Volume 9 / Number 12 / 2015 ISSN 1840-2291

HealthMED

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

Volume 9 / Number 12 / 2015

HealthMED

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

Address Bolnicka bb, 71 000 Sarajevo,
Bosnia and Herzegovina.
Editorial Board e-mail: healthmedjournal@gmail.com web page: http://www.healthmed.ba
Published by DRUNPP, Sarajevo
Volume 9 Number 12, 2015
ISSN 1840-2291 e-ISSN 1986-8103

HealthMED journal is indexed in:

- EBSCO Academic Search Complete
- EBSCO Academic Search Premier,
- EMBASE,
- SJR Scopus,
- Index Copernicus,
- Universal Impact Factor: Impact Factor is 1.0312 (UIF 2012)
- Electronic Social and Science Citation Index (ESSCI),
- Direct Science,
- ISI - institute of science index,
- SCImago Journal and Country Rank,
- ISC Master Journal List,
- Genamics Journal Seek,
- World Cat,
- Research Gate,
- CIRRIE,
- getCITED and etc.

Sadržaj / Table of Contents

Relationship between unilateraly localized brain MRI lesions and interictal EEG findings in children with Epilepsies **493**
Smail Zubcevic, Maja Milos, Feriha Catibusic, Sajra Uzicanin

Assessment of quality of infrastructure and clinical care performance of HCPs during MNH services at district and sub-district level government hospitals, Bangladesh **500**
Farzana Islam, Aminur Rahman, Abdul Halim, Charli Eriksson, Fazlur Rahman, Koustuv Dalal

Correlation of Urinary Monocyte Chemoattractant Protein-1 Level with Disease Activity among Lupus Nephritis Patients **511**
Azreen Syazril Adnan, Ahmad Suhaimi Bin Mustafa, Raja Ahsan Aftab, Fauziah Jummaat, Amer Hayat Khan

Sleep quality and related factors in patients with Fibromyalgia syndrome **517**
Ekrem Akkurt, Haluk Gumus, Halim Yilmaz, Ilknur Albayrak, Alper Murat Ulasli, Halime Cevik, Gulten Karaca, Umit Dundar

Epidemiologic aspects of urolithiasis in our clinical material **523**
Arber Ejup Neziri, Flamur Tartari, Mustafa Xhani, Avni Fetahu, Liridon Selmani, Ilir Miftari

Premature and extremely low birth weight newborn with Clavicular fracture: A case report **532**
Yazdan Ghandi, Mojtaba Sharafkhah, Alireza Zemani

The evaluation of muscular force physical activity after acute coronary infarction during the first phase of rehabilitation **535**
Sebahat Zeqiri, Nexhmi Zeqiri

Instructions for the authors **540**

Relationship between unilateraly localized brain MRI lesions and interictal EEG findings in children with Epilepsies

Smail Zubcevic, Maja Milos, Feriha Catibusic, Sajra Uzicanin

Pediatric Hospital, University Clinical Center Sarajevo, Bosnia and Herzegovina.

Abstract

Neuroimaging procedures and electroencephalography (EEG) are basic parts of investigation of patients with epilepsies.

We tried to assess relationship between unilaterally localized brain lesions found in routine management of children with newly diagnosed epilepsy and their interictal EEG findings. Out of 361 investigated children with diagnosed epilepsy 46 filled criteria for inclusion in the study. There were 21 girls (45,6%) and 25 boys (54,3%). Neurological examination was normal in 32 cases (69. 6%), with bilateral changes in 6 patients (13,4%) and unilateral in 8 (17,4%). Epilepsy with generalized seizures was present in 41,3%, with focal seizures in 52,2%, while 6,5% of children had epileptic spasms. Most prominent brain MRI findings were cysts that were found in 21,7% and focal dysplasia (15,2%), while in 28,3% neuroradiologists did not classify changes. In 41,3% of patients interictal EEG changes were found to be solely localized on one side or predominant on one side, while they were generalized or bilateral in 28,3%. Five children had normal interictal EEG on repeated recordings (10,9%). Multinomial logistic regression found statistically significant relationship between lateralized EEG epileptic discharges and unilateral focal brain MRI lesions at level $p<0,01$, and was close to be significant with generalized and bilateral EEG discharges.

We conclude that our data are showing relationship between unilateraly localized brain MRI lesions and interictal uniletaral or predominantely unilateral EEG findings in children with newly diagnosed epilepsies.

Key words: epilepsy, brain MRI, EEG, children

Introduction

Diagnostic procedures for establishing diagnosis of epilepsy are usually consisting of neurological examination, neurophysiological studies (electroencephalography - EEG) and neuroimaging studies, preferably magnetic resonance imaging (MRI) in children population. Neuroimaging is important procedure in trying to uncover underlying causes of epilepsies. Epilepsies are often associated with gross or subtle structural lesions or metabolic disorders of the brain. Structural neuroimaging plays an important role in the evaluation, management, and treatment of the child with epilepsy (1,2,3). EEG is most often used to diagnose epilepsy, which causes abnormalities in EEG readings. (4). The practice parameter for a first afebrile seizure recommended EEG as a standard part of diagnostic investigation, but in it neuroimaging was considered optional (5). Until new epilepsy classification in 2014, and new practical definition of epilepsy (6) that added as diagnostic possibility one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk, children rarely got diagnosis of epilepsy after the first unprovoked seizure. At this point we started to have situation where after the first unprovoked seizure we can establish diagnosis of epilepsy, and the need for doing neuroimaging and neurophysiological studies has to be reconsidered. After that we have a new recommendation (7) by ILAE Commission of Pediatrics that neuroimaging is recommended at all levels of care for infants presenting with epilepsy, with magnetic resonance imaging (MRI) recommended as the standard investigation at tertiary level (level A recommendation).

What are the essential diagnostic tools for evaluation of newly diagnosed epilepsy can still be a source of debate. Some authors have disputed

the need for EEG as a standard part of the investigation after the first unprovoked seizure, suggesting that EEG results do not significantly affect treatment decisions, but this should be put in reconsideration as well (8, 9).

Relationships between MRI findings and interictal EEG findings have been studied relatively rarely, and were studied mostly in a way that EEG findings of different kinds were compared with brain MRI findings. If relationships between structural abnormalities identified on MRI and physiologic abnormalities identified on the EEG are found, they could provide important information to assist in the assessment of children with new-onset seizures (10). Berg et al, have reported that focal epileptiform discharges were not found to be predictive of MRI lesions; however, focal slowing was a significant predictor (11), while an abnormal motor examination was the strongest predictor of imaging abnormalities. More research is needed to explore relationships between MRI and EEG findings to determine their relevance in the diagnosis and treatment of children with newly diagnosed epilepsy, especially regarding new epilepsy definitions and classifications.

In this study we wanted to investigate relationship between localized unilateral brain MRI abnormal findings and interictal EEG, and to determine EEG pattern that is expected in these children.

Materials and methods

This survey assessed the population of patients aged from 1 month to 18 years of age, who were diagnosed as epilepsy or some of the epileptic syndromes according to International Classification of Diseases (ICD-10) code G40 (12), using criteria set by International League Against Epilepsy - ILAE (6), in four year period 2011. - 2014. The diagnosis was made on Neuropediatric Department, Pediatric Hospital, University Clinical Center Sarajevo, or its outpatient clinic. Out of 361 investigated patients with epilepsy, 46 fulfilled criteria for inclusion in the study, age, newly diagnosed epilepsy, unilateral localized lesion on MRI that was done within 6 months of diagnosis od epilepsy.

Each child had physical and neurological examination, done according to age of a child; we assessed mental status, motor function and balance, sensorium, newborn and infant reflexes in children less than 1 year, muscle stretch reflexes and cranial nerves examination according to age of a child. Examinations were done by child neurologists with special expertise in epilepsy, learning disabilities and other developmental disabilities, attention deficit disorders, sleep disorders, neuromuscular disorders, brain tumors, neurogenetic disorders, neonatal neurology, intellectual disability and cerebral palsy, pediatric neuro-immunology, pediatric multiple sclerosis and related disorders, among other neurological disorders in children.

Findings of neurological examinations were for statistical purposes classified as normal, bilateral and unilateral. Psychologists using tests adequate for the age of patients did psychological investigations.

Each child had an standard MRI scan with at least T1 and T2, sequences performed at the time of establishing diagnosis of epilepsy, or within the period of 6 months. MRI scans was done by 1.5 or 3.0 Tesla units scanner. Trained neuroradiologists interpreted results of brain MRI by visual analysis.

EEGs were done intericataly with electrodes positioned on scalp according to international 10.20 system, on Deymed TrueScan, and Schwarzer neurology systems, using 21 channel system, and reformatting to standard montages. EEG registrations were done as awake routine (20-30 minutes of registration), sleep routine (30-45 minutes), and sleep deprivation (30-45 minutes after at least 6 hours of night sleep deprivation). Children with normal finding on initial EEG registration had repeated registrations; those who had persistent normal findings had serial EEG registrations. The EEG was interpreted by three consultant child neurologist that are authors, trained and experienced in electrophysiological studies.

For statistical purposes interictal scalp EEG findings were classified as normal, nonspecifical changes (non-focal slowing), borderline, generalized (semi generalized) and focal epileptic discharges. Bilateral epileptic changes on EEG with clear predomination on one side were classified as focal (unilateral), as well as clear focal changes, while generalized, semi generalized and synchronous bilateral changes without clear predomination on one side were classified as generalized.

Upon completion of survey, data were analyzed with standard statistical methods using MS

Excel (Microsoft Office Excel 2010) and SPSS for statistical analysis (Statistical Package for Social Sciences, SPSS Inc., Chicago, Illinois, USA), version 22.0. Descriptive statistics and multinomial logistic regression were used as a measure of relationship, and data were found to be statistically significant at the level of $p<0.05$. The results are presented in tables and graphs.

Results

Our investigated sample consisted of 46 patients. Some descriptive statistics of patients are shown on Table 1.

Neurological examination in the moment of making diagnosis of epilepsy was normal in 32 patients. Detailed data about neurological examination findings are shown in the Table 2.

Epilepsy classification was done in a way that children were classified according to major types of seizures as they were recognized, which is shown on the Table 3.

Brain MRI scans in selected patients showed only unilateral localized lesions. Detailed data about brain MRI scan findings are shown in the Table 4.

Children underwent EEG registration or registrations upon arrival to hospital when they were

Table 1. Sex and age at diagnosis of epilepsy

Sex	Male	Female	Total/Average
	25 (54,35%)	**21 (45,65%)**	**46**
Age range at diagnosis of epilepsy	3 months to 17 years	4 months to 17 years	3 months to 17 years
Average age on diagnosis of epilepsy	6 years 10 month	7 years 4 months	7 years 1 months (Std. Dev. 5.615)
Median at diagnosis of epilepsy	7 years 6 month	6 years	6 years
Children up to 2 years	7	5	12 (26.1%)
Children 3-6 years	6	8	14 (30.4%)
Children 7-18 years	13	7	20 (43.5%)

Table 2. Neurological examination findings in selected group of patients

Neurological examination	Normal	Changed	
N	32	14	
%	69. 57%	30.43%	
		Bilateral changes	Unilateral Changes
N		6	8
%		42,86%	57,14%

Table 3. Types of seizures in selected group of children

Type of seizures	Male	Female	Total
Generalized	10	9	19 (41,30%)
Focal	13	11	24 (52,17%)
Epileptic spasms	2	1	3 (6,52%)

Table 4. Brain MRI findings at time of diagnosing epilepsy

Type of lesion	N	%
Cyst	10	21.73
Tumor	4	8.69
Posttraumatic lesion	6	13.04
Vascular and congenital brain anomalies	3	6,5
Focal dysplasia	7	15.22
Hippocampal sclerosis	3	6.5
Non-specified lesions	13	28.26

Table 5. Interictal EEG findings in children with diagnosis of epilepsy and unilaterally localized brain lesions on MRI

EEG finding	N	%
Normal	5	10.87
Borderline	3	6.52
Nonspecific changes (non-focal slowing)	6	13.04
Generalized or semi-generalized discharges	5	10.87
Bilateral discharges without clear predominance on one side	8	17.39
Bilateral discharges with clear predominance on one side	10	21.74
Focal discharges	9	19.57

Table 6. Relationship between localized focal brain MRI findings and interictal EEG findings (assessed by multinomial logistic regression)

EEGa		B	Std. Error	Wald	df	Sig.
Borderline	Intercept	-.511	.730	.489	1	.484
	[MRI=localized]	0b	.	.	0	.
Focal	Intercept	1.335	.503	7.055	1	.008
	[MRI= localized]	0b	.	.	0	.
Generalized	Intercept	.956	.526	3.297	1	.069
	[MRI= localized]	0b	.	.	0	.
Nonspecific	Intercept	.182	.606	.091	1	.763
	[MRI= localized]	0b	.	.	0	.

a) The reference category is: Normal.
b) This parameter is set to zero because it is redundant.

diagnosed as epilepsy, and their final finding was classified as follows on Table 5.

For testing relationship between unilaterally localized brain MRI lesions and different EEG findings that were characteristic for each of our patients we used multinomial logistic regression to model nominal outcome variables, after classifying interictal EEG results of each patient in a way described in methodology. Results are shown on Table 6.

Relationship was statically significant between unilateral localized lesions of brain shown on MRI and EEGs with focal discharges on level of $p<0.01$, and showed close to statistically significant values for EEGs classified as with generalized discharges at $p=0.069$.

Discussion

Clinical investigation of children with epilepsies needs further standardization. It consists of procedures that require sophisticated medical equipement and well qualified medical stuff. Lot of progress has been made in the investigation of children with epilepsies in recent decades, particularly with the extraordinary advances in neuroimaging.

There were slightly more boys than girls in our study, and this is something that we did not expect, but some recent studies are emphasizing that focal cortical dysplasia is significantly more represented in boys than girls (13). Studies that show higher incidence of epilepsies in girls are rare (14). Average age of patients in our study was 7 years and one month, with most of them in school age (7-18 years), which was in line with overall incidence and prevalence of epilepsies (15).

Neuroimaging methods have become one of the most important workups in dealing with childhood epilepsies. Focal neurologic deficit is an important predictor of an abnormality in the neuroimaging examination (moderate evidence) (16). In our study normal neurological examination was found in 70% of our patients, and 17,39% had unilateral neurological deficit and unilateral focal lesion on brain MRI, while 13,04% had bilateral. This sets a question of relevance of lesions that were found

on MRI. Berg et al evaluated 613 children ages 1 month to 15 years with newly diagnosed epilepsy; nearly 80% had neuroimaging, and relevant lesions were found in 12.7% of these children (17).

Focal seizures were mostly found in our patients (52,17%), while generalized were present in 41,30%. This is quite opposite to study from Iceland (18) where generalized seizures were represented more, but in our study we have selected group of patients that had unilateral focal lesions on brain MRI, so we expected to have even more patients with focal seizures. This can probably be further explained by recognition of seizure semiology where sometimes focal beginning of seizure is not recognized, as well as partly by significance of different brain lesions as epileptogenic factor.

Most frequent unilateral focal lesions in our study were cysts and focal dysplasia, while 28% of lesions were not specified. Some authors traditionally suggest that arachnoid cysts are often an incidental finding in patients with epilepsy and do not necessarily reflect the location of the seizure focus (19). Still, there are studies that contradict that (20). Focal cortical dysplasias are increasingly recognized as one of the most common causes of refractory epilepsies in childhood (21), and were second on our list of MRI findings. Recognition of dysplasia is hard in children because its appearance changes with brain maturation, sometimes being more visible, and sometimes vanishing with older age (22).

EEG findings in our group of patients were showing interesting results. We expected that there will be larger majority of unilateral EEG changes, but changes strictly on one side, and predominantly on one side were present in about 40% of our cases. In about 28% of cases we had epileptic discharges over both hemispheres. Localizing values of interictal epileptic discharges obtained by scalp EEG are not well described. Simultaneous scalp and intracranial study (23) has found that analysis of scalp spikes, such as source modeling, at their initial rising phase might provide useful localizing information about seizure origins in the same patient. In another study (24) authors reported that good association between side of interictal spikes and clinical seizures recorded on scalp telemetry and that of subdurally recorded seizures and side of effective temporal lobectomy indicates that these scalp EEG features should not be ignored when localizing epileptogenesis, even among patients whose non-invasive data are complex enough to require invasive recordings. As reported in their critical review of role of EEG in epilepsy Noachtar and Remy (26) stated that although surface EEG recordings are less sensitive than invasive studies, they provide the best overview and, therefore, the most efficient way to define the approximate localization of the epileptogenic zone.

About 11% of our patient with localized unilateral brain MRI lesions and diagnosis of epilepsy had normal interictal EEG findings on repeated recordings. Other studies have also confirmed that a normal EEG is not reliably related to a normal MRI (10), and we found that child with epilepsy and normal EEG can have a brain lesion.

At the end it is worth to cite Plummer et al (26) where they state that the EEG as leading source for localization approach, or the one that should be most valued, has not changed much in nearly a century despite the relatively recent boom in anatomical and functional imaging in epilepsy—the scalp recorded EEG in the context of a rigorous patient history. The "multimodal" imaging technology on offer today for spike and seizure localization has limited value if its results are interpreted without due respect for the patient's electroclinical seizure manifestations.

Conclusions

Our data are showing that there exists relationship between unilateraly localized brain MRI lesions and interictal uniletaral or predominantely unilateral EEG findings in children with newly diagnosed epilepises. These data are suggesting that in spite of newly designed technics for epilepsy investigation, role of interictal scalp EEG remains important, as non-invasive and affordable tool in exploration of epilepsies, and that brain MRI should be standard procedure in diagnostics of children at onset of epilepsy.

References

1. *Gaillard WD, Chiron C, Cross JH, Harvey AS, Kuzniecky R, Hertz-Pannier L, Vezina LG. ILAE, Committee for Neuroimaging, Subcommittee for Pediatric. Guidelines for imaging infants and children with recent-onset epilepsy. Epilepsia 2009; 50(9): 2147-53*

2. *Commission on Neuroimaging of the International League Against Epilepsy. Recommendations for neuroimaging of patients with epilepsy. Epilepsia 1997; 38(11): 1255-6*

3. *Gaillard WD, Cross JH, Duncan JS, Stefan H, Theodore WH. Task Force on Practice Parameter Imaging Guidelines for International League Against Epilepsy, Commission for Diagnostics. Epilepsy imaging study guideline criteria: commentary on diagnostic testing study guidelines and practice parameters. Epilepsia 2011; 52(9): 1750-6*

4. *Abou-Khalil B, Musilus KE. Atlas of EEG & Seizure Semiology. Butterworth-Heinemann/Elsevier, 2006*

5. *Hirtz D, Ashwal S, Berg A, et al. Practice parameter: Evaluating a first nonfebrile seizure in children: Report of the Quality Standards Subcommittee of the American Academy of Neurology. The Child Neurology Society, and the American Epilepsy Society. Neurology 2000; 55: 616-623.*

6. *Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014; 55(4): 475-82.*

7. *Wilmshurst JM, Gaillard WD, Vinayan KP, Tsuchida TN, et al. Summary of recommendations for the management of infantile seizures: Task Force Report for the ILAE Commission of Pediatrics. Epilepsia 2015; 56(8): 1185-97.*

8. *Freeman JH. Practice parameter: Evaluating a first nonfebrile seizure in children: Report of the Quality Standards Subcommittee of the American Academy of Neurology, the Child Neurology Society, and the American Epilepsy Society. Neurology 2001; 56: 574.*

9. *Gilbert DL, Bencher CR. An EEG should not be obtained routinely after first unprovoked seizure in childhood. Neurology 2000; 54: 635-641.*

10. *Doescher JS, deGrauw TJ, Musick BS, Dunn DW, Kalnin AJ, et al. Magnetic resonance imaging (MRI) and electroencephalographic (EEG) findings in a cohort of normal children with newly diagnosed seizures. J Child Neurol 2006; 21(6): 491-5.*

11. *Berg AT, Testa FM, Levy SR, Shinnar S. Neuroimaging in children with newly diagnosed epilepsy: A community-based study. Pediatrics 2000; 106: 527-532.*

12. *World Health organization. International Statistical Classification of Diseases and Related Health Problems 10th Revision. http: //apps.who.int/classifications/icd10/browse/2015/en*

13. *Ortiz-González XR, Poduri A, Roberts CM, Sullivan JE, Marsh ED, Porter BE. Focal cortical dysplasia is more common in boys than in girls. Epilepsy Behav 2013; 27(1): 121-3.*

14. *Sidenvall R, Forsgren L, Blomquist HK, et al. A community-based prospective incidence study of epileptic seizures in children. Acta Paediatr 1993; 82(1): 60–65.*

15. *Banerjee PN, Hauser A. Incidence and prevalnece. In: Engel J, Pedley TA, Aicardi (eds). Epilepsy: A Comprehensive Textbook, 2nd ed. Philadelphia. Lippincott Williams & Wilkins, 2007, pp 45-56.*

16. *Bernal B, Altman N. Neuroimaging of Seizures. In: Medina LS, Blackmore CC (eds.). Evidence-Based Imaging: Optimizing Imaging in Patient Care. New York: Springer Science+Business Media, 2006.*

17. *Berg AT, Testa FM, Levy SR, Shinnar S. Neuroimaging in children with newly diagnosed epilepsy: A community-based study. Pediatrics 2000; 106: 527-532.*

18. *Olafsson E, Ludvigsson P, Gudmundsson G, et al. Incidence of unprovoked seizures and epilepsy in Iceland and assessment of the epilepsy syndrome classification: a prospective study. Lancet Neurol 2005; 4(10): 627–634.*

19. *Arroyo S, Santamaria J. What is the relationship between arachnoid cysts and seizure foci? Epilepsia 1997; 38(10): 1098-1102.*

20. *Gan YC, Connolly MB, Steinbok P. Epilepsy associated with a cerebellar arachnoid cyst: seizure control following fenestration of the cyst. Childs Nerv Syst 2008; 24: 125-134.*

21. *Najm IM, Tassi L, Sarnat HB, Holthausen H, Russo GL. Epilepsies associated with focal cortical dysplasias (FCDs). Acta Neuropathol 2014; 128(1): 5-19.*

22. *Jayakar P, Duchowny M. MRI-negative refractory focal epilepsy in childhooe. In: So LE, Ryvlin P (eds). MRI-Negative Epilepsy: Evaluation and Surgical Management. Cambridge University Press, 2015, 198-205.*

23. *Ray A, Tao JX, Hawes-Ebersole SM, Ebersole JS. Localizing value of scalp EEG spikes: a simultaneous scalp and intracranial study. Clin Neurophysiol 2007; 118(1): 69-79.*

24. *Blume WT, Holloway GM, Wiebe S. Temporal epileptogenesis: localizing value of scalp and subdural interictal and ictal EEG data. Epilepsia 2001; 42(4): 508-14.*

25. *Noachtar S, Rémi J. The role of EEG in epilepsy: a critical review. Epilepsy Behav 2009; 15(1): 22-33.*

26. *Plummer C, Harvey AS, Cook M. EEG source localization in focal epilepsy: where are we now? Epilepsia 2008; 49(2): 201-18.*

Corresponding Author
Smail Zubcevic,
Pediatric Hospital,
University Clinical Center Sarajevo,
Sarajevo,
Bosnia and Herzegovina,
E-mail: smail.zubcevic@gmail.com

Assessment of quality of infrastructure and clinical care performance of HCPs during MNH services at district and sub-district level government hospitals, Bangladesh

Farzana Islam[1, 2], Aminur Rahman[2], Abdul Halim[2], Charli Eriksson[1], Fazlur Rahman[2], Koustuv Dalal[1]

[1] School of Health and Medical Sciences, Orebro University, Orebro, Sweden,
[2] Centre for Injury Prevention and Research, Bangladesh (CIPRB), Dhaka, Bangladesh.

Abstract

Background: Despite the progress towards the MDG4 and 5, compared to the developed world maternal and newborn deaths are still high in Bangladesh. Poor quality of maternal and newborn health care is often blamed for this high mortality. However, only few studies assessed the quality of health care of the facilities in Bangladesh. This study assessed the two important components of quality of maternal and newborn health care namely, infrastructure and performance of health care providers (HCPs) of three different levels of health facilities in Bangladesh.

Methodology: A cross sectional survey including observation and document reviews conducted to measure the quality of infrastructures and to assess the clinical care performance of the health care providers related to maternal and newborn services. Two district hospitals, two maternal and child welfare centres, and 10 upazila (sub-district) health complexes were purposively selected from Thakurgaon and Jamalpur districts of Bangladesh to conduct the study. Six components including human resource, physical infrastructure, infection prevention, equipments/logistics/supplies, essential drugs and recordkeeping were assessed under infrastructure. Maternal and newborn care services provided by the health care providers were evaluated during antenatal care, postnatal care, conduction of delivery care and newborn care. Sixteen doctors using pre-tested infrastructure survey and observation checklists collected data between November and December 2011. The average of the sub-items of each item was calculated and then the mean average of the items were calculated and expressed in percentage. Ethical clearance was obtained from a competent authority and informed consent was obtained from the hospital authorities and the persons who participated in the study.

Results: The percentage of mean average scores of all items of infrastructure for district hospitals, maternal and child welfare centres and upazila health complexes were 57.1%, 52.7% and 45.9% respectively, which were below the cut-off point (60.0%). None of the health care providers of three types of government hospitals obtained 100% score in any areas namely antenatal care, post-natal care, delivery care and newborn care.

Conclusion: Quality of infrastructure of health facilities, and clinical care performance of the health care providers during discharging maternal and newborn health services were found poor in the selected three types of public hospitals.

Key words: health care providers, public hospital, infrastructure, maternal and newborn health, performance, quality improvement

Introduction

Bangladesh, with a population of almost 150 million and the 9th largest country in terms of density alone has many challenges in improving the health of its citizens[1-2]. Sharp declines have been noted in maternal and under-5 child mortalities and progressively aiming to accomplish the Millennium Development Goals (MDGs) 4 and 5 at time[3-4]. Despite the progress towards the MDG4 and 5, the mortality rates of both maternal and under-five children including newborns are still high in Bangladesh in comparison to developed countries[5-6].

Similar to other low and middle income countries (LMICs) poor quality of maternal, newborn and child health care remains a significant pro-

blem in Bangladesh. Compromising with the quality of maternal and newborn health (MNH) care is a key contributor to maternal and newborn mortality, which are closely related to health system and the services provided to the clients at health facilities[7-12].

Improving the quality of health care is one of the most important areas among health policy planners, health care providers (HCPs) and public health researchers globally including Bangladesh. However, defining the quality of care, and how to measure it for a particular health context is remained difficult as it depends on the socio-cultural and economic status; and on the health system of the countries [13]. The well accepted definitions of quality improvement of health care defined by the US Agency for Healthcare Research and Quality is "doing the right thing to the right person at the right time at the lowest cost" [14]. Avedis Donabedian, the pioneer of the concept of improving quality health care identified a framework of understanding and evaluating the quality improvement in healthcare. This framework is recognized in the world of quality health care as the "Donabedian Quality Triad" which measures the quality of care and the components of the triad follow a linear relationship of structure, process and outcome. The structure indicates settings of the health facilities where clients obtain services. It is measured by assessing the quality of infrastructure of health facility, HCPs' attributes and administrative characteristics. Facilitation and motivation on structure play key role to create settings a strong base for quality care. Process evaluates whether the health care offering to the patients are acknowledged as quality care. The end result of the patient care is the outcome measures and it is the ultimate indicator of care quality including death, infection, hospitalization, and discharge with restoration of function[15-16].

This paper is describing the quality of infrastructures and clinical care performance of HCPs in MNH services at public hospitals of Bangladesh through structure and process measurements, the first two component of 'Donabedian Quality Triad". However, in this survey we assessed outcome measures as well, which has been published else where[17].

Methodology

A cross sectional survey was conducted to measure the quality of infrastructures. Moreover, observation and document reviews were carried out to assess the performance of the HCPs related to MNH care. Data was collected between November and December 2011. Fourteen public hospitals of Thakurgaon and Jamalpur districts were selected purposively. District-level hospitals, comprising two district hospitals (DHs) and two maternal and child welfare centers (MCWCs), and 10 sub-district-level hospitals called upazila health complexes (UHCs) were included in this study. Upazila health complexes are the primary healthcare centers and the first point of referral. Each of these health complexes serves a population of between 200,000 and 400,000 and has a bed capacity of between 31 and 50. The district hospitals are the secondary level hospitals with 100 beds where more advanced care and specialist services in medicine, surgery, obstetrics and gynecology, pediatrics, ophthalmology, clinical pathology, blood transfusion and public health are provided[17]. Maternal and child welfare centres are also secondary level hospital with 20 beds and provide emergency obstetric care and other related services like antenatal care and family planning[18].

The study was designed based on 'Donabedian Quality Triad" where quality of infrastructure and clinical care performance of the HCPs during MNH services at the selected health facilities of different levels were assessed through structure measurement and process measurement of the quality triad.

In this study human resources, hospital supportive systems including physical infrastructure, infection prevention system and equipment/logistics/supplies, essential drugs and recordkeeping were included as elements of structure measurement[19]. These organizational factors influence the quality of services during MNH care provided by the HCPs. For process measurement clinical care services during antenatal, postnatal, delivery and newborn care provided by the HCPs were evaluated.

Different types of observation checklists were utilized during this study which was developed through a series of workshops with the program personnel of the Ministry of Health and Family Welfare, Government of the People's Republic of

Table 1. Components, items, sub-items and scoring system of assessing the quality of infrastructures of hospitals

Components	Items	Number of Sub-items	Score
1. Human resources including doctors and nurses	Sanctioned post	-1	0 - Post vacant 1 - Post occupied
2. Physical Infrastructures	Status of signboards /billboards	9	
a) Physical infrastructure	Facility for blood transfusion	5	For each sub items
	Facility for communication and electricity	3	the score is 0 or 1
	Water & sanitation status	6	0 - not or
	Facility for pharmacy & drugs	7	unsatisfactory
	Ambulance services	9	1- satisfactorily
b) Laboratory diagnostics	Lab Logistics/supplies	12	available
	diagnostic test available	17	
3. Infection prevention	Admission areas (OPD)	1	For each sub items
a) Cleanliness	Inpatient areas and wards	1	the score is 0 to 2
	Delivery room	1	
	Bed linens and pillows	1	0 - unclean
	Women's toilet/latrine	1	1 - average
	Ground campus	1	2 - Very clean
	Storage areas (clean and dry)	1	
b) Infection control	Emergency	11	
	OPD	11	
	Delivery care ward	11	For each sub items
	Newborn ward	11	the score is 0 or 1
	OT	11	0 - not available
	Maternity ward	11	1 - available
4. Equipments/logistics /supplies	ANC and PNC Room in OPD	13	For each sub items the score is 0 to 5 0 - not available 1 - not functioning 2 - unutilized but possible to repair 3 - utilized but need to replace 4 - functioning but not utilized 5 - functioning and utilized
	Neonatal/Paediatric Room (OPD)	13	
	Labor /delivery Room	28	
	Maternity Ward (Obstetric ward)	9	
	Operation Theatre (OT)	38	
	Neonatal ward	19	
5. **Essential drugs**			For each sub items
a) Essential and Emergency drugs for maternal care	Oral and Injectable Drugs	17	the score is 0 or 1
b) Essential & Emergency drugs for neonatal care	Oral and Injectable Drugs	17	0 - not available 1- available
6. Record keeping		5	
	History	7	For each sub items
	Examination findings	9	the score is 0 or 1
	Record of investigation advised	- (judgmental Obs/	
	Treatment given	Ped specialist with a	0 - not recorded
	Advice record	scale 0 to 10)	1- recorded
		- Judgmental as above	

ANC-antenatal care, PNC-postnatal care, OPD-out-patient department, OT-operation theatre

Bangladesh related to MNH services, obstetricians, pediatricians and anesthesiologists. Considering the country context, socio-economic and cultural context of the service recipients, availability of resources including service providers, capacity of the hospitals and patient load, the workshop participants came to a consensus to finalize the contents for the check lists to assess the quality of care of MNH services of hospitals. Checklists were developed in English and pretested in a public health facility other than the sampled hospitals. The data was collected by four teams, each comprised of one pediatrician and one gynecologist. After receiving extensive training, the data collection teams visited all 14 health facilities and surveyed the status of infrastructure and clinical care performance of the MNH services provided by the HCPs using structured checklists.

Assessing the quality of infrastructures

The instruments used for assessing the quality of infrastructures contained various components and each component consisted of different items and sub-items. The average of the sub-items of each item was calculated and then the mean average of the items were calculated and expressed in percentage. The workshop participants decided that the quality of the infrastructures of each component would be acknowledged as satisfied if the score would 60.0 percent or above.

Assessment of clinical care performance of the HCPs during MNH services

The data collectors observed the services using the structured observation checklist when HCPs including doctors and senior nurses provided care to the patients in MNH related areas namely antenatal, postnatal, delivery and newborn care. Total 240 HCPs of 14 hospitals were assessed for their clinical care performance when they provided services to the clients of the selected areas.

All the mentioned activities were subdivided and scored separately. This observation checklist was a "must do" check list. In other words every activity of each of the component should be performed by the HCPs when they would provide services.

Table 2. Components, activities, sub-activities and scoring system of assessing the clinical care performance of the HCPs

Components	Activities	Number of sub-activities	Score (0-1)
Antenatal care	1. General	4	
	2. History taking	7	
	3. Clinical Examination	5	
	4. Care provision	13	
	5. Record keeping	5	
Postnatal care	1. General	10	
	2. Newborn history	2	
	3. Newborn assessment	6	
	4. Care provision	7	
	5. Record keeping	5	
Delivery care	1. General	19	0 - Not performed
	2. Care during birth	7	1 - Performed
	3. Immediate newborn care	10	
	4. Active management of the third stage of delivery	5	
	5. Immediate postpartum evaluation and care	8	
	6. Infection prevention after birth (if applicable)	3	
	7. Recordkeeping	5	
Newborn care	1. Management of newborn asphyxia	8	
	2. Management of Low Birth Weight (LBW) neonates	5	
	3. Feeding for stable LBW newborn (wt >1800 gm, >34 week):	7	
	4. Prevention of infection:	2	
	5. Management of Neonatal Sepsis	10	

Ethical issues

Ethical Review Committee of the Centre for Injury Prevention and Research, Bangladesh (CIPRB) approved the study including the methodology. The Directorate General of Health Services and Directorate General of Family Planning of Ministry of Health and Family Welfare, Bangladesh provided written permission to conduct the study in the aforementioned hospitals. Informed written consent was obtained from the authorities of each hospital, the HCPs and the clients who participated in the study. For privacy and confidentiality of information, the study participants were reassured that all information received would remain anonymous and the collected data would be used for this research only.

Results

Assessing of quality of infrastructures

The status of human resources, hospital supportive systems (physical infrastructure, infection prevention system and equipment/logistics/supplies), essential drugs and recordkeeping status of the selected hospitals were evaluated to reveal the quality of infrastructures. In this survey the cut-off point for satisfactory level of quality of any component of the infrastructures was considered 60 percent and above which was decided at the national level workshop with the programme personnel.

All three types of surveyed hospitals scored on an average below 60 percent when all the areas considered together. It was revealed that the infra-

Table 3. Distribution of score on different components of hospitals infrastructures by hospitals of different types

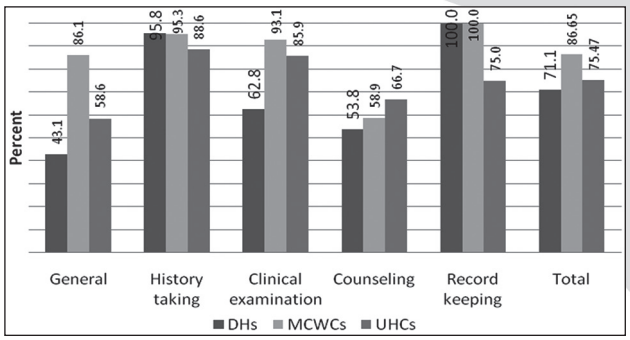
Components of evaluation	DHs	MCWCs	UHCs
	% of average mean	% of average mean	% of average mean
Human resources			
	72.7	**100.0**	**45.6**
Physical infrastructures			
Physical infrastructure	84.6	66.1	66.7
Laboratory diagnostic services	85.7	0.0	62.5
Mean of average mean	**85.2**	**33.1**	**64.6**
Infection prevention			
Cleanliness	46.4	73.3	46.3
Waste management system	8.4	50.0	37.5
Mean of average mean	**27.4**	**61.7**	**41.9**
Equipments/logistics/supplies			
Equip/logistics/supply in ANC and PNC Room in OPD	96.2	87.7	84.9
Equip/logistics/supply in Neonatal/Pediatric Room (OPD)	30.8	0.0	18.7
Equip/logistics/supply in Delivery care /delivery Room	79.6	72.1	68.2
Equip/logistics/supply in Maternity Ward (Obstetric ward)	81.1	58.9	62.2
Equip/logistics/supply in OT Complex	84.8	86.9	46.8
Equip/logistics/supply in Neonatal Ward	55.7	0.0	25.6
Mean of average mean	**71.4**	**50.9**	**51.1**
Essential drugs			
Essential and Emergency drugs for maternal care	73.5	39.7	61.8
Essential & Emergency drugs for neonatal care	29.4	38.2	35.6
Mean of average mean	**51.5**	**39.0**	**48.7**
Record keeping			
Completeness of pt. file in Maternity Ward	48.9	62.5	32.3
Completeness of pt. file in Neonatal Ward	20.0	0.0	15.1
Mean of average mean	**34.5**	**31.3**	**23.7**
Mean average for each type of hospitals	**57.1**	**52.7**	**45.9**

DHs-district hospitals, MCWCs-maternal and child welfare centres, UHCs-upazila health complexes

structure and human resource status were in satisfactory level in district hospitals and maternal and child welfare centres (100 percent and 72.7 percent respectively), however, upazila health complexes scored only 45.6 percent. Human resource component was evaluated on the basis of the actual number of available doctors and nurses against the sanctioned posts. The quality of physical infrastructures was found satisfactory in district hospitals and upazila health complexes (85.2 percent and 64.6 percent respectively), however, infection prevention system was not satisfactory in both types of hospitals (27.4 percent and 41.9 percent respectively). The availability of equipments, logistics and supplies was found above the cut-off point level in district hospitals (71.4 percent). The worst situation was revealed in availability of essential drugs and record keeping system. All three types of hospitals scored below cut-off point ranging from 23.7 percent to 51.5 percent.

Assessing of clinical care performance of the HCPs during MNH services at hospitals

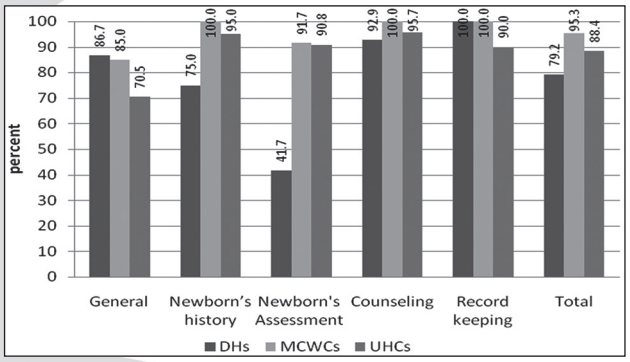
The clinical care performance of HCPs including doctors and senior nurses was assessed when they provided care to the patients in the MNH areas namely antenatal, postnatal, delivery and newborn care. In the observation check list each health care provider should accomplish all the activities including their sub-activities correctly. In other words, healthcare providers should obtain 100 percent score in all activities listed in the check lists.



DHs-district hospitals, MCWCs-maternal and child welfare centres, UHCs-upazila health complexes

Figure 1. Distribution of performance of HCPs on antenatal care by types of hospitals

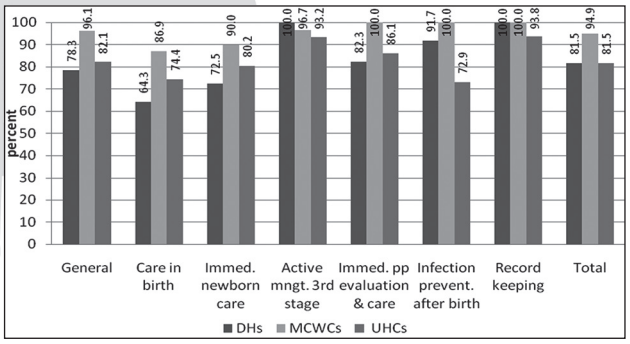
The performance of HCPs who provided antenatal care services in maternal and child welfare centres (Figure 1) were better in all survey areas than district hospitals and upazila health complexes, except counseling of patients which was found better in upazila health complexes. The HCPs scored 100 percent only in record keeping at district hospitals and maternal and child welfare centres. However, when all the activities measured together, HCPs of all three types of hospitals did not able to score 100 percent and the range was 71.1 percent to 86.7 percent.



DHs-district hospitals, MCWCs-maternal and child welfare centres, UHCs-upazila health complexes

Figure 2. Distribution of performance of HCPs on postnatal care by types of hospitals

Performance score of HCPs during postnatal care (Figure 2) was found less than 100 percent when all the activities considered together (ranging from 79.2 percent to 88.4 percent). However, the performance score was found better in maternal and child welfare centres than district hospitals and upazila health complexes. The HCPs of maternal and child welfare centres scored 100 percent in three out of five types of activities.



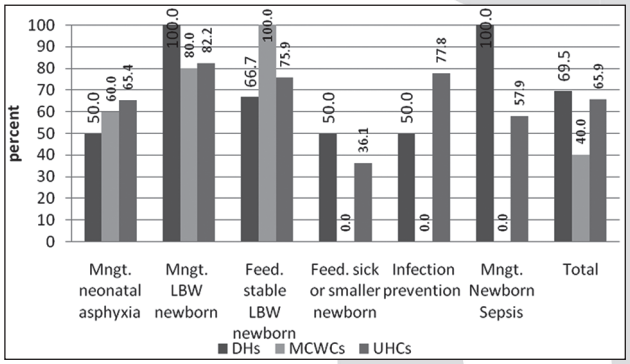
DHs-district hospitals, MCWCs-maternal and child welfare centres, UHCs-upazila health complexes

Figure 3. Distribution of performance of HCPs on delivery care by types of hospitals

However, the HCPs of upazila health complexes did not score 100 percent in any of the ac-

tivities. Regarding newborn assessment the HCPs of district hospitals scored only 41.7 percent whereas the HCPs of maternal and child welfare centres and upazila health complexes scored 91.7 and 95.0 percent respectively.

Similar to antenatal and post natal care, the performance score during delivery care (Figure 3) was found below 100 percent in all three types of hospitals, however, the score was found better in maternal and child welfare centres (94.9 percent) than district hospitals and upazila health complexes (81.5 percent each). Moreover, the HCPs of maternal and child welfare centres scored 100.0 percent in active management of 3rd stage of delivery, immediate postpartum evaluation and care, and infection prevention after birth. Although, performance score of HCPs of district hospitals and upazila health complexes found below 100 percent in almost all individual activities.



DHs-district hospitals, MCWCs-maternal and child welfare centres, UHCs-upazila health complexes LBW-low birth weight

Figure 4. Distribution of performance of HCPs on newborn care by types of hospitals

During the survey it was revealed that the clinical care performance score of HCPs during newborn care (Figure 4) of all three types of health facilities was below 100.0 percent when the activities considered together (ranging from 40.0 percent to 69.5 percent). The HCPs of maternal and child welfare centres scored zero in activities regarding feeding of sick or low bith weight newborns, infection prevention and management of newborn sepsis. On the other hand, performance score of HCPs of district hospitals was found 100.0 percent in management of low birth weight newborns and management of newborn sepsis.

Discussion

We discussed the survey results based on the first two components of the "Donabedian Quality Triad" which include structure and process measurements. In this survey we assessed quality of infrastructure and clinical care performance of HCPs during MNH services at district and sub-district level government hospitals of Bangladesh through structure and process measurements as proposed by Donabedian's quality triad. Quality of health care could be measured in any of the points namely structure, process and outcome measurements or all three together. Structure measure is easy to assess and the main advantage of it is that this measure gives a concrete answer. For example, whether the hospital has pediatrician for providing newborn care 24/7 or the hospital has essential and emergency drugs for neonatal care. Process comprises all the activities which take place among the HCPs and their clients. Donabedian emphasized on technical skill of HCPs during process measurement. Similar to structure, process measures have also some advantages as they are very precise and logical for both the clients and HCPs. Through process measurement it is very simple to get the answer of the question: "are the HCPs doing the right things for his clients?" The strength of process measures is accomplishment of an action through which quality of care could be assessed[15-16].

The instruments those were used in our survey for structure measurement and process measurement had the uniqueness that it could assess a component as a whole and also the items and sub-items of each component. As a result these instruments not only helped to identify the status of the quality of infrastructures and performance of HCPs as a whole, but also provided information at the component and item or sub-item level which will eventually help to identify areas where QI interventions would be required.

Structure measures

In the study it was observed that the organizational factors of structure measurement were poor. There were inadequacy of human resources, lack of hospital supportive systems (physical infrastructure, infection prevention system and equipment/logistics /supplies) and essential dru-

gs, and poor record keeping which influenced the MNH services.

Inadequate human resources

Similar to our study, other studies conducted in Bangladesh showed that lack of human resources including doctors and nurses are one of the main barriers of providing quality care especially in MNH related services in public hospitals. As per the report of World Health Organization, Bangladesh is among the 57 countries where there is severe shortage of health personnel for hospitals[20]. Khan MM *et al.* in their study showed that lack of doctors and nurses were present in all types of health facilities including district hospitals, maternal and child welfare centres and upazila health complexes. They found a significant gap between the need of HCPs throughout the country and sanctioned post authorized by the Ministry of Health and Family Welfare. The gap was found high in maternal and child welfare centres and upazila health complexes (90.0 percent and 22.0 percent respectively), however, the minimum gap was found in district hospitals (2.0 percent). In this survey, it was also revealed that the actual number of doctors and nurses appointed were much more less than the sanctioned post[21]. In another study Mridha M K *et al.* revealed that there was scarcity in skilled human resources in emergency obstetric care in hospitals of Bangladesh[22]. In our study, we found that sanctioned post was fulfilled with 100.0 percent HCPs in maternal and child welfare centres; however, the situation was worse in district hospitals and upazila health complexes for MNH services. More than one fourth of sanctioned post for doctors and nurses of district hospitals and over half of the sanctioned post of upazila health complexes were found vacant. Shortage of human resources usually contributes to working overload. As a result the HCPs often compromise with the quality of services[17].

Lack of hospital supportive systems (physical infrastructure, laboratory diagnostic services, infection prevention system and equipment/ logistics /supplies) and essential drugs, and poor record keeping

Along with adequate skilled health personnel, hospitals need supportive system including physical infrastructure, laboratory diagnostic services, infection prevention system and equipment/logistics /supplies and availability of drugs. These are the basic requirements of a hospital to provide health care services to their clients. It is not possible to provide quality health services if the HCPs have inadequacy in essential drugs or lack of support systems. Through several studies it was identified that hospitals of most of the developing countries including Bangladesh are facing the challenges on adequacy in supportive system and availability of essential drugs and compromising with the quality of health services which are consistent with our study findings[17,23-24]. Our study findings showed that the quality of infrastructure as a whole was poor in all three types of hospitals. However, some of the components of the infrastructures were found satisfactory. In this study it was revealed that the status of physical infrastructure was within the satisfactory level in all types of hospitals and the same types of finding were revealed in a study conducted in Bangladesh[25]. Consistent with the result of a survey conducted in India we found that most of the equipments, logistics and supplies were available and functioning in district level hospitals and but deficiencies were noted in maternal and child welfare centres and upazila health complexes[26]. The status of infection prevention system was found very poor in all types of health facilities which is a common scenario of many hospitals of developing countries[27].

Patient record keeping is very important because of monitoring the patients' condition which contributes to further diagnosis especially for pregnant women and newborns. Moreover, the recorded data often use in administrative, financial, quality assurance, forensic and lawful issues, as well as in public health research. Documentation and record keeping has an important role on quality improvement. Good quality data can provide the scenario of current quality of health care services and help to identify the gap and design suitable intervention program for the particular areas. In this recent study the record keeping system both in maternal and newborn wards was found insufficient. Inadequacy in record keeping is not a major problem for developing countries only, there are evidence that record keeping frequently drop down its quality even in USA, Australia and Scandinavia[28].

Process measures

The process measure for this study was clinical care performance of the HCPs during MNH services which influenced delivery outcome. The assessment covered antenatal, postnatal, delivery and newborn care services and showed that the quality of clinical care performance of the HCPs was poor.

Antenatal and postnatal cares are very important component of MNH services. These two components of MNH services provide opportunity to a woman and her family to be familiar with the risks associated with pregnancy and post pregnancy. These MNH services assist the women to prepare themselves mentally and physically regarding challenges facing during pregnancy and childbirth. Moreover, antenatal and postnatal care influence positively on their health seeking practices and decision making. To prevent maternal and newborn morbidity and mortality, delivery and newborn care are equally important as antenatal and postnatal care. Consistent with other studies conducted in Bangladesh and other developing countries, we found that quality of clinical care performance during MNH services was compromised[25,27,29]. The lowest score was revealed in newborn care among all four areas assessed; and the HCPs working in maternal and child welfare centres performed worse. The poorest performances were found in management of newborn sepsis, feeding of sick or smaller newborn and infection prevention and they scored zero. Findings of a study conducted in Albania, Turkmenistan and Kazakhstan together showed that the performance of HCPs of these three countries is slightly better in newborn care than obstetric care which are contradictory to our study findings[27].

When to sick help and where to give birth are the two most important elements which influence the outcome of pregnancy and appropriate counseling during antenatal care is the source of learning about these elements. Our study findings showed that the performance score in counseling in antenatal care in all three types of hospitals was very low (ranging from 53.8 percent to 66.7 percent). This might be a sign of poor interrelationship between the HCPs and clients. However, the study result of Mansur *et al.* conducted in Bangladesh showed the performance was better in counseling during antenatal care[25].

There are some limitations existed in the current study. We did not go for randomization during district selection. Due to marginal resources only two districts were selected purposively. We did not check whether the hospital equipments were functioning or not, rather we relied on the HCPs responses. As there is no standard scoring system to measure the quality of infrastructure and performance of HCPs, the results of the current study could not be compared directly.

Conclusion

Quality of infrastructure of health facilities, and the performance of the HCPs during discharging MNH care were found poor in the selected different levels of health facilities. Despite the required number of sanctioned posts there was a shortage of human resource particularly in the district and upazila level health facilities, which is a pre-requisite to provide quality care. Although the district and upazila level hospitals scored above the cut-off point (60 percent) in physical infrastructure, the condition in the MCWCs was much poor. Apart from MCWCs, the infection prevention measures were found poor in the other two types of health facilities. Equipment, logistics and supplies scored below the cut-off point in MCWCs and UHCs. There was a lack of essential drugs and poor record keeping system of all types of health facilities. At none of the health facilities the HCPs' performance was not optimum in all items of each patient care component namely, antenatal, delivery and post-natal care and care of the sick babies. Finally, it could be concluded that on the whole the quality of care of the said three different levels of health facilities was poor.

Similar to many of the developing countries, Bangladesh is facing challenges in decreasing maternal and newborn deaths. Most of the deaths could be prevented through proper antenatal care, quality emergency obstetric and newborn care as this avoidable occurrence take place either during delivery or immediate after birth.

To address the current situation, a policy should be developed to ensure optimum number of HCPs, equipments, logistics and supplies according to the level of health facilities. HCPs should receive regular training related to MNH care for improving their performance.

Authors' contributions

FI have contributed actively in designing the methodology and implementation of the study. Under the supervision of FR, AR, CE, AH and KD, FI carried out data analysis, conducted literature review and wrote down the manuscript. AH and FR are guarantors. All authors read and approved the final manuscript.

Authors' information

The authors have been involved in research activities in MNH for the last 20 years in Bangladesh.

Acknowledgments

We gratefully acknowledge World Health Organization-Bangladesh for funding the research project. We would like to thank to the Directorate General of Health Services and Directorate General of Family Planning, Ministry of Health and Family Welfare of the Government of the people's republic of Bangladesh for extending their cooperation throughout the study period. We thank the civil surgeons and deputy directors of Family Planning Department in Jamalpur and Thakurgaon districts, the healthcare facility managers, service providers, and their clients for their support in the study. We are also thankful to the professional experts including programmer, gynecologists, pediatricians and anesthesiologists for their contribution in the workshops for developing the instruments using in this study. We gratefully acknowledge Col. AHM Kamal (Rtd) for English language editing of the manuscript.

References

1. *Population Census-2011, Bangladesh.*
2. *Bangladesh Fact. Bangladesh population 2014-World population review.*
3. *National Institute of Population Research and Training (NIPORT). Bangladesh demographic and health survey 2014 key indicators. NIPORT: Dhaka, Bangladesh; 2015.*
4. *Arifeen S El, Hill K, Ahsan KZ, Jamil K, Nahar Q, Streatfield PK. Maternal mortality in Bangladesh: a Countdown to 2015 country case study. Lancet. 2014; 384(9951): 1366-1374.*
5. *WHO. Level and trends in child mortality: report 2013. Estimates Developed by the UN Inter-agency group for child mortality estimation. Geneva, Switzerland: World Health Organization; 2013.*
6. *Zere1 E, Suehiro Y, Arifeen A, Moonesinghe L, Chanda SK, Kirigia JM. Equity in reproductive and maternal health services in Bangladesh. International Journal for Equity in Health. 2013; 12: 90. http: // www.equityhealthj.com/content/12/1/90. Accessed 20 June 2015.*
7. *Campbell OM, Graham WJ. Strategies for reducing maternal mortality: getting on with what works. Lancet 2006; 368: 1284–99.*
8. *Koblinsky M, Matthews Z, Hussein J, Mavalankar D, Mridha MK, Anwar I, et al. Going to scale with professional skilled care. Lancet. 2006; 368(9544): 1377–86.*
9. *Friberg IK, Kinney MV, Lawn JE, Kerber KJ, Odubanjo MO, et al. Sub-Saharan Africa's mothers, newborns, and children: how many lives could be saved with targeted health interventions. PLoS Med. 2010; 7(6): e1000295.*
10. *Van den Broek NR, Graham WJ. Quality of care for maternal and newborn health: the neglected agenda. BJOG. 2009; 116(1): 18–21.*
11. *Lassi Z S, Salam R A, Das J K, Bhutta Z A. Essential interventions for maternal, newborn and child health: background and methodology. Reproductive Health. 2014; 11(Suppl 1): S1.*
12. *Sameena C, Syed AH, Halim A. Assessment of quality of care in maternal and newborn health services available in public health care facilities in Bangladesh. Bangladesh Med Res Counc Bull. 2009; 35(2): 53–56.*

13. *Krumholz HM, Brass LM, Spertus JA, Bazzarre T, Cohen DJ, Hlatky MA, et al. Measuring and improving quality of care: a report from the American Heart Association/American College of Cardiology First Scientific Forum on Assessment of Healthcare Quality in Cardiovascular Disease and Stroke. Circulation. 2000; 101(12): 1483-93.*

14. *Ferlie E B, Shortell S M. Improving the quality of health care in the United Kingdom and the United States: a framework for change. The Milbank Quarterly. 2001; 79(2): 281-315.*

15. *Donabedian A. The Definition of Quality and Approaches of its Assessment. Volume 1: Explorations in Quality Assessment and Monitoring. Ann Arbor, MI. Health Administration Press, 1981.*

16. *Donabedian A. Evaluating the Quality of Medical Care. The Milbank Quarterly.2005; 83(4): 691-729.*

17. *Islam F, Rahman A, Halim A, Eriksson C, Rahman F, Dalal K. Perceptions of HCPs and patients on quality of care in maternal and neonatal health in fourteen Bangladesh government healthcare facilities: a mixed-method study. BMC Health Serv Res. 2015; 15: 237.*

18. *Government of the People's Republic of Bangladesh Ministry of Health and Family Welfare. Health bulletin 2009. Dhaka: Management Information System (MIS), Directorate General of Health Services (DGHS), Government of the People's Republic of Bangladesh Ministry of Health and Family Welfare; 2009.*

19. *Scholz S, Ngoli B, Flessa S. Rapid assessment of infrastructure of primary health care facilities – a relevant instrument for health care systems management. BMC Health Serv Res. 2015; 15: 183.*

20. *WHO. World health report 2006: working together for health. Geneva, Switzerland: WHO; 2006.*

21. *Khan MM, Hotchkiss DR, Dmytraczenko3 T, Karar ZA. Use of a Balanced Scorecard in strengthening health systems in developing countries: an analysis based on nationally representative Bangladesh Health Facility Survey. Int J Health Plann Mgmt. 2013; 28: 202–215.*

22. *Mridha M K, Anwar I, Koblinsky M. Public-sector maternal health programmes and services for rural Bangladesh. J Helath Popul Nutr. 2009; 27(2): 124-138.*

23. *Anwar I, Kalim N, Koblinsky M. Quality of obstetric care in public-sector facilities and constraints to implementing emergency obstetric care services: Evidence from high- and low-performing districts of Bangladesh. J Helath Popul Nutr. 2009; 27(2): 139-155.*

24. *Chodzaza E, Bultemeier K. Service providers' perception of the quality of emergency obsteric care provided and factors indentified which affect the provision of quality care. Malawi Medical Journal. 2010; 22(4): 104-111*

25. *Mansur AMSA, Karim MR, Hoque MM, Chowdhury S. Quality of Antenatal Care in Primary Health Care Centers of Bangladesh. Journal of Family and Reproductive Health. 2014; 8(4): 175-181.*

26. *Malhotra S, Zodpey SP, Vidyasagaran AL, Sharma K, Raj SS, Neogi SB, et al. Assessment of essential newborn care services in secondary-level facilities from two districts of India. J Helath Popul Nutr. 2014; 32(1): 130-141.*

27. *Tamburlini G, Siupsinskas G, Bacci A. Quality of maternal and neonatal care in Albania, Turkmenistan and Kazakhstan: a systematic, standard-based, participatory assessment. PLoS ONE. 2011; 6(12): e28763.*

28. *Morgan RG. Quality evaluation of clinical records of a group of general dental practitioners entering a quality assurance programme. Br Dent J. 2001; 191(8): 436-41.*

29. *Muhammad AM, Hasnain S, Akram J, Siddiqui A, Memon ZA. Coverage and quality of antenatal care provided at primary health care facilities in the 'Punjab' Province of 'Pakistan'. PLos ONE. 2014; 9(11): e113390.*

Corresponding Author
Farzana Islam
School of Health and Medical Sciences,
Department of Public Health,
Orebro University,
Orebro,
Sweden,

Research Associate
Centre for Injury Prevention and Research,
Bangladesh (CIPRB),
Dhaka,
Bangladesh,
E-mails: farzana.islam@oru.se;
farzaana21@hotmail.com

Correlation of Urinary Monocyte Chemoattractant Protein-1 Level with Disease Activity among Lupus Nephritis Patients

Azreen Syazril Adnan[1], Ahmad Suhaimi Bin Mustafa[2], Raja Ahsan Aftab[3], Fauziah Jummaat[4], Amer Hayat Khan[3]

[1] CKD Resource Center, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia,
[2] Dept Of Medicine, Hospital Kemaman, Jln Da Omar, 24000 Chukai. Terengganu, Malaysia,
[3] Department of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia,
[4] Department of Obstetrics & Gynecology, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia.

Abstract

Background: Lupus nephritis is a well-known type of SLE that causes morbidity and mortality. Various clinical, biochemical and laboratory markers are used in assessing and monitoring disease activity.

Aims and objective: The current study was designed to assess the level of urinary MCP-1 level in lupus nephritis patients in correlation to disease activity and to further evaluate its usage as one of the markers to be used in clinical setting with comparison to SLEDAI biomarker. To measure the standard cut off level of urinary MCP-1 level

Methodology: A cross-sectional study that involved 30 lupus nephritis patients recruited from Nephrology clinic/CKD resource centre of Hospital Universiti Sains Malaysia, Malaysia. The study population was divided into active and inactive lupus nephritis according to SLEDAI scoring system. Urine samples were collected from each subject to test for urinary MCP-1 level and 24-hr urine protein level. Blood samples were also taken to assess the level of laboratory markers. Data collected were analyzed using SPSS version 20.

Results: Of the 30 patients, 16 were in active disease at the time of recruitment. From the analysis, urinary MCP-1 level was noted to be in correlation with disease activity. Mean level in active disease was 389.43 (± 377.72) pg/ml and in inactive disease was 112.45 (± 142.42) pg/ml with the mean difference of 276.98 pg/ml (p= 0.013). There were statistically significant positive correlation between urine MCP-1 level and ESR, 24-hr urine protein and renal SLEDAI ($p<0.001$). Based on the ROC curve analysis, the cut-off level measured was 84.426 pg/ml with the sensitivity of 81.25% and specificity of 64.29%, LR+ 2.2750 and LR- 0.2917.

Conclusion: Urinary MCP-1 level was proven to be useful and valid in assessing disease activity as it showed positive correlation with disease activity and SLEDAI scoring system which was used as a validated monitoring tool for disease activity

Key words: Urinary Monocyte Chemoattractant Protein-1, Lupus Nephritis Patients, Disease Activity

Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disease that is common affecting many individuals across the globe. The prevalence was estimated to be between 40-400 cases per 100,000 individuals [1]. In Asian alone, the prevalence of SLE was estimated to be 30-50/100,00 individuals. In Malaysia whereby the population is multiracial, the distribution of this disease can be seen across the races with the prevalence of Chinese (57/100, 00), Malay (33/100,00), and Indian as the least (14/100,00) [2,3]. The cumulative incidence across the globe was detected to be higher in Asian (55%) compared to Caucasian (14%) [4]. In general, the survival rates of 5-year and 10-year were reported to be 82% and 70% respectively. As for the outcome of lupus nephritis, the 5-year and 10-year survival rates was obtained to range between 83 to 93% and 74 to 84% respectively [5].

Lupus nephritis in its active disease state could represent a spectrum from mild cases to most severe cases at which dialysis sometimes required. Individuals with lupus nephritis could also be in the inactive disease state or in remission. The severity of this disease spectrum can be measured by using various biomarkers that are currently available. Current laboratory investigations are unable to predict disease flare therefore unable to prevent unwanted outcomes. The research on these biomarkers has been carried out to find novel biomarker for detecting and monitoring disease activity of lupus nephritisat best sensitivity and acceptable specificity. MCP-1 chemokines can be detected in urine and serum. In active SLE patients, serum MCP-1 was found in patients with or without renal involvement. As comparison to urine MCP-1, it was found higher in patients with active lupus nephritis. Alzawawy and colleagues compared SLE without lupus nephritis and SLE with lupus nephritis using SLEDAI as a tool to divide active and inactive lupus nephritis. They report that the urinary MCP-1 significantly higher in SLE with active lupus nephritis as compared to SLE alone and SLE with inactive lupus nephritis. Serum MCP-1 was higher in SLE with active lupus nephritis compared to inactive lupus however it was not statistically significant [6].

The current study was designed to investigate the usefulness of urine MCP-1 as disease activity assessment tool. Experimental Studies in non-clinical settings have shown urine MCP-1 has good correlation with disease activity of lupus nephritis. Although it has been shown to be useful tool in research, its usefulness in clinical setting is unknown .

Methodology

A cross sectional study was designed from February 2013 to April 2013, conducted at Nephrology clinic / chronic kidney disease (CKD) Resource Center, Hospital University Science Malaysia (HUSM) KubangKerian, Kelantan, Malaysia. All patient diagnosed with lupus nephritis attended to Nephrology clinic/ CKD Resource Center were recruited for current study. Patient suffering from concurrent infection, Pregnancy or postpartum were excluded from study population.

Research Tool

SLEDAI scoring was used as it was validated for the purpose of disease activity in SLE. Derivation on SLEDAI was performed by Bombardier and colleagues based on descriptors present within organ systems involvement in SLE [7]. Nine organ systems involved were central nervous system, vascular, renal, musculoskeletal, serosal, dermal, immunologic, hematological and constitutional. Each organ systems have its descriptors that described active symptoms present. Descriptors for renal as organ systems were pyuria, urinary casts, hematuria and proteinuria. Each carries weight 4, which comprises total of 16 points.

Urinary casts were defined as presence of red blood cell casts, while hematuria defined by >5 red blood cells high power field which need to exclude stone, infection, or other cause. Proteinuria were significant if proteinuria of >0.5 g/day either new onset or recent increase of more than 0.5g/day. Patient was said to have pyuria if >5 white blood cellshigh power field detected.

Urinary MCP-1

Urinary MCP-1 Elisa kit was obtained from Invitrogen via local distributors. It performed by appointed laboratory technician of Immunology department, Hospital UniversitiSains Malaysia whom has experience in running the test. Duplication of samples was done and mean level was obtained. Sample of urine of patient were kept in cold refrigerator. Once sample obtained and collected for all 30 patients, the tests were run simultaneously.

Data collection

Eligible subjects were explained thoroughly regarding the study and informed consent was signed by patient or guardians. Information such as demographic data and medication history will be collected after patient signing informed consent. They were asked history to suggest active disease according to SLEDAI questionnaire score and filled in the SLEDAI scoring form.

Urine for examination and microscopic examination (UFEME) was done to look for proteinuria, hematuria, pyuria and urinary casts as part of renal SLEDAI scoring. If presence of any, secondary causes were excluded such as concurrent urinary

tract infection, menses, and other conditions lead to similar presentation. Blood investigations were taken to fulfill either SLEDAI scoring requirement or for the purpose to monitoring disease activity as similar during clinic follow up. Based on SLEDAI scoring, patients were categorized into active or inactive group lupus nephritis. SPSS version 20 was used for all statistical analysis.

Study approval

This study was approved by the Research and Ethic Committee Universiti Sains Malaysia. Reference number: USMKK/PPP/JEPeM [257.3(7)]

Results

This study includes 30 lupus nephritis patient attending CKD resource center, HUSM. Out of thirty patients, 28 were female while remaining 2 were male age ranging from 14 to 45 years old with mean age of 28.167 (8.47). Majority of patients (29 patients) were Malay while only one patient was Chinese by ethnicity. 83.3% or 25 patients had normal BMI, 4 patients underweight and one patient overweight. Twelve patients or 40% had secondary hypertension. Most patients diagnosed histologically class IV comprising about 22 patients or 73.3%, 6 patients (20%) were class III lupus nephritis. The remaining 2 patients, each diagnosed to have class II and class V lupus nephritis.

Thirty patients were enrolled in the study. Based on renal SLEDAI scoring above 4 points was classified as active group. From 30 patients, 16 patients were score more than 4 points and included in active group lupus nephritis (table 1)

Correlation of Urinary MCP-1 with Clinical Parameters

Pearson correlation was used to correlate urinary MCP-1 and clinical parameters. Several parameters were measured which includes ESR, C3 and C4 level, 24-hour urine protein, serum albumin, e-GFR measurement, and renal SLEDAI score. Urinary MCP-1 level correlates with C3, C4 level, ESR, serum albumin, 24-hour urine protein and renal SLEDAI however not with eGFR. ESR, 24-hour urine protein and renal SLEDAI had positive correlation with statistical significant ($p<0.001$). Urine MCP-1 had negative correlation with C3 level ($p<0.001$), C4 level ($p=0.006$) and serum albumin ($p<0.001$) (table 2)

Table 1. Patient Characteristics

Variables		n	(%)
Gender	Male	2	6.7
	Female	28	93.3
Race	Malay	29	96.7
	Chinese	1	3.3
	Indian	0	0
	Others	0	0
Age		28.167 (8.47)[a]	
BMI	Underweight	4	13.3
	Normal	25	83.3
	Overweight	1	3.3
	Obese	0	0
Hypertension	Yes	12	40.0
	No	18	60.0
Lupus Nephritis class	I	0	0
	II	1	3.3
	III	6	20.0
	IV	22	73.3
	V	1	3.3
	VI	0	0
Distribution of Lupus Nephritis	Active	16	
	Inactive	14	

Table 2. Correlation of Urinary MCP-1 with clinical parameters

Variables	Pearson Correlation	Sig. (2-tailed)
ESR	0.594	0.001
e-GFR	-0.312	0.093
C3	-0.605	<0.001
C4	-0.493	0.006
24-Hr Urine Protein	0.756	<0.001
Serum Albumin	-0.764	<0.001
Renal SLEDAI	0.737	<0.001

Correlation of Urinary MCP-1 with disease activity

Mean urinary MCP-1 level was compared with active and inactive group lupus nephritis using independent t-test. Mean urinary MCP-1 level in active group was 389.43 ± 377.72 compared to inactive group 112.45 ± 142.42, mean different 276.98 (95% CI = 64.37,489.58) with p value 0.013 (table 3)

Table 3. Correlation between mean urinary MCP-1 with disease activity

MCP-1	Mean (SD)	Mean diff	95% CI	t-stat (df)	p-value
Active	389.43 (377.72)	276.98	(64.37, 489.58)	2.720 (20)	0.013
Inactive	112.45 (1422.42)				

Cut-off points urinary MCP-1 level

Level of urinary MCP-1 was further evaluated to find the cut-off point of urinary MCP-1 level to attain active disease of lupus nephritis. Using ROC curve method, level was determined by high sensitivity and high specificity. The area under curve calculated 0.741 (Asymptotic 95% CI 0.557, 0.925) with p=0.025. Referring to the coordinates of the curve done using STRATA software, a value of equal or greater than 84.426 pg/ml of urinary MCP-1 indicates active lupus nephritis in this study population. The value was translated into 81.25% sensitivity and 64.29% specificity with LR+ 2.2750 and LR- 0.2917 (figure 1)

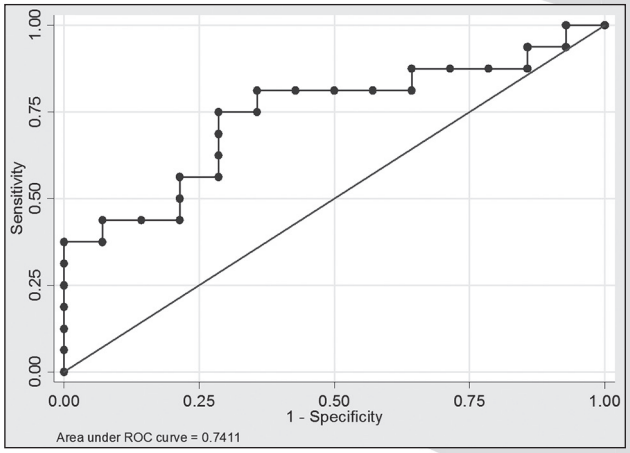


Figure 1. Cut-off points urinary MCP-1 level

Discussions

Majority of our study population were female (93.3%). This is consistent with proportion of disease distribution, which is more common among female. Since the current study was carried out Kelantan with a predominant Malay population, majority of patients recruited for current study were of Malay ethnicity [8]. However, this did not represent the disease population in the country, which was more common in Chinese by which the prevalence was 57/100 000 per population and Malay was 33/100 000 per population [8] Twenty two patients were of class IV lupus nephritis and another 6 patients in class III concludes collectively denotes proportion of patients being followed up in nephrology clinic. Out of 30-recruited patient, 16 patients were classified as active lupus nephritis using renal SLEDAI scoring as opposed to 14 patients inactive.

In the current study, a correlation was observed between urinary MCP-1 and few other clinical parameters when these were used during clinic follow up. Positive correlation were seen on usage of ESR, 24-hour urine protein and renal SLEDAI in relation to urinary MCP-1 with statistical significant (p<0.001). Moderate correlation was seen in 24-hour urine protein and renal SLEDAI. Meanwhile negative correlation was found with C3, C4 level and serum albumin as compared to urinary MCP-1 (p<0.001). Therefore, the usage of urinary MCP-1 as a disease activity marker during clinic follow-up was consistent and correlates well with clinical assessment using SLEDAI and common laboratory examinations in determining disease activity in lupus nephritis patient.

Correlation between urinary MCP-1 and proteinuria in this study consistent with other studies [9]. Alzawawy and colleagues found correlation urinary MCP-1 with renal SLEDAI score which similar to the finding in this study [6]. Negative correlation of urinary MCP-1 to C3 level was noted in few study (kiani and Jason) [10], as well as with C4 level [1]. Hence, clinical parameters and laboratory investigations for assessment of disease activity during clinic session were expected to be consistent with urinary MCP-1 level.

Mean urinary MCP-1 level in active group of lupus nephritis patient was noted to be 389.43 (±377.72) pg/ml as compared to inactive group 112.45 (±142.42) pg/ml. This finding however has lower value as compared to Samia et al which using similar unit conversion [11]. They had recorded mean urinary MCP-1 level of 2409.8 (±516.3) pg/ml in active lupus nephritis group. Differences in terms of urinary MCP-1 level could be related to the severity of disease activity. Other studies had used different conversion unit thus comparatively

not possible [12]. Another explanation of different in the finding relates to possibility of laboratory technique, test kit, preparation and dilution.

The urine MCP-1 levels can be detected in both active and inactive disease and could be attributed by the ongoing inflammatory response. In those patients whom were on immunosuppressive medications, the positivity of urine MCP-1 level was expected to be in concordance with disease activity parameters as described in various studies which was expected to be low. However, many other factors still need to be taken into consideration, which may affect the positivity of urinary MCP-1 level. In this group of patients, the issues such as dosage inadequacy, and the combination of multiple medications may cause the urinary MCP-1 level to still be higher than the expected value. Thus, the positivity of urine MCP-1 level in lupus nephritis patients regardless of disease activity status should not be looked at solely but still need to be tailored to the clinical parameters of patients. Until recent times, there are still lack of studies that could strongly pin point the cut off value for urinary MCP-1 to be significantly positive in determining disease activity solely. Thus, until further researches are done to ascertain the level of MCP-1 in determining disease activity, therefore urine MCP-1 level should be used in correlation with clinical parameters.

Researchers had managed to established good correlation between urine MCP-1 and the disease activity in lupus nephritis patients [11,12]. Thus its usage as one of the assessment tools should be considered. However, limitation exists especially in determining the cut off positive value. This had limited its use among the clinicians, as they are unable to use urine MCP-1 as assessment tools in clinical setting due to unavailability of standard value of reference. As up to date, the usage of urine MCP-1 only limited to research-based purposes. In order for the usage to be expanded into clinical setting as a standard assessment tool, therefore the need for further studies to be carried out to ascertain the standard, acceptable cut off point for urine MCP-1 is crucial.

Limitation of study

This study was a single-centered based study, thus there was limitation of availability of lupus nephritis patients seen during clinic. Multicenter study with a larger sample size would yield interesting results. Nevertheless, despite with the presence of limitations mentioned above, this study had managed to show statistically significant correlation among the studied variables.

The assessment of urine MCP-1 level could be improved and better translated if the measurement was done at time interval. Measurement of urine MCP-1 level could be done at visit one and visit two so that the level of urine MCP-1 can be compared accurately correlating with disease activity. However, the limited duration of study had made follow up interval not possible to be carried out.

Conclusion

The study had shown good correlation between urinary MCP-1 with other blood investigations used to monitor SLE disease activity during clinic. On top of that, it also resulted in positive correlation with SLEDAI which was used as validated disease activity monitoring tool. However its clinical use during clinic was not addressed before. Urinary MCP-1 indeed has a value in assessing disease activity of lupus nephritis as many studies have shown this biomarker has good correlation with disease activity similar to renal SLEDAI and laboratory investigations. Future direction of urinary MCP-1 should look into prediction of disease activity and flare of disease in order to prevent disease progression and irreversible damage to the kidneys

References

1. *Abujam B, Cheekatla S, Aggarwal A. Urinary CXCL-10/IP-10 and MCP-1 as markers to assess activity of lupus nephritis. Lupus. 2013 May; 22(6): 614-23.*

2. *Chai HC, Phipps ME, Chua KH. Genetic Risk Factors of Systemic Lupus Erythematosus in the Malaysian Population: A Minireview. Clinical and Developmental Immunology, 2012; Article ID 963730, 9 pages.*

3. *Boumpas DT, Balow JE. Outcome criteria for lupus nephritis trials: A critical overview. Lupus 1998; 7: 622.*

4. *Balow JE. Clinical presentation and monitoring of lupus nephritis Lupus 2005; 14: 25–30.*

5. *Salgado AdZ, Herrera-Diaz C. Lupus Nephritis: An Overview of Recent Findings. Autoimmune Diseases, 2012; Article ID 849684, 21 pages.*

6. *Alzawawy A, Magdy Z, Magdy A, Mona E. Estimation of monocyte-chemoattractant protein-1 (Mcp-1) level in patients with lupus nephritis. International Journal of Rheumatic Diseases. Volume 12, Issue 4, December 2009; 311–318.*

7. *Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH, et al. Derivation of the SLEDAI. A disease activity index for lupus patients. Arthritis & Rheumatism, 1992; 35(6): 630-640.*

8. *Wang F, Wang CL, Tan CT, Manivasagar M. Systemic lupus erythematosus in Malaysia: a study of 539 patients and comparison of prevalence and disease expression in different racial and gender groups. Lupus, 1997; 6(3): 248–253.*

9. *Rovin BH, Phan LT. Chemotactic factors and renal inflammation. Am J Kidney Dis. 1998; 31: 1065–84.*

10. *Mirfeizi Z, Mahmoudi M, Naghibi M, Hatef M, Sharifipour F, et al. Urine Monocyte Chemoattractant Protein-1(UMCP-1) as a Biomarker of Renal Involvement in Systemic Lupus Erythematosus. Iran J Basic Med Sci. 2012 Nov-Dec; 15(6): 1191–1195.*

11. *Samia MA Ramadan, Yasser A Abdel-Hamid, Hala A Agina, Khaled M Belal, Eman A Baraka. Study of the Monocyte Chemoattractant Protein-1 (MCP-1) as a Biomarker of Lupus Nephritis Clinical Status. Life Science Journal 2012; 9(3).*

12. *Singh RG, Usha, Rathore SS, Behura HK, Singh NK. Urinary MCP-1 as diagnostic and prognostic marker in patients with lupus nephritis flare. Lupus. 2012 Oct; 21(11): 1214-8.*

Corresponding Author
Amer Hayat Khan,
Department of Clinical Pharmacy,
School of Pharmaceutical Sciences,
Universiti Sains Malaysia,
Penang,
Malaysia,
E-mail: dramer2006@gmail.com

Sleep quality and related factors in patients with Fibromyalgia syndrome

Ekrem Akkurt[1], Haluk Gumus[3], Halim Yilmaz[1], Ilknur Albayrak[4], Alper Murat Ulasli[2], Halime Cevik[2], Gulten Karaca[1], Umit Dundar[2]

[1] Physical Therapy and Rehabilitation Clinic, Konya Training and Research Hospital, Konya, Turkey,
[2] Department of Physical Therapy and Rehabilitation, Medical School, Afyon Kocatepe University, Afyon, Turkey,
[3] Neurology Clinic, Konya Training and Research Hospital, Konya, Turkey,
[4] Department of Physical Medicine and Rehabilitation, Medical School of Selcuk University, Konya, Turkey.

Abstract

Background: Fibromyalgia syndrome (FMS) is a chronic pain syndrome whose etiology is not well known and evident in form of widespread pain, sleep disorder, tenderness in some anatomic spots, and fatigue. Symptoms such as poor quality sleep, restless sleep, fatigue, morning stiffness have been reported to be higher than 70% in a number of studies. The aim of the present study is to determine the parameters affecting FMS patients' sleep quality. 100 female patients diagnosed with FMS and 85 healthy individuals were included in the study. All of the participants' pain conditions, sleep quality, Number of Tender Points(NTP), depressive mood were evaluated by using 0-10 cm visual analogue scale(VAS), Pittsburgh Sleep Quality Beck Index(PSQI), digital pressure, and Depression Scale(BDS) respectively. Only patients' disease activity was evaluated by Fibromyalgia Impact Questionnaire(FIQ). When NTP, BDS, PSQI values of FMS and control groups were compared, it was observed that they were significantly higher in FMS group. A correlation was determined between PSQI values and BDS measures, BMI, NTP and FIQ. Sleep quality in FMS patients is affected severely, and it is associated with disease activity and depressive mood. Therefore, sleep quality should be considered in treatment programs of FMS patients.

The aim of the present study is to determine parameters affecting sleep quality of FMS patients.

Methods: In the study, 100 female FMS patients diagnosed according to 1990 American College of Rheumatology (ACR) criteria, and 85 healthy female controls were included. Patients were evaluated with regard to age, body mass indexes (BMI), Pittsburgh Sleep Quality Index (PSQI), Fibromyalgia Impact Questionnaire (FIQ), Number of tender Points (NTP), and Beck Depression Scale (BDI). Control group were evaluated with regard to age, body mass indexes (BMI), Pittsburgh Sleep Quality Index (PSQI), Number of tender Points (NTP), and Beck Depression Scale (BDI). Standard deviation, independent samples T test, and pearson correlation analyses were used in the analysis of the data.

Results: Both groups were similar in terms of BMI and age (P> 0.05). When NTP, BDS, PSQI values of FMS and control groups were compared, it was observed that they were significantly higher in FMS group. Among FMS patients, the correlation between PSQI values and VAS, NTP, FIQ, duration of complaints, and BDS were assessed. A moderate correlation was determined between PSQI values and BDS measures (r = 0.431, P= 0.000), FIQ (r = 0.264, P= 0.008). A Weak correlation was observed between PSQI values and NTP (r = 0.197, P= 0.050), BMI (r = 0.222, P: 0.026).

Conclusions: The result of our study shows that sleep quality in FMS patients was severely affected, and it was associated with disease activity, BDS, and depressive mood. Therefore, sleep quality and its causative factors should be considered in treatment programs of FMS patients.

Key words: Fibromyalgia Syndrome; Sleep Quality; Depression; Female, Pain Syndrome

Introduction

Fibromyalgia syndrome (FMS) is a chronic pain syndrome whose etiology is not well known and evident in form of widespread pain, tenderness in some anatomic spots, and fatigue. 80-90

% of FMS patients comprises women aged 40-60 years [1-5]. The most common symptoms accompanying FMS are fatigue, sleep disturbances, and morning stiffness. Other symptoms experienced at different degrees are irritable bowel syndrome, subjective swelling, non-dermatomal paresthesia, psychological disorders, dysmenorrhea, pollakiuria, angina pectoris, gnathalgia, stomachache, Raynaud's phenomenon, sicca symptoms, skin sensitivity, reticular skin color change, hypermobility syndrome, restless leg syndrome, mitral valve prolapse, significant functional insufficiencies, and especially headache [6-9]. FMS decreases patients' life quality, and it causes difficulties for patients in coping up with their daily life activities.

The aim of the present study was to determine parameters affecting sleep quality of FMS patients.

Materials and Method

Participants

In the study, 100 female patients who applied to outpatient clinic of Physical Therapy and Rehabilitation with widespread pain, and were diagnosed with FMS according to 1990 American College of Rheumatology (ACR) criteria [10] after physical examination, laboratory findings, and imaging examinations were included. Those who had systemic chronic disease, rheumatologic disease, major psychiatric disease history; used antidepressants and anxiolytic drugs in the last 6 months; had cervical and lumbar radiculopathy, myelopathy were excluded from the study. In addition, 85 healthy women at the same age range were included in the study as the control group.

Number of Tender Points (NTP)

Eighteen tender points were defined for diagnostic purposes in line with ACR diagnostic criteria in patients with FMS [10]. NTPs were determined by exerting digital pressure on patients. Palpation was performed with the thumb, and pressure rating was 4 kg/cm^2 (until the finger nail bed became white) [11]. Patients were evaluated by using this test, and their sensitive spots were identified and recorded.

Evaluation of Depression

Beck Depression Scale (BDS), developed by Beck in 1961, was used to assess depressive symptoms in patients [12]. BDS is a 21-item self-reported assessment scale evaluating the depressive mood. The items on the scale were scored from 0 to 3 according to the severity of depression. Increasing the BDS scores indicated severe depression. The Turkish validated version of BDS was used in the study [13].

Assessment of Disease Activity

In order to assess clinical severity of FMS, the Turkish version of Fibromyalgia Impact Questionnaire (FIQ) was used [14]. Validity and reliability studies of FIQ in Turkish were performed in and it has been in use effectively to evaluate clinical severity and treatment efficacies of different modalities in FMS [15]. FIQ consists of 10 items, which measures wellness, fatigue, morning stiffness, pain, sleep, anxiety, depression, job status, and physical condition. Each item is assessed on a 0-10 scale (maximum total score 100). Higher scores indicate further deterioration.

Assessment of Sleep Quality

Patient sleep quality was measured by validated Turkish version of Pittsburgh Sleep Quality Index (PSQI). PSQI consists of seven subscales measuring subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medication, and day dysfunction due to sleepiness. The reply to each question was scored from 0 to 3 according to symptom frequency. If there was no complaint in the last month, patient received 0 point; if complaint was less than once a week, the point was 1; if once or twice a week, then the point was 2; and if three times or more in a week, the point was 3. The score range was between 0-21 points; higher the scores, the worse the sleep quality. If the total score was 5 and above, it indicated that that sleep quality was clinically significantly worse. Diagnostic sensitivity and specificity of the index were 89.6% and 86.5%, respectively [16-18].

Procedure

Participants in the study were asked not to use any analgesic therapy 24 hours before evaluation.

Table 1. Demographic characteristics of both groups

	FMS	Control group	P
Age	35.20 ± 6.50	35.75 ± 6.88	0.575
BMI	27.05±5.06	25.98±5.23	0.175

BMI, Body Mass Index.

Table 2. TPS, BDS, PSQI of both groups

	FMS	Control group	P
NTP	14.84±2.53	2.98±2.39	0.000
BDS	15.19±8.83	7.23±6.25	0.000
PSQI	12.43±3.25	8.05±2.76	0.000

NTP, Number of tender Points; BDS, Beck Depression Scale; PSQI, Pitsburg Sleep Quality Inventory.

During the evaluation, routine physical examinations were performed, and age, duration of complaints, body mass indexes (BMI) were recorded. Overall pain conditions were evaluated by using 0-10 cm visual analogue scale (VAS) for pain scores. Sleep quality was evaluated by PSQI; disease activity was evaluated by FIQ and NTP; and depressive mood was evaluated by BDI.

Results

A total of 100 female patients diagnosed with FMS according to American College of Rheumatology (ACR) 1990 criteria [10], and 85 healthy individuals were included in the study. Both groups were similar in terms of BMI and age (P> 0.05). Demographic data of participants are given in Table 1.

When NTP, BDS, PSQI values of FMS and control groups were compared, it was observed that they were significantly higher in FMS group (Table 2).

Among FMS patients, the correlation between PSQI values and VAS, NTP, FIQ, duration of complaints, and BDS were assessed. A moderate correlation was determined between PSQI values and BDS measures (r = 0.431, P= 0.000), FIQ (r = 0.264, P= 0.008). A Weak correlation was observed between PSQI values and NTP (r = 0.197, P= 0.050), BMI (r = 0.222, P: 0.026); but there was no correlation with the duration of complaint (r= 0.105, P= 0.299).

Discussion

The present study was carried out on 100 female patients diagnosed with FMS, and 85 healthy controls. It was determined that sleep quality and BDS scores in FMS group were significantly higher than healthy controls. When parameters affecting sleep quality were examined, a moderate correlation between depression and disease activity, and a weak correlation between NTP and BMI were defined. Another symptom that FMS patients complained about most was the sleep disorder. Symptoms such as poor quality sleep, restless sleep, fatigue, morning stiffness have been reported to be higher than 70% in a number of studies [19,20]. In our study, we determined that PSQI scores were 5 and above in line with other studies.

PSQI is an easy, simple, and effective method to evaluate sleep quality. Its efficacy and reliability have been proven in various pathologies. In order to determine sleep quality of fibromyalgia patients in the present study, PSQI was used [16-18].

There are also many other studies that investigated the underlying reasons of sleep disorders in FMS patients with polysomnographic analysis conducted in sleep-labs [20-22]. Slow-wave sleep, REM sleep, and total sleep time in FMS patients are determined to be shorter; yet all these sleep disorders are nonspecific [21]. There are studies showing that sleep duration in FMS patients does not differ compared to healthy individuals; yet the quality of sleep disorders. Wilson et. al determined in their study that the patients who suffered from chronic musculoskeletal pain throughout the day had less total sleep time. However, in

FMS patients, the focus was more on the quality of sleep, because the majority of researches stated that there was no difference in terms of total sleep time in patients with FMS and healthy individuals [23]. In this study, we did not evaluate sleep duration, but sleep quality; and we determined sleep quality disorders in FMS patients.

In many studies, it was determined that there was a correlation between sleep problems, pain and depression in FMS [24]. Staud et al. demonstrated the importance of negative mood in pain experienced in FMS [25]. The presence of depression in the diseases that cause chronic pain such as FMS, points at more severe pain and functional limitations. The concurrence of negative mood and pain show similarities with the underlying biological and behavioral mechanisms. Brain regions associated with emotional stability (amygdala, hypothalamus, medial prefrontal cortex) and pain modulations (periaquaductal gray) are intricately linked with each other. Therefore, pessimism, depression and negative emotions are reported to intensify perceived pain signals and thus increase pain intensity and duration [26]. In the present study, it was determined in line with previous studies that there was a moderate correlation between sleep quality and depressive mood. In studies conducted with depressive fibromyalgia patients, it was reported that there was an increase in day time sleepiness and decrease in the activity, and during the night there was an increase in sleep distortion and in the activities during the sleep [27]. One of the prognostic factors of FMS is depression. Depression with FMS and various other diseases has an adverse impact on sleep quality. However, it seems that it is impossible to comment on whether pain and depression cause sleeping problem, or sleeping problem inherent in the disease increases pain and depression. [28,29]. Hamilton et al. reported a moderate correlation between pain and sleep in FMS [30]. The correlation we defined in our study between sleep quality and FMS disease activity was not FMS specific, because the relationships between sleep quality and disease activity of different pathologies (osteoarthritis, rheumatoid arthritis, systemic lupus erythematosus) were established [31-34].

A statistical relationship was established between disease activity in FMS and NTP and BMI in other studies [35,36]. In our study, a weak correlation between BMI, NTP and sleep quality was determined. The relationships between NTP, BMI, and sleep quality and disease activity were important for the consistency of our work.

Limitations of our study may be summarized as absence of sleep duration evaluation, and treatment efficacy results.

In conclusion; sleep quality in FMS patients is affected severely when compared with healthy population, and it is associated with disease activity and depressive mood. Therefore, sleep quality of FMS patients and their influential factors should be considered in treatment programs of FMS patients.

References

1. *Hernandez EH, Beceril E, Perez M, Leff P, Anton B, Estrada S, et al. Proinflamatory cytokine levels in fibromyalgia patients are independent of body mass index. BMC Res Notes 2010; 3(1): 156.*

2. *Fontaine KR, Conn L, Clauw DJ. Effects of lifestyle physical activity on perceived symptoms and physical function in adults with fibromyalgia: results of a randomized trial. Arthritis Res Ther. 2010; 12(2): R55.*

3. *Nordahl HM, Stiles TC. Personality styles in patients with fibromyalgia, major depression and healthy controls. Ann Gen Psychiatry. 2007 Mar 9; 6: 9.*

4. *Küçükşen S, Sallı A, Akkurt HE. Fibromiyaljili Kadın Hastalarda Essitalopram İle Gabapentin Tedavilerinin Karşılaştırılması. Selçuk Üniv Tıp Derg 2011;27(2):88-91.*

5. *İnanıcı F. Fibromiyalji ve Miyofasiyal Ağrı Sendromları. Türkiye Klinikleri J Med Sci 2005; 1: 11-8.*

6. *Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990; 33(2): 160-72.*

7. *Bennett RM. The fibromyalgia syndrome. In: Kelley WN, Harris ED, Ruddy S, Sledge CB, (eds). Textbook of Rheumatology. 5th edition. Philadelphia: W.B. Saunders Company, 1997: 511-9.*

8. *Krsnich-Shriwise S. Fibromyalgia syndrome: an overview. Physical Therapy 1997; 77(1): 68-75.*

9. *McCain GA. A cost effective approach to the diagnosis and treatment of fibromyalgia. Rheum Dis Clin North Am 1996; 22(2): 323-349.*

10. *Katz RS, Wolfe F, Michaud K. Fibromyalgia diagnosis: a comparison of clinical, survey, and American College of Rheumatology criteria. Arthritis Rheum. 2006; 54(1): 169–176.*

11. *Tastekin N, Birtane M, Uzunca K. Which of the three different tender points assessment methods is more useful for predicting the severity of fibromyalgia syndrome? Rheumatol Int 2007; 27(5): 447–451.*

12. *Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961; 4: 561-571.*

13. *Hisli N. Beck Depresyon Envanteri'nin geçerliği üzerine bir çalışma. Türk Psikoloji Dergisi 1988; 6(22): 118-126.*

14. *Sarmer S, Ergin S, Yavuzer G. The validity and reliability of the Turkish version of the Fibromyalgia Impact Questionnaire. Rheumatol Int. 2000; 20(1): 9-12.*

15. *Bennett R. The Fibromyalgia Impact Questionnaire (FIQ): a review of its development, current version, operating characteristics and uses. Clin Exp Rheumatol. 2005; 23(5 Suppl 39): S154-62.*

16. *Agargun MY, Kara H, Anlar O. Pittsburgh Uyku Kalitesi İndeksinin gecerliği ve guvenirliği. Turk Psikiyatri Derg1996;7: 107-15.*

17. *Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. Psychiatry Res 1989; 28: 193-213.*

18. *Buysse DJ, Reynolds CF 3rd, Monk TH, Hoch CC, Yeager AL, Kupfer DJ. Quantification of subjective sleep quality in healthy elderly men and women using the Pittsburgh Sleep Quality Index (PSQI). Sleep 1991; 14(4): 331-338.*

19. *Harding SM. Sleep in fibromyalgia patients: subjective and objective findings. Am J Med Sci 1998; 315(6): 367-376.*

20. *Alvarez Lario B, Alonso Valdivielso JL, Alegre Lopez J, Martel Soteres C, Viejo Banuelos JL, Maranon Cabello A. Fibromyalgia syndrome: overnight falls in arterial oxygen saturation. Am J Med 1996; 101(1): 54-60.*

21. *Rizzi M, Sarzi-Puttini P, Atzeni F, Capsoni F, Andreoli A, Pecis M, et al. Cyclic alternating pattern: a new marker of sleep alteration in patients with fibromyalgia? J Rheumatol 2004; 31(6): 1193-1199.*

22. *Landis CA, Frey CA, Lentz MJ, Rothermel J, Buchwald D, Shaver JL. Self-reported sleep quality and fatigue correlates with actigraphy in midlife women with fibromyalgia. Nurs Res 2003; 52(3): 140-147.*

23. *Shaver JL, Lentz M, Landis CA, Heitkemper MM, Buchwald DS, Woods NF. Sleep, psychological distress, and stress arousal in women with fibromyalgia. Res Nurs Health. 1997; 20(3): 247-257.*

24. *Anch AM, Lue FA, MacLean AW, Moldofsky H. Sleep physiology and psychological aspects of the fibrositis (fibromyalgia) syndrome. Can J Psychol. 1991; 45(2): 179-84.*

25. *Staud R, Weyl EE, Riley JL 3rd, Fillingim RB. Slow temporal summation of pain for assessment of central pain sensitivity and clinical pain of fibromyalgia patients. PLoS One. 2014; 9(2): e89086.*

26. *Landis CA, Lentz MJ, Rothermel J, Buchwald D, Shaver JL. Decreased sleep spindles and spindle activity in midlife women with fibromyalgia and pain. Sleep. 2004; 27(4): 741-750.*

27. *Korszun A, Young EA, Engleberg NC, Brucksch CB, Greden JF, Crofford LA. Use of actigraphy for monitoring sleep and activity levels in patients with fibromyalgia and depression. J Psychosom Res. 2002; 52(6): 439-443.*

28. *Anch AM, Lue FA, MacLean AW, Moldofsky H. Sleep physiology and psychological aspects of the fibrositis (fibromyalgia) syndrome. Can J Psychol. 1991; 45(2): 179-184.*

29. *Bigatti SM, Hernandez AM, Cronan TA, Rand KL. Sleep disturbances in fibromyalgia syndrome: relationship to pain and depression. Arthritis Rheum. 2008; 59(7): 961-967.*

30. *Hamilton NA, Catley D, Karlson C. Sleep and the affective response to stress and pain. Health Psychol. 2007; 26(3): 288-295.*

31. *Chandrasekhara PK, Jayachandran NV, Rajasekhar L, Thomas J, Narsimulu G. The prevalence and associations of sleep disturbances in patients with systemic lupus erythematosus. Mod. Rheumatol. 2009; 19(4): 407–415.*

32. *Hawker GA, French MR, Waugh EJ, Gignac MA, Cheung C, Murray BJ. The multidimensionality of sleep quality and its relationship to fatigue in older adults with painful osteoarthritis. Osteoarthritis Cartilage 2010; 18(11): 1365–1371.*

33. *Nicassio PM, Wallston KA. Longitudinal relationships among pain, sleep problems, and depression in rheumatoid arthritis. J Abnorm Psychol. 1992; 101(3): 514–520.*

34. *Affleck G, Urrows S, Tennen H, Higgins P, Abeles M. Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia. Pain. 1996; 68(2): 363–368.*

35. *Salli A, Yilmaz H, Ugurlu H. The relationship between tender point count and disease severity in patients with primary fibromyalgia. Rheumatol Int. 2012; 32(1): 105-107.*

Corresponding Author
Ekrem Akkurt,
Physical Therapy and Rehabilitation Clinic,
Konya Training and Research Hospital,
Konya,
Turkey,
E-mail: ekremakkurt@yahoo.com

Epidemiologic aspects of urolithiasis in our clinical material

Arber Ejup Neziri[1], Flamur Tartari[2], Mustafa Xhani[2], Avni Fetahu[1], Liridon Selmani[1], Ilir Miftari[1]

[1] Urology Clinic, University Clinical Center of Kosovo, Prishtina, Kosovo,
[2] Service of Urology M. Tereza, Tirana, Albania.

Abstract

Objective: Analysis of Epidemiological aspects of patients operated in UCC Urology Clinic with a diagnosis of urolithiasis, and patients who underwent ESWL treatment in UCC Urology Clinic in Pristina.

Material and methods: Operated patients in the UCC –Clinic of Urology diagnosed with urolithiasis were analyzed in prospectively and retrospectively manner between the time period January 2001-December 2012.

Data analysis was realized using the statistical package InStat 3. Obtained results are presented by tables and graphics.

Results: In male patients treated with nephrolithiasis we found a slight significant difference with 52.5% compared with female patients of 47.5%.

In cases with nephrolithiasis, the age group of 20 - 39 years old was mostly attacked, about 44.7% of patients and despite the age group of 40-59 years old represented with 13.5% of all cases.

The largest number of cases treated in the UCC in Pristina in the analyzed period where represented from the municipality of Prishtina with 572 cases or 23.5% of the total patients.

From 2001 to 2012, at the University Clinical Centre of Kosovo - Urology Clinic 2,438 patients diagnosed with urolithiasis have undergone surgery or ESWL. The prevalence was 135.4 cases in 100,000 people, while the incidence was 11.3 cases in 100,000 people.

Conclusion: Kosovo represents a country in which urolithiasis is quite widespread in males and females as well. As a disease affects the most productive age group of the population and therefore early detection of the disease, then the application of modern methods of treatment plays an important role of fighting the disease.

Key words: Urolithiasis, Epidemiologic aspects, University Clinical Center of Kosovo, Surgery, ESWL.

Introduction

Kidney stones have afflicted human kind since antiquity. The prevalence of urinary tract stone

disease is estimated to be 2% to 15%. Urolithiasis is an entity, which has high morbidity and socio-economical impact, and low mortality.

Urinary stones were a major health problem in developed countries until the 1980s, with a significant proportion of patients requiring extensive surgical procedures and a sizeable minority

losing a kidney. One study showed that about 20% of patients with recurrent stone disease who underwent surgery for obstruction and infection went on to develop mild renal insufficiency [1].

The advent of extracorporeal techniques for stone destruction and the refinements in endoscopic surgery, however, have greatly decreased the morbidity associated with stone surgery, and the disorder is changing from a major health problem to a major nuisance. One unfortunate result of this technologic success is that advances in medical management of stone disease and research in prevention have languished. Surgical procedures treat stones but do not prevent them; however, as anyone who has passed a kidney stone can tell, this may be what the majority of patients with stone disease needs.

Epidemiologic Aspects

Urolithiasis is a common clinical disorder. Its frequency has risen with the development of humanity and varies with the country, geographic area, etc.

Its world prevalence is estimated between 1 to 5%, in developed countries 2-13% (with a great

variation among them), and in developing countries 0.5-1%[1,2,3,4]. The overall probability of forming stones differs in various parts of the world: 1-5% in Asia, 5-9% in Europe, 13% in North America, 20% in Saudi Arabia[2,3,4]. Lifetime prevalences in the USA and Europe range between 8 and 15%, annual incidences of kidney stones are about 0.1-0.4% of the population and the likelihood that a white man will develop stone disease by age 70 years is about 1 in 8[5]. The prevalence among elderly men over 65 is 4.7% in Italy[6]. On the other hand, silent kidney stone, which can be a presentation of urolithiasis, could have prevalence around 3% as has been found in Pakistan[7].

Stone in the upper urinary tract appear to relate to the life-style, being more frequent among affluent people, living in developed countries, with high animal protein consumption. Bladder stones are nowadays mainly seen in the Third World, on account of very poor socio-economic conditions[2]. The later has been decreasing in most countries in the so-called endemic bladder stone belt with gradual improvements in levels of nutrition, especially in proteins. However, as living standards increase, particularly in the urban areas of the more affluent developing countries, so the incidence of upper urinary tract stones in adults is increasing.

The stone problem in the tropics is compounded by low urine volumes resulting in some areas from poor drinking water, which causes chronic diarrhoea, and in others from the hot climate and fluid losses through the skin. As nutrition improves in these countries, the formation of bladder stones gives way to upper urinary tract stones consisting of calcium oxalate, often mixed with calcium phosphate or uric acid, such as are formed in most Western countries.

Objective

Analysis of Epidemiological aspects of patients operated in UCC Urology Clinic with a diagnosis of urolithiasis, and patients who underwent ESWL treatment in UCC Urology clinic in Pristina.

Material and methods

Operated patients in the UCC – Clinic of Urology diagnosed with urolithiasis were analyzed in prospectively and retrospectively manner between the time period January 2001-December 2012. As a data source we used for patients who underwent surgery during this time period in the Urology Clinic in UCC as well as ESWL Protocol in the UCC for the time periods January 2001 January 2012.

Data analysis was realized using the statistical package InStat 3. Obtained results are presented by tables and graphics. Statistical parameters such as the arithmetic mean, standard deviation, median, minimum and maximum values were calculated. Qualitative Data were tested using the X2 test. Quantitative data which did not present a normal distribution were tested using the Kruskal - Wallis test and Mann Whitney test. Testing verification testing is realized with 99.7% confidence level ($p < 0.01$) and reliability of 95% ($p < 0.05$).

Results

I. Epidemiological characteristics of urolithiasis in UCCK treated patients

Table 1. Urolithiasis in University Clinical Center of Kosova patients treated in the Total during years

Year	N	%
2001	182	7.5
2002	325	13.3
2003	214	8.8
2004	220	9.0
2005	227	9.3
2006	153	6.3
2007	174	7.1
2008	179	7.3
2009	290	11.9
2010	286	11.7
2011	92	3.8
2012	96	3.9
Total	**2438**	**100.0**

In a 12 year period, 2001 – 2012 a number of 2438 patients were treated in the University Clinical Centre of Kosova – Urology Clinic due to surgery or ESWL as a consequence of stones in the urinary system (Table 1). The course of University Clinical Center of Kosova treated for kidney stones in the UCCK is variable. In the last two years, 2011 and 2012 a lower number of University Clinical Center of Kosova was presented as

a consequence of data presented only for surgery and not for patients treated with ESWL (Chart 1).

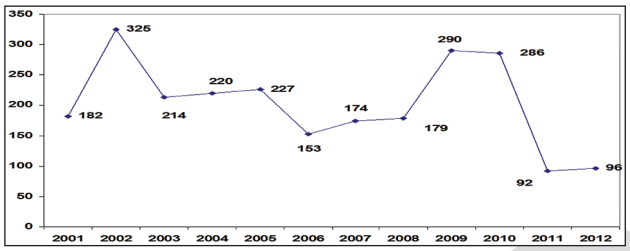


Chart 1. The course of urolithiasis University Clinical Center of Kosova treated in the Total during years

In 100 000 inhabitants the prevalence was proven to be 135.4 in University Clinical Center of Kosova, and the incidence was 11.3 in University Clinical Center of Kosova in 100 000 inhabitants. Total number of University Clinical Center of Kosova for 12 years - 2438 multiplied with 100 000 and divided with the number of Kosova inhabitants (1 800 000). Average of patients treated in the University Clinical Center of Kosova per year - 203 is multiplied with 100 000 and divided with the number of Kosova inhabitants (1 800 000)

Table 2. Kidney stone University Clinical Center of Kosova treated in the University Clinical Center of Kosova according to gender

Gender	N	%	
F	1157	47.5	X^2=6.31
M	1281	52.5	P=0.012
Total	**2438**	**100.0**	

Table 2 proves a slight significant domination (P<0.05) of males in 52.5% (Chart 2).

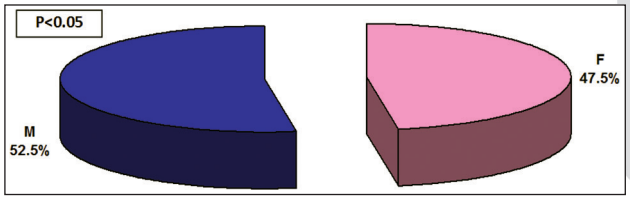


Chart 2. Structure of treated University Clinical Center of Kosova according to gender

Kidney and urinary channel stones University Clinical Center of Kosova belong to different age groups, with a domination of University Clinical Center of Kosova between ages 20-39 with 44.7%, therefore the age group of 40-59 year old with 36.2%, age group of 60-79 years old with 13.5%, age group 10-19 years old with 4.1%, younger than 10 years with 1.0%, and older than 80 years with 0.4% (Table 3).

Table 3. Urolithiasis treated University Clinical Center of Kosova in the University Clinical Center of Kosova according to age-group

Age-group	N	%
<10	24	1.0
10-19	101	4.1
20-39	1091	44.7
40-59	883	36.2
60-79	329	13.5
80+	10	0.4
Total	**2438**	**100.0**

Table 4. Urolithiasis in cases treated in the University Clinical Center of Kosova according to residence

Residence	N	%
Dardanë	26	1.1
Deqan	34	1.4
Dragash	10	0.4
Drenas	116	4.8
F.kosovë	46	1.9
Ferizaj	137	5.6
Gjakovë	98	4.0
Gjilan	90	3.7
Hani i Elezit	3	0.1
Istog	33	1.4
Kacanik	84	3.4
Kastriot	42	1.7
Klinë	42	1.7
Lipjan	87	3.6
Malishevë	56	2.3
Mitrovicë	161	6.6
Novobërd	1	0.0
Pejë	55	2.3
Podujevë	163	6.7
Prishtinë	572	23.5
Prizren	95	3.9
Rahovec	39	1.6
Shtime	53	2.2
Skënderaj	84	3.4
Therandë	104	4.3
Viti	32	1.3
Vushtrri	175	7.2
Total	**2438**	**100.0**

The greater number of patients, treated for urinary stones in the UCCK for the analyzed time period, belonged to the municipality of Pristina 572 University Clinical Center of Kosova or 23.5%, afterwards Vushtrria with 175 or 7.2%, Podujeva with 163 University Clinical Center of Kosova or 6.7%, Mitrovica with 161 casesor 6.6%, Ferizaj with 137 or 5.7% and few cases were treated from small municipalities such as Hani I Elezit 3 and Novobërda one case (Table 4 and Chart 3).

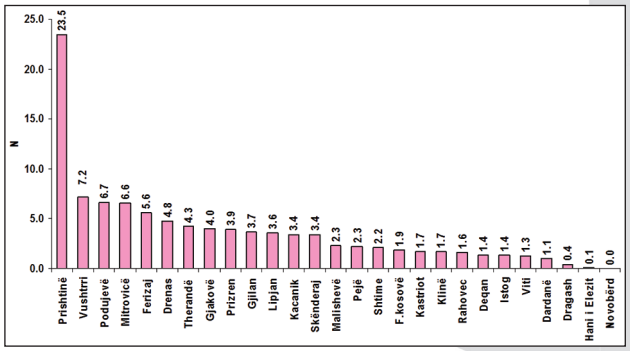


Chart 3. Range of kidney stone cases treated in the University Clinical Center of Kosova according to residence

5. Discussion

In a twelve year period, 2001-2012 in the University Clinical Center of Kosova – in Urologic Clinic 2438 patients underwent surgery or ESWL as a consequence of kidney stones or urinary channel stones (Table 1). The course of University Clinical Center of Kosova treated for kidney stones in the UCCK is variable. In the last two years, 2011 and 2012 a lower number of University Clinical Center of Kosova was presented as a consequence of data presented only for surgery and not for patients treated with ESWL (Chart 1).

In 100 000 inhabitants the prevalence was proven to be 135.4 University Clinical Center of Kosova, and the incidence was 11.3 University Clinical Center of Kosova in 100 000 inhabitants. Total number of University Clinical Center of Kosova for 12 years - 2438 multiplied with 100 000 and divided with the number of Kosova inhabitants (1 800 000).

The incidence was calculated when the average of cases per year – 203 is multiplied with 100 000 and divided with the number of Kosova inhabitants (1 800 000)

Urolithiasis incidenceis defined as the number of new cases of urolithiasis patients in a population, during a certain period of time, usually within one year.

Prevalence is defined as the number of present stones in a monitored population in a certain moment of time.

Life Prevalence is defined as the presence of urinary tract stones in every moment of time during patient's lifetime.

In a 25 years urolithiasis incidence study starting from 1950 until 1974 in the population of Rochesterit, Minesota, the general male ratio was 109.5 in 100 000 inhabitants and for females was 36.0 in 100 000. This would suggest an increase of urolithiasis incidence through the last three decades.

In an Italian study conducted between years 1993-1994 the incidence was calculated to be 168 for 100 000 inhabitants.

Also in a study administered by Japanese urolithiasis incidence in 1995 was calculated to be 100.1 in 100 000 inhabitants, in which males were 55.4, compared to a study mentored by Yoshida and asoc., which provided the result of 81.3in 100 000 inhabitants in males and 29.5 in 100 000 for females, we have concluded that there is a fast increase in annual incidence of urolithiasis in Japan in the last 30 years. (23)

According to **Gary C. Curhan** Med. Asoc. prof., medical department the Brigham Hospital and Harward Medical Hospital, in his paper regarding the Urolithiasis Epidemiology, highlights the risk factor of diseaseoccurrence in USA is above 12% in males and 6% in females. However, **urolithiasis prevalence** depends on age, gender and race.

Urolithiasis prevalence is also high in other countries including Japan and Germany. Urolithiasis prevalence within USA depends on race. Prevalence is highest in old Caucasian males around 10% and lowest in Afro-American females around 1%. The prevalence in Asians and Hispanic population is within these values. (16)

Some studies have shown variable incidence rates within age, gender and race.

As prevalence, incidence was higher in Caucasian males. In males incidence starts to increase after the age of 20 and reaches its peak between the ages of 40-60 with 3 new cases in 1000 inha-

bitants, afterwards starts decreasing. Female incidence rates seem to be higher in late twenties than decreases in one case in 1000 inhabitantsin their fifties.

Although early studies have shown an increase in the incidence rate in the USA, latest studies from Rochester-Minnesota reveal different changes in trends.

Using the same technology from the study performed30 years ago, which proves an incidence increase in males and females between 1950-1974, latest studies have manifested that incidence rates starting from 1990 can decrease in males and reach the peak in females. (15, 16).

Recurrence – if cases are untreated, there is a 30-40% chance of nephrolithiasis recurrence in the first 5 years. On the other side, in treated cases pathology recurrence decreased to 50%.

This reduction using medicines or diet proves that urolithiasis prevention is possible. (16)

Our study concludes a slight significant domination of males with 52%patients treated with urolithiasis.

Table 2 shows a slight significant domination ($P<0.05$) in males with 52.5%. Males form more stones than females, gender ratio is ranged 2.5: 1 n Japan, to 1.15: 1 in Iran. (24)

Kidney and urinary stones cases belonged to age groups of 20-39 year olds with 44.7%, than the age group of 40-59 year olds with 36.2%, age group of 60-79year olds with 13.5%, age group of 10-19 year olds with 4.1%, younger than 1 year old with 0% and older than 80 year olds with 0.4% (Table 3).

In Irani, Japan and USA the culmination of incidence is found in the age group of 40-49 year olds, except Japan where the age group of 50-59 is most attacked. The actual incidence ratio is similar for males in USA and Japan age group of 40-49 year olds, and Iran with younger age. Prevalence grows continually with ageing.(24).

As far as race is considered prevalence and incidence in USA were higher in Caucasians, than in Hispanics, Afro-Americans and Asians. As a conclusion, Caucasian males showed the highest incidence while Asian females had the lowest rate of urolithiasis.(24).

The higher number of cases with kidney stones treated in UCCK in the analyzed period of time belonged to the Pristina municipality with 572 casesor 23.5%, than Vushtrria with 175 or 7.2%, Podujeva with 163 casesor 6.7%, Mitrovica with 161 casesor 6.6%, Ferizaj with 137 or 5.7% andfew cases were treated from small municipalities such as Hani i Elezit 3 and Novobërda one case (Table 4 and Chart 3).

This is obvious from the fact that Pristina represents the most populated city in the Republic of Kosova, with a population living in urban style, although after the war underwent a high population influx and mixture of inhabitants structure.

After data analysis we came to a conclusion that incidence and prevalence were higher in our material, corresponding to the growth of these parameters in USA and other countries of the world. The exact cause of this phenomenon is unclear, but it is thought that urolithiasis presence is effected by genetic and environmental factors.

However changes in the genetic material, as a urolithiasis risk factor are rarely proven, on the other side environmental factor such as I. Dietand II. Climate changes have impact on these trends.

Diet role in stone formation is already known. During the last century a urolithiasis growth was present as a consequence of food quality improvement, when corn was the main element of feeding.

Growth of consummation in minced cereal food has encouraged obesity, which represents one of the reasons in urolithiasis formation (25, 26, 27).

The impact of modern agriculture resulted with epidemic obesity in many countries especially in USA. Obesity prevalence in USA was followed since 1960.

Obesity in adults increased from 14.6% in 1971 up to 35.2% inn 2005. This trend was present also in children; in 2005 11 to 17% of children were obese. Fast food and fructose rich drinks consuming is thought to be promoters of this epidemic appearance.

In USA the percentage of meals coming from fast food restaurants increased from 9.6% to 23.5% in the time period 1977-1996.

These diet changes appeared in many countries such as China, Egypt, Russia, Filipinas etc.

Also, there are accurate evidences that reduction in fluid intake and excessive consumption of calcium appear as risk factors. Also, oxalate, sodi-

um salts and animal proteins intake are risk factors for urolithiasis.

However, randomized prospective food studies have demonstrated that sodium salts, animal proteins reduction, controlled calcium intake alleviate recurrences in hyper-calcium urolithiasis.

Global climate changes are also factors that affect urolithiasis frequency. It is a general consensus that mean global temperature are rising. Lately two studies have shown a correlation between high temperature exposure and nephrolithiasis occurrence.

Evans and Costabile compared the time of USA soldiers arrival in Kuwait and the time of renal pain appearance in the military hospital. Also, Documerc has registered the number of patients coplaning on renal pain and temperature in a French center of tertiary care between years 2002-2004. On the other side, many studies in USA show that high temperature regions have higher urolithiasis frequency.

This correlation between high environment temperatures and increase of kidney stone cases supports the conclusion that global warming is a key factor in kidney stones development.

Considering these facts we can conclude that kidney stones incidence and prevalence is rising globally. This growth is present in gender, race and age aspects. Diet changes and global warming is shown to be moving forces that influence this trend.

Conclusion

Kosovo represents a country in which urolithiasis is quite widespread in males and females as well. As a disease affects the most productive age group of the population and therefore early detection of the disease, then the application of modern methods of treatment plays an important role of fighting the disease. The application of ESWL and URS Lithotripsy in Kosovo, had a high impact in the disease combating, still percutaneus nefrolitholapaxy represents one of the immediate needs of Kosovo Urology.

References

1. *Leonardo R. Reyes Raban.l, CIN 2003. M.D. Clinical epidemiology of urolithiasis in tropical areas page 1-23.*
2. *Menon M, Koul H. Clinical review 32: Calcium oxalate nephrolithiasis. J Clin Endocrinol Metab 1992; 74: 703–707.*
3. *Ramello A, Vitale C, Marangella M. Epidemiology of nephrolithiasis. J Nephrol 2000 Nov-Dec; 13 Suppl 3: S45-50.*
4. *Kim H, Jo MK, Kwak C, Park SK, Yoo KY, Kang D, Lee C. Prevalence and epidemiologic characteristics of urolithiasis in Seoul, Korea. Urology. 2002; 59(4): 517- 21.*
5. *Lee YH, Huang WC, Tsai JY, Lu CM, Chen WC, Lee MH, et al. Epidemiological studies on the prevalence of upper urinary calculi in Taiwan. Urol Int. 2002; 68(3): 172-7.*
6. *Hess B. Pathophysiology, diagnosis and conservative therapy in calcium kidney calculi. Ther Umsch. 2003 Feb; 60(2): 79-87.*
7. *Serio A, Fraioli A. Epidemiology of Nephrolithiasis. Nephron 1999; 81(suppl 1): 26-30.*
8. *Buchholz NP, Abbas F, Afzal M, Khan R, Rizvi I, Talati J. The prevalence of silent kidney stones-an ultrasonographic screening study. J Pak Med Assoc. 2003; 53(1): 24.*
9. *Sutor DJ. The nature of urinary stones. In Finalayson B (ed): Urolithiasis: Physical Aspects. Washington DC, National Academy of Sciences, 1972; 43.*
10. *Curhan GC, Willett WC, Rimm EB, Stampfer MJ. Family history and risk of kidney stones. J Am Soc Nephrol 1997; 8: 1568–1573.1*
11. *Resnick M, Pridgen DB, Goodman HO. Genetic predisposition to formation of calcium oxalate renal calculi. N Engl J Med 1968; 278: 1313–1318.*
12. *Turk C, Knoll T, et al. Guidelines on urolithiasis, Europian Association on Urology Edition, 2011; 7-103.*
13. *Tanagho EA, McAninnch. Smith's General Urology. USA. Mc.Graw Hill companies 17th edition. Marshall L. Staler, MD Urinary Stone Disease, 2008; 246-275.*
14. *Favus JM. Professor and Vice Chair for appointments and promotions. Department of medicine. University of Pritzker School of Medicine. Chicago. Chapter 14. Nephrolithiasis. May 1, 2010.*

15. *Lieske JC, Pena de la Vega LS, Slezak JM, Bergstralh EJ, Leibson CL, Ho KL, et al. Renal stone epidemiology in Rochester, Minnesota: an update. Kidney Int. 2006; 69(4): 760–4. [PubMed]*

16. *Curhan CG, Epidemiology of Stone Disease, Urol Clin North Am. 2007 August; 34(3): 287–293.*

17. *Tiselius HG, Department of Urology, Huddinge University Hospital and Centre for Surgical Sciences, Karolinska Institutet, Stockholm, Sweden, ©, Epidemiology and medical management of stone disease, BJU International | 2003; 91: 758–767 | doi: 10.1046/j.1464-410X.2003.04208*

18. *Lopez M, Hoppe B. History, epidemiology and regional diversities of urolithiasis. Pediatr (Nephrol) 2010; 25: 49/59.*

19. *Does Hard Water Cause Kidney Stones? Singh et al, 1993; Ripa et al, 1995; Kohri et al, 1993; Kohri et al, 1989*

20. *Hughes P. Kidney stones epidemiology. NEPHROLOGY 2007; 12: S26–S30.*

21. *Curhan CG. Epidemiology of stone disease Urol Clin North Am. 2007 August; 34(3): 287–293. doi: 10.1016/j.ucl.2007.04.003 UK. PUBMED Central.*

22. *Hesse A, Brandle E, Wilbert D, Kohrmann KU, Alken P. Study on the prevalence and incidence of urolithiasis in Germany comparing the years 1979 vs 2000. Eur Urol. 2003; 44(6): 709–13. [PubMed]*

23. *Marshall L. Stoller MD, Maxwell V, Meng MD. Urinary Stone Disease. Humana Press. Incx Totowa, New Jersey, 2007; 27-55.*

24. *Victoriano Romero et al, Kidney stones. A global picture of prevalence, Incidence and Associated Risk Factors. Wake Forest University School of Medicine, Winston/Salem, NC. 2010 Med Reviews. LLC.*

25. *Soucie JM, Thun MJ, et al. Demographic and geographic variability of kidney stones in the United States. Kidney int. 1994; 46: 893-899.*

26. *Amato M, Lusini ML, Nelli F. Epidemiology of nephrolithiasis today. Urol Int. 2004; 72(suppl 1): 1-5.*

27. *Taylor EN, Stampfer M, Curhan GC. Obesity, weight gain, and the risk of kidney stones. JAMA. 2005; 293: 455-462.*

28. *Rajveer S. Purohit, Marshall L. Stoler. Laterality of symptomatic Cystine calculi. From the Department Of Urology, University of California, San Francisco, School of Medicine. Submitted: February 7, 2003 accepted March 27, 2003.*

29. *Kidney stones. University of Maryland Medical Center. Last reviewed by: Harvey Simon, MD. editor in Chief, associate Professor of Medicine, Harvard Medical School/last reviewed on 08.27.2012.*

30. *Haxhiu I, Çuni Xh, Hyseni S, Aliu H, Baftiu N, Haxhiu A, Haxhiu E. Modalithy treatments of coraliform stones European Urology Supplements, 2011; 10(9): ISSN 1569-9056 590: 591.*

31. *Haxhiu I, Çuni Xh, Haxhiu A. "Chemical structure of urolithiasis in Kosovo" EAU 4 th South Eastern European Meeting, 17-18 tetor 2008, Tiranë.*

32. *Haxhiu I, Çuni Xh, Hyseni A, Aliu A, Baftiu I, Haxhiu A, Haxhiu E, Morphology of urolithiasis in Kosovo European Urology Supplements, 2011; 10(7): ISSN 1569-9056.*

33. *Türk C, Knoll T, Petrik A, Sarica K, Straub M, Seitz C. Guidelines on Urolithiasis"Europian association of Urology" 2012; 7-101.*

34. *Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. Renal stone epidemiology: a 25-year study in Rochester, Minnesota. Kidney Int. 1979; 16(5): 624–31. [PubMed]*

35. *Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC. Time trends in reported prevalence of kidney stones in the United States: 1976–1994. Kidney Int. 2003; 63(5): 1817–23. [PubMed]*

36. *Yoshida O, Okada Y. Epidemiology of urolithiasis in Japan: a chronological and geographical study. Urologia Internationalis. 1990; 45: 104–111. [PubMed]*

37. *Soucie JM, Thun MJ, Coates RJ, McClellan W, Austin H. Demographic and geographic variability of kidney stones in the United States. Kidney Int. 1994; 46(3): 893–9. [PubMed]*

38. *Soucie J, Coates R, McClellan W, Austin H, Thun M. Relation between geographic variability in kidney stones prevalence and risk factors for stones. Am J Epidemiol. 1996; 143: 487–495. [PubMed]*

39. *Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. N Engl J Med. 1993; 328: 833–838. [PubMed]*

40. *Hiatt RA, Dales LG, Friedman GD, Hunkeler EM. Frequency of urolithiasis in a prepaid medical care program. Am J Epidemiol. 1982; 115: 255–265. [PubMed]*

41. *Curhan G, Willett W, Speizer F, Spiegelman D, Stampfer M. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. Ann Intern Med. 1997; 126: 497–504. [PubMed]*

42. *Curhan GC, Willett WC, Knight EL, Stampfer MJ. Dietary factors and the risk of incident kidney stones in younger women (Nurses' Health Study II) Arch Intern Med. 2004; 164: 885–891. [PubMed]*

43. *Lieske JC, Pena de la Vega LS, Slezak JM, Bergstralh EJ, Leibson CL, Ho KL, et al. Renal stone epidemiology in Rochester, Minnesota: an update. Kidney Int. 2006; 69(4): 760–4. [PubMed]*

44. *Borghi L, Schianchi T, Meschi T, Guerra A, Allegri F, Maggiore U, et al. Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. N Engl J Med. 2002; 346(2): 77–84. [PubMed]*

45. *Ettinger B, Pak CY, Citron JT, Thomas C, Adams-Huet B, Vangessel A. Potassium-magnesium citrate is an effective prophylaxis against recurrent calcium oxalate nephrolithiasis. J Urol. 1997; 158(6): 2069–73. [PubMed]*

46. *Ettinger B, Tang A, Citron JT, Livermore B, Williams T. Randomized trial of allopurinol in the prevention of calcium oxalate calculi. N Engl J Med. 1986; 315(22): 1386–9. [PubMed]*

47. *Ettinger B, Citron JT, Livermore B, Dolman LI. Chlorthalidone reduces calcium oxalate calculous recurrence but magnesium hydroxide does not. J Urol. 1988; 139(4): 679–84. [PubMed]*

48. *Curhan G, Willett W, Rimm E, Stampfer M. Family history and risk of kidney stones. J Am Soc Nephrol. 1997; 8: 1568–1573. [PubMed]*

49. *Resnick M, Pridgen DB, Goodman HO. Genetic predisposition to formation of calcium oxalate renal calculi. N Engl J Med. 1968; 278(24): 1313–8. [PubMed]*

50. *D'Angelo A, Calo L, Cantaro S, Giannini S. Calciotropic hormones and nephrolithiasis. Miner Electrolyte Metab. 1997; 23(3–6): 269–72. [PubMed]*

51. *Taylor EN, Stampfer MJ, Curhan GC. Obesity, weight gain, and the risk of kidney stones. Jama. 2005; 293(4): 455–62. [PubMed]*

52. *Kramer HM, Curhan G. The association between gout and nephrolithiasis: the National Health and Nutrition Examination Survey III, 1988–1994. Am J Kidney Dis. 2002; 40(1): 37–42. [PubMed]*

53. *Kramer HJ, Choi HK, Atkinson K, Stampfer M, Curhan GC. The association between gout and nephrolithiasis in men: The Health Professionals' Follow-Up Study. Kidney Int. 2003; 64(3): 1022–6. [PubMed]*

54. *Taylor EN, Stampfer MJ, Curhan GC. Diabetes mellitus and the risk of nephrolithiasis. Kidney Int. 2005; 68(3): 1230–5. [PubMed]*

55. *Atan L, Andreoni C, Ortiz V, Silva EK, Pitta R, Atan F, et al. High kidney stone risk in men working in steel industry at hot temperatures. Urology. 2005; 65(5): 858–61. [PubMed]*

56. *Robertson WG, Peacock M, Hodgkinson A. Dietary changes and the incidence of urinary calculi in the U.K. between 1958 and 1976. J Chron Dis. 1979; 32: 469–476. [PubMed]*

57. *Larsson L, Tiselius HG. Hyperoxaluria. Miner Electrolyte Metab. 1987; 13(4): 242–50. [PubMed]*

58. *Muldowney FP, Freaney R, Moloney MF. Importance of dietary sodium in the hypercalciuria syndrome. Kidney International. 1982; 22: 292–296. [PubMed]*

59. *Lemann J, Jr, Piering WF, Lennon EJ. Possible role of carbohydrate-induced calciuria in calcium oxalate kidney-stone formation. N Engl J Med. 1969; 280(5): 232–7. [PubMed]*

60. *Johansson G, Backman U, Danielson BG, Fellstrom B, Ljunghall S, Wikstrom B. Biochemical and clinical effects of the prophylactic treatment of renal calcium stones with magnesium hydroxide. J Urol. 1980; 124: 770–774. [PubMed]*

61. *Lemann J, Jr, Pleuss JA, Gray RW, Hoffmann RG. Potassium administration reduces and potassium deprivation increases urinary calcium excretion in healthy adults [corrected] Kidney Int. 1991; 39(5): 973–83. [PubMed]*

62. *Menon M, Koul H. Clinical review 32: Calcium oxalate nephrolithiasis. J Clin Endocrinol Metab 1992; 74: 703–707.*

63. *Ramello A, Vitale C, Marangella M. Epidemiology of nephrolithiasis. J Nephrol 2000 Nov-Dec; 13 Suppl 3: S45-50.*

64. *Kim H, Jo MK, Kwak C, Park SK, Yoo KY, Kang D, Lee C. Prevalence and epidemiologic characteristics of urolithiasis in Seoul, Korea. Urology. 2002; 59(4): 517- 21.*

65. *Lee YH, Huang WC, Tsai JY, Lu CM, Chen WC, Lee MH, et al. Epidemiological studies on the preva-*

lence of upper urinary calculi in Taiwan. Urol Int. 2002; 68(3): 172-7.

66. *Hess B. Pathophysiology, diagnosis and conservative therapy in calcium kidney calculi. Ther Umsch. 2003 Feb; 60(2): 79-87. Serio A, Fraioli A. Epidemiology of Nephrolithiasis. Nephron 1999; 81(suppl 1): 26-30.*

67. *Buchholz NP, Abbas F, Afzal M, Khan R, Rizvi I, Talati J. The prevalence of silent kidney stones-an ultrasonographic screening study. J Pak Med Assoc. 2003; 53(1): 24-5.*

68. *Sutor DJ. The nature of urinary stones. In Finalayson B (ed): Urolithiasis: Physical Aspects. Washington DC, National Academy of Sciences, 1972; 43.*

Corresponding Author
Arber Ejup Neziri,
Urology Clinic,
University Clinical Center of Kosovo,
Prishtina,
Kosovo,
E-mail: arberlindialtini@hotmail.com

Premature and extremely low birth weight newborn with Clavicular fracture: A case report

Yazdan Ghandi[1], Mojtaba Sharafkhah[2], Alireza Zemani[3]

[1] Department of Pediatrics, School of Medicine, Arak University of Medical Sciences, Arak, Iran,
[2] Students Research Committee, School of Medicine, Arak University of Medical Sciences, Arak, Iran,
[3] School of Medicine, Arak University of Medical Sciences, Arak, Iran.

Abstract

Clavicular fractures are the most commonly reported fractures in neonates. This fracture usually occurs in term newborns with a high birth weight and other predisposing conditions to birth trauma. We report a premature (29 week) and extremely low birth weight (ELBW) (960 gr) newborn with right clavicular fracture. His mother was 35 year during pregnancy and had no pelvic anomalies. The mother was not suffering from diabetes or other chronic diseases during pregnancy. The newborn was born with vertex presentation. No vacuums or forceps were used during childbirth. In examination, there was a significant decrease in active movements of the right arm alongside the body and crepitus over right clavicle. However, there were no deformity, tenderness, cervical subcutaneous emphysema, and pain on passive movements of limb. Fracture was diagnosed with chest-x ray. Patient was recovered without any sequel at two months of age. Premature and LBW newborns with no predisposing factors for birth trauma can also be susceptible to clavicle fracture.

Key Words: Birth Injuries; Clavicle Fracture; Newborn; Premature Birth

Introduction

Clavicular fractures are the most commonly reported fractures in neonates**.** Based upon data from large case series, the incidence of clavicle fractures due to birth trauma ranges from 0.5 to 1.6 percent (1-3). Most clavicular fractures are of the greenstick type, but occasionaly the fracture is complete (4). According to the evidence, clavicle fracture in newborns can be associated with neonatal factors (birth weight, presentations, utero fetal position) (4), maternal factors (maternal age, maternal pelvic anatomy) (1, 4, 5), and other factors such as abnormal forces of labor (5). However, clavicular fractures also occur in infants who are products of a normal spontaneous vaginal (5). Clavicle fracture usually occurs in term newborns with a high birth weight and other predisposing conditions to birth trauma, whereas this fracture is extremely rare in preterm and low birth weight (LBW) newborns. Because of its rarity we present a premature and extremely low birth weight (ELBW) neonatal with clavicle fracture.

Case presentation

A male newborn with a birth weight, length, and head circumference (HC) of 960 g (ELBW: birth weight of less than 1000g (6)), 37 cm, 26 cm, respectively, was born in week 29 of pregnancy through vaginal delivery. Abdominal circumference and head-to-abdominal circumference ratio were 24 cm and 1.08, respectively. His mother was 35 year during pregnancy, and considering her weight (73 kg) and height (1.68 m), her body mass index (BMI) (weight (kg)/height ((m)^2) was 25.8 (normal BMI). The mother had no pelvic anomalies. The mother was not suffering from diabetes or other chronic diseases during pregnancy. The newborn was born with vertex presentation. No vacuums or forceps were used during childbirth. Moreover, shoulder dystocia did not occur.

Due to respiratory distress and prematurity, the newborn was transferred to a neonatal intensive care unit (NICU). The newborn had tachypnea at the time of hospitalization (respiratory rate (RR): 50). In examination, there was a significant decrease in active movements of the right arm alongside the body and crepitus over right clavicle. However, there were no deformity, tenderness, cervical subcutaneous emphysema, and pain on passive movements of limb. The right Moro reflex

was absent but bilateral grasp reflex was normal. The newborn's cell blood count (CBC) was normal, and C-reactive protein (CRP) and blood culture (B/C) were negative.

Complete fracture of right clavicle was observed in radiograph of his chest on the second day of hospitalization (Fig. 1). No other abnormalities such as pneumomediastinum were observed in CXR. No brachial plexus palsy was observed. Respiratory distress resolved on the fourth day of hospitalization. The newborn was discharged from the hospital 12 weeks after birth and clavicle fracture was recovered completely at two months of age.

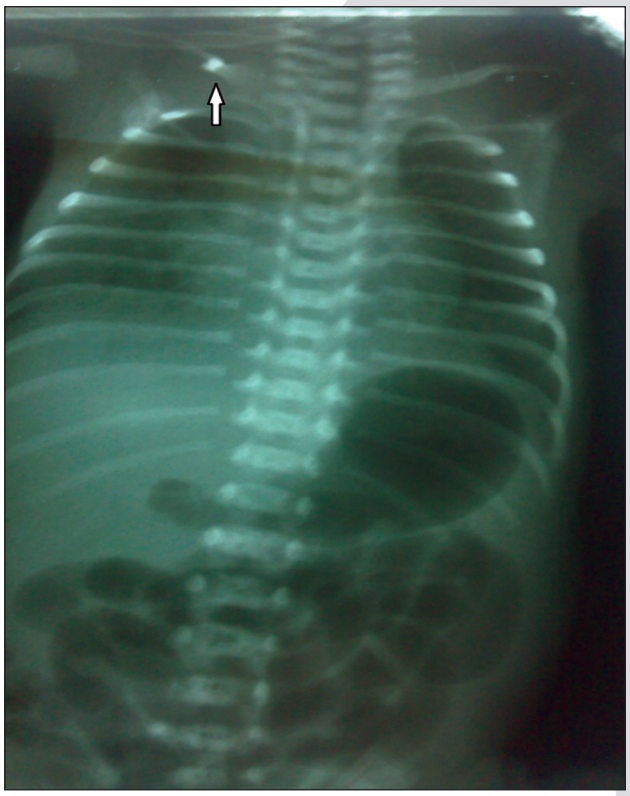


Figure 1. Chest radiograph shows right clavicular fracture

Discussion

Fracture of the clavicle is one of the commonest birth injuries of the neonate. Although, according to some evidence, clavicle fracture may also occur during a natural childbirth (5), various studies have shown that some factors are associated with clavicle fracture in newborns. Shoulder dystocia (3), higher birth weight (macrosomic newborns) (1,2,4,6,7), abnormal fetal presentation, particularly breech presentation (8), maternal pelvic abnormalities (5), difficult delivery and sequential use of vacuum extraction and forceps (2, 7), lower head-to-abdominal circumference ratio (2), abnormal forces of labor (5) and increased maternal age (1) were significantly associated with clavicular fracture.

Our newborn was not susceptible to birth trauma due to lack of maternal pelvic abnormality, appropriate presentation, being ELBW, lack of indication of using labor tools such as vacuum, forceps, and normal forces of labor.

Clavicle fracture in newborns is often asymptomatic (9, 10). However, some symptoms such as decrease or lack of arm movements, pain on passive movements of limbs, absence of newborn reflexes (such as Moro and Grasping), and sometimes crepitus and deformity (9) can reinforce clinical suspicion of limb disorders so that necessary measures are taken to evaluate clavicle fracture and its other differential diagnosis such as congenital pseudoarthrosis, congenital muscular torticollis ،brachial plexus palsy, sternocleidomastoid muscle spasm, traumatic separation of the proximal humeral epiphysis, humeral shaft fractures, and dislocations of the shoulder (4, 10). CXR is used to diagnose clavicle fracture (4, 10). In our patient, the only clinical symptoms were decrease in active movements of the right arm and feeling crepitus, which arose clinical suspicion of clavicle fracture.

Hsu TY et al. (2) diagnosed clavicle fracture in most newborns during the first three days. Ahn ES et al. (7) diagnosed clavicle fracture in 86.2% of newborns before hospital discharge. We diagnosed clavicle fracture on the second day after birth. According to evidence, type of fracture is one of the determining factors in diagnosing clavicle fracture (11). Greenstick fractures (due to its asymptomatic) are often diagnosed late (days 7-10), whereas due to lack of or decrease in arm movements alongside the body, complete fractures and some greenstick fractures are diagnosed earlier (11). In our case, compared to other studies, complete fracture can be the main reason for early diagnosis.

Given the low incidence of clavicle fracture, its asymptomatic nature in many cases, various differential diagnoses, and even simultaneity of these differential diagnoses such as brachial plexus palsy

with clavicle fracture (4), studies recommend to examine newborns with risk factors for birth trauma (1-5, 7). However, our case showed that newborns with no risk factor for birth trauma could also be susceptible to clavicle fracture. This is a significant finding about premature and low birth weight newborns due to the following two reasons: 1) given their weight and other somatometric characteristics, these newborns are less susceptible to birth trauma, 2) compared to mature newborns, investigating clinical signs and symptoms is more limited in these newborns.

As a conclusion, premature and LBW newborns with no predisposing factors for birth trauma can also be susceptible to clavicle fracture, therefore it can be recommended to evaluate newborns with no risk factors for clavicle fracture at birth.

Conclusion

Premature and LBW newborns with no predisposing factors for birth trauma can also be susceptible to clavicle fracture

References

1. *Beall MH, Ross MG. Clavicle fracture in labor: risk factors and associated morbidities. J Perinatol 2001; 21: 513.*
2. *Hsu TY, Hung FC, Lu YJ, Ou CY, Roan CJ, et al. Neonatal clavicular fracture: clinical analysis of incidence, predisposing factors, diagnosis, and outcome. Am J Perinatol. 2002; 19: 17-21.*
3. *Lam MH, Wong GY, Lao TT. Reappraisal of neonatal clavicular fracture: relationship between infant size and neonatal morbidity. Obstet Gynecol 2002; 100: 115.*
4. *Kanik A, Sutcuoglu S, Aydinlioglu H, Erdemir A, Arun Ozer E. Bilateral clavicle fracture in two newborn infants. Iran J Pediatr. 2011; 21: 553-5.*
5. *Peleg D, Hasnin J, Shalev E. Fractured clavicle and Erb's palsy unrelated to birth trauma. Am J Obstet Gynecol 1997; 177: 1038-40.*
6. *Moczygemba CK, Paramsothy P, Meikle S, Kourtis AP, Barfield WD, et al. Route of delivery and neonatal birth trauma. Am J Obstet Gynecol. 2010; 202: 361.e1-6.*
7. *Ahn ES, Jung MS, Lee YK, Ko SY, Shin SM, Hahn MH. Neonatal clavicular fracture: Recent 10year study. Pediatr Int. 2014 Sep 9.*
8. *Mangurten HH. Birth injuries. In: Martin RJ, Fanaroff AA, Walsh MC (editors). Fanaroff and Martin's Neonatal and Perinatal Medicine. Disease of the fetuses and infant. 8th ed. Philadelphia: Mosby Elsevier. 2006; 529-59.*
9. *Herring JA. Upper extremity fractures. In: Herring JA (editor) Tachdjian's Pediatric Orthopaedics. 3rd ed. Philadelphia. Saunders. 2002; 2115-250.*
10. *Oppenheim WL, Davis A, Growdon WA, Dorey FJ, Davlin LB. Clavicle fractures in the newborn. Clin Orthop Relat Res. 1990; 176-80.*
11. *Joseph PR, Rosenfeld W. Clavicular fractures in neonates. Am J Dis Child 1990; 144: 165-7.*

Corresponding Author
Mojtaba Sharafkhah,
Arak University of Medical Sciences,
Arak,
Iran,
E-mail: sharafkhah@arakmu.ac.ir

The evaluation of muscular force physical activity after acute coronary infarction during the first phase of rehabilitation

Sebahat Zeqiri[1], Nexhmi Zeqiri[2]

[1] QKUK - Pristine, Physiatrist Clinic, Pristine, Kosovo,
[2] QKUK – Pristine, Intern Clinic – Cardiologist Service, Pristine, Kosovo.

Abstract

The rehabilitation of patients with acute myocardial infarction depends on the patient's conditions and the degree of complications. Early mobilization is done in order to elute bed rest complications (lowered minute volume, orthostatic hypotension, hypovolemia-induced tachycardia, cardiovascular reflex deficiency, increased blood viscosity and thromboembolic incidence tendency, decreased lung ventilation and hypostatic inflation tendencies, decreased muscular force and muscular contractile force).The purpose of this study was to investigate saved or increased muscular force through physical activity in patients with acute myocardial infarction during the first phase of rehabilitation. Concurrently other parameters were evaluated which suggested eventual patient overburden, such as: arterial pressure, pulse, breathing frequency, skin color, subjective condition. The parameters were measured before and after the physical activity. The research material were patients with AMI during first phase of rehabilitation medical records. The study involved 64 patients with AMI, to whom were applied physical activities based on exercise protocols. The control group consisted of 10 patients with AMI, every study case had patient's confirmation and agreement also the aim of study was explained. Physical activities started applying 72 hours after patients were admitted at Coronary Unit, the protocol was divided in 7 stages. The physical activity was conducted for 10 days in a row and individually applied to every patient, by respecting activity protocol 5. Data measurement, muscular testing (a method to evaluate muscular force), after using physiotherapists manual resistance as measuring tool, hence test is named as manual muscle test. According to manual muscle test, evaluations for muscle force range from 0 to 5. Arterial pressure, pulse, breathing frequency are additional parameters that suggest eventual overload, ECG was performed every day consulting cardiologist, on 12 day Ergometer was performed. The result show an increase on rates of muscular force at female patients on an average of 3.47-4.72 after 10 exercises on a row. In the control group that wasn't part of the program, the rates were lower 3.2-4.0. The results obtained after applied physical activity for 10 days in a row show and increased rate of muscular force by 3.52-4.97 at male patients.

Discussion, all these results were satisfactory thanks to mutual patient-doctor corporation, this corporation was well accepted by the patients because the benefits of these activities were correctly explained to them and this alliance elated them and positively increased their subjective condition.

Taking in consideration the fact that those who suffer from IAM are anxious, physical activity has elevated the patient's confidence and gave them a more realistic approach towards their future. This way they give an end to their negative thoughts and give meaning to their lives.

Conclusion, physical activity is a crucial and inseparable part of IAM treatment and its purpose is to bring the patient back to their normal lives as soon as it is possible. To those suffering from IAM who were mobilized and made active earlier, the level of the functional restore of heart was accomplished two weeks earlier than to those who were not. Applying physical activity during the first phase of rehabilitation is not financially damaging, it is easy to learn, practice and it doesn't require any special environment. Physical activity excellently uses all the existing environmental conditions.

Key words: Physical activity, Acute Myocardial Infraction, Muscular Force

Introduction

Rehabilitation of patients with myocardial infarction depends on patient conditions and the degree of complications. Early mobilization is done in order to elute bed rest complications (lowered minute volume, orthostatic hypotension, hypovolemia-induced tachycardia, cardiovascular reflex deficiency, increased blood viscosity and thromboembolic incidence tendency, decreased lung ventilation and hypostatic inflation tendencies, decreased muscular force and muscular contractile force).(1). The working group of world health national organization (February 1968) prepared the physical activity plan for these patients, in order to decline reduction of their physical condition (2). The rehabilitation of patients with cardiac diseases is not a new discipline. It has been a part of cardiac patient's treatment for many years. Early on physical activity was considered to be harmful for cardiac patients, since 1952 Levin insisted on getting up from bed early on after infarction, by showing the benefits that result from that. This idea was accepted on the 60s when it started being implemented on developed countries. By composing a rehabilitation program by working group of European and American Cardiologist Organization (1994), the definite objective that to be achieved is: physical, psychological, professional and social rehabilitation (3).

Purpose of the study

The purpose of this study was to investigate saved or increased muscular force through physical activity in patients with acute myocardial infarction during the first phase of rehabilitation. Concurrently other parameters were evaluated which suggested eventual patient overburden, such as: arterial pressure, pulse, breathing frequency, skin color, subjective condition. The parameters were measured before and after the physical activity

Material and Method

The research material were patients with AMI during first phase of rehabilitation medical records. Study involved 64 patients with AMI 18 females and 46 males to whom physical activities were applied based on exercise protocol. Control group were 10 patients with AMI, from them 5 females and 5 males, all of them were on Coronary Unit in Clinical and University Center of Kosovo. Every study case had patient's confirmation and agreement also the aim of study was explained. Physical activities started applying 72 hours after patients were admitted at Coronary Unit. The physical activity was conducted for 10 days in a row and individually applied to every patient, by respecting activity protocol. The study was done in series and included patients with AMI on the first phase of rehabilitation on a period of time October 2006-April 2007 a total number of 64 patients. For a patient in order to be part of the study certain diagnostic criteria were considered: typical chest pain, increase of cardio specific enzymes, abnormal Q wave on ECG. From the study were excluded cases with AMI that had additional complications or health issues: patients older than 70 years, patients with cerebrovascular insult, pulse patterns, resistant arterial hypertension, cardiogenic shock signs, and patients with cardiac insufficiency NYHA III, IV. The method ,application of physical activity protocol started 72 hours after acute infarction, strictly applied during bed resting on Coronary Unit, strictly applied individualy,dozed acording to strict principals of cardiologic loading tests and gradual kinesology treatments (5.6)

Protocol is diveded in 7 periods.

First period is 1-3 days long, exercises are done in supine position, starts talking to patient, foot masage for 1-2 minutes, flexion and extension on joints on upper limbs and lower limbs, neck movements, and deep respirations. All these activites are applied 5 times once to 4-6 times a day on each individual.

Second period is 1-2 days long, exercises are done in semi supine position, on the first time excercises are repeated 5-10 times, 4 to 6 times a day individualy.

Third period is 1-2 days long, all exercises are applied on sitting postion or standing acording to patients abilities, 50 meters walking is alowed. Exercises are repeated 4-6 times a day.

Forth period is 1-2 days long, all exercises are repeated more intensly, controlled walking to 100 meters, exercises are repeated 4-6 times a day.

Fifth period is 1-2 days long, independed walk, all exercises are repeated, walking to 200 meters, repeated 4-6 times a day.

Sixth period is 1-3 days long, progressive stair stepping, all other exercises are repeated, Milinov stairs are applied(three steps down , three steps up – this procedure is repeated 5 times and is similar as reaching first floor), exercisses are repeated 4-6 times a day

Seventh period is 1-3 days long, preperations for home program are done, precursory exercises are repeated, walking 200-400 meters, second floor reaching is tried , short walks outside the clinic, cicloergometry with submaximal loadings. Applied physical activity induced relaxition and feelings of joy in patient.

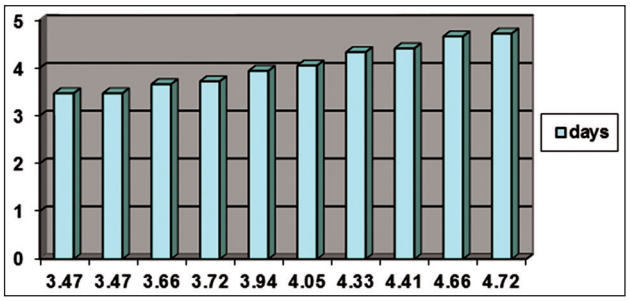
Intensity and durance of exercisses were applied acording to patients conditions, also according to their wish and motivation. During the time of exercisses patients were under proffesional surviliance of Physiatrist and Cardiologyst.

Data measurement, muscular testing (a method to evaluate muscular force), after using physiotherapists manual resistance as measuring tool, hence test is named as manual muscle test. According to manual muscle test, evaluations for muscle force range from 0 to 5 (value 0-no muscular activity, value 1 minimal muscular contraction, value 2 muscular contraction is achieved without gravity, value 3 muscular contraction is achieved with gravity, value 4 muscular contraction is the same as value 3 plus it resists therapeutics manual force, value 5 shows that muscle can do full movement and can resists maximal manual force). Part of this evaluation is plus (+) and minus (-) as an objective value of muscular force. Muscular force is measured on upper limbs and lower limbs, before and after physical activity and is recorded on protocol.

Arterial pressure, pulse, breathing frequency are additional parameters that suggest eventual overload, ECG performed every was, on 12 day Ergometer was performed.

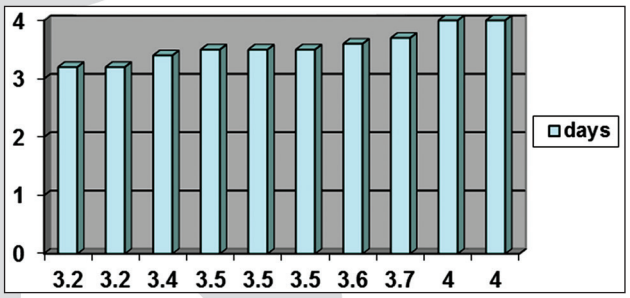
Results

Obtained results for evaluation of muscular force after applied physical activity in patients with AMI on the first rehabilitation phase are applied in graphs. 1st graph presents obtained results after applied physical activity on muscular force for 10 days in a row on females after AMI on first phase of rehabilitation.



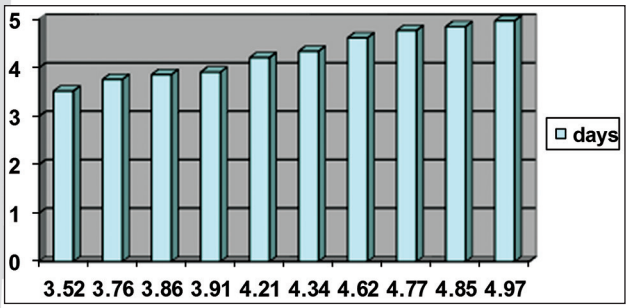
Graph 1.

Obtained results show an increase on muscular force values from 3.47-.4.72 after 10 days exercises in a row. 2nd graph presents muscular force on female's group control with AMI



Graph 2.

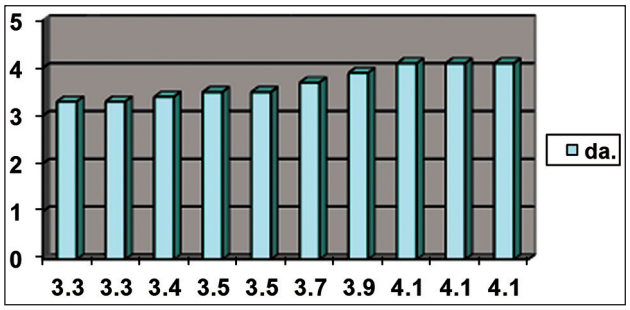
On the group control to whom physical activities were not applied muscular force was increased continually from 3.3-4.1. 3d graph present resulst after aplication of physical activity on musclar force for 10 days continously to patiens with IAM



Graph 3.

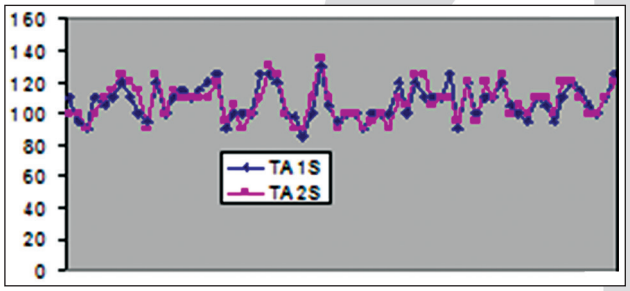
4d graph presents muscular force on male's group control

Control group that has not applied physical acitvity, growth of muscular strength is from 3.3-4.1 and is done in continuel bases.

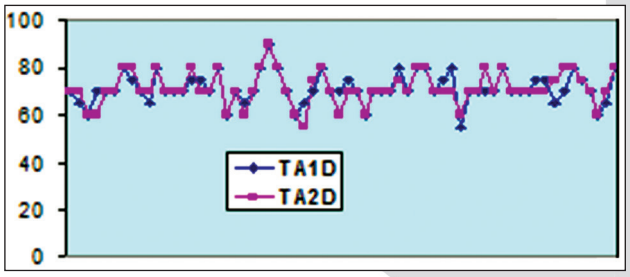


Graph 4.

5th and 6th graphs present values of systolic and diastolic pressure before and after physical activity, resulting with increased values: systolic 20mm. Hg,+0.6mm/Hg, diastolic 10mmHg+0.1mmHg.



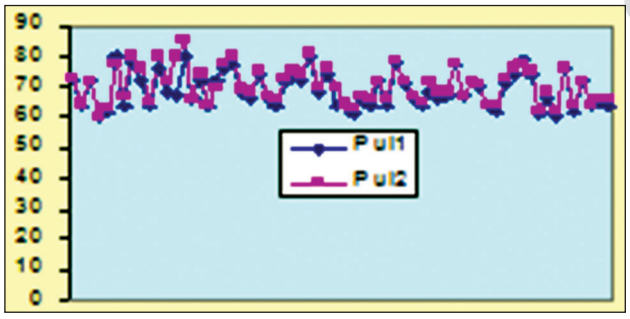
Graph 5.



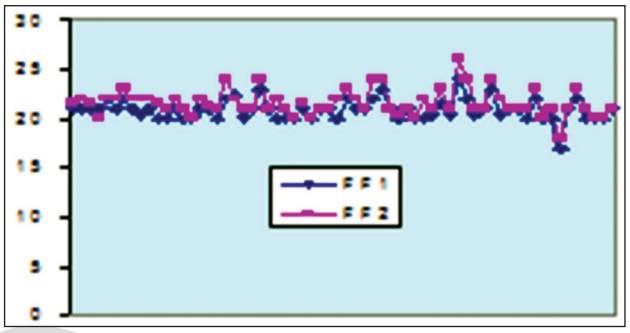
Graph 6.

From these results it is showed that patients were not overburdened after physical activity.

7th and 8th graphs present values of pulse and breathing frequency before and after applying physical activities, no significant changes are seen



Graph 7.



Graph 8.

On ECG and Ergometer of patients that were part of the study after the physical activities, no significant changes are seen.

Discussion

The study investigates the engagement of physical activities on patients with AMI muscular force during the first phase of rehabilitation. Additional parameters (arterial pressure, pulse, breathing frequency, subjective condition) served the purpose of detecting eventual overburden. According to international studies physical activity holds and important role on rehabilitation of AMI patients.

De Busk 1992, Ades et al 2000 and others, based on studies have suggested that patients with AMI to be included in rehabilitation programs in order to have benefits for patient and society. It has been proved that prolonged bed rest of AMI patients resulted in reduced muscular mass, decreased muscular force of skeletal muscles, thrombolytic changes on lower limbs (7), osteoporosis, humeroscapular per arthritis , atelectasis, pulmonary infections, psychological disorders, anxiety, insecurity, all these factors interrupt absolute bed rest. Based on these possible complications, physical activity was included on conservative treatment of AMI patients. The crucial element of this statement is early movement of AMI patients, education, physical toughening, rehabilitation, vices improvement (tobacco, alcohol), working days and life prolongation, overall life quality improvement. During this study the appliance of physical activity on the first phase of rehabilitation brought improvement of muscular force almost on all patients, after 10 days of exercises. All these results were satisfactory thanks to mutual patient-doctor corporation, this corporation was well accepted by

the patients because the benefits of these activities were correctly explained to them and this alliance elated them and positively increased their subjective condition.

Taking in consideration the fact that those who suffer from IAM are anxious, physical activity has elevated the patient's confidence and gave them a more realistic approach towards their future. This way they give an end to their negative thoughts and give meaning to their lives

Conclusion

The appliance of physical activity on AMI patients is an inseparable part of treatment and its purpose is enhancement of patient's capabilities for a normal life as soon as possible. Early mobilized AMI patients were soon activated, their heart regenerative abilities were increased 2 weeks earlier than patients that were not mobilized nor activated. Physical activity improves peripheral blood circulation by reducing cardiac overload. Physical activity on patients groups induced positive changes on their lifestyle, which results on later reduction of risk factors. Appliance of physical activity should be part of daily therapy on non complicated AMI patients. Applying physical activity during the first phase of rehabilitation is not financially damaging, it is easy to learn, practice and it doesn't require any special environment. Physical activity excellently uses all the existing environmental conditions.

References

1. *Weger NK, Rehabilitation of the coronary patient: Status 1986. Prog CardiovascDis 1986; 29: 181.*

2. *Rehabilitation after myocardial infarction Public. Public Health in Europe 24: WHO Regional Ofice for Europe, 1985.*

3. *Istvanovic N. Rehabilitacia bolesnika s kardiovaskularnim bolestima i urednici. Fizikalna medicina i rehabilitacija u Hrvatskoj, Zagreb, 2000: 187-201.*

4. *Hadzi-Pesic Lj. i sar: Fizikalna aktivnost irehabilitacia srcanih bolesnika, Prosveta Nis, 1992; 3-36, 142-182.*

5. *Jevtic M. Klinicka kineziterapija. Medicinski fakultet, Kragujevac, 2001.*

6. *Haskel LW. Design and Rehabilitation of cardiac conditioning programs. In: Wanger KN Helerstein KH. Rehabilitation of coronary patiens. John Wiler and sons. New York, 1978: 203-241.*

7. *Nedvedek B. Osnovi fizikalne medicine i medicinske rehabilitacie, medicinski fakultet, Novi Sad, 1991.*

8. *Hort W, Stahl C. Healing of myocardial infarcion and exercize. Morphologic Findings. In Early mobilization and testing after myocardial infarction. Council on rehabilitation. International Society of Cardiology. Symposium Munich, March 1979.*

9. *Squires RW, Gau GT, Miler TD. Allison TG, Lavie CJ. Cardiovascular Rehabilitation: Status, Mayo Clin. Proc., 1990; 65: 731 – 755.*

Corresponding Author
Sebahat Zeqiri,
QKUK-Pristine,
Physiatrist Clinic,
Kosovo,
E-mail: sebahatzeqiri@hotmail.com

Instructions for the authors

All papers need to be sent to e-mail: healthmedjournal@gmail.com

Preparing Article for HealthMED Journal

First Author[1], Second Author[2], Third Author[3]

[1] First affiliation, Address, City, Country,
[2] Second affiliation, Address, City, Country,
[3] Third affiliation, Address, City, Country.

Abstract

In this paper the instructions for preparing camera ready paper for the Journal are given. The recommended, but not limited text processor is Microsoft Word. Insert an abstract of 50-100 words, giving a brief account of the most relevant aspects of the paper. It is recommended to use up to 5 key words.

Key words: Camera ready paper, Journal.

Introduction

In order to effect high quality of Papers, the authors are requested to follow instructions given in this sample paper. Regular length of the papers is 5 to 12 pages. Articles must be proofread by an expert native speaker of English language. Can't be accepted articles with grammatical and spelling errors.

Instructions for the authors

Times New Roman 12 points font should be used for normal text. Manuscript have to be prepared in a two column separated by 5 mm. The margins for A4 (210×297 mm2) paper are given in Table 1.

Table 1. Page layout description

Paper size	A4
Top margin	20 mm
Bottom margin	20 mm
Left margin	20 mm
Right margin	18 mm
Column Spacing	5 mm

Regular paper may be divided in a number of sections. Section titles (including references and acknowledgement) should be typed using 12 pt fonts with **bold** option. For numbering use Times New Roman number. Sections can be split in subsection, which should be typed 12 pt *Italic* option. Figures should be one column wide. If it is impossible to place figure in one column, two column wide figures is allowed. Each figure must have a caption under the figure. Figures must be a resolution of 300 DPI, saved in TIFF format, width 10 cm min. For the figure captions 12 pt *Italic* font should be used. (1)

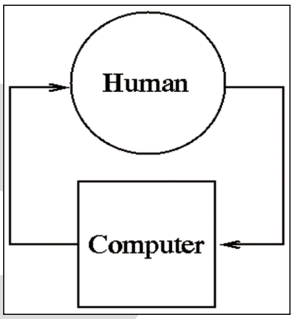


Figure 1. Text here

Conclusion

Be brief and give most important conclusion from your paper. Do not use equations and figures here.

Acknowledgements (If any)

These and the Reference headings are in bold but have no numbers.

References

1. *Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. N Engl J Med 1999; 341: 1284–1291.*
2. *Stewart SM, Lam TH, Beston CL, et al. A Prospective Analysis of Stress and Academic Performance in the first two years of Medical School. Med Educ 1999; 33(4): 243- 50.*

Corresponding Author
Name Surname,
Institution,
City,
Country,
E-mail: