgesia, inadequate anesthesia and postoperative analgesia, post-surgical rehabilitation, breathing and relaxation training during Cesarean birthing, mental control, and postpartum care for baby and mother. All these items were discussed at length with the parturient and her partner. However, in the non-psychological visiting program, the educating nurses merely provided information in a narrative language, which was in contrast to the psychological language full of feelings in the comparison, and did not provide further discussion on the contents such as how to treat complications and inadequate anesthesia and postoperative analgesia. In addition, no information regarding post-surgical rehabilitation, breathing and relaxation training, and postnatal care were given to the participating educatees.

Each woman was given two self-assessment psychometric tests for anxiety and depression evaluation one day before surgery. A self-rating anxiety scale (SAS) (18) and a self-rating depression scale (SDS) (19) were used for scoring participant's anxiolytic and depressive states. Each testing questionnaire consists of 20 items based upon spontaneous statements deriving from communication between visited women and studying personnel. Both of the rating scales change from a minimal scoring of 20 to a maximal scoring of 80 (four levels from 1 to 4 of each item in both anxiety and depression scales exist). The characteristics of these SAS and SDS measurements are linked anxiety with depressive symptoms or anxiolytic reaction psychoneurosis. Baseline values of anxiety and depression were determined prior to randomization. Additional scorings of anxiety and depression with self rating scales were measured at the following time points: (i) 30 min after psychological or non-psychological intervention; (ii) 30 min prior to surgery began; (iii) 10 min after the surgery has begun; (iv) 30 min after the surgery completed. All the testing questionnaires were asked the participants by the data collecting members but not the preoperative educating nursing staff. There would not be any information given as did preoperatively during the posteriori period of the study after the preoperative intervention. The salivary sample was collected at the same time points as were the psychometric parameters for cortisol measurement.

Anesthesia Management

Approximately 500-1 000 ml lactated Ringer's solution was titrated before spinal anesthesia performed. During spinal anesthesia, the L3-L4 vertebral interspace was punctured in the left-lateral jackknife position, and hyperbaric 0.5% bupivacaine 2 ml (10 mg) plus morphine 50 μg was administered intrathecally. After completion of the anesthetic procedures, patients were immediately repositioned supine with a 15-30° left lateral

*Table 1. Preoperative non-psychological and psychological visiting models.**

Items	Non-psychological Visiting	Psychological Visiting
Anesthesia		
Techniques	√	√
Complications	√	√
Dealing with complications		√
Inadequate anesthesia	√	√
Dealing with inadequate anesthesia		√
Effects on neonate	√	√
Postoperative analgesia		
Techniques	√	√
Analgesia complications	√	√
How to treat complications		√
Inadequate pain relief	√	√
Methods to treat inadequate pain relief		√
Surgery		
Procedures	√	√
Complications	√	√
Dealing with complications	√	√
Postpartum rehabilitation		√
Influence on next pregnancy		√
Childbirth		
Breathing and relaxing during birthing		√
Regimens for mental control		√
How to treat babies after they were born		√
Mother-baby contact	√	√
Gender role for the couple	√	√
After Birthing		
Where-to-go after birthing		
Maternal ICU	√	√
Surgical ward	√	√
Breastfeeding	√	√
Care for baby		√
Role transition to parents		√
Postpartum psychoses		√
How to treat postpartum psychoses		√

** Items ticked up refer to giving corresponding information and having a discussion with patients in detail.*

tilt for uterine deplacement. The highest sensory block was checked and confirmed at the level of T3-T5 determined with loss-to-pinprick method bilaterally at 5 min and 10 min after spinal drug administration. Motor block was measured with modified Bromage scale (0, no block; 1, inability to raise extended leg; 2, inability to flex knee; 3, inability to flex ankle and foot).

After the anesthesia was completed, arterial blood pressure was measured every minute for 20 min and then every 3 min for the duration of the study. Hypotension was referred to the reduction of systolic blood pressure (SBP) > 20% of baseline. Baseline arterial blood pressure was determined via measuring the patient three times every 5 min at supine position with left uterine displacement

one day before entering into operating theater by data collectors. All women who encountered hypotension were prescribed a repeatable ephedrine 6-10 mg intravenously. The maternal parameters monitored during the study period included the heart rate by three-lead electrocardiograph, respiratory rate, noninvasive systolic and diastolic blood pressure, mean arterial pressure, oral temperature and fingertip pulse oximetry. Ondanstron 4 mg can be administered intravenously if nausea or vomiting was persisted even when hypotension had been corrected. After delivery of the baby, 20 IU of oxytocin was titrated following lactated Ringer's solution.

Surgery and Postoperative Analgesia

All surgical procedures in this study were standardized and unified, and performed by the same group of obstetricians. A horizontal incision at the low abdominal wall was made to each woman. Blood samples from umbilical cord artery and vein were collected for pH values after the umbilical cord was blocked and cut off. After surgery, all subjects received intravenous patient controlled analgesia (PCA) pumps containing morphine for postoperative pain relief. The parameters of the PCA pump were as follows: a bolus of morphine 0.02 mg/kg, a lockout interval of 30 min, four hour limit 20mg, and no background infusion was given. Ondansetron 0.15 mg/kg was administrated prophylactically 10 min before the conclusion of the surgery, but patients still could receive metoclopramide 10 mg intravenously every 6 h administered at the discretion of the nurses on the surgical ward. Intravenous diphenhydramine, an antihistamine, 25 mg was delivered for treating pruritus if not allergic to it, but not for patients with narrow-angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction or bladder-neck obstruction. The visual analog scale (VAS) of pain were measured with the 100-mm gauge (based on a 0-100 linear VAS, 0 = no pain; 100 = worst pain imaginable). A VAS pain score of less than or equal to 3 was considered to represent effective analgesia. During the period of postoperative analgesia, patients were monitored continuously for blood pressure, heart rate, respiratory rate and oxygen saturation with pulse oxymetry. A ventilatory frequency of less than 8 breathes per minute was defined respiratory depression alarmed by the monitor, and subsequently the morphine was reversed with intravenous antagonist naloxone 0.5-1.0 mg plus high-volume (8-10 l/min) oxygen.

Primary Outcome

The participant self rated scores of anxiety using the SAS system after preoperative psychological or non-psychological visiting was selected as the primary outcome of this study.

Secondary Outcomes

The following maternal measures were selected as the secondary outcomes: ratings with the SDS gauge; preoperative visiting duration; volumes of crystalloid, bleeding and urine; ephedrine requirement; adverse events; time of onset of lactation; 6-wk breastfeeding; overall intensity of VAS rated pain; interval of first morphine request; 48-h total morphine consumption; satisfaction with Cesarean experience rated with a VAS gauge; first time left form bed; and length of hospital stay. Infant outcomes include the body weight, Apgar scorings at the first and fifth minutes, umbilical-cord blood gas measurement, gender status, and Neurobehavioral Assessment Scale (NBAS) with an 11 items scale (20) by pediatric personnel.

Moreover, the association between the maternal demographic variables and the anxiolytic levels was investigated using a multivariate regression modeling. Each one unit increase in age (Δ = 1 year), BMI (Δ = 1 unit), height (Δ = 1 cm), smoking status, nulliparous/multiparous status, education and family economic statuses, history of psychological interview, and pregnancy education are assessed.

Enzyme Immunoassay for Salivary Cortisol

The levels of cortisol from saliva of the participants during different time points were detected using a newly developed specific Enzyme Immunoassay (EIA) kit purchased from the ArborAssays (DetectX®). In brief, a standard curve was generated according to the kit's guidance. The sample was diluted in a 1:5 with the provided Assay buffer, of which 50 μl was pipetted into a clear microtiter plate coated with an antibody to capture mouse IgG. Then a 25 μl of cortisol-peroxidase conjugate was added into the wells and followed by adding 25 μl monoclonal antibody to cortisol to

each well and incubated for 1 h at room temperature. Then the plate was washed 4 times with washing buffer, and 100 µl of tetramethylbenzidine substrate was added. After 30-min incubation, the reaction was stopped by adding 50 µl stop solution and the intensity of the generated color is detected in a microtiter plate reader capable of measuring 450 nm wavelength with correction between 570 and 590 nm. The concentration of the cortisol in the sample was calculated using suitable correction for the dilution of the sample. The detection sensitivity of cortisol was < 17.3 pg/ml.

Sample Size

In a priori study, we established a power table where the mean difference between both of the groups in the SAS rated scorings was 34 ± 9 and 30 ± 8 in the non-psychological and psychological visiting groups, respectively. We set the alpha error level at 5%, the beta error level at 20%, and the statistical power at 80%, of which resulted in a minimum need for sample size for each group was 56. During this pre-study observation, a total of 25 parturients were screened for eligibility. However, there were 11 women exclude because of following reasons: five had a study protocol violation (3 in the non-psychological group and 2 in the psychological group have received information which might included in our educating leaflet), four refused for participation, one with twin pregnancy, and one withdrew after randomization. Therefore, approximately 45% women were excluded due to different reasons. Given the specialty of psychological intervention, during which many gravidas are prone to seeking corresponding information regarding the processes of pregnancy, surgery, anesthesia, analgesia and postpartum rehabilitation etc. that would be in conflict to our interventions. So these may be the underlying reasons for such a high rate of exclusion. Finally, in guaranteeing enough samples could be enrolled, we increased the sample size to 85 in each group to account for potential drop-outs, missing data and protocol violation.

Statistics

Statistical analyses were performed using GraphPad Prism v5.0 (GraphPad Software Inc., San Diego, CA) or SPSS 13.0 (SPSS Inc., Chicago, IL). Values are expressed as the mean, standard deviation (SD), median, interquartile range (IQR) or numbers. All categorical data were analyzed with a Chi-square test. The difference in parametric data including the demographic data and background characteristics were compared with Student's t test. Mann-Whitney U test was used in analyzing non-normally distributed variables and presented as the medians and IQRs including gestational age, SAS and SDS scorings, preoperative visiting time, sensory block level, Apgar ratings and NBAS scores, VAS ratings of pain and satisfaction, morphine consumption, and time interval of first analgesic request. We treated data on the intention to treat (ITT) and per protocol (PP) analyses basis. Namely data from those who were excluded after randomization were considered have negative results after corresponding interventions and analyzed in an ITT standard.

We carried out multivariable logistic regression analyses to assess the adjusted association between maternal baseline variables and priori operative anxiolytic level. First, bivariate analyses were performed using a liberal significance level of $p < 0.25$ to identify which baseline variables were independently associated with the primary outcome for inclusion in the modeling after controlling for the other variables. Modeling, then, was performed by stepwise forward method with a criterion of $p < 0.05$ for variable retention in the models. In the logistic regression model, the independent variables assessed included age, height, BMI, smoking status, history of labor and delivery, education status, family economic status, pregnancy education and history of prior psychological interview. Smoking status (0 = No; 1 = Yes), history of labor and delivery (0 = nulliparous; 1 = multiparous), pregnancy education status (0 = No; 1 = Yes), history of prior psychological interview (0 = No; 1 = Yes) were entered as dichotomous variables for the logistic regression analysis. In addition, college education and middle income were referred as references for education status and family economic status, respectively during regression analysis. A Pearson correlation matrix of variables was used to identify collinear predictive variables. Furthermore, Hosmer-Lemeshow test was used to assess the models' fit (larger p value means better fit or calibration), and predictive accuracy was assessed by the c-index as recommended elsewhere (21). The

odds ratio (OR) and its 95% confidence interval (95% CI) were calculated. All p values were two-sided and less than 0.05 was considered with statistical significance.

Results

A total of 170 parturients were assessed for eligibility. Twenty four of them were excluded for reasons presented in Figure 1, and 146 underwent randomization with 72 in the non-psychological group and 74 in the psychological group. Three women withdrew without any good reasons after random allocation. Fourteen in the non-psychological and nine in the psychological were ruled out because they received additional informal information after the visiting intervention which might negatively influence the primary evaluation of our results. One woman lost follow-up owing to migration to her hometown where far from our hospital which led to difficulty in contacting her. Finally, 57 in the non-psychological visiting and 62 in the psychological visiting completed the study, and their data were used for primary analyses. The data from those excluded after randomization were analyzed in the ITTs.

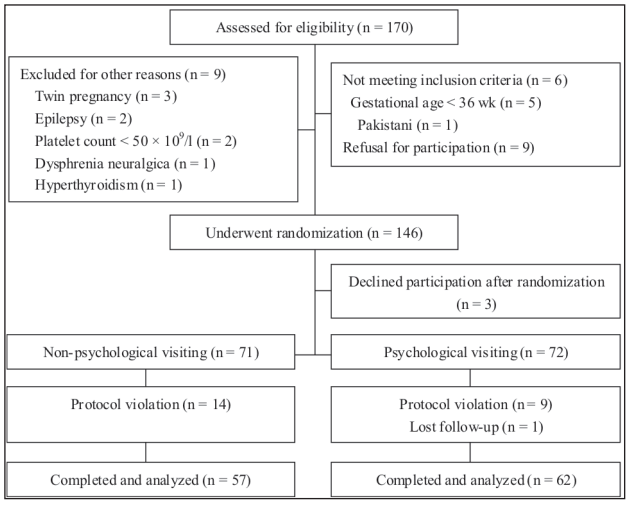

Figure 1. Flowchart of patients' enrollment and randomization.

Table 2 shows the background and demographic data of the subjects, and they were comparable between the two interventional groups. Vital signs all were within the physiological ranges.

Table 3 summarizes the maternal and infant outcomes of both the groups. Two group women had same levels of anxiety prior to the visiting, however, preoperative psychoprophylactic visiting produced considerable effect on alleviating anxiolytic level of parturients undergoing Cesarean section than those without psychological intervention. Further, patients given psychological intervention experienced relatively lower anxiety during the peri-surgical period after the psychological prophylaxis compared with the baseline (all ps < 0.01). No matter which intervention was given, the levels of post-operative anxiety in both groups were lower than did the intra-operative ones ($p < 0.05$). Interestingly, we did not find any significant intergroup and intragroup differences in the levels of depression. The median visiting time of the psychological group was 53 min (IQR, 37-62 min), but 21 min (IQR, 16-28 min) in the non-psychological group ($p = 0.008$). There was not marked difference in the incidence of each adverse event between the two groups, but overallly, 29 and 20 adverse events in the non-psychological and psychological visiting groups, respectively were experienced by the subjects in both groups totally, the difference was statistically significant ($p = 0.039$). A total of eight infants in the non-psychological group and three in the psychological group had lowered arterial or/and venous pH (< 7.20) ($p = 0.083$).

Salivary cortisol was measured in this study to testify the stress levels of the participants. Preoperative psychological visiting significantly reduced the production of salivary cortisol 30 min posteriori which did not appear additional increase during the perioperative period when compared with corresponding non-psychological comparisons (Figure 2). However, non-psychological intervention could not suppress the secretion of salivary cortisol. In our study, we found that intraoperative levels of salivary cortisol in both groups reached peaks, but subsequently, they markedly decreased after the conclusion of the surgery ($p < 0.05$).

Cortisol was measured with Enzyme Immunoassay (EIA) kit. *$p < 0.01$ versus baseline; $^{\#}p < 0.05$ psychological visiting *vs.* non-psychological visiting. 1: baseline; 2: 30 min posteriori intervention; 3: 30 min before operation; 4: 10 min after surgery began; 5: 30 min after surgery completed.

*Table 2. Demographic and baseline characteristics of the patients.**

Characteristic	Non-psychological Visiting (n = 57)	Psychological Visiting (n = 62)
Age, yr	27 ± 6	28 ± 5
Height, cm	162 ± 11	159 ± 9
BMI		
≤ 18.5	0	0
18.5 – 24.9	16 (28.1)	18 (29.0)
25 – 29.9	36 (63.1)	37 (59.7)
≥ 30	5 (8.8)	7 (11.3)
Gestational age, wk		
Median	38	38
IQR	36 – 40	37 – 40
Nullipara/Multipara, n	52 (91.2)/5 (8.8)	56 (90.3)/6 (9.7)
Current smoker, n	1 (1.8)	1 (1.6)
Education status, n †		
Middle school or below	30 (52.6)	34 (54.8)
College	23 (40.4)	25 (40.3)
Postgraduate	4 (7.0)	3 (4.9)
History of psychological interview, n		
Yes	8 (14.1)	6 (9.7)
No	49 (85.9)	56 (90.3)
Pregnancy education, n ‡		
Yes	36 (63.2)	42 (67.7)
No	21 (36.8)	20 (32.3)
Family economic status, n ¶		
Lower	5 (8.8)	4 (6.5)
Middle	41 (71.9)	45 (72.6)
Higher	11 (19.3)	13 (20.9)
Blood pressure, mmHg		
Systolic pressure	117 ± 12	122 ± 15
Diastolic pressure	72 ± 8	70 ± 9
Heart rate, beats per min	76 ± 6	74 ± 7
Respiratory rate, breaths per min	17 ± 2	16 ± 2
Oral temperature, °C	36.6 ± 0.3	36.8 ± 0.4

** Data are presented as mean ± standard deviation (SD) or number (%) if not indicated;*
† Middle school or below includes those received primary or/and advanced middle school education, and those received middle professional training education, and illiterate; college education includes those received formal undergraduate education and advanced professional training education; postgraduate includes those received master, doctorate or/and postdoctoral education.
‡ Pregnancy education refers to the gravida received education about pregnancy process, fetal development, knowledge of labor and delivery, and antenatal education;
¶ Family economic status calculated according to the overall family year incomes in CNY, lower means below 50,000, middle means between 50,000 to 150,000, and higher means over 150,000; CNY 700 ≈ USD 100.
IQR: interquartile range

*Table 3. Maternal and infant outcomes.**

Outcome	Non-psychological Visiting (n = 57)	Psychological Visiting (n = 62)	p value
SAS scoring (20 – 80) †			
Baseline	43 (38 – 56)	45 (36 – 59)	0.82
Posteriori intervention	41 (37 – 50)	28 (24 – 31) **	0.029
Prior operation	35 (31 – 40)	30 (25 – 34) **	0.004
Intra-operation	39 (36 – 46)	34 (27 – 36) **	0.04
Post-operation	28 (25 – 34)	22 (21 – 26)**	0.009
SDS scoring (20 – 80) ‡			
Baseline	48 (45 – 61)	44 (40 – 62)	0.48
Posteriori intervention	44 (40 – 52)	42 (38 – 49)	0.49
Prior operation	41 (38 – 47)	38 (34 – 42)	0.39
Intra-operation	43 (38 – 50)	40 (35 – 45)	0.37
Post-operation	36 (32 – 43)	32 (29 – 39)	0.50
Visiting time, min	21 (16 – 28)	53 (37 – 62)	0.008
Highest level of sensory block	T7 (T9 – T5)	T6 (T9 – T5)	0.81
Pre-anesthesia crystalloid, ml	822 ± 103	806 ± 126	0.87
Total fluid, ml	1,470 ± 185	1,330 ± 170	0.39
Bleed volume, ml	360 ± 75	380 ± 50	0.72
Urine volume, ml	160 ± 45	175 ± 60	0.75
Ephedrine usage, mg	14 ± 4	13 ± 4	0.77
Adverse event, n			0.039
Nausea/Retching	9 (15.8)	8 (12.9)	0.65
Vomiting	1 (1.8)	1 (1.6)	0.95
Fatigue	4 (7.0)	2 (3.2)	0.34
Dyspnea	6 (10.5)	3 (4.8)	0.24
Hypotension ¶	8 (14.0)	5 (8.1)	0.29
Vertigo	0	1 (1.6)	0.33
Mass bleeding	1 (1.8)	0	0.29
Infant outcomes			
Weight, g	3,100 ± 150	3,200 ± 100	0.39
Female/Male, n	26/31	28/34	0.96
One-min Apgar score	9 (9 – 10)	10 (9 – 10)	0.69
Five-min Apgar score	10 (10 – 10)	10 (10 – 10)	1.0
Umbilical cord blood gases, n			
Arterial pH < 7.20	5 (8.8)	2 (3.2)	0.19
Venous pH < 7.20	6 (10.5)	2 (3.2)	0.11
NBAS scoring (11 – 55) §	15 (13 – 23)	17 (12 – 25)	0.45

** Data are presented as median (interquartile range, IQR), mean ± standard deviation (SD) or number (%);*
† SAS refers to patient Self-rating Anxiety Scale with a 20 items scale; ‡ SDS refers to patient Self-rating Depression Scale with a 20 items scale; ¶ Hypotension is defined as systolic blood pressure (SBP) < 20% of baseline;
§ NBAS means Neurobehavioral Assessment Scale with an 11 items scale;
*** Indicates p<0.01 compared with the baseline; Bracket shows p<0.05 compared between the intra-operation and the post-operation.*

Cortisol secretion reached peaks intraoperatively in both groups, of which decreased significantly after the end of the surgery. Psychological visiting markedly reduced the production of cortisol than did the non-psychologicla one.

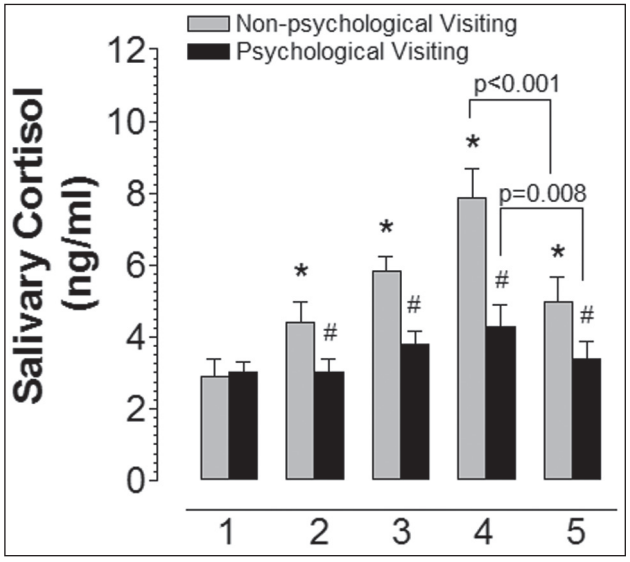

Figure 2. Salivary cortisol levels

Postoperative data are displayed in the Table 4. The rate of onset of lactation during the first 72 h after operation in the psychological subjects differed from that of the non-psychological ones (p = 0.004), but this difference tended to disappear six weeks later (p = 0.11). Besides, postoperative analgesia was significantly improved by the psychological visiting than the comparison, i.e. the interval of the first morphine request was prolonged (p = 0.016), 48 h morphine consumption was lessened (p = 0.02), and finally the overall pain intensity was ameliorated (p = 0.032). Patient's satisfaction with anesthesia in the psychological group was higher than that of the non-psychological group (p = 0.034). Moreover, the rate of urinary indwelling catheter > 24 h was considerably less in the psychological women than that of the non-psychological (p = 0.036). Nevertheless, no significant differences were found in the first time left from bed and the length of hospital stay between the two groups.

We concluded similar results when performing the ITT analyses on maternal and infant outcomes as were the PP analyses above.

Table 5 summarizes the association between the maternal demographic and background variables and the priori operative anxiolytic levels analyzed with multivariate logistic regression. We found that each one unit increase in age over 30 yr and BMI > 30, and nulliparous, postgraduate education, and lower and higher family economic statuses are positive factors that associated with anxiety (the adjusted ORs were 1.11, 1.47, 1.32, 1.62, 1.06 and 1.82, respectively; all ps < 0.05); and priori pregnancy education was negative factor that influences the priori operative anxiolytic level (OR = 0.31, 95% CI 0.11-0.73; P = 0.004). No significant association was detected between other demographic parameters and the level of priori operative anxiety in this study.

Table 4. Postoperative maternal outcomes

Outcome	Non-psychological Visiting (n = 57)	Psychological Visiting (n = 62)	p value
72 h Successful breastfeeding after Cesarean, n	21 (36.8)	39 (62.9)	0.004
Six-week breastfeeding, n	42 (73.7)	53 (85.8)	0.11
Overall postoperative pain intensity (VAS, 0 – 100 mm) *	35 (28 – 56)	22 (13 – 37)	0.032
Time interval of the first morphine request, h *	3.1 (2.5 – 3.9)	4.6 (3.8 – 6.8)	0.016
48-h Total morphine consumption, mg *	57.3 (45.3 – 71.2)	43.2 (39.8 – 50.1)	0.02
Overall satisfaction with Cesarean experience (VAS, 0 – 100 mm) *	88 (75 – 93)	94 (85 – 98)	0.034
Urinary indwelling catheter > 24 h, n	23 (40.3)	14 (22.6)	0.036
First time left from bed, day	1.8 ± 0.5	1.6 ± 0.4	0.62
LOS in hospital, day	3.4 ± 0.7	3.5 ± 0.9	0.89

Data are the means ± standard deviation (SD) or number (%) if not indicated.
** Refers to median and interquartile range (IQR), and is compared with Mann-Whitney U test.*
LOS: Length of stay in hospital after surgery

Table 5. Logistic regression to evaluate the association between the demographic characteristics and the priori operative anxiety levels

Variable	Coefficient	Standard Error	Simple OR (95% CI)	p value	Adjusted OR (95% CI) *	p value
Age (each 1-yr increase)						
≤ 30 yr	0.47	0.22	0.61 (0.35 – 1.83)	0.54	0.63 (0.40 – 1.89)	0.58
31 – 40 yr	0.63	0.59	1.07 (1.03 – 2.32)	0.041	1.11 (1.06 – 2.67)	0.03
> 40 yr	0.97	0.46	2.15 (1.74 – 3.80)	< 0.001	2.18 (1.81 – 3.89)	< 0.001
Height (each 1-cm increase)	0.55	0.48	0.74 (0.19 – 1.53)	0.35	0.75 (0.23 – 1.58)	0.39
BMI (each 1-unit increase)						
≤ 18.5	0.49	0.34	0.70 (0.46 – 1.82)	0.69	0.77 (0.52 – 1.93)	0.74
18.5 – 24.9	0.32	0.29	0.80 (0.65 – 1.47)	0.71	0.84 (0.73 – 1.48)	0.79
25 – 29.9	0.44	0.38	0.53 (0.39 – 1.08)	0.36	0.55 (0.43 – 1.12)	0.40
≥ 30	0.51	0.39	1.46 (1.15 – 1.87)	0.022	1.47 (1.18 – 1.90)	0.02
Nulliparous †	– 0.56	0.44	1.28 (1.05 – 2.15)	0.037	1.32 (1.13 – 2.21)	0.031
Current smoker †	– 0.27	0.51	0.54 (0.39 – 1.13)	0.12	0.54 (0.40 – 1.15)	0.16
Education status ‡						
Middle school or below	0.68	0.53	0.35 (0.24 – 1.06)	0.085	0.43 (0.26 – 1.14)	0.087
Postgraduate	0.40	0.27	1.59 (1.25 – 2.66)	0.004	1.62 (1.28 – 2.79)	0.003
History of psychological interview †	– 0.18	0.36	0.81 (0.57 – 1.39)	0.26	0.84 (0.57 – 1.42)	0.29
Pregnancy education †	– 0.43	0.38	0.36 (0.12 – 0.85)	0.005	0.31 (0.11 – 0.73)	0.004
Family economic status ‡						
Lower income	0.68	0.47	1.03 (1.01 – 1.35)	0.042	1.06 (1.02 – 1.49)	0.038
Higher income	0.53	0.40	1.78 (1.46 – 2.77)	0.011	1.82 (1.56 – 2.93)	0.009

** Odds ratios (ORs) are adjusted for other terms included in the model;*
† Binary variables are calculated by referring to following variable as the reference: "multiparous" for nulliparous, "no smoker" for yes smoker, "with prior psychological interview" for without history of psychological interview, "received pregnancy education" for no pregnancy education;
‡ "College education" and "middle income" are referred as the references for education and family economic statuses, respectively.

Discussion

This randomized, double-blind and controlled study provides evidence that preoperative psychoprophylactic visiting of the Cesarean parturients effectively ameliorates peri-surgical anxiolytic and stressful responses, and improves maternal outcomes: (i) anxiety level rated with SAS system was markedly alleviated after psychological intervention before Cesarean section; (ii) depressive ratings did not display any changes in both the psychological and non-psychological women; (iii) the secretion of salivary measures of cortisol was decreased by the psychological visiting during the study period; (iv) the total incidence of adverse events was lower in the psychological group than the comparison; (v) postoperative maternal variables such as the onset of lactation in the first 24 h, PCA analgesia request and morphine consumption, satisfaction with anesthesia, and urinary indwelling catheter > 24 h were superior in the psychological subjects to those of the non-psychological ones; (vi) multivariate logistic regression revealed that age over 30 yr, BMI > 30, nulliparous, postgraduate education, lower and higher family economic statuses, and priori pregnancy education are associated factors affecting the anxiolytic responses.

In the present study, we used two preoperative interventional programs that were defined as psychological and non-psychological visiting. The major difference between both methods is the contents included in the visiting leaflets and communication with the participants. In the psychological group, relatively detailed information on anesthesia, surgery, childbirth and after birthing

was given and discussed with them at length; besides, training on breathing and relaxation was performed, and how to deal with the complications and adverse events during study period was given. However, in the non-psychological group, information was delivered in narrative language, and without in-depth explanation and discussion on them; further, no training on breathing and relaxation was done. All these differentiated performance resulted in a longer visiting time for the psychological group (median, 53 min; IQR, 37 to 62 min) than the non-psychological control was (median, 21 min; IQR, 16 to 28 min). Some women in both groups had received beforehand information related with our visiting ones at home, and some even sought information which had been given during visiting time after planned interventions, while we had discussed these with participants for the importance prior to starting this trial to guarantee that they can adhere to the study protocol. To these women, we performed subgroup analyses upon their potential influence on our primary outcome, and found information obtained before entering hospital did not produce detectable influence on the outcome analyses (data were not shown). In addition, those who did not follow up the study protocol, i.e. sought and obtained information after visiting intervention, had been excluded during the PP analyses, but when their data were added and analyzed in the ITT manner, similar results were received as were the PP analyses.

Anxiety, the primary endpoint of this study, displayed considerable alleviation after preoperative psychological visiting by interventional nursing members in Cesarean patients. This was inconsistent with that explored in natural childbirth (22), during which antenatal psychological preparation did not improve the birth experience and decrease parental stress in early parenthood in nulliparous women. One major reason for this difference is likely to the long-lasting education before birthing makes pregnant women habituate what the educator might say, of which cannot really suppress anxiolytic responses when the birthing approaching. However, our short-term psychoprophylaxis given before Cesarean delivery answered questions raised by parturients and discussed them in detail of which built up a trusting relationship between gravidas and health-care professionals, which has been confirmed by a *post hoc*-visiting that women received psychological intervention had higher satisfaction with Cesarean birth and postoperative analgesia than those without psychological intervention. Additionally, Marucci and colleagues found that spinal anesthesia itself could decrease Cesarean alertness assessed with SAS and observer's assessment of alertness/sedation (OAA/S) gauges (23). Herein we also used spinal anesthesia for all participating subjects, of which might produce a synergic effect with psychoprophylaxis. Although so, we could not find detectable role for spinal anesthesia in alleviating anxiety in the non-psychological women.

Although antepartum depression is a psychological morbidity associated with adverse obstetric and neonatal outcomes (24), and can be treated with psychological methods (25), but we did not find any beneficial effect of psychological intervention on antenatal depression as concluded in a Cochrane systematic review (26).

Maternal psychological distress leads to dysregulation of the hypothalamic-pituitary axis (HPA) which results in elevated production of cortisol during pregnancy (27). In the present study, we measured salivary cortisol as the indicator of stressful responses, and found that psychological intervention can effectively decrease the production of cortisol in Cesarean women. Besides, the changing trajectory of cortisol in our trial was concert with as was the anxiety level, although correlation between them was not measured in this study with the exception of other reports in elsewhere that apparent non-linear relationship existed between cortisol level and anxiety, but not depression (28). An interesting finding in our trial was the levels of anxiety and cortisol in both groups markedly decreased after the conclusion of the surgical procedures, which indirectly reflects women undergoing Cesarean section have elevated psychological distress that may be evoked by the fear for Cesarean itself.

Cesarean section has been identified as a risk factor for delayed onset of lactogenesis with an OR of 2.40 (95% CI, 1.28 to 4.51) (29). Moreover, studies have shown that acute physical and mental stress can impair the milk ejection reflex which resulted in delayed onset of lactation (30, 31).We hereby observed the successful breastfee-

ding in the first 72 h after Cesarean delivery, and found that psychological intervention considerably increased the successful rate of breastfeeding than the non-psychological comparisons. In addition, all multiparous women in both groups and more primiparous women in the psychological group breastfed successfully after Cesarean section, which was concordant with previous report that nulliparous women had a higher risk of delayed onset of lactation with an OR of 3.16 (95% CI, 1.58 to 6.33) (29). Although 72 h onset of lactation was significantly different between both groups, no marked difference was observed on the rate of six-week breastfeeding in the two groups. Therefore, our data are backing up the previous results that effective strategies should be performed to alleviate Cesarean-related stressful and anxiolytic responses for reducing psychological distress-associated delay of lactogenesis.

As was Caumo and colleagues reported that anxiety and depressive mood were risk factors associated with postoperative pain intensity (32), so preventive strategies should be designed to relieve patient's suffering. In our trial, preoperative psychological intervention reduced postoperative pain intensity rated with VAS system, prolonged time interval of the first analgesic request, and spared the total consumption of morphine when compared with the non-psychological women. The role for psychological interventional language in postoperative analgesia has been confirmed previously that postoperative negative words but not positive words resulted in failure of postoperative PCA regimen after abdominal surgeries (33), and then, in further, the present study provided evidence that preoperative psychological preparation could enhance the analgesic effect of postoperative PCA after Cesarean section.

The total adverse events reported in our study and the numbers of patients with urinary indwelling catheter over 24 h were less in the psychological group than that of the control one, of which plus improved outcomes mentioned above seemed to be associated with the higher satisfaction with the Cesarean experience scored via a VAS gauge. In our investigation, we did not find considerable effect of the preoperative maternal psychological intervention on the infant outcomes and length of stay in hospital after Cesarean section.

Stress and anxiety are complex psychological morbidities affected by multiple internal and external factors (34). In our study, we further analyzed the association between maternal demographic variables and the anxiolytic level using multivariate logistic regression. Finally, we figured out that maternal age over 30 yr, BMI > 30, nulliparous, postgraduate education, and lower or higher family economic status were negative factors, and pregnancy education was a positive factor influencing maternal anxiolytic state. They should be considered when rating the psychological distress in women undergoing Cesarean delivery.

Several limitations on our study should be acknowledged before conclusion was drawn. First, participants were masked for group allocation, while it was still possible that they were aware of the group assignment because of the increasing popularity of preoperative education on natural birthing or/and Cesarean delivery and gravidas' avid involvement into antenatal educating classes. Second, we have chosen patient self-rated assessment of anxiety and depression, i.e. SAS and SDS, for psychological distress. These two measurements, to some points, merely give an overall understanding about the anxiolytic and depressive responses. Whether or not other gauges such as state-trait anxiety inventory (STAI) (35), anxiety sensitivity index (ASI) (36), and depression anxiety stress scale (DASS) (37) etc. were more reliable than SAS and SDS in the present studying context should be warranted further. Third, although we investigated the correlationship between maternal demographic variables and anxiety level, we did not perform further analyses if there were association among each risk factor, the preoperative psychological intervention and anxiolytic level. Thus further studies are needed to clarify these points in the context of Cesarean delivery,

In conclusion, preoperative psychoprophylactic visiting for Cesarean patients by trained expert nurses alleviates maternal anxiolytic and stressful levels but not depression, decreases incidence of adverse events and risk of delayed onset of lactogenesis, improves postoperative analgesia with PCA technique, and increases overall satisfaction with Cesarean experience. Further clinical investigations are necessary for confirming our findings.

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The smoking behavior and affecting factors of physical education and sports teachers in Turkey

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Abstract

Aim: This study aims to examine the attitudes and affecting factors of physical education and sports teachers towards smoking.

Methods: Among a total of 20,074 permanent and contract physical education and sports teachers, 2000 (10%) working in various schools located in different cities in Turkey affiliated with Ministry of National Education during the school year of 2010-2011 were selected using "random sampling method". After necessary permissions were granted, an online questionnaire prepared by the researchers was used to collect data, by which 1995 teachers were contacted.

Results: The responses of the 1995 (1345 male, 650 female) teachers that filled in the questionnaire form were evaluated. The mean age was 31.02±4.72 (n=1992). 88.3% of the participants smoked only once during their entire lives. 53.4% smoked everyday, while 11.8% smoked occasionally (n=1990). Gender did not create a statistically significant difference between smoking and non-smoking teachers (n=1990, $p>0.05$). For both gender groups, the majority of smokers started between the age of 16-20. When smoking behavior was analyzed on the basis of age, it was found that the 26-40 age group had the highest smoking rate. When the participants were asked about the primary factors affecting smoking behavior, the response was friends for 38.7% and pretension for 22.1%. A negative relationship was observed between the level of mother's education and smoking ($p<0.05$). Male teachers had higher cigarette dependence scores than females ($p<0.05$).

Conclusion: This study suggests that physical education and sports teachers, who are supposed to be a role-model for their students, have a high smoking rate. An urgent action plan is needed to reduce the smoking rate and to increase the quit rate among physical education and sports teachers.

Key words: Cigarette, Physical Education and Sports Teachers, Habit, Attitude

Introduction

Nicotine in cigarettes is an unhealthy substance that could cause addiction in a short period of time, turn into an economic burden and affect the organism negatively because of the harmful ingredients it contains (1). Cigarette (tobacco) is the most commonly used addictive in the world, and 70% of quitters restart smoking within three months (2).

Cigarette dependency is an important public health issue that requires taking urgent and effective measures because of its harmful effects on human health (3).

While there is a downward trend in smoking rates (tobacco use) in developed countries, the opposite is the case for developing countries. There are 1.2 billion smokers aged over 15 in the world, 80% of which reside in developing countries. As well as being the most important preventable cause of death, smoking (tobacco use) is also the leading cause of premature death in Turkey. There are around 20 million smokers in Turkey, and Turkey ranks 10th in the list of countries with highest rate of tobacco use. In developing countries, smoking (tobacco use) is typically a male behavior, and the smoking rate is quite high among men (even above 50%) and quite low among women (generally below 20%) (4).

According to the " Family Structure Research" conducted by Turkish Statistics Institute in 2006, 33.4% of the individuals aged 18 and over are smokers in Turkey. The smoking rate is 50.6% among men and 16.6% among women (5).

The negative effects of passive smoking make smoking all the more important. The WHO has characterized smoking as the "most rapidly spreading and long-lasting epidemic in the world". According to data provided by the WHO, tobacco causes 5 million deaths every year. With the pre-

sent upward trend in the smoking rate around the world, it is expected that smoking will cause more than 8 million deaths every year by 2030 (4).

Smokers generally start smoking before the age of 18 (6). Taking the behavior of adults as example play a major role in the smoking behavior of adolescents (7). It was found that smoking rate is higher among students, and the students are more likely to start smoking in schools where smoking rate is also high among teachers (8).

Poulsen et al. emphasize how important anti-smoking campaigns addressing teachers as well as banning smoking within school premises are for creating smoke-free schools (9).

Physical education and sports is devoted to maintaining and improving health. It is important that the physical education and sports teachers understand the importance of health themselves before they share their knowledge with students (10). Smokers get tired more easily during exercise and tend to stop earlier (11).

Teachers play an important role in reducing smoking rate in the society, but physical education and sports teachers in particular are all the more responsible since smoking and sports do not mix (12).

This study aims to identify the smoking behavior and affecting factors of physical education and sports teachers in Turkey, who play an important role in the education of the young by serving as a role-model.

Materials and methods

This is a cross-sectional descriptive study that aims to identify the smoking behavior and affecting factors of physical education and sports teachers in Turkey. Among a total of 20074 permanent and contract physical education and sports teachers, 2000 (10%) working in various schools located in different cities in Turkey affiliated with Ministry of National Education during the school year of 2010-2011 were selected using "random sampling method". 1995 teachers were contacted in total.

After necessary permissions were granted, the participating teachers were asked to fill in an online questionnaire developed by the researchers in light of the existing literature on the subject, consisting of questions that identify the participants' demographic characteristics and opinions about smoking as well as determine their level of cigarette dependency (Fagerström Nicotine Dependence Scale). The collected data were processed using SPSS software package and were subjected to percentage, mean, chi-square (X^2) analyses, depending on the variable in question. In this study, mean values in are presented with standard deviation, and $p<0.05$ was taken to indicate statistical significance.

Results

Among all the participating physical education and sports teachers, 67% were male and 32.6% were female. The mean age was 31.02±4.72 (n=1992). 49.9% were married. 88.3% smoked only once during their entire lives. 71.4% smoked at least 100 cigarettes during their entire lives. 53.4% of the participating teachers were regular smokers, while 11.8% smoked occasionally (n=1990). 34.8% (n=1990) were non-smokers.

The mean age that the teachers smoked for the first time was 16.59±2.89 (min.2, max. 30). 16-20 was the age group that both male and female teachers started smoking the most.

Table 1 shows the distribution of the smoking status of physical education and sports teachers across genders (n=1990, $p>0.05$).

When the participants were asked about the factors affecting their smoking behavior, the response was peer influence for 38.7%, pretension for %22.1, mental distress for 10.5%, curiosity for

Table 1. The distribution of the smoking status of physical education and sports teachers across genders

Gender	Smoker		Non-Smoker		Total	Missing	Grand Total	
	n	%	n	%	N	n	n	%
Female	422	32.5	227	32.8	**649**	1	650	32.6
Male	876	67.5	465	67.2	**1341**	4	1345	67.4
Total	1298	100	692	100	**1990**	5	1995	100

p=0.895
(p>0.05)

8.0%, adapting to social environment for 6.2%, pleasure received from smoking for 6.2%, stress for 4.0%, desire to look cool for 2.8%, and smoking parents for 0.5%.

A negative relationship was observed between the level of mother's education and smoking rate among teachers ($p<0.05$). It was found that the age of starting smoking increases as the parents' level of education gets higher ($p<0.05$).

When the smoking behavior of physical education and sports teachers was analyzed from the point of view of age, it was found that the teachers aged between 26-40 smoked more. (Table 2).

A statistically significant relationship was observed between cigarette dependence scores and gender. It was found that male teachers had higher cigarette dependence scores compared to female teachers (Table 3).

The distribution of the opinions of physical education and sports teacher about smoking across genders is shown in Table 4.

91.5% of female physical education and sports teachers indicated that they tried quitting smoking because of its harmful health effects, while 87.5% did so because smoking may affect their health negatively in the future. Among male physical education and sports teachers, 92.9% tried quitting smoking because smoking may affect their health negatively in the future, while 88.8% did so because its harmful health effects (Table 5).

Table 2. The distribution of the smoking status of physical education and sports teachers across age groups

Age group	Smoker			Non-smoker			Total	Grand Total	
	N	Grp%	Gen%	N	Grp%	Gen%	N	N	%
21-25	64	4.9	3.2	77	11.0	3.9	141	1995	7.1
26-30	640	49.3	32.1	298	42.8	14.9	938	1995	47.0
31-35	377	29.0	8.7	204	29.3	10.2	581	1995	29.1
36-40	177	13.6	18.9	83	11.9	4.2	260	1995	13.0
41-45	32	2.5	8.9	29	4.2	1.5	61	1995	3.1
46-50	6	0.5	1.6	3	0.4	0.2	9	1995	0.5
51-55	1	0.1	0.3	1	0.1	0.1	2	1995	0.1
56-60	1	0.1	0.1	2	0.3	0.1	3	1995	0.2
	1298	100.0	65.1	697	100.0	34.9	1995	1995	100.0

p=0.00 (p<0.05)

Table 3.

Cigarette dependence score	Gender					
	Male		Female		Grand total	
	N	%	N	%	N	%
0	134	15.1	113	26.1	247	18.7
1	162	18.2	73	16.9	235	17.8
2	152	17.1	62	14.3	214	16.2
3	101	11.4	50	11.5	151	11.4
4	48	5.4	30	6.9	78	5.9
5	69	7.8	36	8.3	105	7.9
6	51	5.7	24	5.5	75	5.7
7	95	10.7	29	6.7	124	9.4
8	59	6.6	14	3.2	73	5.5
9	17	1.9	2	0.5	19	1.4
Missing	-	-	-	-	674	-
Total	888	100.0	433	100.0	1995	100.0

p=0.00 (p<0.05)

Table 4. The distribution of physical education and sports teacher's opinions about smoking across genders

Variables	Sub-variables	Gender						
		Male		Female		Grand Total		
		n	%	N	%	n	%	p
I think the teachers who smoke in front of their students set a bad example for them.	**Strongly disagree**	10	0.7	4	0.6	14	0.7	**0.034**
	Disagree	29	2.2	7	1.1	36	1.8	
	Undecided	12	0.9	3	0.5	15	0.8	
	Agree	88	6.5	64	9.8	152	7.6	
	Strongly Agree	1206	89.7	572	88.0	1778	89.1	
	TOTAL	1345	100.0	650	100.0	1995	100.0	
I think the students would be encouraged to smoke if their physical education and sports teacher is also a smoker.	**Strongly disagree**	15	1.1	9	1.4	24	1.2	**0.423**
	Disagree	73	5.4	38	5.8	111	5.6	
	Undecided	28	2.1	21	3.2	49	2.5	
	Agree	195	14.5	82	12.6	277	13.9	
	Strongly Agree	1034	76.9	500	76.9	1534	76.9	
	TOTAL	1345	100.0	650	100.0	1995	100.0	
I think physical education and sports teachers smoke more than other teachers.	**Strongly disagree**	129	9.6	47	7.2	176	8.8	**0.000**
	Disagree	117	8.7	39	6.0	156	7.8	
	Undecided	144	10.7	52	8.0	196	9.8	
	Agree	285	21.2	107	16.5	392	19.6	
	Strongly Agree	670	49.8	405	62.3	1075	53.9	
	TOTAL	1345	100.0	650	100.0	1995	100.0	

Table 5. The distribution of physical education and sports teachers' reasons for trying to quit smoking across genders

Reasons for trying to quit smoking		Female		Total	Male		Total	Missing	Grand Total	
		Yes	No	N	Yes	No	N	N	N	%
Illness	n	17	331	348	32	673	705	942	1995	52.8
	%	4.9	95.1	100.0	4.5	95.5	100.0	47.2	-	-
Economic costs	n	177	174	351	355	365	720	924	1995	53.7
	%	50.4	49.6	100.0	49.3	50.7	100.0	46.3	-	-
Harmful health effects	n	325	30	355	653	89	742	898	1995	55.0
	%	91.5	8.5	100.0	88.0	12.0	100.0	45.0	-	-
Harmful effects on the health of friends and family	n	107	241	348	302	395	697	950	1995	52.4
	%	30.7	69.3	100.0	43.3	56.7	100.0	47.6	-	-
Negative effects on health in the future	n	307	44	351	650	50	700	944	1995	52.7
	%	87.5	12.5	100.0	92.9	7.1	100.0	47.3	-	-

Discussion

Of all participants, 67.0% were male, while 32.6% were female. The mean age was 31.02±4.72 (n=1992). 49.9% were married.

65.2% of the participatants (n=1990) were still smokers at the time of study. 53.4% were smoking regularly, while 11.8% were smoking occasionally. In a study conducted in Manisa, it was found that 40.7% of the high school teachers were smoking regularly, and 17.4% were smoking occasionally (13). Using a questionnaire, Turgut et al. found that smoking rate among teachers was 42.2% (14). As for other countries, the smoking rate among high school teachers was found to be 37.2% in Spain, 44.7% in Japan, 33% in Romania, 20% in Malaysia, and 21.4% in India. In Estonia, smoking rate was found to be 40% and 11% for

male and female teachers respectively. In Italy, smoking rate was found to be 35% and 30% for male and female teachers respectively (15).

Several studies conducted in Elazığ, Manisa and Sivas show that smoking rate varies between 51.3% to 83.1% among male teachers and between 16.9% and 54.0% among female teachers (16). These figures resemble the smoking rate suggested by the present study: 67.2% among male teachers and 32.8% among female teachers. While the smoking rate among male teachers was found to be higher than the smoking rate among female teachers, no statistically meaningful relationship was observed between gender and smoking rate. The findings of this study also suggest that the smoking rate among female teachers increase as the level of education gets higher.

The mean age of trying smoking was found to be 16.59±2.89 (min.2, max. 30). The age group that the participants started smoking the most was 16-20 for both gender groups.

Studies show that the majority of students start smoking during high school or college (17).

In this study, when the teachers were asked about their reasons for starting smoking, the most common responses were peer influence (38.7%), pretension (22.1%), mental distress (10.5%), curiosity (8.0%). In a study conducted by Ögüs et al., it was found that students' reasons for starting smoking were curiosity (32%), stress (23%), pretension (19%), desire to look more mature (18%) in the order of decreasing frequency. The popularity of a student at school increases the risk of smoking (18).

It was seen that the age of starting smoking increased, while the parents' level of education got higher ($p<0.05$). Studies conducted in the USA show that there is a relationship between smoking and social class. The smoking rate was found to be lower in groups with higher income levels (19).

In a study conducted by Şahin et al. with the participation of students of faculty of medicine, the mean Fagerström nicotine dependence score was found to be 3.57±2.37 and thus indicated a low degree of dependence. The mean Fagerström nicotine dependence score was 3.04±0.07 in our study, and the score was higher among male teachers.

The rate of those who agreed with the statements that the "teachers who smoke in front of students set a bad example for them" and "physical education and sports teachers smoke more than other teachers" were higher among female teachers ($p<0.05$). Adolescents are affected by their school environments and teachers who serve as their role-models (21).

When physical education and sports teachers were analyzed on the basis of the reasons for quitting or trying to quit smoking, the response was harmful health effects for 91.5% of the female teachers and 88.8% of the male teachers. 87.5% of the female teachers and 96.9% of the male teachers quit or tried to quit smoking because they thought it could affect their health negatively in the future. In a study conducted by Açıkel et al., the most common reason for quitting smoking was found to be "harmful health effects" (71.9%), followed by "economic reasons" (56.3%) (22).

In conclusion, it was observed that smoking is still a very import problem among physical education and sports teachers. General education programs for all teachers as well as anti-smoking programs for smoking teachers in particular are needed in order to ensure that as role-models for students at school teachers are healthy themselves in the first place.

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Growth and Nutritional Status of Children and Adolescents from 7 to 19 Years of Age in the Town of Jagodina (Central Serbia)

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Abstract

Introduction: Growth and nutritional status are influenced by genetic and external factors. The nature and intensity of influence of these factors vary in population groups. Surveillance of the nutritional status of children and adolescents is of great importance since these are the critical periods for the development of obesity which may adversely affect health in their later life.

Aim: The aim of the study was to investigate growth status and the prevalence of overweight and obesity in children and adolescents aged 7-19 years, from the town of Jagodina - Central Serbia.

Material and methods: The tested group consisted of 1044 individuals, 514 schoolboys and 530 schoolgirls aged 7-19 years. The research focused on height and body weight as well as body mass index (BMI). The demographic factors included parents' level of education and number of children per family. The height and body weight were assessed on the basis of criteria set by WHO (1983), while NHANES I and IOTF were used for assessing the nutritional status. The relation between demographic factors and obesity was set by logistic regression analysis.

Results: The results show that the overall rate of small height is approximately 17%, malnutrition is present in 19% of children and excessive body weight is recorded in 16% of the subjects. In both sexes the overall prevalence of overweight and obesity is 10.8% and 5.6%, respectively. The results of prevalence of overweight and obesity obtained by two different criteria show discrepancy only regarding the prevalence of overweight males.

Conclusion: Although the results indicate that there is no excess of small height, malnutrition and overweight over that which would be expected in a population with a normal distribution of these traits, there is still a need for constant monitoring of growth and nutritional status in order to offer the public information on the number of children with potential health problems.

Key words: Body Mass Index, Growth status, Nutritional status, Obesity, Overweight

Introduction

Growth and nutritional status of children and adolescents are determined by anthropological characteristics. Among these, height and body weight are the traits that are most frequently used for assessing the growth and nutritional status. These traits are often indirect indicators of health status and living conditions of individuals and entire populations. The growth of children and adolescents is a complex process influenced by both genetic and environmental conditions. Although genetic inheritance has a decisive influence on growth patterns, there is evidence that numerous social, demographic, economic and life style factors are also important. Normal growth during the period of puberty may be seriously affected by physical activity or inactivity (1). The nature and intensity of influence of these factors vary in population groups from region to region. The variability in the growth of children and adolescents noticeably indicates differences in environmental quality. A positive correlation between high living standard of parents and many of the anthropometric traits has been reported (2,3). A large-scale study conducted in the region of Vojvodina-North Serbia (4) has shown that parents' level of education and per capita income are most influential factors on children's growth. The study

has also indicated that father's level of education is the most dominant factor since it influences the anthropometric traits in all ages. A permanent measuring of height and weight and determining their ratio, i.e. body mass index (BMI) is very important for monitoring children and adolescents' growth and development (5). Variations in BMI of children and adolescents are indicators of developmental changes during the period of childhood and adolescence (6). Since obesity has become an epidemic in many parts of the modern world a continual monitoring of nutritional status is of great importance. Most of the studies on nutritional status have focused on adult population so far. Children and adolescents have mostly been out of focus due to the lack of comparable representative data, and the use of varying criteria for defining obesity among different countries and researches (7). Childhood and adolescence have been proposed as critical periods for the development of obesity (8). The prevalence of overweight and obesity in children and adolescents is increasing worldwide (9), even in the countries with a high prevalence of underweight, stunting and wasting (10). Obesity in children is a public health problem as it may adversely affect health in their later life (11). An investigation in the city of Novi Sad (Serbia) has shown that the metabolic syndrome prevalence is increasing and that it is directly related to the obesity level in children (12). By preventing obesity it is possible to mitigate a number of mass non-infectious diseases and childhood appears as the most suitable period for the prevention (13). The studies on nutritional status conducted in Serbia have pointed to an increase of obesity in children and adolescents. However, these studies have included only certain geographical regions and not the whole territory of the country. The largest studies so far have been conducted in the north of Serbia, the region of Vojvodina and certain districts of this region. In North Backa district (14) obesity was detected in 6.9% of boys and 6.7% of girls in the period 1995-2002. The studies including subjects from 7 to 18 years of age coming from larger urban areas in the region of Vojvodina (4) recorded the prevalence of obesity in 4.50% of boys and 4.22% of girls, while in South-East Serbia (15) the prevalence of obesity in urban children aged 6-7 was 6.3% in boys and 3.8% in girls, and in rural boys and girls it was 1.1% and 3.3%, respectively.

The aim of this study was to investigate growth status and the prevalence of overweight and obesity in children and adolescents aged 7-19 years from the town of Jagodina, situated in Central Serbia.

Material and methods

A cross-sectional anthropometric study was carried out from March to May 2011. The investigation was performed in Jagodina, a city and municipality located in central Serbia, 136 km south of Belgrade. It is the administrative centre of the Pomoravlje District of Serbia. Applying the random sample method, 2 primary and 2 secondary schools, all located in the city centre, were chosen for this investigation.

The tested group consisted of 1044 individuals, 514 schoolboys and 530 schoolgirls aged 7-19 years. The mean age of boys in the sample was 12.6±3.6 years and of girls 12.8±3.6. For each examinee a decimal age was calculated out of the date of examination and the date of birth.

All anthropometric measurements were carried out by a trained interviewer - a professional specialised both in anthropometry and interviewing subjects, and using specialist GPM Anthropological Instruments for Somatology and Osteology (Sieber Hegner Maschinen AG Zürich, Switzerland). The participants were lightly dressed and without shoes, and were measured in the morning hours. Body height was measured with an anthropometer in the standing erect position, to the nearest 1 mm. Body weight was measured on an electronic digital scale with an accuracy of up to 0.1 kg.

Growth status was assessed by percentile values recommended by WHO (16). The height results were classified in the following way: small height for age $\leq P_{15}$, normal height for age $> P_{15} < P_{85,}$ high height for age $\geq P_{85.}$ As for the weight, the categorization also included three groups: small weight for age $\leq P_{15}$, normal weight for age $> P_{15} < P_{85,}$ overweight for age $\geq P_{85.}$ The nutritional condition was assessed according to reference values of BMI representing the ratio between body weight and body height squared (BMI kg/m^2). The recommendations of the National Health and Nutrition Examination Survey I were applied (NHANES I), according to which the risk for overweight and obesity is represented by BMI values from 85-95th percentiles

and ≥ 95th percentile, respectively (17). The risk for significantly underweight is represented by BMI ≤ P_5, for mildly underweight BMI > P_5 ≤ P_{15} and normal weight is represented by BMI > P_{15} < P_{85}. The assessment of the prevalence of overweight and obesity also relied on International Obesity Task Force (IOTF) references (18) which developed definitions of overweight and obesity based on BMI centile curves that passed through the adult cut-off points of BMI 25 kg/m^2 and 30 kg/m^2.

Among demographic factors, parents' level of education and number of children in the family were analysed. The level of education was classified into the following categories: primary education (eight years of schooling), secondary education (twelve years of schooling), higher education (fourteen years of schooling) and university education (sixteen years of schooling).

Measurements were analysed with the use of the program SPSS for Windows version 10 applying standard statistical methods. The differences between sexes were tested by t-test, while Chi-squared test was used to determine the differences in the prevalence of overweight and obesity. The level of correlation between demographic factors and anthropological characteristics was assessed by Pearson's coefficient of mutual relation. The relation between demographic factors and obesity was assessed by logistic regression analysis, the level of significance being $p<0.05$, $p<0.01$.

All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

Results

Table 1 presents demographic characteristics of the tested group. The largest number of subjects' parents are with secondary education, followed by those with a university degree. On the whole, the number of mothers with higher education is greater than in fathers. The smallest percentage of the parents are those with primary education. In most of the cases, the families are with two children, while the number of those with three children is greater than the number of families with only one child. Approximately 4% of the families are with four children and five or six children per family are found in minor percents.

Table 1. Demographic characteristics of the participants

	Boys		Girls	
	N	%	N	%
Father`s level of education				
Primary	15	2.91	24	4.52
Secondary	367	71.26	373	70.24
High	29	5.63	31	5.84
University	103	20.04	102	19.24
Mother`s level of education				
Primary	22	4.27	32	6.03
Secondary	316	61.36	326	61.39
High	69	13.40	76	14.31
University	107	20.81	96	18.11
Number of children in the family	N		%	
1	151		14.44	
2	645		61.78	
3	198		18.93	
4	44		4.21	
5	4		0.38	
6	2		0.19	

The height ranges from 127.29cm in 7-year old boys to 179.98cm in 19-year old males. As for girls, the height spans from 126.98 to 164.38cm (Table 2). Comparing boys and girls, no significant differences are observed at youngest age. However, at the age of 10 and 11, with entering the puberty phase, girls are with greater height than boys, this difference being significant only for the age of 10 ($p<0.01$). At the age od 12 and 13, girls and boys are again of similar height. Finally, at the age of 14 when boys enter the puberty phase, they are of greater height than girls, this difference being significant from the age of 15 ($p<0.01$).

The weight distribution is very similar to the distribution of height (Table 2). No significant differences are observed till the age of 10. Slightly higher values are recorded in girls of the age 10 and 11, but significant differences appear from the age of 14 when considerebaly higher values are recorded in boys ($p<0.01$). The means of BMI (kg/m^2) are mostly identical in both sexes, with an exception of two oldest age groups in which boys exhibit considerably higher values than girls ($p<0.05$; $p<0.01$).

Table 2. Mean values and standard deviations (SD) for height, weight and BMI for each age group in boys and girls

	Height			Weight		BMI	
	N	Mean	SD	Mean	SD	Mean	SD
Boys							
Age							
7	16	127.29	7.01	27.43	6.79	16.73	2.81
8	54	129.96	4.88	29.03	5.17	17.12	2.54
9	57	136.59	5.92	33.51	8.37	17.79	3.20
10	62	140.20	6.47	36.10	8.98	18.17	3.30
11	50	146.69	7.11	41.62	11.58	19.13	3.86
12	29	152.35	7.22	45.69	10.52	19.51	3.30
13	37	157.12	7.35	51.92	10.57	20.94	3.55
14	30	166.15	7.54	60.00	10.95	21.60	2.80
15	34	171.79	9.36	61.98	12.24	20.89	3.30
16	42	177.74	6.88	71.58	21.93	22.65	6.66
17	40	178.65	7.27	74.48	21.60	23.31	6.75
18	34	179.03	5.66	77.68	21.25	24.31	7.06
19	29	179.98	8.25	75.44	9.17	23.37	3.08
Girls							
7	17	126.98	5.96	27.88	5.93	17.21	3.04
8	56	130.25	5.73	29.75	6.22	17.43	2.87
9	55	134.72	7.35	31.59	8.37	17.17	2.86
10	62	143.35	6.14	38.60	9.74	18.60	3.62
11	41	148.39	8.63	42.53	11.70	19.07	3.88
12	34	152.39	6.85	45.56	10.90	19.45	3.59
13	37	158.31	7.41	50.54	12.30	20.00	3.82
14	33	162.69	7.40	54.31	11.93	20.41	3.52
15	38	164.10	6.76	57.16	9.67	21.15	2.89
16	48	163.23	5.61	55.89	6.52	20.98	2.20
17	43	164.85	5.53	62.02	9.95	22.85	3.79
18	37	165.99	5.83	59.41	8.14	21.58	2.84
19	29	164.38	6.02	57.37	7.10	21.20	2.08

Table 3. Growthand nutritional status distribution according percentile values

Variable Level	Boys (%)	Girls (%)	Total (%)
Height-for-age			
Small height	17.20	16.64	16.92
Normal	69.37	69.92	69.64
High	13.43	13.43	13.43
Weight-for-age			
Underweight	20.96	21.02	20.99
Normal	66.81	64.41	65.61
Overweight	13.22	14.56	13.89
Nutritional status (BMI)			
Significantly underweight	8.75	10.19	9.47
Mildly underweight	9.92	9.43	9.67
Normal	66.54	61.89	64.21
Overweight	8.86	12.74	10.80
Obese	5.80	5.41	5.60

The growth and nutritional status, assessed by percentile values and the WHO categorization, indicate that the majority of boys and girls (approximately 69%) are with normal height values. Small height is observed in 17% of subjects, while 13% of them are characterized by high height values. The applied weight categorization also shows that most of the subjects are of normal weight for their age. Small weight is recorded in 21% of boys and girls, while 14% of them are in the category of overweight. The BMI categorization indicates that the majority of schoolchildren are with normal nutritional status. Approximately 9% of the subjects are significantly underweight, and nearly 6% of boys and girls fall into the category of obese (Table 3).

Distribution of overweight and obesity in boys according to the reference values of NHANES I and IOTF can be seen in Table 4. The categorization points to an unequal distribution of overweight boys at certain ages. A higher prevalence of overweight is obtained on the basis of IOTF cutoff values. According to the reference values of NHANES I standard, 8.9% of boys are overweight. However, a significantly higher prevalence of overweight (22.03%) is observed when the IOTF criterion is applied (χ^2=22.426; p<0.01). The prevalence of

Table 4. Distribution of overweight and obesity according reference values of NHANES I and IOTF in boys

Age	NHANES I overweight		NHANES I obesity		IOTF overweight		IOTF Obesity	
	N	%	N	%	N	%	N	%
7	-	-	2	12.50	1	6.25	2	12.5
8	5	9.09	3	5.45	5	9.09	6	10.91
9	4	6.90	3	5.17	10	17.24	3	5.17
10	3	4.84	4	6.45	10	16.13	5	8.06
11	6	11.76	5	9.80	11	21.57	4	7.84
12	3	10.34	-	-	11	37.93	-	-
13	7	18.92	2	5.41	12	32.43	2	5.40
14	4	13.33	1	3.33	10	30	1	3.33
15	5	14.71	-	-	7	20.58	1	2.94
16	3	7.14	4	9.52	6	14.28	3	7.14
17	2	5.00	2	5.00	6	15	2	2
18	1	2.91	2	5.88	6	17.65	2	5.88
19	3	10.34	2	6.89	9	48.27	1	3.44
Total	46	8.9	30	5.80	104	22.03	32	5.74

Table 5. Distribution of overweight and obesity according reference values of NHANES I and IOTF in girls

Age	NHANES I overweight		NHANES I obesity		IOTF overweight		IOTF Obesity	
	N	%	N	%	N	%	N	%
7	2	11.76	2	11.76	2	11.76	4	23.53
8	7	13.21	4	7.55	9	16.98	7	13.21
9	7	12.28	2	3.51	10	17.54	4	7.01
10	13	21.67	3	5.00	20	33.33	3	5.00
11	5	11.63	4	9.30	6	13.95	4	9.30
12	3	8.82	2	5.88	5	14.70	2	8.33
13	3	8.11	1	2.70	8	21.62	1	2.70
14	4	12.12	1	3.03	4	12.12	1	3.03
15	5	13.51	1	2.70	7	18.42	-	-
16	5	10.42	-	-	5	10.42	-	-
17	9	20.93	4	9.30	11	25.58	1	2.32
18	4	10.81	1	2.70	5	13.51	-	-
19	3	10.34	2	6.89	-	-	-	-
Total	70	12.74	27	5.41	92	16.15	27	5.72

obesity assessed on the above criteria indicates an equal distribution at certain age groups, while considering the total sample, a uniform prevalence of obesity can be observed (approx. 6%).

As it is the case with boys, a slightly higher prevalence of overweight (Table 5) is also observed in girls, applying the IOTF cutoff values. These variations, however, are marginal, and no significant differences are recorded when the total sample is concerned. At some ages almost identical values are obtained and on the whole, the prevalence of obesity is higher than 5%.

The values of Pearson's coefficients of correlations between demographic and anthropological characteristics are shown in Table 6. In both sexes a significant positive correlation is observed between the anthropological traits and the parents' level of education. The level of parents' education negatively correlates with the number of children per family. Fathers' education shows a positive correlation with the height of both boys and girls, and to a lesser extent, it positively correlates with the girls' weight. The number of children per family negatively correlates with the boys' BMI. In both sexes, the weight shows a highly positive correlation with both height and BMI values.

Considering the demographic factors analyzed in this research, only the number of children per family has an influence on both male (OR: 0.722; CI: 0.534-0.798) and female (OR: 0.727; 95% CI: 0.541-0.978) obesity. The parents' level of education shows no effect on the subjects' obesity.

Table 6. Pearson coefficients of correlations between demographic and anthropological characteristics

	Father`s level of education	Mother`s level of education	Number of children in the family	Height	Weight	BMI
Males						
Father`s level of education	1.000	0.505**	-0.145**	0.127**	0.073	0.012
Mother`s level of education		1.000	-0.220**	0.080	0.074	0.049
Number of children in the family			1.000	-0.083	-0.082	-0.139**
Height				1.000	0.836**	1.000
Weight					1.000	0.878**
BMI						1.000
Females						
Father`s level of education	1.000	0.568**	-0.149**	0.136**	0.100*	0.085
Mother`s level of education		1.000	-0.158**	0.058	0.011	-0.043
Number of children in the family			1.000	0.028	-0.007	-0.054
Height				1.000	0.860**	0.509
Weight					1.000	0.867**
BMI						1.000

** *Correlation is significant at the 0.01 level*

* *Correlation is significant at the 0.05 level*

Table 7. Logistic regression analysis between parents education, number of children in the family and obesity

Variable	Beta	SE	OR	p	95.0% CI	
					Lower	Upper
Males						
Father education	-0.249	0.246	0.780	0.312	0.481	1.263
Mother education	0.073	0.219	1.076	0.738	0.700	1.653
Number of children in family	-0.325	0.155	0.722	0.035	0.534	0.798
Females						
Father education	-0.155	0.260	0.856	0.551	0.514	1.426
Mother education	-0.391	0.235	0.676	0.096	0.427	1.072
Number of children in family	-0.318	0.151	0.727	0.035	0.541	0.978

Discussion

In Serbia, more comprehensive researches of growth and nutritional status of children and adolescents have been conducted only in certain geographical regions of the country. Larger-scale researches have been mostly carried out in the north of Serbia, the region of Vojvodina, (4,19), as well as in certain parts of this region (14). Central parts of Serbia, however, have rarely been included in investigations of this kind. Therefore, the main objective of the present study was to explore the growth and nutritional status of children and adolescents from central Serbia, in order to establish similarities and differences within the population of this age coming from other parts of Serbia and the world. Bearing in mind that socioeconomic factors have an impact upon children's growth and development, the study included certain demographic factors such as parents' level of education and number of children per family in order to examine the extent to which these factors influence the subjects' growth and nutritional status.

The obtained results show that at youngest age the height and weight values recorded in this study are very similar, considering different sexes. Differences between boys and girls are noticeable at the age of 10 and 11, when entering pubertal phase, girls are characterised by higher height than boys. A study conducted in the region of Vojvodina (4) has pointed to differences between sexes from the age of 9 to 13, with higher values also recorded in girls. This study, however, has shown considerably smaller differences between boys and girls during the pubertal period of girls. More noticeable differences appear at the age of 14 and 15 when boys exhibit much higher height and weight values than girls of the same age. Comparing the obtained height and weight means with adequate results of recent studies conducted in Vojvodina region (4), it can be concluded that boys and girls living in these two regions of Serbia are characterized with rather similar height and weight values. From the age of 12, slightly higher values are noticed in schoolchildren of Vojvodina, but the differeneces are statistically insignificant. A further comparison of the height results suggests that 18 and 19-year old adolescents from Jagodina have similar height to Slovenian adolescents (20), while they are taller in comparison with the same age populations from Hungary (21), Spain (22) and India (23).

A relative increase in height suggests that there is no significant increase of height after the age 15 in girls and 17 in boys, a phenomenon observed in earlier studies as well (4). The height of both boys and girls positively correlates with fathers' level of education, a result already reported in studies conducted in Serbia (4).

The percentile values indicate that nearly 69% of schoolchildren are of normal height. Small height is recorded in 17% of the subjects, while 13% of them are with high height. The data comply with the results from Vojvodina (4) and the north part of Bačka district (14). However, a recent study in the city of Novi Sad (19) which used the same WHO criteria (16) shows a greater percentage of schoolchildren with high height (23.13%) than it is recorded in this study. The same holds true for schoolchildren of small height, whose presence is recorded in 11.20% of cases in the city of Novi Sad. The weight categories set for certain age groups indicate that the largest number of schoolchildren in Jagodina are of normal weight. Approximately 21% of subjects are with small weight, while the overweight are recorded in 14% of cases. When these results are compared with the study conducted in the city of Novi Sad (19) which reports that small weight is recorded in 11.55% of cases and the percentage of the overweight is 25.79%, the subjects from Jagodina appear to have significantly lower weight values.

According to the obtained results, the prevalence of overweight is slightly higher in girls and the prevalence of obesity is similar in both males and females. In this sample, the average number of children and adolescents with excessive weight, both male and female, equals 16.4%. In 10.80% of the subjects, an overweight problem is observed, while obesity is present in 5.60% of the cases. This implies that there is no excess of overweight nor obesity over that which would be expected in a population with a normal distribution of body mass – overweight individuals are those above 85th percentile, but below 95th percentile (which is about 10% of the population) while obese individuals, defined as those over 95th percentile, should constitute about 5% of a normal population. Comparing the nutritional status of different popu-

lations is often very difficult, because of the lack of a uniform method and common assessment criteria (24). Compared with other studies that included the same size sample and methods, and were conducted in Vojvodina (25), a similar prevalence of overweight and obesity, to this in our study is noticed in males and females (10.0%, 4.9% males and 9.9%, 5.0% in females, respectively). A recent study carried out in Belgrade that included children aged 6-14 (26) reports a slightly higher prevalence of obesity in boys (6.8%) as well as in girls (8.2%). Although obesity in children and adolescents appears as a rapidly increasing sociomedical problem in Serbia, the present study does not show any significant deviations from previous investigations. In 2006, 11.6% and 6.4% of children and adolescents were overweight and obese, respectively. When this is compared with the results obtained in 2000, an increase of 3.4% of the overweight and 2.0% of the obese is noticed, particularly in undeveloped regions of the country (27). Nevertheless, in comparison with the information reported by other investigators (28) and by International Obesity Task Force (29), the prevalence of overweight and obesity in Serbia is still lower than in most European countries.

The trends in child obesity are difficult to quantify or to compare internationally, as a wide variety of definitions of a child obesity are in use. (18). A recent study in the city of Novi Sad (19) reports on a noticeable discrepancy in the results of growth and nutritional status obtained by different assessment criteria, with statistically significant differences observed in numerical and percentile data on different categories of schoolchildren. With this in mind, apart from using NHANES I criteria for assessing overweight and obesity in this study, we decided to use IOTF reference values as well, (18) which developed definitions of overweight and obesity based on BMI centile curves that passed through the adult cut-off points of BMI 25 kg/m^2 and 30 kg/m^2. Applying the IOTF reference values, a higher prevalence of overweight is obtained in both girls and boys, although significant differences are observed only in boys, with 22.03% of these subjects being overweight. In girls, the prevalence is 16.15%, and this result does not significantly differ from the one obtained by NHANES I criterium. Considering both boys and girls, the overall prevalence of obesity assessed on the basis of the two criteria is rather similar, equaling nearly 6%.

Many studies have reported that socioeconomic status (SES) is related to the weight status (30) and that mothers' literacy is a strong predictor of the nutritional status (31). However, the strength of this association varies among countries. In developed countries, low SES may be associated with overweight/obesity, whereas in developing countries the opposite situation could also be the case (32). Many studies have shown that educational achievement of parents, both fathers and mothers, is associated with children's nutritional status (28). This study shows that the number of children per family is the only demographic factor that affects both male and female obesity and this factor negatively correlates with the male BMI. The greater the number of children per family is, the smaller BMI value is obtained. There are also other reports (33,34) claiming that children with siblings have lower BMI and are less likely to be obese than children without siblings. Some other studies (31), however, have found no association between the family size and BMI status. Although it has been reported that the educational attainment of parents could lead to higher income and thus imply greater availability of food and household resources (35), this study shows that parents' level of education has no significant effect upon boys and girls' obesity. Similar results have already been obtained in Vojvodina region (25) in a study that represents the first attempt to investigate the influence of these factors upon the nutritional status of the young portion of Serbian population. The study shows that although a correlation among various socioeconomic factors is observed, the effect of each of these factors upon the nutritional status is absent. This might be explained by an economic crisis in Serbia, a drop of living standards and worsening financial situation in all social classes since the beginning of the last decade of the 20th century.

A limitation of the present study may be found in the fact that it is cross-sectional and of local character. Nevertheless, this study, as well as other similar studies conducted in Serbia so far, contributes to the expansion of the database necessary for further investigations and monitoring of the

nutritional status. The present results therefore offer a better insight into the growth and nutritional status and a potentional relationship between demographic factors and overweight and obesity in Serbia today.

The results of growth and nutritional status of children and adolescents in the town of Jagodina show that the overall rate of small height is approximately 17%, malnutrition is present in 19% of children and excessive body weight is recorded in 16% of the cases. Although the results indicate neither excess of small height, malnutrition nor overweight, they still point to a need for constant monitoring of growth and nutritional status, in order to offer the public information on the number of children with potential health problems.

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Musculoskeletal Complaints of University Students and Associated Physical Activity and Psychosocial Factors

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Abstract

Objective: The aim of this study was to describe the prevalence of musculoskeletal complaints (MSCs) and to evaluate associations of physical activity and psychosocial factors with musculoskeletal complaints in a general population of university students.

Methods: This cross-sectional research included 166 university students. As a data-collecting device, the Physical activity assessment questionnaire (PAAQ), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were used. An additional questionnaire was administered to obtain demographic data.

Results: Among the 166 participants, 58 (34.9 %) reported MSCs and the remaining 108 (65.1%) non-widespread MSCs. Axial skeletal pain in 63 (44.9%), pain above the waist in 59 (37.7%) and pain below the waist in 44 (17.4%) of students with MSCs were determined. Physical activity sport, home activity, travel activity and total were founded statically different between students who were not MSCs and students who were MSCs ($p<0.05$). We found that 21 (36.2%) of the students with MSCs had depressive symptoms (BDI>/= *18*), 29 (50.0 %) had anxiety (BAI >/= *18*). The possibility that the sport and total physical activity scores of the students with MSCs are lower than those without MSCs, and the Beck Depression total score and Beck Anxiety total scores are higher is bigger ($p<0.05$)

Conclusions: In this study, musculoskeletal complaints are common among university students, physical activity and psychosocial factors were associated with musculoskeletal complaints. Future studies should try to clarify whether musculoskeletal complaints are a cause or a consequence of inactivity and psychosocial complaints in university students.

Key words: Musculoskeletal complaints, physical activity, psychosocial factors, depression, anxiety

Introduction

Musculoskeletal complaints (MSCs) is a major public health problem in most countries due to high prevalence rates and considerable burden in terms of medical costs, work disability, and reduced quality of life (1-3). However , its have been studied little among university students (4,5). The prevalence of MSCs among university students has increased over recent decades but the causes of these pains and the reasons for their increase remain obscure. Changes in society, including improving living standards and the increasing use of advanced technologies, obviously impact on the everyday life of students, and may explain some of the changes.

MSCs is a dynamic multi-dimensional concept, with a wide spectrum of causative and conducive factors. The perceptions comprise medical, physical, psychological, and psychosocial aspects and are both culturally and socially context dependent (6,7).

It is prominent in the current literature that psychosocial factors especially depression, anxiety are common associative factors that influence the prevalence of musculoskeletal complaints in adolescents and adults (8,9). It is unknown as to what extent psychosocial factors influence university students'experience of musculoskeletal complaints.

As stated by several indications a physical active life is very important. Recently, strong correlations have been reported between physical activity and

health, while physical inactivity has been found to be a risk factor for a number of chronic diseases (10,11). Low levels of physical activity are associated with increased prevalence of health problems (12). Sundblad et al (13) showed that physically inactive students reported more complaints when compared with physically active ones. Headache, abdominal pain and musculoskeletal pain were the most frequently reported complaints, and these students were found to be more stressed than physically active students. The relationship between physical activity and the MSCs has not been investigated also in the literature in university students.

The aim of this study was to describe the prevalence of musculoskeletal complaints and to evaluate associations of physical activity and psychosocial factors with musculoskeletal complaints in a general population of university students.

Materials and Methods

Study Sample

The study population consisted of the students attending high university in the city of Kayseri (population 800,000) in Turkey. There were 400 students in university in the spring of 2008, a total of 210 students were chosen at random for the study. 39 students were absent at timeof the study. The number of students participating in the study was 171, giving a response rate of 81 %. 5 students were excluded from the final sample because of missing questionnaires. The final sample therefore, consisted of 166 students, of whom 128 were girls and 38 boys.

All the students completed a questionnaire in class in the presence of a teacher and returned it in a sealed envelope. Participants gave their written informed consent to use their records for the study.

The Ethics Committee of the Erciyes University approved the research.

Questionnaires

An additional questionnaire was administered to obtain the students' sociodemographic and health information. These data included age, gender, weight, height, smoking status, where the student lived and family type.

Body mass index (BMI) was calculated as body weight in kilograms divided by height in meters squared.

Musculoskeletal complaints

Participants were asked whether they had suffered pain or stiffness in muscles and joints lasting at least 3 months. Those who responded positively were then asked to indicate one or several of the following nine areas of the body: neck, shoulders, elbows, wrist/hands, upper back, low back, hips, knees and/or ankles/feet.

In the present study individuals with MSCs (pain and/or stiffness ≥ 3 months during the past year) were subdivided into widespread MSCs and non-widespread MSCs. "Widespread MSCs" were defined as pain and/or stiffness ≥ 3 month during the past year and ≥ 15 days with symptoms during the last month from all of the following regions: axial skeletal pain (pain in the neck, chest/abdomen, upper back, or lower back), pain above the waist (neck, shoulders, elbows, wrist/ hands, chest/abdomen, or upper back) and below the waist (lower back, hips, knees, or ankles/feet). Individuals with MSCs not fulfilling the criteria for widespread MSCs were defined as having nonwidespread MSCs.

The numeric pain scale: It was used to measure the intensity of subjective pain.It uses a line.

The it was developed by Breivik et al (14). One end is rated with a 0 to indicate no pain, and the other end is rated with a 10 to indicate the worst possible pain. The student is asked to rate his or her pain by selecting a number to represent intensity.

Measurement of Physical Activity

Physical activity assessment questionnaire (PAAQ)

PAAQ is a self-report questionnaire, which asked the participants to give the weekly average of the number of times, and duration they engaged in physical activity over the last year (15). The work (school for students), travel, home, sport and stair activities were listed as 5 separate categories to estimate the activity of participants during the last year. Respondents indicated whether the activities that are listed under these categories were done and if so, on how many days and how many minutes per day the activity was generally performed in a week. Each activity was assigned an intensity value (Metabolic expenditure units—MET)

based on the work of Ainsworth et al (16) MET/week values are computed by the multiplication of duration, frequency and assigned MET values to each activity (MET/week = Frequency × Duration × MET value of activity). The average weekly energy expenditure in kilocalories (kcal/week) is also computed by using the following formula set:

kcal/week = Frequency x Duration x
x MET value of activity x Weight

PAAQ reveals MET/week and kcal/week values for home, school, travel, sport and stair categories. The sum of the five scores is considered the total physical activity score (MET/week or kcal/week).

PAAQ has been shown to have acceptable validity for research purposes. Two week test–retest reliability was $r = .40$ for MET/week and $r = .53$ for kcal/week in adults (15). The PAAQ has been found to be moderately correlated ($r = .72$; $p < .01$) with 24 h daily writing of the activities (16). In this study, kcal/week scores were used as indicator of exercise behavior.

Data were processed into three activity levels using published cut-points- sedentary (<1000 kcal/week), active (1000-2500 kcal /week) and more active (2500> kcal /week).

Beck Depression Inventory (BDI)

Severity of depression was measured with BDI by a psychologist. The reliability and validity of BDI has been tested for the Turkish population by Hisli (17). Each item on the scale is given 0-3 points. The highest point obtainable is 63. The cut off point of the scale is 17 (18). Students were subdivided using a cut-off score of 18 into two groups, those without depressive symptoms (<18) or with depressive symptoms (>/=18).

Beck Anxiety Inventory (BAI)

The BAI determines the severity of anxiety symptoms; BAI was developed by Beck et al (19) and was adapted to the Turkish population by Ulusoy et al (20). Each item of the inventory scores 0–3 points. The scores range from 0–63, with higher scores representing increased severity of the anxiety experienceshigh total scores show severe anxiety. Students were subdivided using a cut-off score of 18 into two groups, those without anxiety symptoms (<18) or with anxiety symptoms (>/=18).

Statistical Analysis

Data were expressed as mean ± standard deviation. To compare continuous variables, parametric and nonparametric analyses were used and the appropriateness of variables to normal distribution was determined. A Chi-square test was used to compare the qualitative variables.

In the multivariate analyses, using multiple binary logistic regression, we estimated the prevalence odds ratio (OR) with 95% confidence interval (CI) for the association between MSCs (dependent variable) and physical activity and psychosocial factors. The statistical analysis were considered significant if $p<0.05$.

Data analyses were performed with the Statistical Package for the Social Sciences, version 15.0 (SPSS, Chicago, Illinois, USA).

Results

Among the 166 participants, 58 (34.9 %) reported MSCs and the remaining 108 (65.1%) non-widespread MSCs.

Axial skeletal pain in 63 (44.9%), pain above the waist in 59 (37.7%) and pain below the waist in 44 (17.4%) of students with MSCs were determined (Table 1).

Table 1. Location and intensity of musculoskeletal complaint

Locations	n	%	Pain intensity
Axial skeletal pain	63	44.9	4.31±2.13 5 (1-10)
Pain above the waist	59	37.7	4.25±2.24 4.50(1-10)
Pain below the waist	44	17.4	4.18±1.30 4.50 (2-6)

The mean age, gender, smoking, family type, height, weight and BMI were not different between students who were not MSCs and students who were MSCs ($p>0.05$) (Table 2).

Physical activity sport, home activity, travel activity and total were founded statically different between students who were not MSCs and students who were MSCs ($p<0.05$) (Table 3).

Table 2. Sociodemographic Characteristics of Participants with MSCs and Without MSCs

Variables		Participants with MSC n=58 (34.9 %)	Participants Without MSCs n=108 (65.1%)		Total n=166
Age		*21.31±4.44* *20.0(18-39)*	20.90±3.72 20.0(18-39)	U=3066.00 p>0.05	20.93±*3.79* *20(18-39)*
Gender	Girls	*49 38.3%*	79 61.7%	X^2 =2.74	128 77.1%
	Boys	*9 23.7%*	29 76.3%	P>0.05	38 22.9%
Family type	nüclear	*48 33.1%*	36 58.8%	X^2 =1.74 p>0.05	145 87.3%
	Divided	*5 50.0%*	15 66.0%		10 6.0%
	large	*5 45.5%*	36 72.0%		11 6.6%
Where the student lived					
	homeland	*26 41.2%*	36 58.8%	X^2 =2.61	62 47.2%
	With parent	*18 34.0%*	15 66.0%	p>0.05	33 21.1%
	home	*14 28.0%*	36 72.0%		50 32.7%
Smoking	Never	*5 26.7%*	11 73.3%	X^2 =0.552	16 9.3%
	Current	*53 36.3%*	93 63.7%	p>0.05	146 90.7%
Height		*1.64±0.07* *1.63(1.50-1.86)*	1.66±*0.08* *1.66(1.50-1.93)*	U=2426.00 p>0.05	1.66±*0.08* *1.65(1.50-1.93)*
Weight		*57.76±9.69* *57(40-90)*	59.41±*9.71* *58(44-88)*	U=2661.00 p>0.05	59.13±*9.77* *58(40-90)*
BMI	(kg/m2)	*21.23±2.47* *21.29(16.65-29.30)*	21.29±*2.89* *21.09(13.89-29.90)*	t=-0.127 p>0.05	21.37±*2.70* *21.35(13-29.90)*

[mean ± S.D., %, or median (interquartile range)]. BMI = body mass index

Table 3. Physical Activity and Psychosocial Characteristics of Students

Variables	Participants with MSC	Participants Without MSCs		Total
Stair	*91.29±77.04* *81(0-257)*	98.77±*80.45* *90(0-250)*	U=2846.500 p>0.05	88.66±*79.28* *82.60(0-257)*
Sport	*308.23±781.75* *100(0-2300)*	442.83±*641.25* *122.50(0-5000)*	U=2225.000 P<0.05	370.62±*664.38* *97.50(0-5000)*
Home activity	*2024.25±4307.90* *2350 (0-9000)*	5229.16±*5964.47* *3700(0-9000)*	U=2229.000 P<0.05	5034.61±*9524.51* *4050(0-9000)*
Travel activity	*366.90±643.25* *219.37(0-3000)*	672.38±*582.51* *327.50(0-7600)*	2325.500 P<0.05	434.49±*930.19* *230(0-7600)*
School	*3196.24±2031.86* *3000(0-8000)*	3460.27±*1896.15* *3100(0-8000)*	U=2593.000 p>0.05	3304.79±*1947.82* *3000(0-8000)*
Physical activity total	*7117.56±3555.35* *8084.55(400-11520)*	8793.71±*3853.47* *9067.00(400-11795)*	U=2278.500 P<0.05	8515.22±*3793.26* *9050(0-11795)*
Sedanter *Active* *More active*	*6 6.4 %* *1 1.7 %* *50 92.9%*	2 1.9% 4 3.9% 97 94.2%	X^2=0.190 p>0.05	8 4.4 % 5 1.9% 149 93.7%
Beck depression <18 *>/=18*	*37 63.8%* *21 36.2%*	88 81.5% 20 18.5%	X^2=6.31 P=0.01	125 75.3% 41 24.7%
Beck depression total	*14.05±9.40* *14.0(0-44)*	10.31±*8.76* *9.0(0-35)*	U=2346.500 P=0.008	11.44±*9.09* *9.50(0-44)*
Beck anxiety < 18 *>/= 18*	*29 50.0%* *29 50.0%*	73 67.6% 35 32.4%	X^2=4.93 P=0.02	102 61.4% 64 38.6%
Beck anxiety total	*20.48 ±12.62* *17.50(0-58)*	14.18±*11.93* *10(0-50)*	U=2146.00 P=0.001	16.22±*12.58* *14(0-58)*

A summary of psychological variables is provided in Table 3. The Beck Depression total score and Beck Anxiety total score were higher in the participants with MSCs when compared with participants without MSCs ($p<0.05$).

We found that 21 (36.2) % of the students with MSCs had depressive symptoms (BDI>/= *18*), 29 (50.0 %) had anxiety (BAI >/= *18*).

The possibility that the sport and total physical activity scores of the students with MSCs are lower than those without MSCs, and the Beck Depression total score and Beck Anxiety total scores are higher is bigger ($p<0.05$) (Table 4).

Table 4. Results of the analyses concerning the influence of MSCs

Variables	Odds ratio	95% CI	p
Sport	0.81	0.70-0.95	0.05
Physical activity total	1.33	1.34-2.08	0.05
Beck Depression	1.99	0.061-0.304	0.00
Beck Anxiety	1.99	0.061-0.304	0.00

CI: *confidental interval;*

Discussion

The present study confirmed that MSCs were common among university students. It was associated with pysical activity,depression and anxiety.

The prevalence rate of 34.9 % for MSCs obtained in this study is somewhat higher than the prevalence rates of chronic pain reported for comparably aged individuals in nursing students (32.9 %) (21) and young women (25.8 %) (22). In present study, axial skeletal pain in 63 (44.9%), pain above the waist in 59 (37.7%) and pain below the waist in 44 (17.4%) of students with MSCs were determined. In the studies (5,21) while Hupert et al (5), found neck pain in 69 %, hand/wrist complaints in 53 %, shoulder complaints in 49 %, arm complaints in 8 % of the students who use computer, Smith and et al (21) determined low back pain in 59,2 , neck in 34.6 %, knee complaints in 25 % and shoulder complaints in 23,8 % of nursing students.The methodological differences may explain the differences in findings. The notable finding in our study and the other similar epidemiological studies (23,24) is that pain problems are an inherent epidemiological phenomenon and a frequent health problem that people live with, even in this young age group. These results underscore the significance of chronic pain problems, which are possibly present already in this young age group.

It was demonstrated that poor physical activity was associated with a high prevalence of MSCs. In general, it is important to realise that our cross-sectional data do not allow for a distinction between cause and effect: participation in physical activity can influence health (positively or negatively), but health complaints and certainly severe complaints can also limit physical activities. Another mechanism could be involved too. Many positive effects of physical activities are associated primarly with the energetic load , whereas the negative results are related primarly to the mechanical loads during these activities. For symptoms of musculoskeletal system, a focus on energy consumption and physical exertion seems to be inadequate and biomechanical factors, such a twisting, bending and sudden peak loads should also be considered, both in school and in leisure.

In present study , the students with MSCs were more depressive and anxious than the ones without MSCs. MSCs are of multifactorial origin. Both physical and psychosocial factors can contribute to its development, as well as individual factors such as gender, age, and anthropometry (25). It can not be ruled out that anxiety can worsen the symptoms of MSCs . The association between psychosocial factors and MSCs may be explained also by increased muscle tension (26).

The association between psychosocial factors and MSCs among university students has not been published before, but our results are consistent with the results reported on adult populations. Levoska et al (27) found an association between stress symptoms and MSCs among female office workers. Leino et al (28) also reported a connection between stress symptoms and musculoskeletal disorders in metal industry employees.

In view of the cross-sectional nature of this study, we are unable to determine whether psychosocial symptoms are consequences or causes of MSCs in students or whether they are all components of a more generalized syndrome. Although the specific mechanisms underlying the relationship between depressive, anxiety symptoms and pain-related disability are not currently defined, neurochemical changes in serotonergic or noradrenergic function that occur as a consequence of depression could

mediate a potential relationship (29). Such changes are thought to increase sensitivity to painful stimuli and could thereby render affected persons more susceptible to disabling musculoskeletal pain.

Conclusion

The prevalance of MSCs were high in universty students population. Low-level physical activity and psychosocial symptoms in students were associated with higher prevalences of MSCs.

Future studies should try to clarify whether chronic MSCs are a cause or a consequence of activity and psychosocial symptoms. Future research in university students cohorts could also focus on relations between different sports activities, and MSCs in order to understand more about different kinds of physical activities as risk factors for MSCs among students.

The multifactorial nature of the etiology of MSCs can already be seen in young populations, which should be taken into account in the treatment of MSCs. Additional study is necessary to assess the effect of psychotherapy on MSCs in students.

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Relationship between psychosocial and physical health of a child with the dimensions of the functioning of single-parent families

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Abstract

Objectives: To examine global psychophysical health of the children of preschool and school age in single-parent families, as well as to determine the connection between particular components of children's health with the characteristics of family relations.

Methods: Research sample consisted of mothers (248) from Novi Sad. The data were collected using a modified version of the CHQ/Child Health Questionnaire, as well as the The Family Adaptability and Cohesion Evaluation Scale. In data processing, we have used descriptive statistical methods, discriminant analysis, Pearson correlation and factor analysis.

Results: Psychosocial and physical health of children in single-parent families is estimated as globally poorer in relation to the children from two-parent families, and differences are reflected in the following variables: psychosocial health – self-esteem, mental health, social role limitations (emotional problems), problems in behaviour and learning; physical health – presence of chronic health problems. Through research, multiple connectedness of family relations and dimensions of psychosocial and physical health of a child is also determined.

Conclusions: Implication of labour refers to the determination of new social and health measures in order to provide developmentally optimal conditions for adequate functioning of families with one parent.

Key words: psychophysical health, children, single-parent families, family relations

Introduction

Great number of previous theoretical considerations and studies pointed that traditional family based on marriage of biological father and mother is the most optimal environment for child's development, however, constant increase of the number of divorces, one-parent and binuclear families requires that family structure and roles in it are redefined. In newly-established families, it comes to key movements in relations, which can have great impact on individual and overall family health.

According to Family Systems Teory, which is simultaneously a theoretical starting point of our paper, interdependence of the roles of family members is recognized, as well as their contribution to the formation of direction and dynamics of family relations, which are specific for each institution mentioned (1). According to this theory, the deficiency of psychophysical health of any family member is a reflection of chronically dysfunctional family relations, which are reflected in inadequate emotional exchange, unfavourable family atmosphere and inadequate communication between its members. According to Kerr, the abovementioned family relations also have a negative impact on the ability of family to adapt (2).

In accordance with this model, numerous studies have pointed out to significant role of the family in generation of life and general welfare of individual during his life (3, 4). Based on those studies, supporting, caring family environments provide a basis for the development of competence, self-respect and adequate behaviour of children and young people (5, 6).

From some other sources we learn that family structure and transition by themselves have rela-

tively insignificant impact of optimal development of a child, when they are compared with the role that family functioning has (7). One of the findings that is confirmed in numerous studies refers to the expressed behavioural disorders in adolescents and stresses the lack of general family cohesion and control as the most important factors in the genesis of delinquency (8). Similar results were obtained by Kranzler and colleagues (9, 10,11), which say that inadequate family relations and lack of one parent can represent an increased risk for the occurrence of psychopathological disorders in children and that in those families, the problems related to children's health are registered more frequently (Felner et al, according to:12, 13). Some other studies, however, state that individuals who have a good physical and mental health, they also have greater chances to have positive relations within a family (14).

Disintegration of family system and changes in psychophysical functioning of children

Changes in family structure are causing imbalance and disorders in family life and all family members experience that situation in different ways. The crisis that comes from disintegration of family system is a great burden for each of them. When the children are in question, the loss of one parent in everyday contacts (divorce, death, separation) often reflects itself in expressing anxiety and lack of confidence in own abilities. Low self-esteem of the child is further related with self-control and observation of own inefficiency in relation to external world, so it is often expressed in the form of inadequate social behaviour in case of the mentioned children, as well as in the form of withdrawal and avoidance of peers or delinquency in adolescent period (15).

Psychosocial consequences of disintegration of family system for the children are largely conditioned by the age of a child. It is observed that family factors are the strongest predictors of mental health with children of the earliest and primary school age (16, 17), as well as that the problems related to mental health and general functioning, with an increasing exposure of a child to risk factors, are cumulatively increased (18, 19). In that way, unfavourable life events often cause passivity, inhibition, aggression, change of behaviour towards peers, even social isolation, in case of younger children. In physical plan, the occurrence of psychosomatic symptoms, such as headaches, stomach aches and other physical problems also appear very often. More serious disorders and health problems are most frequently diagnosed in the adolescence, but having in mind that growing up is a long-term process, the disorders often originate from an earlier age – childhood (20).

Following the model of Family systems theory and results of previous studies about single-parent families, in this study we tried to examine the characteristics of single-parent families in our environment and determine the differences in relation to the families with both parents. Insufficient exploration of the impact of individual family relations on psychophysical health of the children, as well as specificities and difficulties of everyday life and education procedures of single parents require from us to pay particular scientific attention to this phenomenon.

Methodology

Sample

The study included 176 mothers from two-parent and 72 mothers from single-parent families. The study was organized in the premises of Single Parents Association, Institute for Health Protection of Children and Youth, as well as two primary schools in Novi Sad.

Having in mind the objectives and tasks of the research, the sample consisted of parents whose children are of preschool and/or school age. Group of single-parent families consisted of mothers who educate their children on daily basis and live in separate household, regardless of the previous or current legal marital status (single parents from child's birth; parents who are legally still married but the other parent does not live with them) are regardless of the circumstances in which they occur. The most common reason for absence of the other parent in single-parent families is divorce of parents (86,1 %), while an identical percentage of 6,9 % mothers have mentioned something else as a reason (spouse's mental illness, serving prison

sentence, work abroad, involvement of spouses' parents in family life, rejection of the child by the father from the beginning of pregnancy) and mentioned that they live in single-parent household due to spouse's death. We need to mention that the reasons for the absence of the second parent are not related to marital status, i.e. they do not give any information about whether the marriage between the parents was concluded or not. Average number of years of single-parenthood in our sample is 6,2 years (minimum to 1 year, maximum 21 year).

Instruments

Child Health Questionnaire (21). This questionnaire is designed for the evaluation of physical and psychosocial welfare of healthy, as well as chronically ill children, aged from 5 are more years. Evaluation of mentioned characteristics is performed by parents/educators, while in older primary school age, the questionnaire can be filled in by children themselves. Original version of questionnaire contains 14 subscales. For the needs of our research, there were separated four scales for measuring the Psychosocial and four subscales for measuring the physical health of a child, however factor analysis, as well as Scree plot analysis of the Questionnaire on our sample has shown that it is the most optimal to take seven factors for further analysis, and those seven factors are the following: *Self-esteem, Mental health, Social role limitations depending on emotional state, Problems in behaviour and difficulties related to learning, Presence of health problems that are of psychogenic character as factors of Psychosocial health, while the factors Presence of chronic health problems and General health and frequency of somatic symptoms were taken as the dimensions of Physical health of a child.*

Reliability of such a modified instrument is within acceptable limits, with Cronbach's alpha coefficients that range from .74 to .85. The exception is subscale *Mental health,* whose alpha coefficient is .63, as well as subscale *Presence of chronic health problems* with alpha coefficient .57.

The Family Adaptability and Cohesion Evaluation Scale / FACES III (22). FACES III is a self-expressing instrument, which consists of 20 items, with five-degree scale of Likert type for answers. It is designed for the study of family functioning through two dimensions: family cohesion and family adaptability. On the sample of this study, the Scale has shown satisfactory metric characteristic for the dimension of cohesion (α = .84), while the reliability level for the dimension of adaptability is relatively low (α = .68). By applying factor analysis with Promax rotation, latent space of instrument was examined. According to Kaiser – Guttman criterion, five factors were isolated, which together explain 54% of variance. On particular factors in our research, we have set out the items from both subscales, so we have also defined them having in mind the content of items that they include and height of correlation with the factor. The factors obtained are the following: *Support and time spent together, Inclusion of the child in decision-making within a family, Obligations and rules, Emotional attachment and taking leadership and Roles division.* This analysis has served us to further explain the dynamics of family relations and their relation with dimensions of psychophysical health of a child in our sample.

Results

Structure of differences between single-parent and two-parent families in relation to the evaluation of dimension of psychosocial and physical health of a child. In order to determine the differences between single-parent and two-parent families, when it comes to psychophysical health of a child, discriminant analysis was applied. Grouping variable distinguishes mothers in relation to the family type, and continuous variables are the scores of respondents on Promax – factors obtained in the analysis of the CHQ.

After the analysis performed, a significant discriminant function was singled out. The function obtained is statistically significant at the level of confidence $p<0.01$ ($F=64.98$, $p= .000$).

Coefficient of canonical correlation is substantial and significant (.457), so it is concluded that there is a correlation between discriminant function and two observed groups. Data about it are visible in Table 1.

Table 1. Canonical correlation and significance of discriminant function

Function	Rho	Dtr	F - test	p
1	.457	.209	64.977	.000

Table 2 provides us with an insight into the connectedness of particular variables of psychophysical health of a child and discriminant analysis. In factor structure of this canonical discriminant function, in addition to variables *Mental health* and S*ocial role limitations depending on emotional state,* there are also the *Presence of chronic health problems, Self-esteem,* as well as *Problems with behaviour and difficulties* related to learning.

Table 2. Matrix of the structure of discriminant function

Variable	Structure of the function
Self-esteem	**-.555**
Mental health	**-.849**
Social role limitations depending on emotional state	**-.607**
Problems with behaviour and difficulties related to learning	**-.480**
Presence of health problems that are of psychogenic character	-.090
Presence of chronic health problems	**-.706**
General health and frequency of symptoms	-.218

Relative position of groups in discriminant function is presented by the position of its centroids that are shown in Table 3. Table shows us that children from two-parent families are grouped towards negative pole of discriminant function, while the children from single-parent families are grouped on positive pole. It means that mothers from single-parent families estimate that their children have lower self-esteem, more frequent fluctuation of mood (mental health), greater number of problems in realization of social role that are of emotional character, greater number of problems that are related to behaviour and learning and more frequent chronic health problems in case of children that live in complete families. These results indicate that the children from single-parent families have generally poorer psychosocial and physical health than the children from the single-parent families.

Table 3. Centroids of the groups

	Function 1
Children from two-parent families	-.292
Children from single-parent families	.715

Connection between the dimension of psychophysical health of a child and dimensions of family functioning in single-parent families

In order to determine the connection between psychophysical health of a child and family functioning in single-parent families, the coefficients of correlation among Promax factors were analyzed, which were obtained by analyzing the structure of CHQ and Scale FACES III.

Correlations between such obtained factors of Family functioning and psychophysical health of a child are shown in Table 4.

Based on the results obtained in Table 4, we can see that the correlations between the factors of family functioning and psychophysical health of a child are on average relatively low, but there is a significant correlation between the Support and time spent together of family members and almost all dimensions of Psychosocial health (Self-esteem, Mental health, Social role limitations depending on emotional state, Problems in behaviour), as well as two dimensions of Physical health (Presence of chronic health problems and General health and frequency of somatic symptoms), which means that smaller mutual support of the members and smaller amount of commonly planned activities within the family is related with lower self-esteem, more frequent fluctuation of mood, poorer realization of social role, greater problems in behaviour, more frequent presence of chronic diseases, as well as poorer general health and more frequent presence of somatic symptoms in the child. On the other hand, supporting relations within a family are positively related with mentioned dimensions of psychophysical health of a child.

The results also indicate that the inclusion of a child into decision-making within a family has a negative correlation with self-esteem of a child and a positive correlation with the evaluation of general health and frequency of symptoms. Negative correlation in the paper is found between a great number of obligations and defined rules within the family and mental health, as well as general health and frequency of somatic symptoms in a child.

In this paper, the results obtained show that excessive obligations, as well as rigid rules, which are imposed to children within the family, have a negative correlation with three dimensions of Psychosocial health, and those dimensions are: Mental

Table 4. Correlation between the factors of child's psychophysical health (CHQ) and the quality of family functioning (FACES III) in single - parent families

Psychophysical health of a child	Quality of family functioning				
	Support and time spent together	Inclusion of a child into decision-making within the family	Obligations and rules	Emotional attachment and taking leadership	Roles division
Self-esteem	**.219****	**-.131***	-.032	.086	**-.149***
Mental health	**.319****	.001	**-.223****	**.273***	-.021
Social role limitations (emotional problems)	**.164***	-.105	**-.194***	.020	-.097
Problems in behaviour and difficulties in learning	**.170***	.022	**-.191***	.101	.013
Presence of health problems that are of psychogenic character (asthma, allergies, depression)	-.038	-.059	.005	**.135***	-.058
Presence of chronic health problems	**.176***	-.038	-.079	**.130***	.034
General health and frequency of somatic problems	**.236****	**.184***	-.072	**.125***	**.189***

***p < .01 *p < .05*

- Psychophysical health (CHQ) – lower score, poorer health, presence of symptoms

- Quality of family functioning (FACES III) – lower score, poorer quality of cooperation between family members

health, Social role limitations, as well as the Problems in behaviour and difficulties in learning.

In Table 4, it is also visible that the factor Emotional attachment and taking leadership is related with two dimensions of Psychosocial health (Mental health, Presence of health problems that are of psychogenic character) and two dimensions of Physical health (Presence of chronic health problems and General health and frequency of somatic symptoms).

Discussion

When we speak about the change in family structure, it is important to mention that it does not always lead to disintegration, i.e. lack of unity and cooperation between the members. Poor emotionally – affective connectedness between the members, lack of mutual support and solidarity, frequency of conflicts, lack of limits between subsystems are not the characteristics of single-parent families only, but they are a result of chronic pathological relations in family and they can occur in family systems with two present parents. We speak about the disintegration of a family, when it comes to single-parent families, when a change in family structure make the fulfilment of important family tasks more difficult or impossible, affects its functionality and impairs physical and mental health of an individual.

What is the relation between family functioning in single-parent families and children's health in our research we can see from correlation coefficients between particular dimensions of family dynamics and dimensions of child's health. Greater support and time spent together, as well as greater emotional attachment between family members is significantly related with better mental state of a child, while somewhat lower, but more significant correlation is found between greater support of members with better self-esteem, more successful ability of realizing social role that depends on emotional state, with smaller problems in behaviour, smaller presence of chronic health problems, as well as generally better health and smaller frequency of somatic symptoms in offspring. Having in mind that we have determined in this study that better psychosocial and physical

health is characteristic for the children from two-parent families, and that psychophysical health of children from incomplete families is much more sensitive, explanation for such findings we see in difficult life conditions of children and greater exposure to emotional stress, which are certainly more present in single-parent families (23). In many studies, a significant contribution of unstable life style, variable mental state of mother or guardian is determined, as well as inadequate relations within the family with the feeling of insecurity in children, which are then expressed through poorer general mental health and poorer social functioning of a child (10, 24), so these results are in accordance with our expectations and they are realistic indicators of their mental state. Several authors point out that stress chain reactions after the disintegration of family system (25, 26) can lead up to poorer achievements in school, appearance of risk behaviour for health, earlier initiation of working life, as well as earlier transition to parenting. In research of Piorkowska – Petrović (27), it is stated that the children from binuclear families are more susceptible to psychosomatic illnesses and manifestation of behavioural problems.

Results of our study point out to the presence of negative correlation between a greater number of obligations and defined rules within the family and mental health, as well as general health and frequency of somatic symptoms in a child, which certainly points that the transfer of household duties from parents to a child correlates with worse mood of a child, as well as that the lack of flexibility (limited scale of rules) and lack of decision-making within the family are also negatively associated with mental and physical health of a child (28). The same author also stresses that in single-parent families, child or children have a greater responsibility towards household duties, which can have a negative effect on their relations with peers and effectiveness at school.

It is interesting that the inclusion of a child in decision-making within a family has a negative correlation with child's self-esteem and a positive correlation with the evaluation of general health and frequency of symptoms. Such results are certainly not expected and they are explained by the characteristics of our sample. However, it is possible that the expectation of independence and responsible decision-making from a child of preschool age contributes to the child's feeling that it is not competent enough and ready for such a role, so it has a negative effect of child's self-esteem. However, having in mind that the direction of correlation among variables mentioned is not examined in this research, it is possible that low self-esteem of a child contributes to the parents becoming more engaged in inclusion of a child in making decisions that are related to the family.

Negative correlation in this paper is also found between a greater number of obligations and rules defined within the family and mental health, as well as general health and frequency of somatic symptoms in a child, which certainly points to the fact that transfer of household duties from parent to child correlated is worse mood of a child, as well as that lack of flexibility (limited scale of rules) and lack of decision-making within the family are negatively associated with mental and physical health of a child (28).

Having in mind that the factor Emotional attachment and taking leadership, as well as the factor Support and time spent together mostly gather the items that represent a dimension of cohesion in original version, we are not surprised by the connectedness between the former factor and mental health of a child, because it confirms the concept of the Family systems theory, which advocates the importance of emotional atmosphere and emotional exchange between family members on physical functioning of all family members (1). Such family relations reflect in authoritative educational behaviour of parents and its characteristics are high control, but also a caring approach towards the child, so we are not surprised by the connectedness of this dimension with another three health dimensions. Namely, the analyses show that high emotional attachment and authoritarian relations are related with smaller presence of health problems, which are of psychogenic character, smaller presence of chronic health problems and generally better health and lack of somatic symptoms in a child. Other authors also advocate the thesis about a negative impact of undesirable educational and family relations on individual dimensions of psychosocial health, as well as child's behaviour (29, 6). According to these views, if a parent avoids relationships with a child, it become

incapable of establishing long-lasting emotional relations, it is not persistent in its actions and it can be hostile to its environment (27).

Conclusion

The research presented by this paper has confirmed a multiple connectedness between family relation and psychophysical health of a child in single-parent families. Zdanovicz and associates in their study have also confirmed, tha family factors have a significant effect on health indicators of the individual (31), although in the mentioned research, cohesion between family members had positive, while adaptibility had negative effects on health indicators.

Results obtained in this paper are in accordance with the concept of teh Family systems theory, according to which the symptoms within an individual are reflections of movements in emotional balance of family relations (32), which is, in our research, reflected in behavioural change and more frequent symptoms of children in single-parent families. However, having in mind that this is about the estimation of child's health by the parent, as well as the fact that each individual health problem cannot be related to dysfunctional relations in family, it cannot be spoken about a simple correlation between family functioning and child's health. However, the main implication of the work lies in highlighting health vulnerability of children in single-parent families, and is very important to point out the connection between particular components of children's health with the characteristics of family relations, in order to take adequate measures to protect and improve family health.

Limitation of this paper is that the research only includes one family member and that the data are obtained from the parents, which certainly does not lessen the value of data, but more relevant research would be obtained if the research would include the representatives of a wider macro-system (family doctor, psychological services, teachers, etc...). In addition, it would be desirable to examine the impact of some socio-democratic characteristics, as well as personalities of parents and children, on psychophysical functioning of the children. Having in mind the complexity of structure, the relation between family members and unique contribution of each of them to family dynamics, further studies of family relations should be based on longitudinal studies, in order to obtain more adequate image about development of relations and atmosphere within families and their unique contribution to individual and family health of its members.

It is well-known that social model of health points out that the highest goal in life of an individual is health and that care about oneself and the loving ones is an indicator of human dignity and development (33). Based on the above-mentioned, instead of authoritative, it is necessary to provide supportive education to family members at all social levels in order to raise the awareness about own competence when knowledge, prevention and facing with health problems are in question, as well as to create programmes for raising the awareness of social, political and environmental factors that can influence the outcomes of health within the family. For those reasons, we suggest multidisciplinary approach in studying health, as well as stressing the family and family relations as significant basis and optimal developmental conditions for adequate psychosocial and physical functioning of individuals. Mentioned programmes should certainly be realized firstly through the education of parents, teaching staff in schools, as well as through a method that is based on peer education in educational institutions.

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Effects of illness activity on electrocardiographic parameters in patient with multiple sclerosis

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Abstract

Background: Multiple sclerosis (MS) has been reported to be associated with autonomic dysfunction. QT and P wave duration are clearly related to autonomic nervous system. We compared P wave dispersion (PWD) and corrected QT dispersion (QTcD) in stable phase and active phase MS patients to healthy control subjects.

Method: 76 MS patients and44 healthy control subjects were included. Twelve-lead surface ECG recording was performed all participants. The P and QT wave parameters were measured manually

Results: Maximum P wave and QTc duration were higher in MS patients than control groups. The average PWD and QTcD value of MS patients was also found to be higher than control groups. According to illness activity, statistically differences weren't observed at ECG parameters in patients with MS.

Conclusion: P wave and QTc duration were found to be statistically different in patients with MS and control subjects. But illness activity didn't affect these electrocardiographic parameters as significantly.

Key words: multiple sclerosis, p wave dispersion and QT dispersion

Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system with presumed autoimmune etiology. There are significant researches on the involvement of the autonomic nervous system (ANS) in MS. Autonomic involvement may become manifested by papillary, bowel, bladder, sweating, and sexual problems (1,2). Cardiac autonomic imbalance has already been described in patients with MS (3,4). Cardiovascular autonomic tests, that are easy to perform in clinical practice, include deep breathing, Valsalva maneuver, blood pressure and heart rate variability. QT abnormalities are clearly related to ANS dysfunction (5). In addition, P-wave duration and dispersion have been reported to be affected by the autonomic tone (6) which induces changes in the velocity of atrial impulse propagation (7). P wave dispersion (PWD) is a recent electrocardiographic (ECG) marker that reflects discontinuous and heterogeneous conduction of sinus impulses (8,9). Kocer et al. (10) reported that P-wave duration and dispersion were significantly different in patients with MS compared with the control subjects. This study was planned to compare P wave duration-PWD and corrected QT duration (QTc) and dispersion in stable phase and active phase of MS patients to healthy control subjects.

Method

Total thirty-eight patients with MS (40 patient clinically or Para clinically in the active phase and 36 patient clinically or Para clinically in the stable phase) were enrolled in this study. Duration of at least two months without any significant new symptoms and/or signs was defined as a stable phase. 44 age and gender matched healthy subjects were included the study as the control group. Patients who have valvular heart disease, hypo-hyperthyroidism, chronic obstructive pulmonary disease, congestive heart failure, coronary artery disease, diabetes, alcoholism, collagen disease, ventricular preexcitation, atrioventricular conduction abnormalities in their medical history and those on medications known to alter cardiac conduction were excluded from the study. The study was approved by the local ethics committee of Yuzuncu Yil University Medical School. Signed informed consents were taken from the subjects before study entry.

Twelve-lead surface ECG was obtained from each subject while in the supine position. The ECG was recorded on a paper with a speed of 50 mm/sec and 2 mV/cm standardization. The measurements of the P wave durations were using calipers and magnifying lens. P wave duration; the onset of P-wave was defined as the junction between the isoelectric line and the beginning of P-wave deflection and the offset of P-wave as the junction between the end of P-wave deflection and the isoelectric line. P- wave dispersion was calculated as the differences between the longest (maximum P wave duration) and the shortest measured P-wave durations (minimum P wave duration). QT intervals were taken beginning from the onset of the QRS complex to the end of the T wave, which was defined as its return to the TP baseline. In case of U-wave was presented, the QT interval was measured to the combination of the curve between the T- and U-waves (11). The R-R interval was measured and used for computing the heart rate and for correcting QT interval (QTc) with Bazett's formula. QTc dispersion (QTcD) was determined as the difference between the maximum and minimum QTc interval in different leads. All measurable ECG leads were used in QTcD calculations. Any patient had less than nine measurable leads. The intra observer and inter observer variations for measurements were less than 5% and non-significant.

The echocardiographic examination was performed at rest, with the patient in the left lateral decubitus position, using a commercially available echocardiographic device (Vivid 3, General Electric, Milwaukee, WI, USA) with a 3.0 MHz transducer, by an experienced echocardiographer. Left-ventricular diameters and the left atrial systolic diameter were determined from M-mode traces recorded from parasternal long-axis view according to established standards (12). The pulsed-Doppler sampling volume was placed between the tips of the mitral valve leaflets to obtain maximum filling velocities. Early diastolic flow (E), atrial contraction signal (A), E/A ratio, and E deceleration time (DT) were measured. Isovolumetric relaxation time (IVRT) was determined as the interval between the end of the aortic outflow and the start of the mitral inflow signal. Tissue Doppler was measured from basal lateral and basal septal wall of the left ventricle in a four-chamber view with a gate of 1–2 mm. We determined the average of three measures. We used these measures in order to exclude systolic heart failure and diastolic dysfunction which may affect P and Qt wave duration.

Statistical Analysis

Data were presented as mean ± standard deviation (SD). Using an SPSS package 13.0 (SPSS Inc., Chicago, Illinois, USA) the changes of parameters patients and control groups were assessed by t-tests for quantitative data and Chi-square test for qualitative variables and with Mann-Whitney's U-test for variables without normal distribution. A two-tailed p value < 0.05 was considered significant.

Result

There were no difference between patient with MS and control groups in terms of baseline demographic characteristics and echocardiographic parameters (table 1). Maximum P wave duration and QTc duration were higher in MS patients than controls (126±6 vs. 122±5 ms, p=0.004, 393±25.6 vs 372.7±11.4, p=0,001 respectively). Minimum P wave duration was found to be similar in MS patients and healthy controls (72±8 vs. 75±8 msec, p=0.2), but minimum QTc was statistically different in MS patient than control (393±25.6 vs 372.7±11.4 msn, p=0,01). Mean PWD and QTcD value of MS patients were also found to be higher than controls (53±10 vs. 47±10 msec, p=0.01, 43.8±11.1 msec vs 35.4±8.5 msec, p=0.03 respectively). According to illness activity, statistically differences weren't observed at electrocardiographic parameters in patient with MS (table 2).

Discussion

In this study P wave duration and PWD, QTc duration and QTcD was found to be statistically different in patients with MS and control subjects. But illness activity didn't affect these electrocardiographic parameters as significantly.

Multiple Sclerosis is a chronic inflammatory demyelization disorder of the central nervous system. MS may be accompanied by clinical symptoms of autonomic dysfunction (2,3). Frequently

Table 1. Baseline demographic characteristics and echocardiographic parameters patients with Multiple Sclerosis

	Active (n:40)	Passive (n:36)	Total patient (n:76)	P value
Age (year)	35.6±7.6	33.4±8.6	34.6±8.0	0.39
Duration of illness (year)	3.0±1.8	5.0±2.9	4.0±2.6	0.55
Left atrium (cm)	2.8±0.8	2.7±0.9	2.7±0.9	0.71
Aort (cm)	2.6±0.8	2.5±0.9	2.5±0.9	0.41
LVDD (cm)	4.3±0.3	4.4±0.3	4.5±1.1	0.91
LVSD (cm)	2.4±0.7	2.5±1.0	2.5±0.9	0.41
IVS (cm)	1.1±0.1	1.0±0.1	1.0±0.1	0.89
PW (cm)	1.1±0.1	1.0±0.1	1.0±0.1	0.89
EF (%)	60±7.6	61.5±6.8	62.2±9.4	0.13
E (m/sn)	0.8±0.2	0.9±0.1	0.8±0.1	0.06
A (m/sn)	0.7±0.1	0.6±0.1	0.6±0.1	0.30
Dt (msec)	188.8±18.8	180.5±11	184.7±15.8	0.11
IVRT (msec)	90.3±10.3	87.7±3.5	89±7.7	0.30
E lat (cm/sec)	13.5±2.6	14.2±2.2	13.9±2.4	0.37
A lat (cm/ sec)	9.6±1.8	9.4±2.0	9.5±1.8	0.81
S lat (cm/ sec)	9.5±1.6	9.4±1.0	9.5±1.3	0.92
E sep (cm/ sec)	10.1±1.8	11.4±1.9	11.2±1.8	0.50
A sep (cm/ sec)	8.8±2.3	8.5±2.4	8.7±2.4	0.71
S sep (cm/ sec)	9.0±2.7	9.2±3.5	9.1±3.1	0.82

Table 2. Electrocardiographic parameters in patient with MS and control group

	Active (n:40)	Passive (n:36)	Total patient (n:76)	Control (n:44)	Actif vs Passive	Total patient vs control
Age (year)	35.6±7.6	33.4±8.6	34.6±8.0	35.2±6.5	0.39	
Heart rate	76.6±10.9	74.2±11.5	75.5±11.1	71.5±9.4	0.51	0.16
P max (msec)	96.5±13	93.3±14.5	95±13.7	90.4±7.6	0.48	0.005
P min (msec)	46.5±10.9	43.9±6.9	45.3±9.2	41±6.9	0.39	0.07
PWD (msec)	50±9.2	49.4±13.9	49.7±11.5	39.4±8.9	0.88	0.001
QTc max (msec)	396.2±27.6	389.4±23.4	393±25.6	372.7±11.4	0.41	0.001
QTc min (msec)	351.7±19.7	346.7±25	349.4±22.2	339.7±13.8	0.48	0.001
QTcD (msec)	43.7±12.7	43.8±9.4	43.8±11.1	35.4±8.5	0.97	0.03

observed autonomic nervous system disturbances include bladder, bowel, sphincters, sexual dysfunction and sweating; cardiovascular rhythm disturbances (usually atrial fibrillation) have been observed in acute relapses of MS (13,14). Relapsing-remitting form of MS often causes disturbances of autonomic nervous system. Saari et al. (15) investigated cardiovascular autonomic control in 51 MS patients with standardized cardiovascular tests and they found both reduced blood pressure reactions and heart rate variation indicating disregulation of cardiovascular system. They also found that midbrain lesions in MS patients are associated with cardiovascular dysfunction. It is preferable to combine several tests, especially those which are easy to perform in daily clinical practice like deep breathing, Valsalva maneuver, postural blood pressure changes, when analyze autonomic dysfunction in MS patients. Performing those tests is simple and does not require expensive laboratory equipment. In addition electrocardiography has been used analyze autonomic dysfunction in MS patients (8,16).

P wave dispersion is a new electrocardiographic parameter of noninvasive cardiology. PWD has been advocated as a novel measurement of the heterogeneity of atrial depolarization. The increase in dispersion of atrial refractoriness may favor

a reentry mechanism leading to atrial fibrillation (AF). Further, the correlation between the presence of intraatrial conduction abnormalities and the induction of paroxysmal AF has been well-documented (7,9,17). In addition, PWD have been reported to be affected by the autonomic tone, which induces changes in the velocity of impulse propagation (7). Tukek et al. (6) reported that increased sympathetic activity may cause significant increase in PWD, and valsalva maneuver normalizes these changes. The authors suggested that their finding might be related to the beneficial effects of medications that decrease sympathetic tone. Therefore, it is considered that the effect of autonomic system causes changes in P wave duration (6,8). Our results indicated that MS is associated with prolonged P wave duration and increased PWD, compared to healthy controls as appropriate previous study [7] but illness activity didn't affect P wave duration and PWD.

Another electrocardiographic parameter for assessment autonomic nervous system is QT interval. Increased QT dispersion is generally associated with heterogeneity of ventricular repolarization and has important clinical correlates in patients with a wide range of heart disorders (18,19). Moreover, it has been reported that QTD clearly related to ANS dysfunction (5). Prolongation of QTc suggests that ANS disturbance could play a critical role in sudden cardiac death in MS (20). Therefore QTc interval should be studied before beginning a treatment known to prolong cardiac repolarization, especially in patients with corticospinal signs (16,21). In addition, increased QT interval duration has been shown in MS patients indicating ventricular repolarization abnormalities (21). Our results indicated that MS is associated with prolonged Qtc duration and increased Qtc dispersion compared to healthy controls but illness activity didn't affect QTc duration and QTcD.

Study Limitation

Regardless of the technique used, QTc is difficult to measure. The end of repolarization is a gradual process and therefore it's hard to define. Despite, its poor reproducibility and measurement errors, this simple and cheap method is a strong and independent predictor of ventricular heterogeneity and cardiac mortality. Another limitation in this study is manual calculation of P-wave measurements by using a magnifying lens. Although, digital and signal-averaging ECG systems have been used to evaluate PWD that was measured manually either on paper or on a high-resolution computer screen. In addition, small number of the patients included in the study is another major limitation.

Conclusion

P wave duration and PWD, QTc duration and QTcD was found to be statistically different in patients with MS and control subjects. But illness activity didn't affect these electrocardiographic parameters as significantly.

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The Role of Executive Functions at Dyscalculia

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Abstract

Calculia is considered to be the ability of performing arithmetic operations. Problems in acquiring arithmetic skills can be described as difficulties in counting as well as developmental dyscalculia. The most comman difficulties in counting are: difficulties in logic, difficulties in planning, perseverance of inappropriate (responses) procedures and poor understanding of arithmetic operations.

The aim of the research is to determine the influence of executive functions on the acquisition of mathematical skills and the appearance of dyscalculia at junior schoolchildren. It is operation analized in the following way:

- the determination of the relationship between the ability levels of planning and forming of concepts (as elements of executive functioning) and mastering of mathematical skills of junior schoolchildren
- the determination of the relationship between the elements of executive systems (abilities of planning, flexibility of attention and mental rigidity) at children with difficulties in mastering mathematical skills.

Following tests of neuropsychological test battery were used. The examined variables: planning; perseverance; mental rigidity. WCST- WISCONSIN CARD SORTING TEST – used for evaluation, is the best-known test for the discovery of perseverance and mental rigidity. Control variables are: sex, age and deviant intellect quotient.

In accordance with the set goal of the research to determine the influence of the examined characteristic of EF and their influence on the acquisition of mathematical skills and the appearance of difficulties in it, we concluded that the influence existed and that the role of EF in the acquisition of mathematical skills at junior primary schoolchildren was considerable. The assertion was based on the results which, at children with calculation difficulties, show low efficiency and high connection of the examined cognitive characteristics of EF ($p<0,01$). At children who do not show calculation difficulties, the examined characteristics of EF show high efficiency without any statistically important connection ($p>0,01$).

Key words: difficulties in counting, developmental dyscalculia, cognitive functions, planning, perseverance, working memory, attention

Introduction

Each nerve field and each quality of psychic functions that take part in mastering mathematical skills has its developmental path. It is preconditioned by the genetic heritage and influence of the outer factors which affect the development of neuronal combinations (myelination and synaptogenesis) and thus determine their building rhythm and dynamics of psychic activities. In that way, each structure that builds a cognitive function affects its quality and its functional configuration and makes it specific.

Calculia is defined as an ability of performing mathematical operations. In many languages, the word used for the number (in English “digit”, in Spanish “digito”) comes from the Latin word “digitus” which, at the same time, means a finger and a number. Anthropologically speaking, the decimal system in mathematics has an anatomic origin. During their development, mathematical skills reach a high level of abstraction. The ontogenetic development gives an insight into the aspects of brain organization of mathematical skills. The pattern of mathematical thinking depends on

the quality of structures and functions which participate in its formation. Both hemispheres take part in the anatomofunctional organization of calculia, but the dominant role belongs to the left.

The ability of planning and the organization of activities, the performance of a planned activity, realization, verification of efficiency achievement, the ability of self-correction represent the highest level of functioning of the frontal lobes. The term (EF) executive functions is frequently used for frontal or control cognitive functions in modern reference books. It is thought that EF include a greater number of cognitive skills that appear in various cognitive modalities and that can be seen in all aspects of cognitive functioning. The position of prefrontal cortex, on top of cortical hierarchy, is fundamental for the ability of developing of complex representations of the outer world, including not only symbolic skills, but also complex patterns which we use in problem-solving. The function of frontal lobes is related to the term *executive functions,* but, in fact, it is a neuro-psychological term which denotes certain cognitive operations. Basic cognitive functions are attention, memory, perception, thinking, language and praxis. Executive functions do not belong to any of these basic cognitive domains, but are superior to them.

The aim of the research is to determine the influence of executive functions on the acquisition of mathematical skills and the appearance of dyscalculia at junior schoolchildren. It is operationalized in the following way:

- the determination of the relationship between the ability levels of planning and forming of concepts (as elements of executive functioning) and mastering of mathematical skills of junior schoolchildren
- the determination of the relationship between the elements of executive systems (abilities of planning, flexibility of attention and mental rigidity) at children with difficulties in mastering mathematical skills.

Methods

The examined sample is made of fifty-four third-grade pupils of regular population from two urban primary schools. The examined sample is divided into an experimental and control groups. The examinees from the experimental group were chosen according to the discrepancy between general intellectual potentials, general achievement at school and the success in the field of mathematics shown by a mark (unchanged and in the previous grade).

Control variables are: sex, age and deviant intellect quotient.

The distribution of the sample according to the sex: the total number of boys 30 (14 experimental and 16 control group), the total number of girls 24 (13 experimental and 11 control group). The distribution of the sample according to the age: the age of the examinees in the experimental group was from 9 years 3 months to 10 years 2 months, which was slightly different from the examinees in the control group from 9 years 3 months to 10 years 3 months. The distribution of the sample according to the deviant intellect quotient (DIQ) – DIQ span from 90-103, the total number of 25 examinees (14 from the experimental and 11 from the control group); from 104-115, the total number of 29 examinees (13 from the experimental and 16 from the control group).

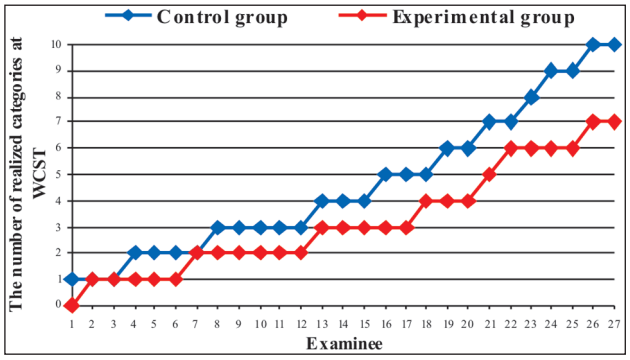
The examined variables: planning; perseverance; mental rigidity. WCST – WISCONSIN CARD SORTING TEST – used for evaluation, is the best-known test for the discovery of perseverance and mental rigidity. It primarily evaluated the ability of abstraction of healthy examinees. It consists of 128 cards with drawn figures: cross, circle, star and triangle, coloured red, yellow, green and blue, the number of figures on a card is from 1-4. All the figures on a card are the same colour. The stimulus cards are presented; an examinee, while putting the other cards under the stimulus ones, should discover the actual principle of card matching, and, on the basis of the feedback of the examiner, also to discover if the answer was right or wrong. The test is sensitive to the planning ability disorder, concept formation and perseverance. Scoring is done according to the eleven categories. As far as clinic work is concerned, the most important scores are the perseverance error score and the number of realized categories.

Statistics

Acquired results are shown in tables and graphs in absolute numbers and percentages. X^2 test and correlation measures were used for data proce-

ssing. The achievements were analyzed in relation to the test qualitative parameters, as well as the aspect of knowledge so far in that scientific field.

Results

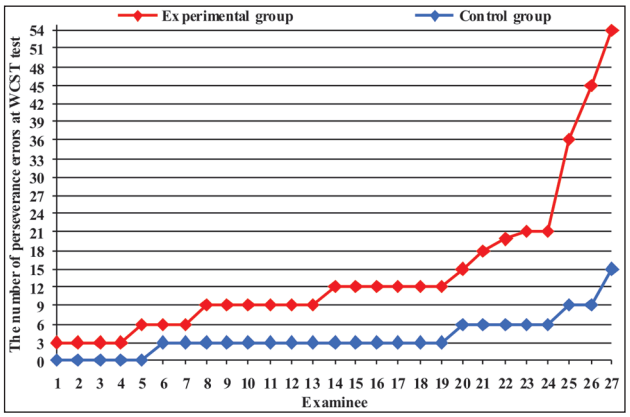


Graph 1. The number of realized categories at WCST

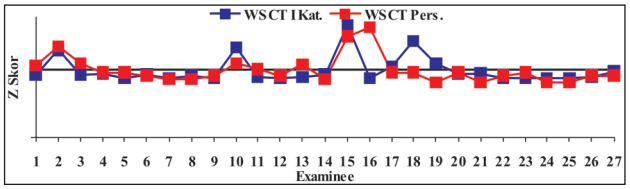
By the observation of both curves, we can draw a conclusion that the examinees from the control group were more efficient because they made, both individually and as a group, a greater number of categories at WCST.

By the observation of both curves, we can notice greater efficiency of the examinees from the control group who had minimal perseverance errors.

By the application of X^2 test we concluded that there was a statistically important relation between two evaluated characteristics at the examinees from the experimental group ($p < 0.01$)



Graph 2. The number of perseverance errors at WCST test



Graph 3. The connection between the planning ability and mental rigidity at WCST test – experimental group

By the observation of the graph, the important connection of the two examined characteristics at WCST test (Shown in Table 1) can be noticed.

Table 1. The connection between the results obtained by the application of WCST test in two evaluated characteristics within the experimental group

WCST / WCST.		WCST Perseverative mistakes							
		I		II		III		∑	
WCST I Kat.	I	3	11,11%	5	18,52%	1	3,70%	9	33,33%
	II	2	7,41%	2	7,41%	4	14,81%	8	29,63%
	III	2	7,41%	5	18,52%	3	11,11%	10	37,04%
	∑	7	25,93%	12	44,44%	8	29,63%	27	

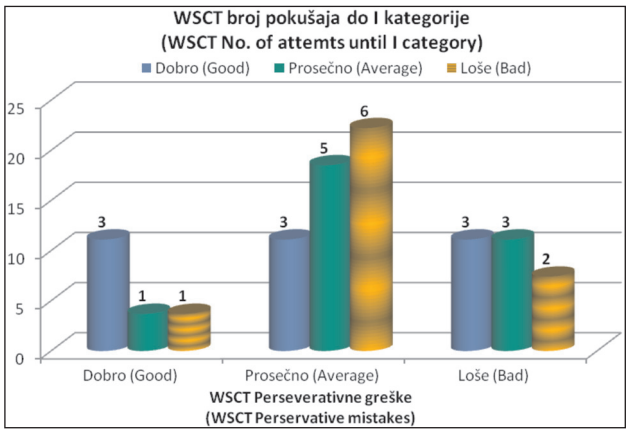
$x^2 = 3,49$; $df = 4$; $p < 0,01$

Table 2. The connection of the results acquired by the application of WCST test in two evaluated characteristics within the control group

WCST / WCST.		WCST Perseverative mistakes							
		I		II		III		∑	
WCST I Kat.	I	3	11,11%	3	11,11%	3	11,11%	9	33,33%
	II	1	3,70%	5	18,52%	3	11,11%	9	33,33%
	III	1	3,70%	6	22,22%	2	7,41%	9	33,33%
	∑	5	18,52%	14	51,85%	8	29,63%	27	

$x^2 = 2,85$; $df = 4$; $p > 0,0$

By the application of X^2 test we concluded that there was a connection of the two evaluated characteristics at the examinees from the control group, but with no statistical importance ($p>0.01$).



Graph 4. The connection between the planning ability and mental rigidity at WCST test – control group

Table 2, presented graphically, also shows that there is no statistically important connection among the evaluated characteristics at the examinees from the control group.

While processing the statistical sample, we concluded that the measurement among the evaluated characteristics within the executive functions was very complex, especially if we compared different parameters.

The results point out their mutual dependence and connection, but with the statistical importance only at the examinees from the experimental group, that is, at those examinees who show difficulties in mastering mathematical skills. As lowly efficient and highly dependent, the evaluated characteristics within the executive functions behave as a disturbing factor in the process of mastering mathematical skills. The connection of examined characteristics at the examinees from the control group was checked in order to confirm the acquired result. The high efficiency of examined characteristics of executive functions was notified and also the connection without any statistical importance which indicates their independence. At the same time, as such, they stimulate the acquisition of mathematical skills.

Discussion

The role of prefrontal regions in the cognitive growth is related to mastering of specific mechanisms which enable an individual a high level of cognitive competence and the realization of autonomous, meaningful and aim-oriented behaviour of a structural change in certain parts of frontal cortex which are carriers of various functions that can cause decrease of cognitive efficiency. The most important aspect of this study lies in the connection of qualitative functioning of certain characteristics within executive functions, their influence on the acquisition of mathematical skills and the appearance of some difficulties in the same process. The received results confirm the important influence of executive functions on the acquisition of mathematical skills. A structural disorder of the ability to understand mathematics lies on the lowered maturity of prefrontal cortex. Most neurologists claim that most arithmetic operations are performed by the left half of encephalon (left hemisphere) and that the cause of difficulties of acquisition of mathematical skills is that children use the right hemisphere more, that is, they have a greater tendency to holistic cognitive strategies, while it is better to deal with mathematics analytically. Dyscalculia is partly a disorder in mastering of mathematical skills which can appear in all or some mathematical areas. Disturbances are usually formed in as early as a developing period and are manifested the moment a child starts the process of acquisition of mathematics. Certain parts of prefrontal and frontal cortex can mature late or mature slowly and by this precondition not only hindered acquisition of mathematical skills, but also some other difficulties. Some studies in the field of developmental disorders show a high interrelation between dyscalculia and dyslexia, ADND and anxiety (Akerbach, Gross-Tsur, Manor & Shalev, 2008). The examined sample in this study did not have any of these disorders registered in the medical documentation. One of the researches concludes that dyscalculia is present at girls with 8.3 %, while at boys it is with 7.2 %. The received results within this study, being analyzed according to the sex, confirm the named research with a slight difference because of the size of the sample (von Aster & Shalev, 2007). A thorough study (Barbaresi et al.2005), having used medical and school docu-

mentation, found out that the percentage of calculation disorders gets higher with the age of the examinees. Within this study, since the examinees were followed for two years, such a difference was not noticed. Neuropsychological markers within this research did not register any developmental slowdown, but they clearly showed that the lowered efficiency in the functioning of EF would cause hindered mastering of mathematical skills. The research study (Geary & Hoard, 2008) claim that EF control the understanding of the procedure. The results of this study correspond to the named research.

Conclusion

In accordance with the set goal of the research to determine the influence of the examined characteristics of EF and their influence on the acquisition of mathematical skills and the appearance of difficulties in it, we concluded that the influence existed and that the role of EF in the acquisition of mathematical skills at junior primary schoolchildren was considerable. The assertion was based on the results which, at children with calculation difficulties, show low efficiency and high connection of the examined cognitive characteristics of EF ($p < 0.01$).

At children who do not show calculation difficulties, the examined characteristics of EF show high efficiency without any statistically important connection ($p < 0.01$). Having illustrated the seriousness of the problem, as well as the fact that the scientific books still discuss this matter very cautiously, we would like the results of this research to serve as a base which will make the experts in the field get to all the secrets of EF and their influence on the dynamics and quality of cognitive skills.

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The Influence of Climate Changes on Respiratory Allergic and Infectious Diseases

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Abstract

Human activities are resulting in changes of global climate and environment.The likelihood that this trend in climate changes is due to antrophogenic causes is over 90%. These changes, in turn, have had, and will continue to have impacts on human health. Antrophogenic climate change is predicted to have range of effects on respiratory allergic and infectious and other allergic diseases over the coming decades, most of them negative. The possible effects of climate change are wide-ranging, and predicted to ocurr in the folowing areas: extreme temperature events, worsening of air pollution, altered aeroallergens, extreme weather events. A number of studies have revealed potential impacts of climate change on human health that may have an enormous clinical and public health significance. While such impacts have received increasing attention in recent years, the impact of climate change on aeroallergens and related allergic diseases have been somehow neglected. There are many research challenges along the road to a more complete understanding of the impact of climate change on aeroallergens and allergic diseases such as bronchial asthma and hay fever, so on the COPD (chronic obstructive pulmonary disease) and respiratory infectious diseases. It is important that public health authorities and health professionals be aware of these changes in the climate and environment, and that research scientist embrace the challenges that face further work in this area.

Key words: climate changes, respiratory diseases

Introduction

The rise in the prevalence of respiratory allergic and infectious diseases in the last decades is well known (1).It has occurred first in western societies especially as to allergic diseases, but as their lifestyle has been more widely adopted, other countries are also experiencing the rise in these diseases. The rapidity of these changes can be explained on the basis of environmental changes, since genetic influences take many generations to have such a profound effect (2, 3).

Climatic changes have a mayor impact on our environment. It is widely acknowledged that climate change is occurring, but there is the debate as to cause. Intense scientific studies point to anthropogenic factors as the mayor driver of these changes, but there is also a point of view that it is independent of human activity and part of a natural circle. This debate has become politicized and in particular the question of what steps should be taken to reverse or even stop this phenomenon (1).

Climate has a major impact on bronchial asthma, COPD, respiratory infections and other allergic diseases through a number of mechanisms (2,3,4,5).

There is a growing awareness that the medical profession has to prepare for changes in diseases brought about by climatic changes. Experts from EAACI (European Academy of Allergy and Clinical Immunology) in Zurich discussed these issues and issued press release on their projections of climate changes and recommendations on changes needed to reduce its impact on human health (5).

Climate change

Climate change is not something that might happen in the future. It is happening now since the middle oh the 20th century. In many countries all over the world average temperatures have raised about 1˚C (6, 7).This has been accompanied by an increase in the frequency of heat-waves, decrease in the numbers of frosts and cold days, and a redistribution of rainfalls from one region to another (7).

Last (2009.) and this (2010.) year will be remembered for extreme bushfires, dust-storms and

lingering rainfall deficiencies, areas of flooding and record-breaking heat waves (7).

The decade just ended (2000.-2009.) was warmest on record in many countries, continuing a trend where each decade since the 1940's has been warmer than that preceding it (7).

The likelihood that this warming trend is due to antrophogenic causes is over 90%_(8). Antrophogenic climate change is predicted to have range of effects on respiratory allergic and infectious and other allergic diseases over the coming decades, most of them negative.

Effects of climate change

The possible effects of climate change are wide-ranging, and predicted to ocurr in the folowing areas:

- Extreme temperature events
- Worsening air pollution
- Altered aeroallergens
- Extreme weather events

Extreme temperature events

The globe is warming and will continue to do so over this century. This process will continue, even if rapid and marked reductions in carbon dioxide emissions occur soon, due to inertia of the global climate system. Mean temperatures will continue to increase, as climate variability (the range of expected maxima and minima). The effect of this two-fold change will be significant increase in the number of very hot days for many areas (8).

The health effects of extreme heat are well-known.The record- breaking 2003. European heat-wave, for example caused tens-of-thousands of premature deaths across several countries especially France (9). Most affected were the elderly, disadvantaged or chronically ill (especially those with respiratory or cardiovascular diseases). There is also evidence from a European study that each 1˚C increases all-cause mortality by up to 3% (and respiratory mortality up to 6%) (10).

As heat waves are expected to become more severe, frequent and prolonged as global warming progresses, strategies to reduce the associated morbidity and mortality must become a public health priority (11).

A paradoxal effect of increased global temperatures is that winters should become warmer, leading to a modest decrease in cold-related morbidity and mortality.

Worsening air pollution

During the last decade, the air pollution is at least one of the important factors among the ones contributing to the negative impact on the immune system and to increase of the allergic diseases worldwide. Air pollutants may be classified as “Primary” – SO2, NO3, CO, volatile organic compounds, and “Secondary”- formed within atmosphere by chemical of physical processes: ozone, fine particles (12). According to their impact on the immune system and allergization they are divided into Type I or “East type” provoking increase of bacterial and viral airway inflammation and Type II or “West type” – associated predominately with allergic sensitization and increasing the allergic diseases (12).

Nowadays it is well proved that the air pollution may affect different mechanisms of action, cytokines and cells playing an important role in immune homeostasis. They inhibit the phagocytic activity, synthesis of GIM-CSF and secretory IgA. They stimulate the release of lymphokines of Th2 type: IL-4, -6, -10, -13 and -16 and have significant inhibition of lymphokines of Th1 type: γ-interferon and IL-2 (11,12). This is the immunological basis for the increase of the allergic diseases and higher sensitization to conventional allergens in the world last decades, especially in the industrialized countries (12).

Petrunov carried out the study using as a model the population of the city of Pernik – highly industrialized and polluted town and the city of Breznik –small town free of air pollution, in order to confirm the above mention data. In the studied people in Pernik he found 22,5% of immune system disorders in comparison with those of Breznik that comprised 8,8%. In 24,4% of the population of Pernik he revealed sensitization to different conventional allergens and only 7,3% of the studied people from Breznik showed any allergic sensitization (12).

The action of air pollutants on different levels and via complex of interactions and maintenance of allergic and toxo-allergic reactions is still being discussed**.**

The relationship between air-pollution, climate change and respiratory illnesses is complex ,and

more research is needed to allow better predictions to be made. Despite this, enough is known about ground-level ozone, nitrous oxides and particulates to inform future research and mitigation/ adaption strategies.

Ground -level ozone. Ozone is a potent oxidising substance known to have several adverse respiratory effects (11):

- Increased new onset asthma
- Decreased lung function
- Exacerbation of COPD
- Allergen sensitisation
- Increased hospital admissions
- Increased all-cause mortality

Ozone (O3) is a component of photochemical smog, produced by the action of sunlight on fossil-fuel combustion products (primaraly vehicle exhaust in cities). Its production is increased by warmer temperatures (especially due to urban heat-island effect) and it is this property that will probably lead to increased ozone formation during the coming years.

Produced by the action of sunlight on exhaust fumes (especially on hot days), high concentrations of ozone found in the Earth's lower atmosphere (troposphere) is hazardous to life.

Although urban areas are most affected, O3 crosses national and even continental boundaries (there is increasing evidence, for example, that Asia is "exporting" its ozone to the USA) (13). The future effects of this issue are difficult to predict due to warming -induced changes in air circulation and wind patterns.

As hydrogen combustion is the main source of ground-level ozone, patterns and levels of future O3 concentrations also become difficult to predict with certainty if carbon-free fuels become dominant.

Other forms of air pollution

Nitrous oxides are produced by high temperature hydocarbon combustion (especially in vehicles). They are important, in part, because they produce an enhanced response to inhaled allergens probably due to bronchial irritation and inflammation (4).

Small ambient particles are also produced by fossil-fuel combustion. Short-term inhalation of these particles increases cardiopulmonary hospital admissions and mortality, while long-term exposure worsens paediatric asthma and causes higher mortality in adults (11). It is difficult to predict future patterns of particle production and exposure, as mitigation strategies (e.g. electric - or hydrogen-powered vehicles) may significantly reduce their production.

Conversely, expected increase in wildfires, droughts and desertification due to climate change may produce more particles, and they may spread over wider areas (11). Wildfires in particular pose many health risks. Apart from the direct threat to life, their smoke may contain plastic, toxic and herbicide & pesticide residues (4).

Climatic conditions have and other effects on increasing air-pollution level. They may contribute to increased pollution, for example through increased power generation required for air-conditioning and cooling (14). Various pollutants have an impact on the severity of existing asthma, and they also have adjuvant effects on allergenicity of pollens. This has been well demonstrated with diesel exhaust particles and Japanese maple and birch pollens (14).

Altered aeroallergens

Global warming is already having demonstrable effects on plant behaviour and distribution (8).There has been a general shifts polewards and upwards (altitude) of plant habitability zones in many regiones, related to warmer conditions. There have also been changes due to altered precipitation patterns and land-use variations.

Flowering times are also changing, with a general trend towards earlier spring flowering (although paradoxically,plants that rely on a longer duration of winter chill to trigger budding are flowering later due to warmer winters) (14).

Many researches suggest that pollen amount and allergenicity is increasing (1).

Pollen appears to be more allergenic, with higher levels of some core proteins (the molecules mainly responsible for triggering allergy) (15). Respiratory allergies may follow dose-response curves: more pollen + more allergenicity = more severe allergies.

Changes in the timing of the pollen season (longer and earlier) may produce worsening allergies if there is overlapping with peak ground-level ozone production in summer.

Other changes due to global -warming include (14):

- Changed wind patterns with disperse pollens in new direction or further than before
- Changed local condition may alter dust-mite and mould distributions
- Changed agricultural practices may alter the level of pollens related to farming activity (e.g. rye grass is a component of farm pasture; the mould Alternaria is related to agricultural production).
- Changed species make up of forests and grasslands (whereby one species is replaced by another due to altered microclimate or species invasion) may also change pollen type and load.

All of these phenomenas have the effect of changing pollen distributions. This exposes new populations to novel allergens that will trigger new-onset allergies, as well as worsening of existing ones (1,3).

Climate change is happening now , and some of the changes described (such as changes in flower times and geographical range) have already been documented by the IPCC (Intergovermental Panel on Climate Change) (8). It is known from paleoclimate research that plants react qiuickly to environmental changes- ice core and ocean sediment data show that significant vegetation changes (in response to previous climate disruptions) have taken just a decade to occur (15).

Pollen allergy is an important driver of respiratory disease. The total pollen load and the distribution of pollen species are dependent on geographic and climatic factors. Changes in these factors can have significant effects on amounts and types of pollens, and can influence other characteristics of pollens. Vegetational changes occur quickly within a decade of climatic changes (1, 15).

The distribution of flora is changing. For example the tundra is receding and is being replaced by more temperate forests which include birch and pine trees, which are major pollinators and cause significant allergic diseases (14). There is also increasing of biomasses of flora associated with the warming environment which leads to increasing amounts of pollens being produced. With global warming there has been demonstrable change in pollinating seasons of flora in many parts of the world (3, 9, 14). Pollen seasons start earlier and are prolonged and there is also evidence of increased allergenicity of pollens (3, 9, 14).

A change in distribution and timing of release of mould spores has also been observed. Mould allergy is an important cause of respiratory allergic disease, although less understood than pollen allergy (1, 3, 14).

Extreme weather events and abnormal weather patterns

Climate change is expected to magnify the hydrological cycle ,causing more frequent droughts but also more hurricanes, storms and extreme precipitation events (8). It has been known for some time that thunderstorms may cause asthma exacerbationts (11). It appears likely that this is due to disruption of pollen particles, thereby exposing their allergenic cores. Heavier rainfalls have the potential to cause floodings and increased mould growth. Both occured after Hurricane Katrina inundated much of New Orleans (15). Following such extreme events, it is likely that population displacement, crowding, drinking contaminated water and malnutrition will increase respiratory infections, especially pneumonia, and possibly increase TB transmission (11).

More frequent floodings ,expected as the hydrological cycle intensified due to global warming, will have different adverse health consequences.

One of the consequences of global warming has been an increase of abnormal and violent weather patterns. A number of asthma epidemics have been related to “thunderstorm asthma” in which large amounts of pollens are transported often over wide distances and deposited to a confined geographic area, resulting in a large increase of number of asthma attacks and their severity (11). Other major weather changes have contributed to major disasters such as the Victorian bushfires in 2009. in Australia which destroyed towns and claimed over 200 lives. Apart from the direct devastation there was an increase in pollution from smoke and from toxic chemicals released from burning of plastic and synthetics (7).

Climatic change has and other effects on human health. There are effects on insect distribution

with resulting increase in insect stings reported in areas such as Alaska and increased distribution of vectors for infections diseases such as dengue fever and malaria (8).

Conclusion

The influences on respiratory allergic and infectious diseses discussed in this article are jast as small part of the adverse health effects that have been occured and predicted to occur over the coming decades due to climate change .The barriers to accepting and acting on anthropogenic global warming are largely psychological and political rather than scientific, as climate change science is now very developed. Health professionals are capable to deal with this risk ,as they do so on a daily basis in clinical practice. They have a unique opportunity to educate and inform their patients , communities and politicians about these issues. Health professionals have an ethical duty to do so in order to limit as much as possible, the expected increased burden of illnesses that is on the horizon. There is a need to include the studying of effects of climate changes on human health in medical student education.

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Knowledge, skills and attitudes of physicians recognition on violence against children

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Abstract

Objective: The aim of this study was to determine the level of knowledge, attitudes and skills of doctors in recognising the problem and treatment in cases of violence against children.

Patients and methods: This research is cross-sectional study involving 40 doctors in Primary care including doctors of General medicine, Pediatricians, Family medicine, Emergency department, and School medicine. doctors who are employed in Health Center and in Regional Medical Center in Mostar voluntarily completed a questionnaire. Questionnaire was taken from Israel study and questions were regarded the knowledge, practice and attitudes aboutchild abuse.

Results: In our sample there was significantly more Family medicine doctors (P> 0,001). Most of the doctors had approximately 5-10 % from total number of children patients (P>0,001). Doctors in age group 41-50 had significantly higher level of attitude in recognition of violence against children, in comparation with doctors aged 30-40 years (P=0,033). Doctors who had more than 20 years of worktime had significantly higher level of attitude towards recognition of violence against children than those who had only 2-5 years of worktime (P=0,044). There wasn t significant difference in doctor s knowledge depending on whether they completed the education about violence against children after graduating from the University (P=0,093).

Conclusion: Older doctors, with more than 20 years of worktime had higher level of attitude than younger doctors while in knowledge and practice wasn t any significant difference. The doctors who finished one-day education about children abuse didn t differ in knowledge and practice compared with doctors who didnt finish education.

Key words: violence, children, doctors, knowledge, attitude, practice.

Introduction

Abuse and neglect of children is a complex psychosocial problem that in recent decades is getting wider scale, both in rich and in poor communities (1). Its complexity and the ability to solve far beyond the scope of medicine or health. Medical aspects of child abuse include individual psychopathology its possible causes and its consequences in the form of physical damage, and particularly devastating effects on mental and emotional health of the child (1-4).

- There are the following forms of abuse:
- Physical neglect
- Mental abuse and neglect
- Sexual abuse
- Psychological neglect

Doctors are often the first professionals to encounter abused child (6). Motivation and the workplace, consider as an important factor in the training of professionals. Graduate and postgraduate training programs in this area are rare not only here but in the world, and continuing education programs are made without collecting the request of those to whom they are intended. Their work is influenced by different factors, the most common allegations are: (a) personal opinion about the problem and motivation to participate in its resolution, (b) work experience, working conditions and opportunities, (c) the knowledge of experts and (d) interprofessional cooperation in the local community (5-8).

First of all, the definition of physical abuse in the law of the United States appeared in1962, when doctors are obliged to report suspicions of abuse during treatment of injuries in children. Research American Academy of Pediatrics 1990 showed that 45% of pediatricians treated or advised patients who have been victims of violence in the previous 8 weeks. American Academy of Pediatrics in 1998 found that 57% of 608 pediatrici-

ans reported that they treated injuries caused by abuse in the past year (14). In the Federation of Bosnia and Herzegovina doctors working in primary health care are going through training programs on procedures in case of domestic violence, which was organized by the Federal Ministry of Health. The program was conducted among doctors in Mostar, in early March 2010.This one-day training based on interactive lectures and solving cases was organized on a voluntary basis and included about 20 doctors employed in Mostar (15).

Methods

The study was conducted at the Health Center, Mostar and Regional Medical Center in Mostar, in April 2010. Research studies in the intersection which included 40 doctors including general practitioners, pediatricians, family specialists, emergency medicine and school. Tested all these specialty doctors employed in the Health and RMC Mostar in Mostar, who agreed to interviews. The survey has been used an anonymous questionnaire designed on the basis of a questionnaire taken from the Israeli study (16). The questionnaire consisted of personal information and 24 questions. Questions were related to knowledge, application and attitude of respondents towards violence against children.

The data obtained were statistically analyzed by the program system SPSS for Windows (version 13.0, SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel (version 11 Microsoft Corporation, WA, USA). The statistical tests used the $\chi 2$ test to compare nominal variables. To display the mean and dispersion measures for symmetric distributions using the arithmetic mean and standard deviation and to compare these variables used the Student t-test and ANOVA test. The level of significance was $P < 0.05$

Results

Doctors, depending on the age group to which they belonged were significantly different in attitude (F=3.897, P=0.029). This significant difference in attitude existed among physicians who belonged to the age group 30-40 and doctors 41-50 (Post hoc test Scheffe test P = 0.033). Doctors in the age group 41-50 had significantly higher levels of attitudes towards violence against children in relation to physicians, aged 30-40 (Scheffe post hoc test, P = 0.033) (Table 1).

Doctors were significantly different in attitude depending on their years of service (F=3.654, P=0.036). This significant difference in attitude existed among physicians who have 2-5 years of experience and a doctor who hamore than 20 years of

Table 1. Knowledge and use of physician attitude towards violence against children in relation to age group

Variables	M±SD* variables considering age groups of respondents			F	*P*
	30-40 year	41-50 year	>50 year		
Knowledge	2,82±0,46	3,10±0,28	3,04±0,25	2,095	0,137
Application	3,04±0,41	3,28±0,52	3,26±0,49	0,632	0,537
Paragraph	2,71±0,94	3,37±0,32‡	3,25±0,43	3,897	0,029

M ± SD = mean ± standarddeviation

‡ Doctors in the age group 41-50 years had significantly higher levels of attitudes towards violence against children in relation to physicians aged 30-40 years (Scheffe post hoc test, P = 0.033).

Table 2. Knowledge, attitude and use of physicians towards violence against children in relation to their years of service

	M±SD* variables considering doctors working experience			F	*P*
	2-5	11-20	>20		
Knowledge	2,82±0,46	3,10±0,24	3,05±0,28	1,971	0,154
Application	3,04±0,41	3,21±0,53	3,31±0,48	0,780	0,466
Paragraph	2,71±0,94	3,29±0,39‡	3,31±0,39	3,654	0,036

*M ± SD * variables for years of service to physicians*

M ± SD = mean ± standarddeviation

‡ Physicians who were > 20 years of service had significantly higher levels of attitudes towards violence against children in relation to physicians, aged 30-40 years (Scheffe post hoc test, P = 0.044).

Table 3. Knowledge, attitude and use of physicians towards violence against children, depending on whether they completed the training on violence against children.

	M ± SD * variables to training on violence against children		T-test	P
	Yes	No		
Knowledge	**3,14±0,35**	**2,96±0,28**	**1,721**	**0,093**
Application	**3,35±0,51**	**3,17±0,47**	**1,111**	**0,274**
Attitude	**3,28±0,44**	**3,15±0,61**	**0,673**	**0,505**

** M ± SD = mean ± standard deviation*

service. Doctors who had more than 20 years had significantly higher levels of attitudes towards violence against children of doctors who have 2-5 years of working experiance (Post hoc Scheffe test P = 0.044) (Table 2). Knowledge of physicians were not significantly different depending on whether they completed the training on violence against children after completing the study (t-test=1.721, df=38, P=0.093) (Table 3). The sample was the most common specialization in family medicine (χ^2 test=31.250, df=4, P<0.001) (Figure 1). Most patients have an approximate percentage of the total number of children 5-10% of patients. (X^2 test=26.600, df=3, P<0.001) (Figure 2).

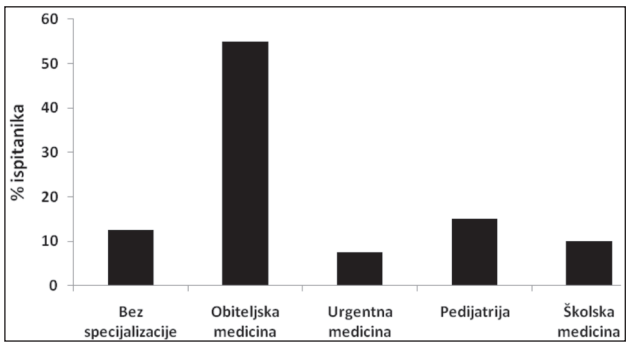

Figure 1. Specialization subjects

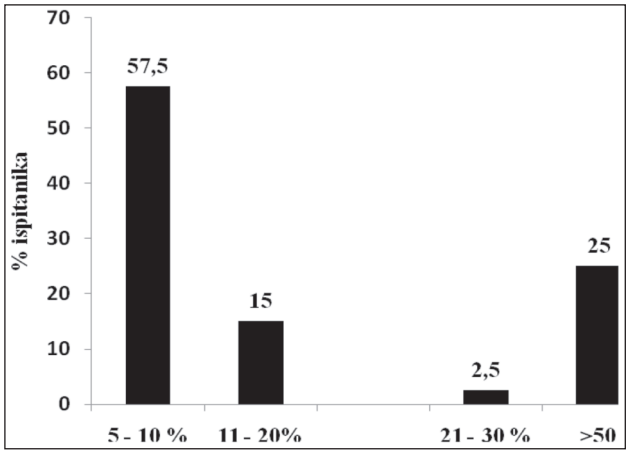

Figure 2. Distribution of respondents by age approximate percentage of children from the total number of patients

Discussion

In this study, we examined knowledge, attitudes and skills of 40 physicians who work in primary care to identify problems and treatment in cases of violence against children. Doctors around the world are not in an equal position to play a key role in the prevention and recognition of violence against children (17). In our study, physicians were significantly different in the attitude towards the recognition of violence against children according to age group they belong to. Doctors who belonged to an older age group and who had more than 20 years of working experience had a higher level position. The reason for this is probably a higher level of experience in the field of domestic violence during their working years. In this study, there was no significant difference in the recognition of violence based on gender, age, experience, reporting and practical applications, as well as in research conducted in Pennsylvania (18-20).

The results of our study in the application of measures against violence coincided with the survey that was conducted in Israel (16). Research conducted in Israel 2004 showed that the most common age group who had sought help from 13-18 (15,16). The results of a study conducted in Mostar, indicate that the most common abuse were sexually (13%) and emotional abuse (13%), while the physical form of violence was present in all (5%) of children. Emotional neglect is very frequent (98%), and significant proportion of those students who experienced physical neglect (85%) (22). The results are probably unreliable because it is still in our midst who is conservative, most abuse is not reported yet (21).

The problem of violence against children is one of the most important public health problem in the Federation. Many physicians do not have adequate training on violence against children (12,13).

Research conducted in Israel showed that physicians do not have enough knowledge, skills and time to identify victims of violence (16). The training focused on the medical staff has proved to be effective in improving knowledge and skills, and recognition of violence. In a study conducted in the U.S. in 42% of physicians reported that prior to participating in training programs, which does not coincide with our research, because most doctors in our research has not participated in training programs on violence against children. .

Doctors who have completed a one-day training did not differ from other colleagues, probably because of the short duration of the training. A study conducted in the U.S. showed that 20% of emergency physicians reported that they had only seven hours training on violence against children, while family physicians had the shortest training programs (9-11). Research from the United States and Israel have shown that there is a large hole between the Violence and its lack of recognition by a physician indicating the urgent need for programs that will increase the recognition of violence against children (16,23,24). Our study has shown that the obstacles faced by our doctors in the recognition of violence were: lack of knowledge, experience, time and psychological barriers, which coincides with the Israeli study (16). To prevent violence against children is necessary to focus on the prevention of child abuse in the family, and not to remove or treat its effects, determine the criteria of mandatory reporting of child abuse and neglect of children in the family and monitor their implementation in practice.

Conclusion

IN our study, physicians were significantly different in the attitude towards the recognition of violence against children according the age group they belong There was no significant difference in the recognition of violence based on gender, age, experience, and practical work.while more reporting has been performed by family physicians . Most respondents had as patinets children, the percentage of the total number of patients, approximately 5-10%. There was a significant difference in attitude compared to a year of service medical doctors were not significantly different in the level of knowledge with respect to their position. Doctors who have completed a one-day training on violence against children did not differ significantly in knowledge and application in relation to physicians who have not completed the training.

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Public health significance of musculoskeletal diseases

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Abstract

Musculoskeletal diseases (MSDs) are public health and individual problem, and with cardiovascular diseases, injuries and mental health disorders, they are the leading causes of increased morbidity and mortality. The hospital MSD registry covering the area of Tuzla Canton (2000.–2005.) provides for the decade activities of care related to the causes and consequences of the diseases. The purpose and objectives of the study aim to establish trends in the incidence and prevalence of MSDs by age and sex, the hospital treatment outcome and the primary diagnosis and MSD comorbidity. The study included 5,825 hospitalized men (43%) and women (57%), divided into the experimental group (4.692) that included inflammatory arthropathy, degenerative forms of rheumatism, metabolic diseases; and the control group covering other MSDs (1.133) within „group M" of ICD-X. The trend in incidence and prevalence of MSD is growing without significant sex-specific differences. New female patients (2.708) with the diagnosis studied are more significantly affected compared to men (1.984). The patients within the studied group of diseases are more significantly affected (3.737) compared to other MSDs (1.008) at the age of <65. The registered individual diagnosis studied (4.594) significantly correlate with a large number of patients from the same group compared to 199 patients with MSD comorbidity. Uncured patients with the diagnosis studied (1.778) and MSD comorbidity (86) are more significant compared to those with cure hospital treatment outcome. It is estimated that every year there is 8% of new patients diagnosed with MSD in the health-care system of the Tuzla Canton, who are mostly <65 years of age, having average five-year hospital treatment frequency of 1,7 times, while women continue to be more significantly affected. The strategies of reducing morbidity, disability and mortality caused by MSDs recommend a cross-cutting approach accompanied with comprehension and acceptance of individual responsibility.

Key words: Musculoskeletal diseases, epidemiology, comorbidity, treatment outcome

Introduction

Musculoskeletal diseases (MSDs) are large public health and individual problem. Cardiovascular diseases, MSDs, injuries and mental health disorders are mass non-communicable diseases accompanied with increased morbidity and mortality. For this reason, MSDs have a large social, medical and economic significance both for the patient, his/her family and for the entire community.

According to the 2001. WHO Report, 40% of the population being >70 years of age suffer from knee osteoarthritis (OA), and 80% of patients suffer from limited movement, 25% of which is unable to carry out daily life activities; 51-59% of patients diagnosed with rheumatoid arthritis (RA) demand change of workplace; 80% of the population has experienced a "low back pain" at least once in a lifetime; it is expected that there will be 6 million people suffering from OP with hip fracture by 2050 [(1)].

The prevalence of MSDs has been constantly on the rise since 1990. in Sweden. It has been registered 15% of men and 21% of women being 16-84 years of age. The immovability is increasing proportionally with age, especially in women being >45 years of age[(2)].

The severity of pain is, in both sexes, the first sign of MSD and it occurs in patients being <45 years of age. The pain caused by MSD occurs in 30%-48% of working women, and in 21%-32% of

men. Women more frequently (40%-60%) experience a long-term disability. It is assumed that the causes are the lack of support and assistance in household, obligations towards children and family and women are mostly sitting at work [3].

The longitudinal study developed by Gjesdal et al. [4] refers to the increase in mortality caused by MSDs and mental health disorders. In around 36% of patients, the registered mortality was 32%. The comorbidity hazard rates are associated with disability (2,9 in women and 2,3 in men). Gjesdal at al. [5] refer to the increase of mortality in the disabled caused by MSDs, who are and are not retired in Sweden and Norway (1990.–1996.). In Sweden, the disabled women died with a mortality rate at 6.1%, men – with a mortality rate at 6,1%, while in Norway, this rate for women was 4,6% and for men – 8,5%.

A patient suffering from MSD has reduced income and opportunities for advancement, is inactive, isolated, with the deteriorating quality of life and uses the health care system to a large extent [6].

The increase in incidence and prevalence of MSDs is expected to be more significant in women and patients being <65 years of age, with significantly uncured outcome and registered primary diagnosis with respect to MSD comorbidity.

Objectives

To identify the trends in standardized incidence and prevalence rates associated with the studied and other musculoskeletal diseases, by sex.

To determine the significance of the diseases studied in relation to other musculoskeletal diseases, by age and sex.

To determine the significance of hospital treatment outcome for the studied group of diseases in relation to the MSD comorbidity.

Methods and Materials

The retrospective study included 10.032 hospital treatments, coded from M00 to M99 according to ICD-X[7]. An MSD Hospital Registry for the Tuzla Canton has been formed; a projection of the Tuzla Canton population was developed by groups of ten-year age span and by sex; the standardized incidence rates (incidence–CI) and prevalence rates (prevalence - CP) are presented in percentages [8]; hospital treatment outcome is presented as: cured, uncured, enabled for his/her work, enabled for work with a change of workplace, enabled for work with the requirement to retrain, enabled merely for performing necessary daily activities and died. To test the hypotheses, the significance and the correlation between the variables of the studied and control group was used, and tested with the t-test at the $p<0.05$ level.

The sample consisted of 5.825 (2.518 men and 3.307 women) patients who live and have been hospitalized in the hospital health care system of Tuzla Canton (TK) in the period from 2000. to 2005. The Experimental - Study Group (4.692) consisted of inflammatory arthropathy, degenerative forms of rheumatism (arthrosis, spondylosis, dorsopathy) and metabolic diseases, while the control group (1.133) included all other MSDs from the „M“ ICD-X group.

Results

The trends of incidence rates (men: from 12% to 25%; women: from 13% to 22%) and prevalence rates (men: from 19% to 32%; women: from 22% to 37%) are on the rise and with no significant sex-specific differences (Figure 1).

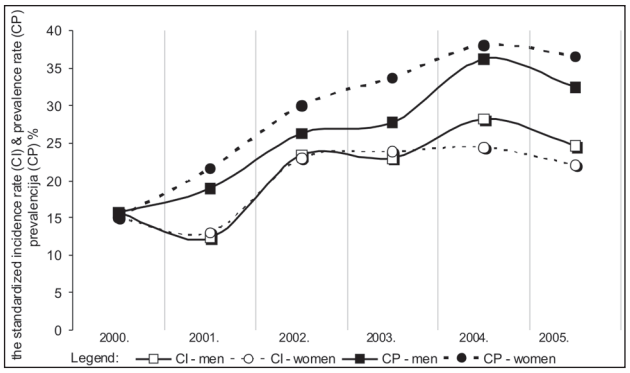

Figure 1. MSD incidence and prevalence trends

The incidence and prevalence rates for the studied MSDs are on the rise and they are significantly higher, in both sexes, for the studied diseases than for the other MSDs (Figure 2: $t= 34,42$ $p<0.05$); (Figure 3: $t=8,66$ $p<0,05$).

There is a significant number of the new patients within the studied group compared to other MSDs ($t=5.40$ $p<0.05$), and within the studied group, the women are more affected (2.708) compared to men (1.984) ($t=1,20$ $p<0,05$) (Figure 4).

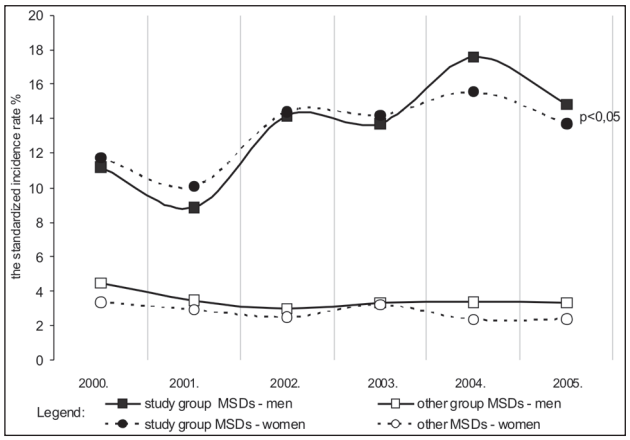

Figure 2. The incidence trend for the studied group and other MSDs by sex

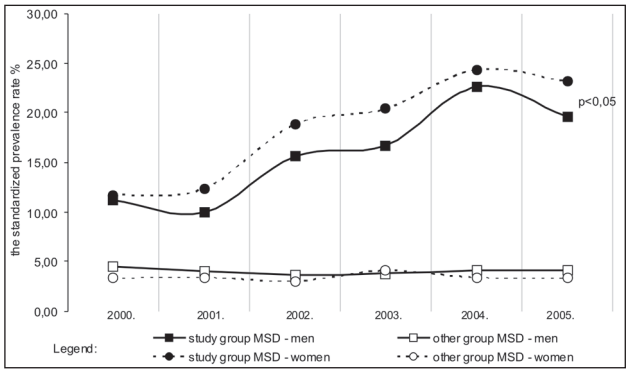

Figure 3. The prevalence trend for the studied group and other MSDs by sex

The patients within the studied group are more significantly affected (3.737) compared to other MSDs (1.008) at the age of <65. (Figure 5: t=1,93 p<0,05).

The hospital outcome for the uncured patients being <65 years of age was 16,3% of women and 10,5% of men (Table 1).

The registered individual diagnosis studied (4.594) significantly correlate with a large number of patients from the same group compared to 199 patients with MSD comorbidity. (Figure 6: t=2,55 *r=0,93* p<0,05).

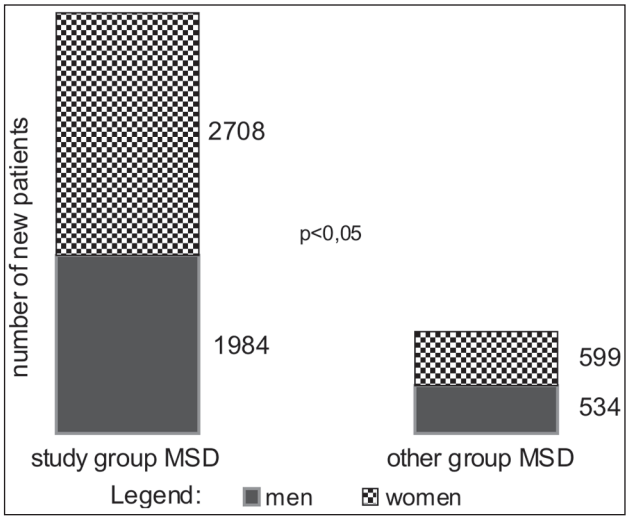

Figure 4. The new patients within the studied group of diseases and other MSDs by sex

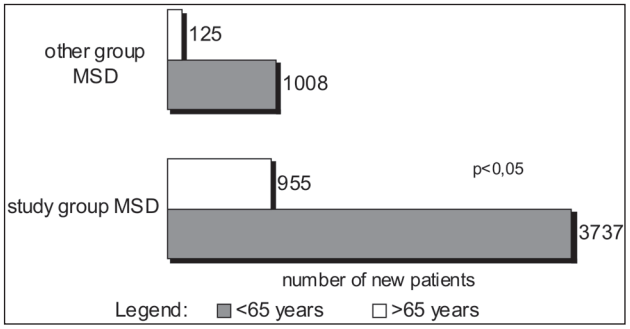

Figure 5. The new patients within the studied group of diseases and other MSDs by age, < and > 65 years of age

The uncured patients with the diagnosis studied (1.778) and MSD comorbidity (86), have been more significantly registered compared to those with cured outcome of hospital treatment (Figure 7: t= 5,38 p<0,05).

Table 1. Hospital treatment outcome by sex and age

Hospital treatment outcome	Total		From the age of <65 year	
	men	women	men	women
Cured	999	834	627	489
Uncured	834	1.377	611	952
Enabled for his/her work	418	540	332	416
Enabled with a change of workplace	47	20	44	18
Enabled for work with the requirement to retraid	22	5	21	4
Enabled merely performing nesessary daily activities	182	513	121	303
Died	16	18	5	7
Total	**2.518**	**3.307**	**1.761**	**2.189**

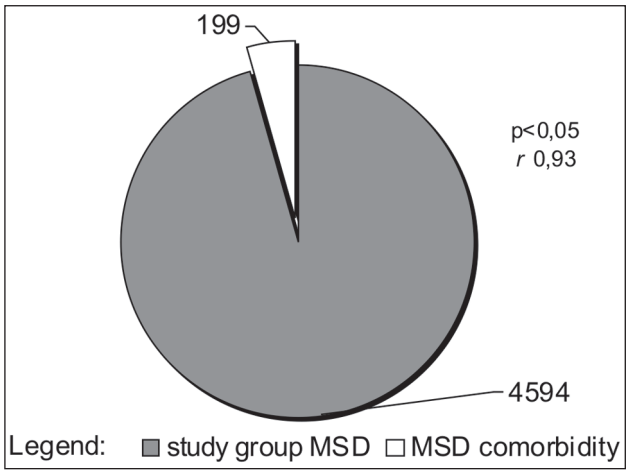

Figure 6. Correlation between the studied group of diseases and MSD comorbidity

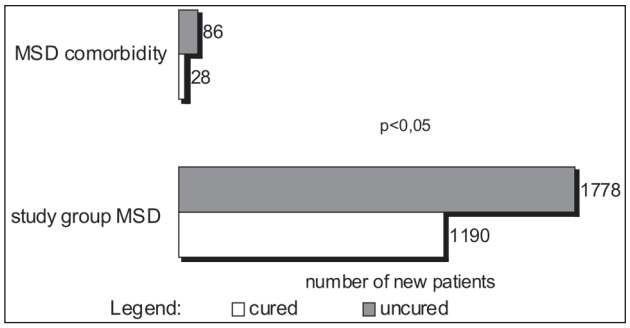

Figure 7. Correlation between the studied group of diseases and MSD comorbidity by treatment outcome

Discussion

The study supports the decade activities of care related to the causes and consequences of the MSDs, and the established hospital registry of the Tuzla Canton (2000. -2005.) is the scientific evidence of the future strategic activities in Bosnia and Herzegovina. The purpose and objectives of the study aim to establish trends in the incidence and prevalence of MSDs by age and sex, the outcome of hospital treatment and the primary diagnosis and MSD comorbidity. The sample (5.825) included hospitalized men (43%) and women (57%), who were divided into the experimental (4.692) and control group (1.133).

According to Specter at al. [9], and WHO and the Board of Bones and Joints Decade [1], it is estimated that every year there is 8% of new patients with MSD in the health-care system of the Tuzla Canton, who are mostly <65 years of age, having average five-year hospital treatment frequency of 1,7 times, while women continue to be more significantly affected (by the studied degenerative forms of rheumatism) compared to men.

In the USA, 43 million people or 18,4% of the population suffers from rheumatic diseases, of which 21,1% are women and 15,7% men. The population aged from 16 to 44 years represents 5%, from 45 to 64 years - 21%, and almost 50% of the population aged over 65 years. In the USA, MSDs are the most frequent cause of a long-term disability. The prevalence of RA in the developed countries ranges between 0,3% - 1%, and in the developing countries, it is lower, as indicated by the rates of 0,1% - 0,2% in this study. In 1999. in the USA, there were 39 million visits to general practitioners out of them 2,4% were treated in hospitals (with average treatment length of 5 days), 2,9 million visits to specialists from other fields of medicine, 2,2 million of emergency visits [10]. According to the Report issued by the Australian Institute of Health and Welfare (AIHW), out of the total number of those suffering from MSD, 1,6 million or 64% were women [11].

The registered individual diagnosis studied significantly correlate with a large number of patients from the same group compared to the patients with MSD comorbidity; however, the other types of comorbidity were not included in this study. Salmi et al. [12] refer to the prevalence of somatic and mental disorders associated with socio-demographic and lifestyle factors. Around 80% of patients have had more than one diagnosis, of which 55% more of somatic diagnoses, mostly in women. For this reason, it is recommended to study comorbidity in different groups of patients with various socio-demographic and health status.

RA is more frequent in women and it requires surgery in 68% of patients. This study points to the development of future guidelines for assessment of ability to work. At the time of recession and reforms, it is important to develop sound perspectives of health, labor productivity and optimal systems of treatment and rehabilitation for MSDs [13].

Morbidity and mortality caused by MSD increases with the increase in obesity prevalence, which is an important causal factor that has not been studied in Bosnia and Herzegovina. The relative risk of different body mass indices (BMI) is related to age and long-term suffering from MSDs, smoking

and the level of education. The obesity is associated with higher mortality rates of all causes, in particular with cardiovascular diseases and MSDs [14]. Increasing BMI by ≥2kg/m^2 increases the risk of OA by >50% in the next 10 years. Weight loss by 10% increases physical functions by 28% [15].

Paget's disease of bone (PDB) – bone deformities after surgery occur in persons being >55 years of age with prevalence of 1-2%; it is more frequent in men, and it rarely occurs in persons being <25 years of age. The symptoms and complications of PDB may be asymptomatic, accompanied with bone pain, fractures, deformities, neurological and cardiovascular disorders, as well as malignant transformations [16].

Work capacity is reduced in patients suffering from MSDs, being 54-65 years of age, which is associated with socio-economic status [17]. In South Africa, girls are exposed to poorer social status, causing significant MSD morbidity in women [18]. The community looses 70% of income due to sick leaves [19].

Ciccolo at al. [20] estimated national profit of 30% of the preserved population health in 2010 in the USA, by introducing measures to improve muscle strength, physical functions and control of depression. The preventive model of "black box" applied in the USA and Sweden is also usable in the prevention of MSDs. To apply this model, the evidence based MSD Registry is necessary [21]. Health for All in the 21st recommended reduction of non-communicable diseases by 2020. with continual reduction in morbidity, disability and mortality caused by MSDs, with the recommendation of cross-cutting responsibility for health in all sectors of the community, with comprehension and acceptance of individual responsibility [22].

Conclusion

The trend in incidence and prevalence of MSD is growing without significant sex-specific differences. New female patients with the diagnosis studied are more significantly affected compared to men. The patients within the studied group of diseases are more significantly affected compared to other MSDs at the age of <65. The registered individual diagnosis studied significantly correlate with a large number of patients from the same group compared to MSD comorbidity. Uncured patients with the diagnosis studied and MSD comorbidity are more significantly registered compared to those with cure hospital treatment outcome. It is estimated that every year there is 8% of new patients with MSD in the health-care system of the Tuzla Canton, who are mostly <65 years of age, while women continue to be more significantly affected.

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