Acta Medica Academica

Journal of Department of Medical Sciences
of Academy of Sciences and Arts of Bosnia and Herzegovina

ISSN 1840-1848 (Print) Volume 42 Number 1 May 2013 ISSN 1840-2879 (Online)

Online First www.ama.ba

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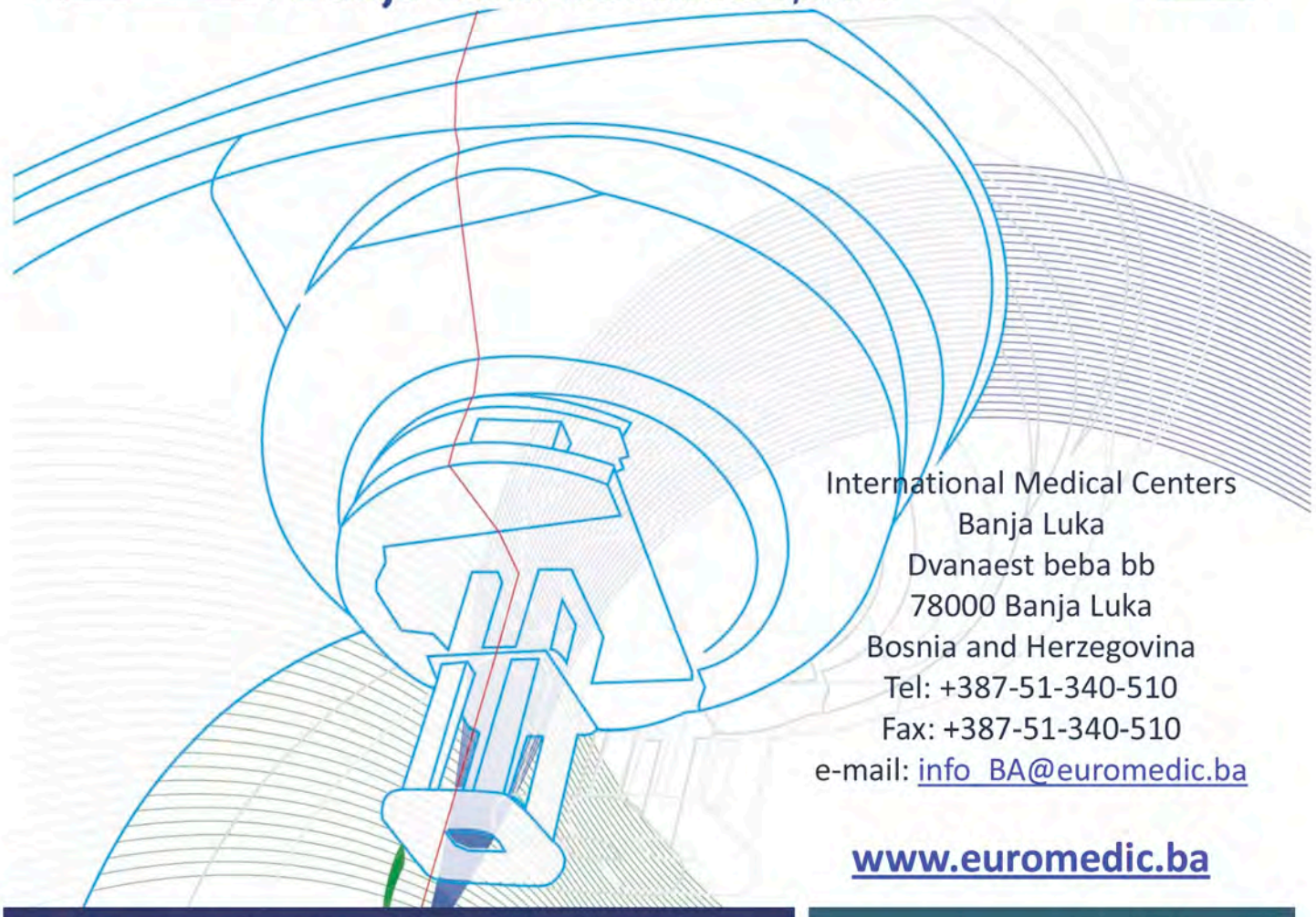

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International Medical Centers Banja Luka (IMC Center for radiotherapy Banja Luka) is a private radiation therapy center in Bosnia and Herzegovina established according to the Public-Private Partnership (PPP) model. The Center has a contract with the local National Health Fund making treatments available to local patients on the basis of a valid health identification card.

Treatments provided in this Center are 3DCRT, BT and IMRT. As of August 2013, RapidArc, the state-of-the-art technique, will be also available.

Euromedic International, the founder of International Medical Centers Banja Luka (IMC Center for radiotherapy Banja Luka), signed a formal agreement with Methodist International (MI), a subsidiary of The Methodist Hospital (TMH) in Houston, Texas, United States of America in February 2012. For the period of three years, a team of MI's eminent clinical and administrative consultants from Houston will focus on the development and establishment of exceptional and distinguishable clinical, operational and quality standards for radiation oncology in Euromedic's Centers for radiotherapy.

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Acta Medica Academica

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AIMS AND SCOPE

Acta Medica Academica is a biannual, peer-reviewed journal that publishes: (1) reports of original research, (2) original clinical observations accompanied by analysis and discussion, (3) analysis of philosophical, ethical, or social aspects of the health profession or biomedical sciences, (4) critical reviews, (5) statistical compilations, (6) descriptions of evaluation of methods or procedures, (7) case reports, and (8) images in clinical medicine. The fields covered include basic biomedical research, clinical and laboratory medicine, veterinary medicine, clinical research, epidemiology, phramacology, public health, oral health, and medical information.

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SUBSCRIPTION

Acta Medica Academica is published semi-annually. The annual subscription fee is € 15 outside of Bosnia and Herzegovina.

PUBLISHER CONTACT INFORMATION

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COVER PHOTO PICTURE

Safet Zec (1943-), "Room", 1978, colored pencil on paper, 1200x900 mm (Artist's collection). Courtesy of author.

INSTRUCTIONS TO AUTHORS

Instructions to authors in English language are published in each new issue. Home page of the Journal www.ama.ba offers free access to all articles and Instructions to authors.

SECRETARY

Nerma Tanović, Sarajevo, BA

TECHNICAL EDITOR

Husref Tahirović, Tuzla, BA

DTP

Narcis Pozderac, Sarajevo, BA

PRINT

SaVart Print, Sarajevo, BA. Printed on acid-free paper.

CIRCULATION

500 copies

THE JOURNAL IS INDEXED IN

Medline/PubMed
EBSCOhost
Index Copernicus
CAB Abstract/Global Health Databases
IndexScholar.com
DOAJ
CrossRef

Acta Medica Academica (ISSN 1840-1848) is an international peer-reviewed biannual journal which is printed as a continuation of the journal Works of the Academy of Sciences and Arts of Bosnia and Herzegovina, Department of Medical Sciences, founded in 1953. *Acta Medica Academica* Online (ISSN 1840-2879) offers free access to all articles at www.ama.ba.

Acta Medica Academica 2013;42(1):1-3
DOI: 10.5644/ama2006-124.64

Acta Medica Academica is now indexed in Medline/PubMed

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Received: 14 April 2013; Accepted: 20 April 2013

Towards the end of last year, on 20.11.2012, we were informed that our journal *Acta Medica Academica (AMA)* had been selected, from the first issue published in 2012, for indexation in Medline/PubMed. The announcement arrived only six months after our first application.

This success comes after six years' hard work by the new editorial board of the journal. Although the *AMA* journal, as the successor to the journal *Radovi*, has a tradition longer than forty years (Volume 41), the revamping of the journal in 2006 in line with the guidelines of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals of the International Committee of Medical Journal Editors (ICMJE) (1, 2) required sweeping changes. This practically meant that the journal set out on a path on which it was necessary to overcome all the difficulties faced by a new journal (3, 4), in an environment, which may with justification be seen to be a small scientific community.

With the new concept of publication, the journal was meant first of all to achieve regularity in publication, as at that time it had not been published for two years. It was necessary to affirm the journal and its work concept and "seek out" manuscripts for publication, in the full meaning of those words.

I would like to mention with much gratitude those who, together with me, have been doing this work with dedication from the very beginning. The former editors of the Croatian Medical Journal made a significant contribution to the affirmation of our journal in Croatia: Prof. Dr. Ana Marušić and Prof. Dr. Matko Marušić. A certain number of their articles, and articles sent to the editorial board thanks to their recommendation, have been published in the AMA journal. They have supported the journal with advice and in many areas in terms of their expertise, and technical and organization details.

Members of the Bosnian-Herzegovinian American Academy of Arts and Sciences – BHAAAS have also contributed to the affirmation of the journal in the United States of America. By publishing their own articles and encouraging their colleagues to publish their articles in our journal, they have

contributed to the better quality and richer content of the latest issues of AMA. In this regard, the most significant contributions came from Prof. Dr. Gordan Srkalović, Dr. Emir Festić and Dr. Ognjen Gajić.

The following also contributed to the affirmation of the journal in their own settings: Doc. Dr. Nermina Arifhodžić from Kuwait, Prof. Dr. Adnan Čustović and Prof. Dr. Predrag Slijepčević from England, Prof. Dr. Bogdan Bošković from Serbia, and Doc. Dr. Mojca Sajko Čižek from Slovenia. They also improved the quality of the journal significantly by sending in their own articles. Indeed, the greatest contribution to achieving this success came from the authors of the articles we published, since they could have published the articles they published in *AMA* in more respected journals.

How have we worked?

In the last six years a significant activity of *AMA* has been individual work with young authors who thus have had the opportunity to learn about writing skills and the medical publishing process. Members of the editorial board of *AMA* do not reject poorly written/prepared manuscripts with relevant themes and/or interesting core data, but repeatedly correct them in close cooperation with the authors ('pre-review') until they are ready for the international review process.

All manuscripts submitted to AMA undergo "double-blind" peer review. They are reviewed by at least three reviewers. In the first round of peer reviewing, a majority of reviewers must recommend at least publication with revisions for the authors to be invited to resubmit their revised articles. In the second round, a majority of the original peer reviewers must recommend publication of the article as it stands. The editors retain final discretion over publication of all articles. Every manuscript accepted for publication is proofread by a lecturer whose native language is English.

AMA was the first journal in Bosnia and Herzegovina to introduce mandatory checking of all submissions for text similarity using CrossCheck. Two members of our editorial team have engaged successfully in plagiarism research. As a result of this work we discovered three plagiarized manuscripts. Also *AMA* is the first journal in the country which informs the public about the best publications by domestic authors in international journals.

The academic community have liked the column, which may increase the journal's visibility. We opted for visibility rather than for profit, because we judged that our readership is not willing or able to pay access to the e-version of the journal. For this very reason, we declined offers to join the commercial electronic package of prestigious journals.

One of the reasons why the *AMA* journal was only a biannual is the rather low number of articles that we received for consideration due to the fact that authors want to publish in journals indexed in respectable bases, as well as due to the fact that *AMA* is known as a journal with strict and harsh criteria with respect to the article review process. Now, after being indexed in Medline/PubMed we hope that we will receive a larger number of articles and that this will enable us to gradually increase the frequency of publication of the journal.

What does the future hold?

In the near future we will retain the current concept of editing the journal. We are also planning to improve our current cooperation with national and foreign scientific institutions and experts in the field of biomedicine, to ensure that the journal will continue to be a form of school for young researchers from BH in scientific research and publication, to make it possible for the journal, in terms of content, to become part of the professional literature used by its read-

ers in their everyday work, to improve the availability of the published articles on an international level, increase the frequency of publication of the journal and achieve more indexations.

Conclusion

In realization of the new concept of the journal we have used our own, but also other people's experience. Together with the reviewers, we have helped those authors who have needed it in their research and in writing articles. All this has, in a relatively short period of time, had a significant impact on the quality of the journal, and has made it possible for us to have today a journal that is indexed in Medline/PubMed – the most important and the largest world index base of biomedical data. Indexation in such a relevant index base means that access to complete articles published in our journal and bibliographic and abstract data from those articles will be free of charge. This will mean that the interest of researchers from the near and further surroundings, but also the entire world, in the *AMA* journal will be even greater.

Conflict of interest: The author declares that he has no conflict of interest.

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Acta Medica Academica 2013;42(1):4-14
DOI: 10.5644/ama2006-124.65

The utilization and perceived usefulness of health care and other support services by people exposed to traumatic events related to the war in the Balkans

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Received: 2 January 2013
Accepted: 20 April 2013

Objective. To explore which health care and other support services people exposed to traumatic events related to the war use, how helpful they perceive them in the course of their post-war adaptation and whether utilization and perceived usefulness depend on the mental health status of participants. **Methods.** A community sample of 3304 adults exposed to at least one war-related traumatic event was randomly selected in different regions in the former Yugoslavia. A specifically designed instrument, the Matrix for the Assessment of Community and Healthcare Services, was used to record service utilization and their perceived usefulness. The mental health status of participants was assessed using the Mini International Neuropsychiatric Interview. **Results.** Primary health care was the most frequently used type of service (80.5%). Services providing help with leisure activities, social support and social contacts were perceived as most helpful. Participants with current post-traumatic stress disorder used all types of health care services and employment support services significantly more often than participants without mental disorders and participants with other mental disorders. They were more satisfied with primary health care services than participants without mental disorders and less satisfied with financial and material support services as compared to participants with other mental disorders. **Conclusions.** The frequency of utilization of different types of services varies greatly in war affected communities. Medical services are widely used and therefore have a central role in the care provision following a war. Services providing help with leisure activities and social support are most appreciated and may be more widely established.

Key words: Survivors of war, Support services utilization, PTSD.

Introduction

War and war traumatization have a negative impact on many aspects of human functioning, from different aspects of social life to physical and mental health. The effects of war can last long after the war has ended (1-3).

War survivors need organized forms of help in many domains of their lives, from accommodation support, to support in overcoming traumatic experiences. Depending on the context, societies after war usually respond by setting up various forms of interventions and services aimed at meeting needs and supporting the traumatized population (4-7).

Providing accommodation and meeting basic human needs is considered to be of primary importance (7-11). However, there are various concepts of defining priorities, forms of help and ways of organizing the provision of services needed in war and post-war environments. These concepts arise from various theories on the mental health effects of war traumatization (12-14).

Studies on the long-term utilization of these services are relatively scarce. The existing studies have mostly been carried out on veteran populations, with the focus on health care utilization (15-17). Measures of quality assessment, (i.e. usefulness of programmes and services) were not adequately defined (18) and conducted by service providers; consequently, there is a lack of information on which services are perceived as the most useful by the users themselves.

The negative impact of traumatic stress on overall health status has been well documented. Several studies have identified a positive association between combat related post-traumatic stress disorder (PTSD) and increased healthcare utilization (19-22). Kartha et al (23) found that trauma exposure was associated with greater mental healthcare utilization among patients presenting to primary care clinics, and the existence of PTSD explained only part of this association.

The war that started in 1991 after the disintegration of Yugoslavia was the largest military confrontation in Europe after the World War II. War activities of different intensity and duration were taking place in ex-Yugoslavia until 2001, resulting in a large number of human victims and causing considerable mental health problems, material damage, and migrations of the population (24, 25). The capacity of the formerly well-developed and accessible local health structures (26-28) was significantly reduced. As a priority, international assistance supported the local health system in ex-Yugoslavia by strengthening primary health care and providing necessary supplies to hospitals and health centres (26). A range of services and activities were organized during and after the war, aimed at helping people. Many of the services were provided within existing governmental organizations, and some were established by various NGOs, which had not previously existed in the countries of former Yugoslavia (9, 29).

In this study, we examined the utilization as well as the perceived usefulness of services provided not only in the combat-related PTSD population but also in wider war-affected community samples. The primary objective of this study was to explore which health care and other support services war-affected people use and how helpful they perceive them to be in the course of their post-war adaptation. A second objective was to examine whether there is a difference in frequency of use and perception of the usefulness of certain types of services depending on the mental health status of participants.

Methods

The research was a part of a larger epidemiological study entitled ”Components, Organization, Costs and Outcomes of Health Care and Community Based Interventions for People with Posttraumatic Stress Following War and Conflict in the Balkans” (CONNECT). The study was conducted in five sites in the Balkans (Serbia, Croatia, Bosnia and Herzegovina, Macedonia and Kosovo).

Details on the rationale, methodology and other findings of CONNECT have been published elsewhere (30).

Participants

We selected households for interviews in each of the Balkan sites based on a combination of regional clusters and random walk technique. First, we determined all the administrative units (regions, counties) that were exposed to the war and then randomly selected approximately 20% of these units. Of each of the selected administrative units, we randomly chose three towns, with a minimum of 3,000 inhabitants, for the interviews. The researchers randomly selected an address as a starting point for the interviews and then selected every fourth household from the random starting point.

The interviews were carried out with adults in the identified households whose birthday was the closest to the date of the interview and who met all the inclusion criteria. If the potential participant was not present, the researchers returned to the household at different times of the day and/or different days of the week. When, even after three visits, no contact was established, the researchers selected another household following the same procedure.

The inclusion criteria were the following: participants were born in the former Yugoslavia, were between 18 and 65 years of

Table 1 Socio-demographic characteristics of the sample

Characteristics	Without disorder	Current PTSD	Other mental disorders	Total
	n (%)	n (%)	n (%)	n (%)
Number of participants	1724 (52.2)	665 (20.1)	915 (27.7)	3304 (100)
Women	868 (48.8)	355 (20.0)	554 (31.2)	1777 (53.2)
Education level				
No education/primary school	456 (26.4)	256 (38.5)	295 (32.2)	1007(30.5)
Secondary school	862 (50.0)	312 (46.9)	439 (48.0)	1613 (48.8)
Higher	406 (23.6)	97 (14.6)	181 (19.8)	684 (20.7)
Total	1724 (100)	665 (100)	915 (100)	3304 (100)
Marital status				
Married/cohabiting	1250 (72.5)	460 (69.2)	613 (67.0)	2323 (70.3)
Single	341 (19.8)	82 (12.3)	181 (19.8)	604 (18.3)
Divorced	62 (3.6)	60 (9.0)	58 (6.3)	180 (5.4)
Widowed	71 (4.1)	63 (9.5)	63 (6.9)	197 (6.0)
Total	1724 (100)	665 (100)	915 (100)	3304 (100)
Employment status				
Employed	734 (42.5)	164 (24.7)	294 (32.1)	1192 (36.1)
Unemployed	724 (42.0)	339 (51.0)	473 (51.7)	1536 (46.5)
Retired	182 (10.6)	149 (22.4)	104 (11.4)	435 (13.1)
Educated/trained	84 (4.9)	13 1.9)	44 (4.8)	141 (4.3)
Total	1724 (100)	665 100)	915 (100)	3304 (100)
Age of participants	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
	42.5 (12.0)	41.5 (12.1)	45.6(10.9)	42.5(12.0)

age on the day of the interview, had been exposed to at least one war-related traumatic event and had been at least 16 years old at the time of the last war-related traumatic event. Mental retardation and/or organically caused mental disturbances were exclusion criteria. The potentially traumatic experience was established using a screening list containing 20 stressful events that people may have experienced during wartime (e.g. shelling, sexual assault, or combat). Participants gave written informed consent for the interviews.

Across all sites 70.1% of the eligible participants were interviewed. Of 5,330 people contacted, 603 (11.3%) did not meet the inclusion criteria and 1414 (26.5%) refused to participate. The final sample consisted of 3304 participants (62.0%). The average age of participants was 42.5±12.0 years. Basic socio-demographic characteristics are shown in Table 1.

Instruments and procedure

The data were obtained through face-to-face interviews conducted in the native language of the participants from January 2005 to November 2006. The interviews were done at places according to participants' preferences – in their homes, community organizations, or research center facilities.

The research teams consisted of qualified psychologists and psychiatrists. They were all trained in using the assessment instruments. The socio-demographic characteristics of participants, including, age, sex, education level, employment status, marital and housing status and information relating to war experience (active or passive participation in the war, staying at home or being a refugee) were obtained from a short structured questionnaire.

The utilization of health care and other support services were assessed using the Matrix for the Assessment of Community and Healthcare Services (MACSI) – an instrument developed within the CONNECT project. The instrument records details of utilization of health care and a wide range of specific and non-specific forms of help (30). It records details of services and forms of help specific for war and post-war periods (accommodation in refugee camps, home reconstruction, humanitarian aid, PTSD treatment programs, compensations and benefits, etc.).

The MACSI is structured in the form of nine tables, each of which stands for a category of services/forms of help: Primary health care, Mental health care, Specialist physical health care, Accommodation support, Employment support, Leisure activities – social contacts, Financial and material help, Legal support, Informing and advocacy,

The categories contain details on services used by participants from the beginning of the war (for instance, a visit to the family doctor, psychotherapy, a surgery operation, humanitarian aid in form of food or clothes, material for house reconstruction, etc.) until the present date. They also contain information about the year when a service was used for the first time, the number of times it was used and the period of use (if applicable). Finally, participants rated the usefulness of each service or intervention on a 10-point scale (1 – not helpful at all, 10 – very helpful).

Mental health status of the participants was assessed using the Mini International Neuropsychiatric Interview (MINI) (31). The MINI is a short, structured, diagnostic interview based on the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV (32). It is divided into modules, each corresponding to a diagnostic category with DSM Axis-I disorders (32). Modules consist of precise questions about psychological problems or symptoms, and the clinical assessment consists of evaluation of the participants' answers in terms of clinically relevant dimensions (ie, time frame, fre-

quency, severity). Clinical judgment of each symptom is then registered in the form of *yes* (symptom was clinically relevant) or *no* (symptom was not clinically relevant) answers. At the end of each module there is a diagnostic frame, which documents if the diagnostic criteria were met for each disorder. Compared with more extensive and time-consuming clinical interviews (such as the Structured Clinical Interview for DSM Disorders), MINI has similar metrical characteristics and satisfying levels of sensitivity and specificity (31, 33).

Statistical analysis

The results are shown in the form of frequencies (percentages) and arithmetic means ± standard deviations. We first conducted descriptive statistical analysis of the sociodemographic characteristics of the sample, and then presented the frequency of utilization of a particular service category. Due to the large number of missing data (e.g., the number of visits to the physician, duration and period of treatment, etc.), the utilization of particular services was assessed in terms of dichotomous outcomes ("used" or "did not use" a particular service). The variables of service categories were also dichotomized. If the respondent used at least one service from a particular group of services, the category was coded as "used" (e.g., if the respondent visited the cardiologist, the "specialist physical health care" category was coded as 1, i.e. "used"). In order to test differences in the frequency of use and the perceived usefulness of certain services according to the mental health status, the participants were divided into three groups: current PTSD, other mental disorders, or without disorders. To test the differences in frequency of use among the three groups, the chi square test was preformed. One-way analysis of variance was used to test the difference in perceived satisfaction, followed by the Scheffe post-hoc test in order to test the significance of differences between the three groups. Statistical analyses were performed using the Statistical Package for the Social Sciences, version 11.0 (SPSS Inc., Chicago, IL, USA). The significance level was set at $p<0.05$.

Results

The frequency of services used and perceived usefulness

People exposed to traumatic events related to the war used a wide range of services during and after the war, as summarized in Table 2. Primary health care and specialist physical health care were the most frequently used forms of help. The frequency of using other forms of interventions varied widely. Participants found health care services and help with leisure activities, social support and contact the most helpful.

Participants suffering from PTSD were significantly more likely to use support in employment and all types of health care interventions compared to the other participants (Table 2). The Scheffe post-hoc test showed that participants with PTSD were significantly more satisfied with the interventions of primary health care compared to participants without a mental disorder, and reported significantly lower satisfaction with financial and material support compared with the participants with other mental disorders (Table 3).

Table 2 Differences in the frequency of utilization of services according to mental status (current PTSD, other mental disorders, or without disorders) of participates assessed

Service categories	Groups	Utilization of services			Chi square
		Yes	No	Total	
		n (%)	n (%)	n (%)	
Primary health care	Without disorders	1345 (78.0)	379 (22.0)	1724 (100.0)	p <0.05
	Current PTSD	570 (85.7)	95 (14.3)	665 (100.0)	
	Other mental disorders	745 (81.4)	170 (18.6)	915 (100.0)	
	Total	2660 (80.5)	664 (19.5)	3304 (100.0)	
Mental health care	Without disorders	242 (14.0)	1482 (86.0)	1724 (100.0)	p <0.05
	Current PTSD	175 (26.3)	490 (73.7)	665 (100.0)	
	Other mental disorders	166 (18.1)	749 (81.9)	915 (100.0)	
	Total	583 (17.6)	2721 (84.2)	3304 (100.0)	
Specialist physical health care	Without disorders	959 (55.6)	765 (44.4)	1724 (100.0)	p <0.05
	Current PTSD	456 (68.6)	209 (31.4)	665 (100.0)	
	Other mental disorders	554 (60.5)	361 (39.5)	915 (100.0)	
	Total	1969 (59.5)	1335 (40.4)	3304 (100.0)	
Accommodation support	Without disorders	468 (27.1)	1256 (72.9)	1724 (100.0)	NS
	Current PTSD	203 (30.5)	462 (69.5)	665 (100.0)	
	Other mental disorders	231 (25.2)	684 (74.8)	915 (100.0)	
	Total	902 (27.3)	2402 (72.7)	3304 (100.0)	
Employment support	Without disorders	295 (17.1)	1429 (82.9)	1724 (100.0)	p <0.05
	Current PTSD	136 (20.5)	529 (79.5)	665 (100.0)	
	Other mental disorders	138 (15.1)	777 (84.9)	915 (100.0)	
	Total	569 (17.2)	2735 (82.8)	3304 (100.0)	
Leisure, social support and contacts	Without disorders	127 (7.4)	1597 (92.6)	1724 (100.0)	NS
	Current PTSD	54 (8.1)	611 (91.9)	665 (100.0)	
	Other mental disorders	64 (7.0)	851 (93.0)	915 (100.0)	
	Total	245 (7.4)	3059 (92.6)	3304 (100.0)	
Financial and material support	Without disorders	690 (40.0)	1034 (60.0)	1724 (100.0)	NS
	Current PTSD	288 (43.3)	377 (56.7)	665 (100.0)	
	Other mental disorders	405 (44.3)	510 (55.7)	915 (100.0)	
	Total	1383 (41.9)	1921 (58.1)	3304 (100.0)	
Legal support	Without disorders	67 (3.9)	1657 (96.1)	1724 (100.0)	NS
	Current PTSD	23 (3.5)	642 (96.5)	665 (100.0)	
	Other mental disorders	32 (3.5)	883 (96.5)	915 (100.0)	
	Total	122 (3.7)	3182 (96.3)	3304 (100.0)	
Informing and advocacy	Without disorders	19 (1.1)	1705 (98.9)	1724 (100.0)	NS
	Current PTSD	5 (0.8)	660 (99.2)	665 (100.0)	
	Other mental disorders	10 (1.1)	905 (98.9)	915 (100.0)	
	Total	34 (1.0)	3270 (99.0)	3304 (100.0)	

PTSD = post-traumatic stress disorder; NS = not significant.

Table 3 Differences in the perceived usefulness of certain categories of intervention between groups of participants (current PTSD, other mental disorders, or without disorders) assessed with one-way analysis of variance and results of the Scheffe post-hoc test

SERVICE CATEGORIES	Groups	N	M	SD	F	P	Scheffe	p
Primary health care	Without disorders	1345	7.78	2.25	3.34	0.039*	1stand 2nd group	0.041*
	Current PTSD	570	8.06	2.15			1st and 3rd group	0.871
	Other mental disorders	745	7.84	2.14			2nd and 3rd group	0.185
	Total	2660	7.89	2.18				
Mental health care	Without disorders	242	7.91	2.43	2.45	0.087	1stand 2nd group	0.345
	Current PTSD	175	8.26	2.34			1st and 3rd group	0.660
	Other mental disorders	166	7.69	2.34			2nd and 3rd group	0.093
	Total	583	7.95	2.37				
Specialist physical health care	Without disorders	959	8.10	2.16	1.64	0.194	1stand 2nd group	0.775
	Current PTSD	456	8.19	2.08			1st and 3rd group	0.419
	Other mental disorders	554	7.95	2.23			2nd and 3rd group	0.214
	Total	1969	8.08	2.16				
Accommodation support	Without disorders	468	6.18	2.83	1.15	0.317	1stand 2nd group	0.624
	Current PTSD	203	5.95	2.88			1st and 3rd group	0.370
	Other mental disorders	231	5.85	3.02			2nd and 3rd group	0.946
	Total	902	6.00	2.91				
Employment support	Without disorders	295	5.56	3.29	1.52	0.220	1st and 2nd group	0.409
	Current PTSD	136	5.10	3.33			1st and 3rd group	0.817
	Other mental disorders	138	5.78	3.42			2nd and 3rd group	0.241
	Total	569	5.48	3.35				
Leisure, social support and contacts	Without disorders	127	8.41	2.34	0.120	0.887	1st and 2nd group	0.930
	Current PTSD	54	8.26	2.51			1st and 3rd group	0.986
	Other mental disorders	64	8.47	2.25			2nd and 3rd group	0.893
	Total	245	8.38	2.37				
Financial and material support	Without disorders	690	5.73	2.93	4.02	0.018*	1st and 2nd group	0.674
	Current PTSD	288	5.55	2.87			1st and 3rd group	0.080
	Other mental disorders	405	6.13	2.71			2nd and 3rd group	0.031*
	Total	1383	5.80	2.84				
Legal support	Without disorders	67	6.06	3.72	2.27	0.108	1st and 2nd group	0.227
	Current PTSD	23	4.54	3.01			1st and 3rd group	0.247
	Other mental disorders	32	4.75	3.80			2nd and 3rd group	0.978
	Total	122	5.12	3.51				
Informing and advocacy	Without disorders	19	7.47	2.87	0.238	0.789	1st and 2nd group	0.995
	Current PTSD	5	7.63	2.89			1st and 3rd group	0.821
	Other mental disorders	10	6.73	3.35			2nd and 3rd group	0.863
	Total	34	7.28	3.04				

1st group = without disorder; 2nd group = current PTSD; 3rd group = other mental disorder; *p<0.05.

Discussion

This study showed that the war-affected population used a wide range of organized forms of help and services during and after the war. Primary health care was the most frequently used form of help and overall health care services were perceived as more helpful compared with other support services. However, when specific interventions were compared, services providing help with leisure activities, social support and social contacts had the highest average values of perceived usefulness.

Participants with current PTSD were significantly more frequent users of all types of health care services and employment support services than participants without mental disorders and participants with other mental disorders. They were significantly more satisfied with primary health care services as compared to participants without mental disorders, and significantly less satisfied with financial and material support services as compared with participants with other mental disorders.

The study used strict selection criteria and a rigorous probabilistic sampling method. However, it also has several limitations. Since this is a retrospective study covering a long period of time (in some countries up to 15 years), many data are missing simply because the participants could no longer remember all events (for instance, the number of visits to the doctor, medications they had been taking, the sum of financial support they received, etc). Furthermore, it is very likely that some of the data were not accurate due to memory bias. This may imply that the frequency of utilization of some or all services has been underestimated, which would put the data established in this study at the lower end of the true service utilization.

The frequency of utilization of primary health care services was 80.5%, followed by specialist physical health care with 59.5% utilization. In the five countries of the former Yugoslavia, the primary health care system was relatively well developed and organized, and therefore more accessible than other forms of help (34, 35). Furthermore, the primary health care system has a gate keeping function of referring patients to other specialist health care systems so that patients intending to receive specialist care still need to see a primary care doctor first. Bearing in mind that primary health care in the region functioned continuously even during the most difficult periods of the war, it may have been the safest and most reliable service to obtain some form of help (36). The frequent utilization and high appreciation of the usefulness of health care services demonstrate the importance of a functioning health care system in war and post-war conditions.

The relatively unfavorable perception of the usefulness of services helping with accommodation and employment, and of financial support might reflect that the provider organizations of services had not been prepared and equipped to cope with the extraordinary challenges they faced at the beginning of the war. Besides, compared to the health care system, which had a well established funding arrangement, organizations providing other services lacked the material resources to provide better and more popular support.

Services providing help with leisure activities, social support and social contacts were used by a relatively small number of participants. These services were mostly organized by NGOs through projects initiated and funded from abroad, and their number was therefore limited (5, 37). One reason for the highest perceived usefulness of such services may be that they were seen as an increased social support and expansion of social networks (5).

The highly perceived usefulness of this type of service may indicate their impor-

tance for recovery from war traumatization. This is inconsistent with the opinion of some professionals that the role of community-based services is less important or even ineffective (6). In any case, we should take the perceived usefulness of these services into consideration when designing, organizing and implementing services in the future.

Legal support, informing and advocacy were used by a small number of participants. These services were mostly organized by governmental organizations, but to a lesser extent and only in some areas was the organization of such services practically feasible. Moreover, these services, for the most part, did not actively search for people in need and had not been commonly used in the pre-war period, which might have resulted in these services not being recognized by potential users.

The significantly more frequent use of health care by persons with PTSD was also reported in previous studies (19-22). Due to their mental health problems, persons with PTSD are more likely to need specialized health care, such as psychiatric care. They may also have a number of physical complaints that require medical care (38, 39). Recent studies have shown a link between PTSD and cardiovascular disorders (40, 41), frequent painful syndromes (42-44), increased use of tobacco, alcohol and other addictive substances (45) and difficult social and family functioning (46), all of which can contribute to utilizing primary and specialized health services. To avoid the stigmatization associated with seeking help from a psychiatrist, individuals with symptoms of PTSD may decide to seek help through primary health care.

Although there is some data on the utilization (22, 39, 47, 48) and treatment cost (49) of medical services for people with PTSD in the literature, to our knowledge patients' perception of the usefulness of such services has not been systematically studied. In our study, we found that people with PTSD were highly satisfied with the health care they received. This might be explained in the context of the organization of the health care system, which can respond quickly and efficiently to patients' needs, unlike other forms of assistance (primarily services providing financial and material support), where the system is much slower and dependent on bureaucratic procedures and the various requirements that people have to meet before obtaining help. This may have led to the dissatisfaction of traumatized people with such services.

Conclusion

People exposed to traumatic events related to the war from the areas of the former Yugoslavia used a broad range of services. The frequency of utilization varied significantly, but in general, medical services were the most frequently used and the participants were relatively satisfied with the care provided. Participants were most satisfied with services providing help with leisure activities and structuring their free time. Whilst health care services play a central role in providing care to war affected communities – and are particularly appreciated by patients with PTSD – services helping with leisure activities and social contacts may be more widely established so they can meet the needs of people in post-conflict areas.

Authors' contributions: Conception and design: TF, ZŠ, MB, SP; Acquisition, analysis and interpretation of data: TF, ZŠ, ZT, DA, MB, AK, DLT, NM, MP, SP; Drafting the article: TF, ZŠ, ZT; Revising it critically for important intellectual content: TF, ZŠ, ZT, DA, MB, AK, DLT, NM, MP, SP.

Conflict of interest: The authors declare that they have no conflict of interest.

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Acta Medica Academica 2013;42(1):15-24
DOI: 10.5644/ama2006-124.66

Comparison of double disk synergy test, VITEK 2 and Check-MDR CT102 for detection of ESBL producing isolates

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Received: 17 January 2013
Accepted: 7 May 2013

Objective. This study is to define the statistical significance for detection of ESBL producers by the double disk synergy test and molecular test (Check-MDR CT_{102}), microdilution test (VITEK 2 with AES) and double disk synergy test (DDST), as well as the microdilution test and molecular test. **Materials and methods.** Phenotypic testing of 55 isolates *Enterobacteriaceae* (*Escherichia coli* (14/55), *Klebsiella pneumoniae* (34/55), *Klebsiella oxytoca* (3/55) and *Proteus mirabilis* (4/55) was performed by VITEK 2 Compact/AES. When this test showed positive results for the ESBL phenotype, then DDST with amoxicillin/clavulanate, ceftazidime, cefpodoxime, aztreonam, ceftriaxone and cefoxitin disks was performed along with Check-MDR CT_{102} which identified CTX-M, TEM and SHV β-lactamases. **Results.** Applying the McNemar test, we determined that there was a statistically significant difference in the results of detection of ESBLs bacteria using DDST compared to molecular methods (95% CI=41.92 to 54.55; p<0.0001), as well as a DDST and VITEK 2/AES (95% CI=40.13 to 52.73; p<0.0001). We did not find any statistically significant difference in the results of detection of ESBL producers using molecular techniques and VITEK 2/AES (CI=-4,43 to 5,36; p=1). Also we did not find any statistical.. difference between the resistance to cefpodoxime and ceftriaxone (50/50) compared to the results of molecular tests. **Conclusion**. In routine daily testing, good detection of ESBLs bacteria, especially CTX-M can be obtained with phenotypic methods with VITEK 2/AES and by DDST with cefpodoxime, and ceftriaksone disks.

Key words: ESBL, DDST, VITEK 2/AES, Check-MDR CT_{102}.

Introduction

Extended spectrum β lactamases (ESBL) are a group of enzymes which have the capability of hydrolyzing third-generation cephalosporins and aztreonam (but not cephamycins and carbapenems) and which are sensitive to inhibitors such as clavulanic acid, sulbactam and tazobactam. They developed from point mutation of genes which code production of primordial TEM-1, TEM-2, or SHV-1 β lactamases with replacement of the configuration of amino acids at an active site for these enzymes (1). In 1989, Philippon, Labia and Jacoby presented the first example where resistance to β-lactam antibiotics mediated by β lactamases was a result of important changes in the spectrum of

substrates of these enzymes (2). Due to their activity, they can hydrolyze a wide range of ß-lactam antibiotics, such as penicillins and cephalosporins. Besides *Klebsiella pneumoniae* and *Escherichia coli*, which represent the most important pathogens producing ESBLs, other ESBL producers, such as *Klebsiella oxytoca, Enterobacter cloacae, Enterobacter aerogenes, Serratia marcescens, Citrobacter diversus, Providencia stuartii, Proteus mirabilis, Salmonella typhimurium, Pseudomonas aeruginosa, Burkholderia cepacia* and *Acinetobacter spp*. have been registered lately.

To date, 890 various ESBLs have been discovered worldwide. They are classified according to two basic schemes: the molecular classification scheme according to Ambler and the functional classification system according to Bush-Jacoby-Medieros (3, 4).

Phenotypic testing of bacteria (disk diffusion and microdilution methods) is performed according to the recommendations of the Clinical and Laboratory Standards Institute in the Performance Standards for Antimicrobial Susceptibility Testing (M100-S21 Vol. 31 No 1) which we used in our study, or the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST), January 5, 2011, version 1.3 (5, 6). Using the disk diffusion method, a typical phenotypic profile of ESBLs shows resistance to third-generation cephalosporins (ceftazidime, cefpodoxime, ceftriaxone) and monobactams (aztreonam), an increase of the zone of inhibition for amoxicillin/clavulonate towards third-generation cephalosporins, and sensitivity to cefoxitin. Besides standard phenotypic methods, automated systems can also be used for the detection of resistance. VITEK 2 cards contain an ESBL test which monitors susceptibility of *Escherichia coli* and *Klebsiella species* to cefepime, ceftazidime and cefotaxime alone and in combination with clavulanic acid. The logarithmic reduction of growth within wells containing clavulanic acid and those which do not contain clavulanic acid indicates expression of an ESBL. The ESBL test, in combination with the VITEK 2 Advanced Expert System (AES), represents a very sensitive methodology for detection of ESBLs in clinical isolates. AES indicates possible inconsistent results in the antibiogram and, using existing knowledge about resistence mechanisms and CLSI standards, it indicates a phenotype for each isolate. Examples of phenotypes detected by AES are: ESBL, AmpC, carbapenemases (metallo or KPC β lactamases), as well as co-existing mechanisms of resistence (ESBL and AmpC) in the same isolate, where it may be necessary to apply molecular detection methods. The majority of VITEK 2 results are available on the same day that the VITEK 2 card is set up and VITEK 2 gives comments about the susceptibility test results, which can be used as guidelines by a clinician for antibiotic therapy.

Molecular diagnosis of ESBL is performed by the application of various methods, such as PFGE (pulsed field gel electrophoresis), multiplex PCR (polymerase chain reaction), sequencing of deoxyribonucleic acid (DNA) or pyrosequencing. One of the most sensitive methods, which is based on multiplex PCR and provides results in 24 hours, is the Check Points method. The principle of the Check Points diagnostic system is based on molecular recognition of the amplified target DNA sequence and subsequences with universal primers. The test uses highly-specific DNA markers necessary for differentiation of "real" ESBLs from non-ESBL variants TEM and SHV. This test detects and differentiates genes of different CTX-M families of enzymes, as well as SHV and TEM. Unlike conventional phenotypic methods, this test enables results to be obtained in one day.

Since results of genotypic testing methods are a reliable indicator of the existence

of genes for resistance due to the presence of ESBLs, this study aims to define statistical significance for detection of ESBL producers by the DDST and molecular test (Check-MDR CT_{102}), microdilution test (VITEK 2 with AES) and DDST, as well as microdilution test and molecular test.

Material and methods

This research was conducted at the Polyclinic for Laboratory Diagnostics, Institute of Microbiology University Clinical Centre, Tuzla in Bosnia and Herzegovina. The research included 55 isolates of *Enterobacteriaceae* (*Escherichia coli* (14/55), *Klebsiella pneumoniae* (34/55), *Klebsiella oxytoca* (3/55) and *Proteus mirabilis* (4/55)) where production of extended spectrum beta-lactamases had been detected using the microdilution method in VITEK 2/AES [AST-GN27 card, (bioMérieux, Marcy l'Étoile, France)], according to the procedure contained in the manufacturer's instructions. In this study we used the *Klebsiella pneumoniae* ATCC 700 603 strain as a positive control, and *Escherichia coli* ATCC 25922 strain as a negative control.

We examined each confirmed isolate with the double disk synergy test and molecular test. We applied the double disk synergy test (BD BBL™ Sensi-Disc™ Antimicrobial susceptibility Test Discs; Mueller Hinton agar, Liofilchem s.r.l. Bacteriology products) with disks cefpodoxime, ceftazidime, cefotaxime, ceftriaxone, aztreonam and cefoxitin according to recommendations by Thomson et al. (7) respectively, and we used 20 mm disk spacing.

Klebsiella pneumoniae, *Klebsiella oxytoca* and *Escherichia coli* were considered resistant to cefpodoxime disks of 10 μg if the zone of inhibition was ≤17 mm, and ≤22 mm for *Proteus mirabilis*. Strains were considered resistant to: ceftazidime disks of 30 μg if the zone of inhibition was ≤22 mm, cefotaxime disks of 30 μg if the zone of inhibition was ≤27 mm, ceftriaxone disks of 30 μg if the zone of inhibition was ≤25 mm, aztreonam disks of 30 μg if the zone of inhibition was ≤27 mm (5). We considered the screening test as positive if the zones of inhibition for the mentioned antibiotics were resistant, except for the zone of inhibition regarding cefoxitin, which was in the susceptible zone, i.e. ≥18 mm.

Genotyping of phenotypically confirmed ESBL isolates was performed with the multiplex PCR application of the commercially available Check-MDR CT102 (Check-Points Health BV) for detection of TEM, SHV and CTX-M genes according to the manufacturer's instructions. Before performing PCR, a DNA extraction from a pure culture of each isolate was made using the mini-kit QIAamp DNA (Qiagen, Sample & Assay Technologies).

Statistical analysis

The commercial statistical program Arcus Quickstat Biomedical was applied for data entry and basic statistical analysis. We used the chi-square test (McNemar) and statistical significance was tested at the 0.05 level.

Results

By using the VITEK 2 Compact system with AES, 14/55 *Escherichia coli,* 34/*55 Klebsiella pneumonie,* 3/55 *Klebsiella oxytoca* and 4/55 *Proteus mirabilis* were identified in a total of 55 *Enterobacteriaceae* isolates. The ESBL phenotype was identified in 49 isolates (89.09%) while ESBL/AmpC resistance phenotype was identified in 6 isolates (10.90%) (Figure 1).

Double-disk synergy test and molecular method Check-MDR CT_{102} were performed for all isolates. A positive result was found in 50 isolates (90.90%) tested by Check-MDR CT_{102} and in 21 isolates (38.18%) tested by double-disk synergy test

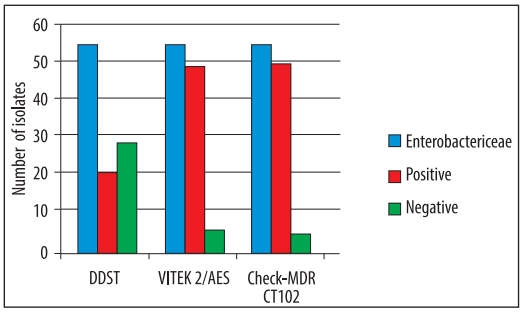

Figure 1 Results of ESBL detection by molecular, microdilution and DDST.

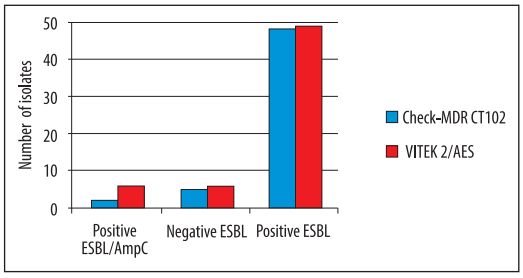

Figure 2 Results of the identification of ESBL using microdilution and molecular methods.

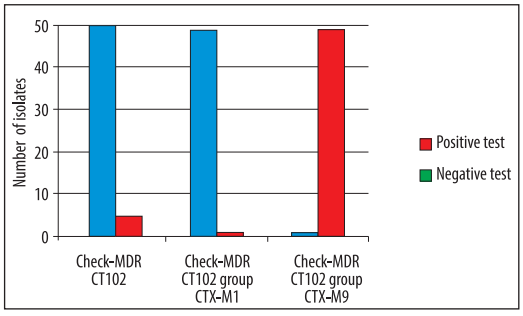

Figure 3 Illustration of ESBL genotypes.

Results obtained by the VITEK 2/AES

Consecutive samples of positive ESBL isolates were taken, using VITEK 2/AES from our routine work. Out of 55 isolates of *Enterobacteriaceae* which were tested, 49 isolates tested by the VITEK 2 Compact system/AES were positive for phenotype ESBL. Out of those, 48/49 also tested positive for phenotype by Check-MDR CT_{102}. One isolate which was positive on this test did not prove positive for genotype of ESBL. Out of 6 isolates tested by the VITEK 2 Compact/AES and positive for a combined phenotype ESBL/AmpC, 2 tested by Check-MDR CT_{102} confirmed the presence of ESBL genotype (Figure 2).

Results obtained by Check-MDR CT_{102}

50 out of 55 isolates tested by Check-MDR CT_{102} were positive. In 49 isolates the group CTX-M1 beta-lactamases was identified and the group CTX-M9 was identified in the remaining one (Figure 3).

Results obtained by the double-disk synergy test

All 55 isolates were tested by the double-disk synergy test. A typical phenotype profile of ESBL was found in 21 (38.18%). By considering the results of the molecular test Check-MDR CT_{102} positive, we found a phenotypic profile in 21/50 (42%) isolates. Furthermore, we found 15 different phenotype profiles in the remaining isolates, 29/50 (58%) (Table 1).

Out of 6 isolates which were positive (ESBL/ApmC) by the VITEK 2/AES, the phenotypic profile of AmpC beta-lactamases using DDST (when the diameter zone for ceftazidime, cefpotaxime, ceftriaxone or aztreonam was inside the zone of resistance, when there is no synergizing with clavulonic acid and when the organism is resistant to cefoxitin was found in 3 isolates) (Table 2).

Comparison of results obtained by double disk synergy test, Check-MDR CT102 and VITEK 2/AES

50 isolates tested by the molecular test were positive for genotype ESBL. Out of those, 21 were also positive by the double-disk synergy test. We found that the results of these two tests in detection of ESBL are significantly different (CI=41.92 to 54.55; $p<0.0001$). The sensitivity of double-disk synergy test was 48%.

Table 1 Phenotypic profile of ESBL isolates confirmed with Check-MDR CT_{102} and DDST negative

Phenotypic profile ESBL	Antibiotics					
	AMC	CAZ	CPD	ATM	CRO	FOX
I combination	5/S	5/R	5/R	5/R	5/R	5/R
II combination	9/R	9/R	9/R	9/R	9/R	9/I
III combination	1/I	1/R	1/R	1/I	1/R	1/R.
IV combination	2/I	2/I	2/R	2/I	2/R	2/R
V combination	1/I	1/R	1/R	1/I	1/R	1/S
VI combination	2/R	2/I	2/R	2/R	2/R	2/S
VII combination	1/I	1/S	1/R	1/R	1/R	1/S
VIII combination	1/I	1/S	1/R	1/S	1/R	1/S
IX combination	1/S	1/I	1/R	1/R	1/R	1/I
X combination	1/I	1/I	1/R	1/R	1/R	1/I
XI combination	1/I	1/S	1/R	1/S	1/R	1/I
XII combination	1/I	1/I	1/R	1/I	1/R	1/S
XIII combination	1/R	1/S	1/R	1/I	1/R	1/S
XIV combination	1/R	1/I	1/R	1/R	1/R	1/I
XV combination	1/R	1/R	1/R	1/I	1/R	1/I

AMC=amoxicillin/clavulanate; CAZ=ceftazidime; CPD= cefpodoxime; ATM=aztreonam; CRO=ceftriaxone; FOX= cefoxitin.

Table 2 Phenotypic profile of ESBL/AmpC isolates detected by the VITEK 2, ESBL test in conjunction with AES

Phenotype	Antibiotics					
	AMC	CAZ	CPD	ATM	CRO	FOX
I combination	2/R	2/S	2/I	2/S	2/I	2/S
II combination	1/R	1/I	1/I	1/S	1/S	1/R
III combination	3/R	3/R	3/R	3/R	3/R	3/R

AMC=amoxicillin/clavulanate; CAZ=ceftazidime; CPD= cefpodoxime; ATM=aztreonam; CRO=ceftriaxone; FOX= cefoxitin.

Table 3 Correlation of Check-MDR CT_{102} and phenotypic methods in detection of ESBL isolates

Methods for detection of ESBLs	95% CI	p
Check-MDR CT_{102}/ double disk synergy test	41.92 to 54.55	p<0.0001
Check-MDR CT_{102}/VITEK 2 compact /AES	-4.43 to 5.36	p=1.0
VITEK 2 compact /AES/double disk synergy test	40.13 to 52.73	p<0.0001

Out of 50 isolates which tested positive for genotype ESBL by the molecular test, 48 were positive by the VITEK 2/AES. By applying the Chi$_{\iota}$ square test (McNemar) we found that the results of these two tests in detection of ESBL are not significantly different (95% CI=-4.43 to 5.36; p=1.0). The sensitivity of the VITEK 2/AES was 96%.

Out of 48 isolates which tested positive by the VITEK 2/AES, 21 were also positive by double-disk synergy test. By applying the Chi square test we found that these two tests are significantly different in detection of ESBL (95% CI=40.13 to 52.73; p<0.0001). The susceptibility of the test is 43% (Table3).

Table 4 Correlation of molecular tests and resistance of ESBL isolates to amoxicillin/ clavulanate, aztreonam, and cefoxitin

Methods for detection of ESBLs	95% CI	p
Check-MDR CT_{102}/ DDST amoxicilline/clavulanate	-6.05 to 9.96	p=0.6875
Check-MDR CT_{102}/DDST aztreonam	-0.71 to 19.09	p=0.065
Check-MDR CT_{102}/DDST cefoxitin	23.46 to 41.73	p<0.0001

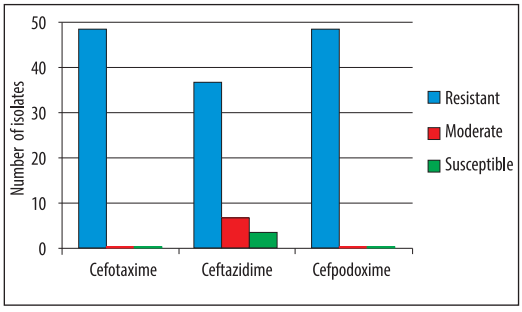

Figure 4 Susceptibility of ESBL isolates confirmed by the molecular test.

Sensitivity of ESBL isolates confirmed by molecular test on the cephalosporin's of III generation

50 isolates tested positive by molecular test. Out of those, 38 isolates were resistant to ceftazidime, 8 were intermediary susceptible and 4 were susceptible. All 50 isolates was resistant to ceftriaxon and cefpodoxime.

By applying the Chi square test, we found a statistically significant difference (95% CI=6.60 to 23.54, p=0.0034) between the results of the molecular test (where a positive result implies resistance to third-generation cephalosporins) and resistance to ceftazidime, whereas no statistical difference was found between the resistance to cefpodoxime and ceftriaxone (50/50) compared to the results of the molecular test (Figure 4).

Resistance of ESBL isolates to amoxicilline/ clavulonate, aztreonam and cefoxitin confirmed by the molecular test

Considering 50 isolates confirmed by the molecular test, we applied the Chi square test and did not find a statistically significant difference between the results of the molecular test and resistance to amoksicillin/clavulonate (95% CI=-6.05 to 9.96; p=0.6875), and aztreonam (95% CI=-0.71 to 19.09; p=0.0654) but we found a statistically significant difference between the results of molecular test and cefoxitin (95% CI=23.46 to 41.73; p<0.0001) (Table 4).

Discussion

The number of newly discovered ß –lactamases from *Enterobacteriaceae* has been rising annually, increasing the need for the introduction of new methods for their detection.

Many existing methods for detection of ESBL, AmpC or carbapenemases with *Enterobacteriaceae* and slow-fermentative Gram negative bacilli are technically demanding and their performance requires a great deal of time and special skills in a microbiologist. Small laboratories, which do not have appropriate equipment for molecular confirmation of individual types of resistance, must have a sensitive and specific method available for phenotypic detection of the same. According to the CLSI recommendations in M100-S21 Vol. 31 No. 1, phenotypic detection of ESBL by disk diffusion or broth dilution is based on the increased activity of cefotaxime or ceftazidime in the presence of clavulanic acid. Commercial methods, such as Etest, VITEK 2 and Phoenix, have developed phenotypic ESBL tests using CLSI methods as the reference comparative method. Molecular detection is based on the detection of resistance genes or

their products. Results of phenotypic methods for detection of ESBL isolates are relative, and applying different systems gives different results. Genotypic methods can detect resistance but lack of resistance does not indicate susceptibility. Resistance proven in this way is absolute – it is either present or not.

Application of the disk diffusion method with ceftazidime, amoxicillin/clavulanate, and cefotaxime disks, which are placed 30 mm from the center of one to the center of another disk, was first described by Jarlier et al. in 1988. This method has remained a reliable method in clinical laboratories, although reading is sometimes difficult. The sensitivity of this test can be increased if disks are set at the distance of 30 mm and 20 mm (7). In our study we used 20 mm disk spacing.

The sensitivity of a screening test for the detection of ESBLs with *Enterobacteriaceae* varies, depending on the antibiotic used as a predictor of their existence. Application of more than one antibiotic increases the sensitivity of the test. Cefpodoxime and ceftazidime show the greatest sensitivity for detection of ESBLs. Phenotypic confirmation tests do not detect all ESBLs. Besides ESBLs, some bacteria possess other β-lactamases which can mask detection of ESBLs during phenotypic testing, resulting in false-negatives. This includes AmpC β-lactamases and TEM β-lactamases resistant to inhibitors. Hyper production of TEM and SHV β-lactamases in bacteria with ESBLs can also give false-negative results in phenotypic confirmation tests. This is why it is necessary to apply molecular detection methods to detect bacteria with the presence of multiple β-lactamases. However, molecular methods are not available in all laboratories (5).

The susceptibility of double-disk synergy test in our research was 48%. 50 isolates tested by the molecular test were positive for genotype ESBL. Out of those, 21 were also positive by double-disk synergy test. We found that the results of these two tests in detection of ESBL are significantly different (95% CI=41.92 to 54.55; $p<0.0001$). In our study we found that DDST failed in AMC R isolates and we assume that narrowing the disk spacing might improve ESBL detection in AMC R isolates. The reason for these results is probably due to the joined resistance we found using VITEK 2/AES.

According to the recommendations of Livermore and Woodford from 2004, determining the susceptibility of isolated bacteria to ceftazidime and cefotaxime or to cefpodoxime should be the first line in detection of ESBLs. A confirmatory test should be done when resistance to any of the above mentioned antibiotics is found. To confirm the mechanism of resistance, it is very important to identify the organism to the species level, or at least for those isolates that are resistant to the above mentioned antibiotics. This is necessary because with *Klebsiella pneumoniae* and *Escherichia coli,* the cefpodoxime clavulanate combined disk is used as a confirmation test for the detection of ESBL, while with *Enterobacter species* and *Citrobacter freundii,* the cefpirome/clavulanate combination disk is used. According to the same author, the best choice of a cephalosporin is the one that can reveal all ESBLs, even when their production is rare, because since 2001, CTX-M enzymes, as well as TEM and SHV mutants, have been isolated in clinical and in outpatient specimens. For this reason, the best choice for detection of TEM and SHV ESBLs is resistance to ceftazidime and variable to cefotaxime, CTX-M ESBLs, are always resistant to cefotaxime and variable to ceftazidime and for all ESBLs resistance to cefpodoxime is compulsory (8). In our research, comparing disk diffusion and Check-MDR CT_{102}, we defined that the best predictor for ESBLs is resistance to cefpodoxime and ceftriaxone, because in all 50 molecular test confirmed isolates we found resistance by the double disk synergy

test, but also we found a statistically significant difference between the results of the molecular test and resistance to cefoxitin using disk diffusing testing (95% CI=23.46 to 41.73; p<0.0001). Out of 50 ESBL isolates confirmed by molecular tests, 28 isolates showed sensitivity to cefoxitin, 14 isolates had intermediate sensitivity and 8 isolates showed resistance. It was not a good predictor of ESBLs

Resistance to ceftazidime is used in practice to indicate the presence of an ESBL, and ceftazidime is the best substrate for TEM and SHV ESBLs. When ceftazidime is used alone in practice, then CTX-M producing isolates will not be detected, since they are susceptible to ceftazidime. Many ESBLs show an "inoculum effect" where MICs of broad-spectrum cephalosporins increase if the inoculum increases. To avoid the possibility of omission in the detection of the CTX-M enzymes, it is important to examine susceptibility to cefotaxime, besides the susceptibility to ceftazidime. Applying the double synergy test in our work, we found a typical phenotypic profile for ESBLs in 42% (21/50) of ESBL isolates which were confirmed by Check-MDR CT_{102}. However, in 24% (12/50) of ESBL isolates we found that ceftazidime results were intermediate (8/50) or susceptible (4/50). Such findings can be explained by the fact that the ESBL isolates from our research belonged to the CTX-M genotype, for which ceftazidime zone diameters are intermediate or susceptible in *in vitro* conditions (9).

In the study of Peer et al., (10), 10.8%, 9.5% and 5.4% of ESBL producing bacteria had false susceptibility to third-generation cephalosporins (ceftazidime, cefotaxime and ceftriaxone) with interpretation of a routine disk diffusion method. In our research, 4/50 isolates (8%), confirmed by the molecular method, had false susceptibility to ceftazidime and none of the isolates had false susceptibility to ceftriaxone using DDST and VITEK 2/AES.

According to Peer et al. (10), usage of more than one antibiotic, such as ceftazidime, cefotaxime, ceftriaxone, aztreonam and cefpodoxime, significantly improves the sensitivity of ESBL detection. The same authors underline that using DDST, (double-disk synergy test), PCDDTs (Phenotypic Confirmatory Disk Diffusion Tests) and cefoxitin for the screening of ESBL/AmpC beta-lactamases in positive *Klebsiella* isolates, resulted in ESBL detection for 69.5% (64/92) of the isolates, AmpC beta-lactamase detection in 19.5% (18/92) of the isolates, and detection of both mechanisms of resistance in 10.8% (10/92) of the isolates (10).

Although specificity of DDST is well documented, its sensitivity is variable and varies between 76.5%, 93.3%, 87% and 79% in different studies. This difference in DDST sensitivity appears in different studies because standards set for performance of DDST are often complicated and very precise. Different DDST sensitivity also appears because of the application of different disks (11).

In our research, out of 55 isolates examined with VITEK 2/AES (ESBL screening test includes the resistance on one of III generation cephalospofins) we found ESBL confirmation in 89.09% (49/55) of the isolates and in 10.9% (6/55) we found two phenotypes, AmpC and ESBL. However, after application of the molecular method Check-MDR CT_{102} for ESBL detection, we obtained a positive result in 90.90% (50/55) isolates. With these isolates and using the double disk synergy test, we detected an ESBL phenotype in 42% (21/50) of the isolates. VITEK 2 /AES detected an ESBL/AmpC phenotype in 6 isolates and there was a phenotypic profile corresponding to the presence of AmpC β lactamases in 3/6 (50%) of the isolates by double disk synergy test.

In a multicenter evaluation of the VITEK 2 Advanced Expert System for interpretive reading of antimicrobial resistance, Livermore et al. determined that for 126 of

137 reference genotypes there was a phenotypic match with the results obtained using the VITEK 2 Advanced Expert System; in 4 isolates there was a partial match, while in 6 isolates the results were discrepant. With 1 isolate the result could not be interpreted. The same study proved that discrepancies were found in only 64 of 963 interpretations in 10 European countries, which indicates that errors are minimal if the VITEK 2 and AES systems are used in an appropriate manner (12). In our research, out of 50 isolates which tested positive for genotype ESBL by the molecular test, 48 were positive by the VITEK 2/AES. By applying the Chi square test, we found that the results of these two tests in detection of ESBL are not significantly different (p=1.0).The sensitivity of the VITEK 2/AES is 96%.

To analyze the sensitivity of the VITEK 2 ESBL test, in Spanu et al. (2006), as well as our research, molecular ESBL identification was applied as a confirmation test and the sensitivity of the VITEK 2 ESBL test was found to be 98.1% (306/312). False positive results were found in 0.24% (2/817). In this research, out of the 50 positive results obtained by Check-MDR CT102, 48 were positive on the VITEK 2 Compact system and sensitivity was 96%. In 2 isolates which were positive by Check-MDR CT102, VITEK 2/AES detected the AmpC/ESBL phenotype. In 5/55 isolates that were negative by Check-MDR CT102, the AmpC/ESBL phenotype (VITEK 2/AES) was found in 4/5 (80%). The ESBL phenotype was detected by VITEK 2/AES in 1/5 (20%) of Check-MDR CT102 negative isolates. From our results and from results obtained by other authors, it can be concluded that VITEK 2 is a fast and reliable/practical tool for the routine identification of ESBL producing *Enterobacteriaceae* isolates (13).

Limitations of study

During preparation of this work we had some limitations. One of them was the study's small sample size, which is a consequence of the inability to purchase a set of performance analysis of a large number of molecular tests, and the other was the domination of one ESBL type.

Conclusion

In conclusion, this study shows that in addition to molecular methods, which reliably detect genes for each individual mechanism of resistance in routine daily testing, good detection of ESBL-producing bacteria, especially CTX-M, can be obtained with phenotypic methods i.e. microdilution method in VITEK 2 Compact apparatus with AES and the disk diffusion test with a cefpodoxime, and ceftriaksone disk.

Authors' contributions: Conception and design: FN, MH; Acquisition, analysis and interpretation of data: FN, MG; Drafting the article: FN, ZD, SP; Revising it critically for important intellectual content: FN, MH, NT.

Conflict of interest: The authors declare that they have no conflict of interest.

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Acta Medica Academica 2013;42(1):25-31
DOI: 10.5644/ama2006-124.67

An outbreak of multidrug-resistant *Serratia marcescens*: The importance of continuous monitoring of nosocomial infections

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Received: 11 March 2013
Accepted: 10 May 2013

Objectives. *Serratia marcescens* is a well-established as a nosocomial pathogen, resulting in considerable morbidity and mortality in immunocompromised patients. The aim of this study was to investigate an outbreak of *Serratia marcescens* at the Orthopaedic Clinic of the Clinical Center University of Sarajevo. **Methods.** A total of 96 strains from 79 patients were isolated. The isolates were identified by conventional methods. Susceptibility testing was performed by the disc-diffusion method following CLSI guidelines. Results were confirmed by VITEC-2 Compact. **Results.** From January to December 2010, 96 strains from 79 patients were isolated at the Orthopaedic Clinic of the Clinical Center, University of Sarajevo.The strains were isolated from wound swabs, blood cultures and cerebrospinal fluid. The strains were identifed using current phenotypic methods as *Serratia marcescens* with identical biochemical characteristics and antibiotic susceptibility patterns. All strains were susceptible to imipenem, meropenem, amikacin, ciprofloxacin, levofloxacin and piperacillin/tazobactam. The infection control team was alerted and after investigation they discovered the same phenotype of *Serratia marcescens* in the anaesthetic vials used in procedures. This outbreak was extremely difficult to terminate, even with cohorting of patients, sterilisation of equipment, reinforcement of handwashing and deep-cleaning of facilities. The implementation of new control measures terminated the outbreak in February 2011. **Conclusion.** Continuous monitoring of nosocomial infections is indispensable. Phenotypic characterization of the isolates is useful for studying the relationship of microbial pathogens. The relationship of one clinical isolate to another during an outbreak is important in motivating the search for a common source or mode of transmission.

Key words: Nosocomial infection, Phenotyping, *Serratia marcescens.*

Introduction

Serratia marcescens is an opportunistic pathogen, which is now well established as a nosocomial pathogen, resulting in considerable morbidity and mortality in susceptible patients. *Serratia marcescens* has been implicated as an aetiological agent in every conceivable kind of infection, including respiratory tract infection, urinary tract infection, septicaemia, meningitis and wound infection (1, 2). Patients most at risk are those in intensive care units who are subjected to medical devices, especially central venous

catheters, and those treated with broad-spectrum antimicrobial drugs (2). The first description of nosocomial infection caused by *Serratia marcescens* was Wheat's report of 11 cases over a 6-month period in 1951 at Stanford University Hospital (3). Infections caused by this organism have been reported with increasing frequency since 1960 (4). Since the emergence of *Serratia marcescens* as a cause of infections was noticed, many aspects of the pathogenicity and virulence of the organism have been studied, including adherence and hydrophobicity, lipopolisaccharide (LPS) and extracellular products (chitinase, several proteases, nuclease and lipase) (2). *Serratia marcescens* has expressed the ability to survive and grow under extreme conditions, including in disinfectants, antiseptics and double-distilled water (5-7).

Nosocomial epidemics of infections caused by *Serratia marcescens* have been described in a variety of clinical settings, and different environmental sources have been identifed as reservoirs. Outbreaks have been traced to multiple sources, including contaminated solutions and disinfectants, intravenous fluids, mechanical respirators, intravenous catheters, ultrasonic nebulizers, fiberoptic bronchoscopes, and hand-to-hand transmission by hospital personnel (4-7).

In addition, *Serratia marcescens* often demonstrates multiple mechanisms of antibiotic resistance (2, 8-10), necessitating the use of antibiotics usually kept in reserve. The antibiotics of choice to treat a variety of infections are β-lactam agents such as penicillins, cephalosporins, monobactams and carbapenems. The introduction of them into therapy was rapidly followed by reports of resistance (11, 12). Microorganisms producing extended-spectrum β-lactamases (ESBLs) were identifed in the early 1980-ies (12). Production of ESBLs is the major mechanism of resistance to oxymino-cephalosporins and aztreonam in Gram-negative bacteria (12, 13). Carbapenems are generally the last resort in the treatment of infections caused by *Serratia marcescens* ESBL, because they are not affected by most β-lactamases, including ESBLs (12, 13).

The subject of this study was the investigation of an outbreak of *Serratia marcescens,* using phenotypic methods and to emphasize the importance of continuous monitoring of nosocomial infections.

Material and methods

Patient data

From January to December 2010, we observed an outbreak of *Serratia marcescens* involving 79 patients, at the Orthopaedic Clinic of the Clinical Center, University of Sarajevo. Before the onset of infection, all patients had been treated by orthopedic surgeons. Approximately within 48 hours after surgery the symptoms of infections occured.

Bacterial isolates and identification

A total of 96 isolates of *Serratia marcescens* were collected from 79 patients involved in the outbreak. The strains were isolated from wound swabs (78), blood cultures (17) and cerebrospinal fluid (1). Culture were made at the Institute of Clinical Microbiology of the University of Sarajevo Clinic Centre. Samples were plated on blood agar and Mac Conkey agar (Becton Dickinson, New Jersey, United States). Mac Conkey agar was used for selective isolation of *Enterobacteriacae*. These media are specially designed to distinguish lactose fermenting (pink to red) from non lactose–fermenting colonies (colourless or slightly beige). The plates were incubated overnight at 37^0 C in bacteriological incubators. All isolates were identified by conventional biochemical testing (14) and interpretative criteria established by the Clinical Laboratory Standards Institute (CLSI) guidelines (15). Results were con-

firmed by VITEC 2 Compact (bioMerieux, Marcy l'Etoile, France). Use of the VITEC 2 Compact with the Gram-negative cards (GN13) validated for use with the instrument identifed the isolates as *Serratia marcescens.*

Susceptibility testing

Antimicrobial susceptibility testing was performed by the Kirby-Bauer disc-diffusion method on Mueller-Hinton agar (14), according to CLSI guidelines (15). Bacterial inocula were prepared by suspending the freshly grown bacteria in normal sterile saline adjusted to a 0.5 McFarland standard. Antimicrobial susceptibility was determined for ampicillin, amoxiclilin/clavulanic acid, cefotaxime, ceftazidime, ceftriaxone, cefepime, gentamicin, amikacin, ciprofloxacin, levofloxacin, piperacillin/tazobactam, imipenem and meropenem. Results of antimicrobial susceptibility testing were confirmed by VITEC 2 Compact with AST cards.

Infection control

In June 2010, it became apparent that an outbreak was occuring and infection control measures were reviewed. Patients known to be infected or colonised were isolated in single rooms, where possible. Extensive environmental microbiological investigations were started. Swabs were taken from numerous surfaces, including walls, floors with their edges and corners, doors and door handles, sinks, ventilators, stethoscopes and other personal medical devices. To address the possibility of human carriage, the hands and cellular phones of some of the healthcare workers were checked. Bottles of saline used for dilutions and one phosphate buffer, multiple-dose vials of anaesthetics, drug bottles and boxes, soaps and disinfectants were swabbed and subcultured. The only positive result for the epidemic strain *Serratia marcescens* was from a multiple-dose vial of anaesthetics used intravenously during procedures.

Statistical analysis

The statistical data were analyzed by descriptive statistical values (statistical measures of counting-frequencies, percentages).

Ethical statement

Ethical principles outlined in the World Medical Association Declaration of Helsinki were applied in this study.

Results

From January to December 2010, in 79 patients hospitalized in the Orthopedic Clinic of the Clinical Center, University of Sarajevo, *Serratia marcescens* infections were registered. Before the onset of infection, all patients had been treated by orthopedic surgeons. Approximately within 48 hours after surgery, the symptoms of infection occurred. Laboratory findings showed elevated CRP 74 mg/l (range18-166), ESR 40 mm/1h (range 6-88), leukocytosis 12.8x10^9/l (range7.9-18.6). Wound swabs, blood cultures and one sample of cerebrospinal fluid from patients were sent to the Institute of Clinical Microbiology and all were positive for *Serratia marcescens,* with identical biochemical characteristics and antibiotic susceptibility patterns. The gender structure of patients was: 31 (39%) males and 48 (61%) females. The average age of the patients was 48 years (range from 20 to 76). Most of the patients (n=52; 65%) were older than 50 years.

A total of 96 samples from 79 patients involved in the outbreak were collected. The strains were isolated from wound swabs (78/96; 81%), blood cultures (17/96; 18%)

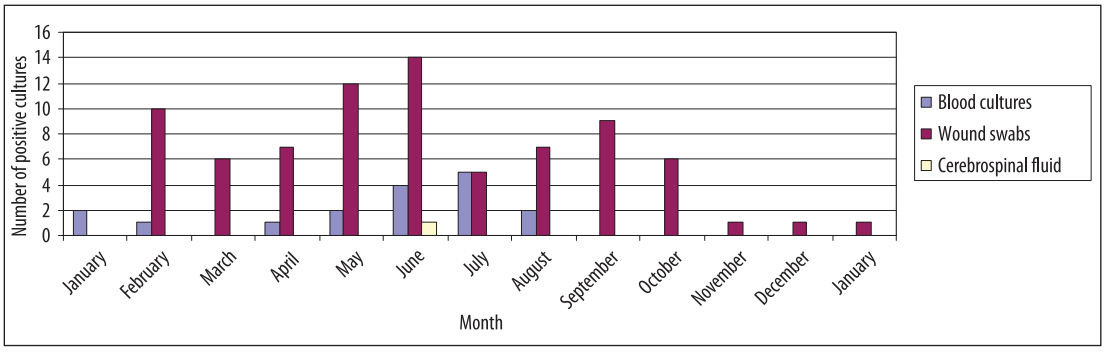

Figure 1 Laboratory-reported positive Serratia marcescens culture (cerebrospinal fluid, blood cultures, wound swabs) by month and culture site, January 2010 – January 2011.

and cerebrospinal fluid (1/96; 1%).The highest number of positive cultures were registered in May and June (33/96; 34.3%) (Figure 1).

The strains were identified with current phenotypic methods as *Serratia marcescens* with identical biochemical characteristics and antibiotic susceptibility patterns. The isolates showed resistance to ampicillin, amoxycillin-clavulanic acid, cefotaxime, ceftriaxon, ceftazidime, cefepime, trimethoprim/sulfometaxazole and gentamicin. Isolates remained susceptible to imipenem, meropenem, amikacin, ciprofloxacin, levofloxacin and piperacillin/tazobactam.

The infection control team was alerted and, after investigation, discovered the same phenotype of *Serratia marcescens* in a multiple-dose vial of anesthetic used during procedures.

All other environmental screens were negative for *Serratia marcescens*. The multiple-dose vial of anesthetic was changed with a separate vial in January 2011. Enhancement infection control measures were implemented and the outbreak was terminated in February 2011.

Discussion

Over the last 40 years, *Serratia marcescens* has become an important cause of nosocomial infections. There have been many reports concerning the identification, antibiotic susceptibility, pathogenicity and epidemiological investigation of this microorganism (2, 8). Outbreaks have been described in a variety of clinical settings and different environmental sources have been identified as reservoirs (1, 2, 8). Accurate identification is important in defining outbreaks (1, 11).

In this study, we examined an outbreak of *Serratia marcescens* involving 79 patients, in the Orthopedic Clinic of the Clinical Center, University of Sarajevo. Before the onset of infections, all patients had been treated by orthopedic surgeons. Approximately within 48 hours after surgery the symptoms of infections occured. Laboratory findings showed elevated CRP, ESR, leukocytosis. Wound swabs, blood cultures and one cerebrospinal fluid sample from patients were sent to the Institute of Clinical Microbiology and all were positive for *Serratia marcescens,* with identical biochemical characteristics and antibiotic susceptibility patterns. All patients had episodes of clinically significant infection and required therapy with antibiotics. There were 17 episodes of septicemia, one meningitis and 78 wound infections. The situation was dramatic, and we decided to start an investigation. The Infection Control Team was alerted and an investigation carried out. Of the several pos-

sible mechanisms for the pathogenesis of infections, given the nature of the outbreak (rapid onset post-surgery, complexity of the surgeries, severity of disease) a direct intravenous bolus of bacteria was suspected. This could have occurred if one or more of the following were contaminated: medications used during surgery, instruments, skin overlaying the site of surgery, or the hands of personnel performing the procedure (16, 17). Extensive environmental microbiological investigations were performed. A positive result for the epidemic strain of *Serratia marcescens* came from a multiple-dose vial of anesthetic used intravenously to provide general anesthesia during surgical procedures. All other environmental screens were negative for *Serratia marcescens*.

Both the epidemiologic and microbiologic evidence supported the contaminated vial of anesthetic as the cause of this outbreak. This is a very important finding, especially since in available literature we found very rare similar cases (16, 17). Halaby et al. (17) reported a case of fatal bacterial meningitis after spinal anesthesia. Several studies described infections caused by *Serratia marcescens* associated with contaminated disinfectants and antiseptics (5, 6, 18-20). Sauter et al. (6) reported a case of meningitis associated with contamination of a skin antiseptic solution containing benzalkonium chloride. Bosi et al. (20) reported an outbreak of *Serratia marcescens* infection in the neurosurgery intensive care unit due to contamination of hexetidine solutions.

The outbreak in our hospital was extremely difficult to terminate, even with cohorting of patients, sterilization of equipment, reinforcement of hand-washing and deep-cleaning of facilities. As a result, enhancement infection control measures were implemented, as well as a recommendation for use of single vials. It was suggested that use of multi-dose vials is a constant threat, and separate vials should be used. Separate vials of medicines should be used for patients and the approach to procedures should be with all aseptic precautions.

Knowledge and practice of infection control measures are mandatory and should always be emphasized to staff. Continuous monitoring of nosocomial infections is essential. Nosocomial infections with multidrug-resistant organisms (MDROs) are a major cause of morbidity and mortality (1). A lot of patients were colonized with MDROs on admission, indicating the importance of screening on admission to intensive care units (ICUs). Screening on admission allows early detection and limits dissemination of these strains with application of appropriate control measures (21). The factors which predispose colonization and infection with MDROs are most often transmitted among patients by the hands of personnel. So, it was suggested that permanent control of personnel is necessary (21). The implementation of new control measures and replacement the multiple-dose vials of anesthetic with separate vials terminated the outbreak in February 2011.

We examined the outbreak using phenotypic methods. Phenotypic characterization of the isolates is useful for studying the relatedness of microbial pathogens. Relatedness of one clinical isolate to another during an outbreak is important in motivating the search for a common source or mode of transmission. Epidemiologically unrelated isolates could have similar characteristics and they may not be distinguished by phenotypic methods. Genotypic characterization of the isolates is necessary in these cases.

Unfortunately, in this study we did not characterize the examined isolates by using molecular methods because these methods have not been applied in our Institute. We know that it is limitation of this investigation, but we solved the problem using simple resources in the environment. Lately, molecular methods are being used more frequent-

ly worldwide in typing hospital pathogens, since they allow genotypic characterization of the isolates (22). More recent studies with a wide range of strains and different primers have confirmed that RAPD-PCR is a promising method (22). Molecular methods have many advantages such as reproducibility, discriminatory power, ease of interpretation and performance. By applying this technique to all new isolates it should be possible to detect rapidly an outbreak of infection and allow the problem to be monitored and the source of the initial infection traced (22). This approach ensures a rapid and more adequate response by the infection control team, contributes to a reduction in the number of hospital infections and improvement of the quality of patient health care.

Conclusion

We examined the outbreak in our hospital using phenotypic methods. A positive result for the epidemic strain *Serratia marcescens* came from a multiple-dose vial of anesthetic used during procedures. Phenotypic characterization of the isolates is useful for studying the relatedness of microbial pathogens. Relatedness of one clinical isolate to another during an outbreak is important in motivating the search for a common source or mode of transmission. Phenotypic methods have some limitations, which can be overcome by using genotypic methods. Continuous monitoring of nosocomial infections is essential. Knowledge and practice of infection control measures is mandatory and should be always emphasized to staff.

Authors' contributions: Conception and design: MŠ; Acquisition, analysis and interpretation of data: MŠ; Drafting the article: MŠ; Revising it critically for important intellectual content: MH.

Conflict of interest: The authors declare that they have no conflict of interest.

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Acta Medica Academica 2013;42(1):32-40
DOI: 10.5644/ama2006-124.68

Impact of a recruitment campaign on students' applications to medical school

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Received: 29 March 2013
Accepted: 18 April 2013

Objective. Medical schools might benefit if they have information about the activities that may help them to increase the number of applicants with superior academic qualifications. **Methods.** The study was carried out at the Split University School of Medicine, Croatia. Medical school applicants were surveyed in 2007 and 2009. Promotional activities consisted of presentations on medical education covering six general high-schools in 2008, and a presentation on regional television, aired in 2008 and 2009 shortly before the admission term. **Results**. The survey response rate was 79% (299/379). The number of applicants in 2009 increased by 37% and the percentage of applicants from general high schools increased by 10%, in relation to 2007. The percentage of students with the best grades in all four years of high school was 42% in the both surveys. Presumed quality was a major influencing factor for choosing Split University Medical School. However, the medical school in the Croatian capital remained the first choice for students. Only a few applicants stated that the medical schools' promotional campaigns influenced their decision about where to study; 9.7% and 1.5%, respectively. **Conclusion.** Presentations in elected general high schools and a television campaign should be further explored as possible activities that regional schools may use to recruit potential applicants.

Key words: Medical school applicants, Recruitment, Television campaign, Medical education.

Introduction

A number of studies have been carried out to identify proper strategies to recruit high quality applicants to medical studies. Campaigns were undertaken due the low interest of students for certain medical disciplines (1), the shortage of professionals in unattractive geographic regions (2), or to recruit underrepresented racial and ethnic minorities (3).

The outreach and recruitment strategies used by medical schools were diverse, ranging from a nationwide campaign, to the specific activities of particular medical schools. Depending on the educational system of a country, potential applicants were targeted among high school students or among col-

lege students. One example of an intensive recruitment program is the Joint Admission Medical Program (JAMP) in Texas, USA, which is aimed at recruitment of economically disadvantaged students. The program was based on a partnership between the public and private colleges and the medical schools. The JAMP program provides a number of entering class positions in medical schools for qualified JAMP participants, and provides a variety of support measures during undergraduate study, such as additional learning activities, review of students' academic progress, counseling, mentoring and tutoring, summer internships and limited scholarship support. Various types of support at medical school were also provided (4).

To enhance the diversity of applicants, in 2009 the University of Oklahoma College of Medicine introduced a Summer Medical Program for high school students, with instructions on proper applications to medical school, providing interaction with minority physicians and distinguished physicians suitable to serve as role models in the medical profession, and senior students (5). At the University of Chicago, Pritzker School of Medicine, the curriculum was changed to suit the goals emphasized in a recruitment strategy.

By introducing a compulsory course on health disparities in 2005, the school acquired the reputation of being an institution aware of health disparities and social justice issues, which in due course has contributed to a substantial increase in the enrollment of underrepresented minority students (6).

Recruitment and promotional activities for prospective medical students, aimed at enlistment of a sufficient number of candidates for medical studies in rural areas, have been reported in Canada and Australia. Medical students in Canada, whose medical education curriculum integrates courses on rural medicine and hands-on learning, is aimed at developing a full understanding of the people living in rural areas and the specifics of their health needs. Such courses have caused more students to select rural practice as their career choice (7). The Rural Student Recruitment Program of The University of Western Australia includes promotional visits to rural high schools. Traveling and accommodation costs during the application and interviews are supported, too (8). In Australia, the percentage of medical students from rural regions has more than doubled as a result of national policies and initiatives (7). Another Australian study proved that the revision of selection criteria can significantly influence gender balance and student ethnicity (9).

However, there is a sparsity of studies on recruitment activities aimed at enlargement of the applicant pool at medical schools. In Croatia there are four medical schools, all of which are state-owned and located in the four major cities. The intention of the authorities is to ensure that the best students from regional medical schools stay in the regional cities instead of applying for the medical school in the capital, Zagreb.

The aim of this study was to analyze whether promotional activity could recruit more high quality applicants to apply to regional medical schools. We hypothesized that presentations to high school students and the use of a TV campaign could increase the overall number of applicants and the number of applicants with higher academic qualifications.

Methods

Setting

The University of Split, School of Medicine is located in Split, the second largest city in Croatia, being one of four medical schools in Croatia. The other three schools are in Zagreb – the capital of the Republic of Croatia,

Rijeka – the third largest city and in Osijek – the fourth largest city in Croatia. The Split School annually enrolls 75 students for a 6-year medical curriculum (10).

Participants

In 2007 and 2009, one academic year before and after the television media campaign, we surveyed the applications for medical studies collected in the Students' Affairs Office. All students who personally submitted their application documents to the Students' Office were invited to participate in the study, and none of them declined. Students whose applications were submitted by another person, or who sent application by mail were not included in the study.

Promotional activities

The University of Split, School of Medicine conducted a one-year promotional campaign consisting of presentations at targeted high schools and a campaign on regional television in 2008 and 2009. TV presentations were organized as four one-hour series, specially devised to present the Split Medical School and the study of medicine. In Croatia, students enter university after a 3-year or 4-year high school course, which may be vocational or a general high school. Vocational high schools last 3 or 4 years and emphasize the acquisition of specialized skills in chosen professions, such as hair dresser or plumber. In contrast, 4-year general high schools have a broad general curriculum. Some of these schools have a curriculum which emphasizes courses in languages or mathematics. The aim of the general high schools is to provide the students with a broad background knowledge, to allow them to enroll in any of the existing university courses. General high schools admit only students with outstanding academic achievements in primary school. Therefore, our promotional activity was targeted at general high school students in Split, Croatia, and covered 6 general high-schools that were visited once. At the end of each of the presentations, at least half an hour of discussion followed.

The presentations were given by the Dean and Vice-Dean for Education on three consecutive Saturdays at the beginning of the 2008-2009 school year, with fourth-year students attending. Each presentation was devoted to students from humanist, mathematical and language-oriented general high schools. The presentations lasted 45 minutes and each was attended by 40-50 students, which represents 25% of all students attending those schools. The Dean and Vice-Dean for Education gave presentations about the history of the School, the number of students, the organization of classes, the application procedure, the curriculum, research activities, opportunities for students to engage in research, employment opportunities for graduate physicians, different career opportunities, advantages of studying in Split and the Bologna Process. After the presentation, students had the opportunity to ask questions. At the end of the presentation, the Head of the Students' Affairs Office at the University of Split, School of Medicine was available to answer questions about formal admissions procedures.

The television campaign consisted of four 1-hour television programs, which were professionally filmed in a regional television studio, TV Jadran. In these television programs the School management and students promoted the School and pointed out to the benefits of studying in Split. The topics were, as follows: the role of the Medical School in the concept of a knowledge-based society, the achievements of the University of Split, School of Medicine (success stories about the development of the School) and medicine as a career choice. The presentations were shown on TV in April and September 2008 and in April and June 2009. The first presentation was in the evening, at 8 PM on TV

Jadran, and during the next week the presentations were replayed three times during the afternoons. TV Jadran is essentially available free of charge to the population of Central Dalmatia, but TV Jadran participates in a Croatian television cable network too and its program is available nation-wide.

The admissions to the University of Split, School of Medicine took place at the end of the June 2009, and all activities were completed by that date.

Survey

The survey was conducting using a questionnaire, which consists of 6 questions: about the applicants' city of residence, gender, high school, high school grade average, the reasons which influenced the student to choose this medical school and a request to rate the four Croatian medical schools in regard to the students' study preferences (Supplement 1). For the question about the reasons for choosing a medical school, multiple answers were allowed.

Ethics statement

The study was approved by the University of Split, School of Medicine Ethics Committee. As this study involved anonymous data collection, informed consent was not required.

Statistical analysis

Each completed questionnaire was marked by numeric code. The collected data were entered into electronic data sheets, and analysis was performed using GraphPad Prism 4.00 software (GraphPad Software Inc., La Jolla, CA, USA). Frequencies were reported as numbers and percentages. The differences in response frequencies between the two years were calculated using Fisher's exact test. Categorical variables were compared using the chi-squared test. Statistical significance was set at $p<0.05$.

Results

Out of total of 379 applicants in 2007 and 2009, 299 (79%) submitted their application personally (103 in 2007 and 196 in 2009) and were eligible to participate in the study. All of them agreed to participate and to fill out the questionnaire. More women applied in both analyzed years in comparison to men. In both years the majority of the applicants were from general high schools (Table 1).

The number of applicants to the University of Split, School of Medicine increased, from 147 in 2007 to 232 in 2009. Among applicants who participated in the study, the number of applicants from general high schools, where a promotional campaign was carried out, increased by 10%. In 2007, 42.7% (44/103) of participants were students with the best grades during all four years of high school, compared to 41.8% (82/196) in 2009.

However, the average high school grade of applicants was lower in 2009, compared to 2007. The percentage of applicants from the Split-Dalmatian County, where the School is located, remained almost the same, while the percentage of applicants from the neighboring counties – Dubrovnik-Neretva County, Zadar County and Sibenik County – showed an increase in 2009 (Table 1). The majority of the applicants were from three counties in Croatia: the Split-Dalmatia County, the Dubrovnik-Neretva County and Zadar County, and from the neighboring country, Bosnia and Herzegovina (Table 1).

In both years, the applicants' first choice was the medical school in Zagreb, and second choice was the school in Split. For the majority of the applicants, the most important selection factor was the medical school's quality. There were 10 applicants in 2009 and 3 applicants in 2007 who stated that the school's promotional campaign was an important factor in their decision about where to study (Table 1). The percentage

of applicants who deemed the promotional campaign of the medical school important when deciding where to study was significantly higher in 2007, than in 2009 (9.7% vs. 1.5%, respectively). Separate analyses were conducted for the subgroup of students from Split, and the only categorical variable among the reasons for choosing a medical school that was significantly different between the analyzed years was the number of students who indicated the promotional campaign as a reason (Table 1).

Table 1 Comparison of medical school applicants' responses in 2007 and 2009. The number of respondents in 2007 was 103, and in 2009 it was 196

Applicants' responses	2007	2009
Gender		
M	42 (40.8)	59 (30.1)
F	61 (59.2)	133 (67.8)
Missing values	0	4 (2%)
High school		
General high school	65 (63.1)	142 (72.4)
Vocational school	35 (33.9)	47 (21.4)
Other	0	3 (1.5)
Missing values	3 (2.9)	4 (2)
Best grade in all four years of high school, N (%)	44 (42.7)	82 (41.8)
Reasons for choosing a medical school among all applicants included in the study, N (%)*		
Quality of the studies	84 (81.6)	159 (81.1)
Reputation of a specific medical school	33 (32.0)	64 (33.0)
Cost of studying	28 (28.0)	33 (17.0) †
Friends' recommendations	8 (8.0)	22 (11.2) †
Quality of the student life	15 (15.0)	18 (9.1)
Promotional campaign of the medical school	10 (9.7)	3 (1.5) †
Reasons for choosing a medical school among applicants from Split, N (%)*		
Quality of the studies	58 (79.4)	99 (81.1)
Reputation of a specific medical school	25 (34.2)	40 (32.8)
Cost of studying	23 (31.5)	27 (22.1)
Friends' recommendations	5 (6.8)	16 (13.1)
Quality of the student life	11 (15.1)	11 (9.0)
Promotional campaign of the medical school	7 (9.6)	3 (2.5) †
First choice medical school		
Osijek	1 (0.9)	1 (0.5)
Rijeka	2 (1.9)	0
Split	15 (14.6)	15 (7.6)
Zagreb	74 (71.8)	168 (85.7) †
Missing values	11 (10.7)	12 (6.1)
County of residence		
Split-Dalmatian County	81 (78.4)	149 (76.0)
Dubrovnik-Neretva County	4 (3.8)	10 (5.1)
Zadar County	3 (2.9)	6 (3.0)
Sibenik-Knin County	1 (0.9)	6 (3.0)
Brod-Posavina County	1 (0.9)	-
Vukovar-Syrmia County	1 (0.9)	1 (0.5)
Krapina-Zagora County	0	1 (0.5)
Bosnia and Herzegovina ‡	10 (9.7)	16 (8.1)

*Multiple responses allowed; †Significant difference between the observed years; P <0.05; ‡All applicants from neighboring country Bosnia and Herzegovina were entered as one category.

Discussion

In this study we analyzed whether one-year promotional activities, consisting of presentations in elected high schools and a campaign on a regional television may have an effect on the applicant pool of a regional medical school. Compared to the year before the promotional activity, the number of applicants after the promotional activity increased by 37%. The number of applicants to this School has been fluctuating between 100 and 200 over the past decade (11), and the year after our promotional activity was the first time since 1999 that there were more than 200 applicants. The number of applicants from general high schools increased by 10% in the observed period, which may be considered a positive trend, because high schools provide a broader knowledge base in comparison to vocational schools.

However, only 9.7% of students in 2007 and 1.5% of students in 2009 stated that the promotional campaign of the medical school was their principal reason for choosing Split medical school. It is possible that the campaign had an influence, but students do not perceive presentations in high schools and television series as a 'promotional campaign', because they were not designated in that way.

Our data suggest that further research will be needed to improve the recruitment strategy, in order to recruit more high quality applicants and to retain the majority of prospective students in the region. Strategies that will create the image of a high quality school could influence prospective students to choose a regional school as their first choice, because the students stated that the quality of the medical school was the most important factor in choosing schools. Our promotional activity did not affect gender ratio. The predominance of women applicants has been present since the founding of the School of Medicine in Split (12).

The medical school in Split is among the smallest medical schools in Croatia in terms of the number of available positions, and our previous study indicated that other schools have a larger applicant pool, corresponding to the number of enrolment positions available (11). Considering the overall number of high school students interested in becoming medical students, there is potential for increasing the applicant pool of regional medical students.

In a 2005 study, Agrawal et al. studied recruitment methods used by American medical schools to recruit underrepresented and minority (URM) students, where the deans of student affairs were asked to indicate which interventions they used, and to rate the effectiveness of those programs (3). The interventions that were listed and rated were: site visits to school pre-admission, pre-admission counseling, career development outreach in primary or secondary schools, financial aid, early targeting of minority students, URM student recruiters, enrichment programs, community based education programs, alumni involvement, application assistance and partnerships with various organizations, such as education or labor state departments and foundations (3). Regional schools could consider using the extensive list of promotional activities, based on studies reporting on outreach to minority students, to increase their attractiveness among future medical students.

Hemphill et al. wrote about a marketing approach to recruitment, emphasizing that marketing theory deals with perceptions of value, satisfaction and practice selection, and that new perspectives in research-based market segment-specific solutions can be sought (13). Building on the suggestions of Hemphill et al. (13), high school students may be viewed as customers, medical schools as corporations and the entire country as the market of competition. Adopting this philosophy, coordinating mechanisms to integrate dissemination of information, and marketing the service supply between

the three elements may help in student recruitment to a specific school.

The University of Split, School of Medicine should emphasize its strengths to potential students, and advertise its advantages to potential candidates. For example, this school has a very high focus on evidence-based medicine and it is home to the national branch of The Cochrane Collaboration (14-18). We have reported previously that students from the University of Split, School of Medicine have more knowledge and more positive attitudes on evidence-based medicine, compared to students from other medical schools in Croatia and in Mostar, Bosnia and Herzegovina (19). Acta Medica Academica published a series of manuscripts in 2012, showing that the University of Split, School of Medicine is continuously improving its curriculum (20), placing the emphasis on clinical skills (21), and providing students with enhanced experience in the field of family medicine (22-25). All this could be an advantage for prospective students.

This study had several limitations. Only applicants from Split would have been potentially exposed to the promotional activities in the high schools and the survey did not question whether the survey respondents had heard the school presentation or seen the television broadcast. Since few students indicated that the promotional activities of the School were important in their decision, it is possible that there were other confounding variables that influenced the 37% increase in the number of applicants post-promotion. In the study we did not have a comparison group to show the differences between a medical school with a promotional activity and one without any. We did not have any means for measuring the viewership of the television series. Furthermore, in 2007, there were 70% of applicants who participated in the survey, and 84% in 2009. The proportion of applicants from general and vocational schools among those who did not fill out the survey does not necessarily need to be the same as among those who did participate in the study in 2007 and 2009. The 10% difference in the number of applicants from general high schools between 2007 and 2009 might be due to the fact that more students from general high schools came in person to submit their applications in 2009.

Conclusion

The number of applicants increased by 37% after the promotional activities, but the students did not indicate that the promotional campaign was a reason for choosing a medical school. Presentations in targeted general high schools and a television media campaign should be further studied, as possible activities that regional schools may use to reach out to potential applicants.

Acknowledgements: We are grateful to the study participants. We appreciate the help provided by Mr. Josip Baric from the Students' Affairs Office at the School of Medicine in Split, for providing valuable information and assistance in distribution of questionnaires.

Authors' contributions: Conception and design: DS, LP; Acquisition, analysis and interpretation of data: LK, TM, TM, DS, LP; Drafting the article: LP; Revising it critically for important intellectual content: LK, TM, TM, DS, LP; Approving final version of the manuscript: LK, TM, TM, DS, LP.

Conflict of interest: The authors declare that they have no conflict of interest.

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Supplement 1

QUESTIONNAIRE FOR MEDICAL SCHOOL APPLICANTS

1. Please indicate the city in which you live:				
2. Gender	○ male			
	○ female			
3. Your high school was:	○ general high school			
	○ vocational high school in the field of medicine			
	○ other vocational high school			
4. Your average academic success in high school:	Excellent (grade 5)	Very good (grade 4)	Other	
1st grade	○	○	○	
2nd grade	○	○	○	
3rd grade	○	○	○	
4th grade	○	○	○	
5. What were your reasons for choosing a particular medical school among all Croatian schools? (multiple answers allowed)	○ Quality of the studies	○ Friends' recommendations		
	○ Reputation of a specific medical school	○ Quality of the student life		
	○ Cost of studying	○ Promotional campaign of the medical school		
6. If you could choose a city where you would ideally like to study, what would be the order of your preference?	1st choice	2nd choice	3rd choice	4th choice
Osijek	○	○	○	○
Rijeka	○	○	○	○
Split	○	○	○	○
Zagreb	○	○	○	○

Acta Medica Academica 2013;42(1):41-45
DOI: 10.5644/ama2006-124.69

Occipitalization of the atlas: Its incidence and clinical implications

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Received: 24 January 2013
Accepted: 17 April 2013

Objective. The aim of the present study was to investigate the incidence of occipitalization of the atlas among Thai dried skulls, in order to contribute to baseline awareness of this condition. **Materials and methods**. The skulls of 633 adult Thais from the collection maintained in the Department of Anatomy, Faculty of Medicine, Khon Kaen University, Thailand, were examined for evidence of occipitalization of the atlas. The skulls were well-preserved and did not show any traits of craniofacial deformation. The skulls for which the age and sex were unknown were excluded from the analysis. From the cadaveric records on each individual, we learned that the skulls belonged to 373 men (age of decease between 25 and 90 years), and 260 women (age of decease between 28 and 92 years). **Results**. Occipitalization of the atlas was detected in 2 skulls (0.32%). The first case was a male skull (54 years of age at decease), where the atlas was partially fused to the occipital bone. The second case was also a male skull (59 years of age at decease) showing complete fusion of the anterior arch of the atlas. **Conclusion**. The incidence of occipitalization of the atlas is low; however, if present this abnormality may cause a wide range of neurological problems. Knowledge of occipitalization of the atlas may be of substantial importance to orthopedists, neurosurgeons, physiotherapists and radiologists dealing with abnormalities of the cervical spine. Mistaken diagnoses have led to delayed treatment and at times adverse results.

Key words: Occipitalization, Atlas, Incidence, Neurological problems.

Introduction

Occipitalization of the atlas, or atlanto-occipital fusion, is one of the most common skeletal abnormalities found at the craniocervical junction (1). Occipitalization is caused by assimilation of the first cervical vertebra (the atlas) into the basicranium (2, 3). The incidence ranges between 0.14 and 3.63 % (4-9) and it can be partial or complete (10-12), with the latter being the most common (13). Multiple variations of partial occipitalization have been reported, and many involve some aspect of atlanto-occipital articulation (14). Atlantal occipitalization may be congenital or acquired (15). Most of the mechanism of occipitalization is believed to be the malformation of the embryological development of the upper axial skeleton (16). Congenital malformation of the

cervico-occipital region is of considerable consequence because of its proximity to the spinomedullary region, with the possibility of neurological compression syndrome. Occipitalization of the atlas can produce a wide range of neurological signs and symptoms, which vary from a transitory headache to a full-blown neurological syndrome (17), leading to occipitocervical instability. The onset of neurological symptoms is usually in the third or fourth decade. The presence of blocked vertebrae below this level may accelerate the development of symptoms, due to compensatory motion at the atlantoaxial joint (6).

Standard anatomy text books do not pay much attention to occipitalization of the atlas, and research on it is the only source of information (4). Thus, the aim of the present study was to investigate the incidence of occipitalization of the atlas among Thai dried skulls, in order to contribute to baseline awareness of this condition.

Methods

We examined 633 skulls of adult Thais from the bone collection maintained in the Department of Anatomy at the Faculty of Medicine, Khon Kaen University, Thailand. The skulls were well preserved and did not show any trait of craniofacial deformation. The external and internal surfaces of the entire occipital bone were observed by visual inspection. The age and sex of the deceased were recorded by the technicians. The skulls for which the age and sex were unknown were excluded from the analysis. From the cadaveric records on each individual, we learned that the skulls belonged to 373 men (age of decease between 25 and 90 years), and 260 women (age of decease between 28 and 92 years). All of the skulls came from individuals who had donated their bodies to the Department. The proposal for this research project was approved by the Research and Ethics Committee of the Faculty of Medicine, Khon Kaen University.

Results

Of the 633 dried occipital bones, occipitalization of the atlas was found in two subjects (0.32%). The first case was a male skull (54 years of age at decease), where the atlas was partially fused to the occipital bone (Figure 1).

The posterior arch was incompletely fused in the midline. The anterior arch of the atlas was completely fused with the basilar part of the occipital bone, except for a slit-like opening above the anterior tubercle. The lateral masses were completely fused to the occipital bone. The superior articular facets of the atlas were totally fused to the occipital bone in the region of the occipital condyles. The left transverse process had no foramen transversarium. The respective maximum vertical length and transverse width of the right vs. left inferior articular facets were 19 and 14 mm, vs.17 and 16 mm. The respective transverse and sagittal diameter of the foramen magnum were 25.4 and 28 mm.

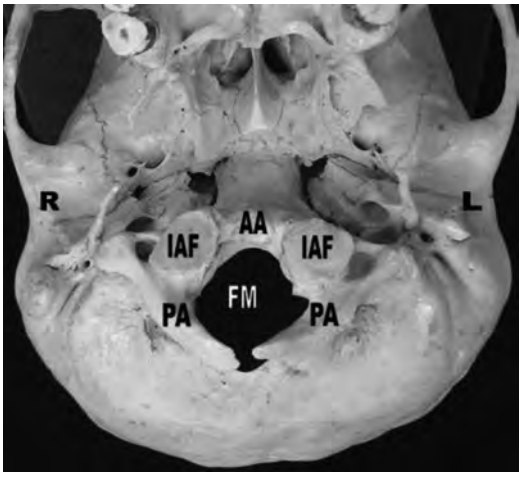

Figure 1 Photograph of the base of the skull showing a central deficit of the posterior arch of the atlas and fusion existing between the occipital bone and the right and left parts of the posterior arch. (R – right side, L – left side, AA – anterior arch of the atlas, IAF – inferior articular facets of the atlas, FM – foramen magnum, PA – posterior arch of the atlas).

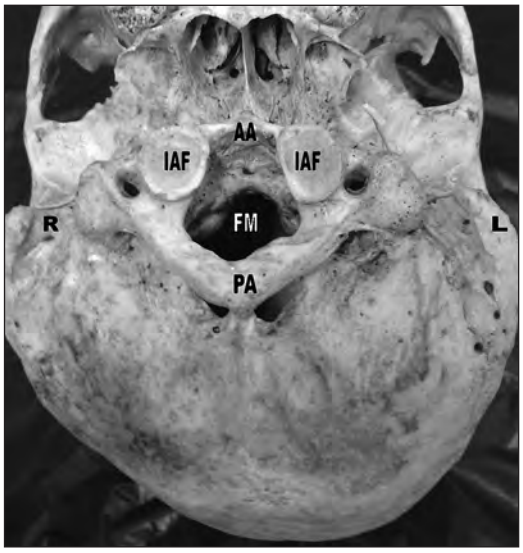

Figure 2 Photograph of the base of the skull showed fusion between the occipital bone and the right and left parts of the posterior arch and the posterior tubercle. (R – right side, L – left side, AA – anterior arch of the atlas, IAF – inferior articular facets of the atlas, FM – foramen magnum, PA – posterior arch of the atlas).

The second case was also a male skull (59 years of age at decease) showing complete fusion of the anterior arch of the atlas (Figure 2).

The posterior arch was also fused with the squamous part of the occipital bone. There were some perforations between the posterior arch and the occipital bone. The lateral masses were completely fused to the occipital bone. Both the left and right superior articular facets of the atlas were fused with the corresponding occipital condyles. The respective maximum vertical length and transverse width of the right vs. left inferior articular facets were 18 and 16 mm, vs.20 and 15 mm. The respective transverse and sagittal diameter of the foramen magnum were 26.2 and 32.6 mm.

Discussion

The cause of occipitalization of the atlas may be congenital or acquired (15). The acquired cases may be due to tuberculosis (16) or other infectious disease. They may also result from mechanical injuries of the cervical region of the vertebral column. The injuries may concern ligaments and/or bones. By comparison, the congenital causes are connected with the appearance of disorders (teratogenic factors, genetic anomalies) during the third week of fetal life, when the occipital and cervical sclerotomes are developing. Occipitalization of the atlas takes place if the first cervical sclerotome does not divide into the cranial and caudal components, and the atlas gets assimilated into the occipital components, because the caudal part of the fourth occipital sclerotome unites with the whole first cervical sclerotome (7, 16).

Atlanto-occipital fusion can cause numerous neurological deficits because the dimensions of the foramen magnum undergo reduction. The symptoms concomitant with occipitalization are connected with compression on the medulla oblongata, spinal cord, vertebral artery and venous plexus (10, 17). The sagittal diameter of the foramen magnum is a crucial landmark in symptomatic patients (18). In our second case, this diameter was considered abnormal as it was < 30 mm (18). This can lead to clinically manifesting symptoms.

Vega et al. (19) reported that the range of the transverse diameter of the foramen magnum is between 28-40 mm. The respective transverse diameter of the foramen magnum of both of our cases was narrower than the normal range. This report is in agreement with Sani et al. (9), Tun et al. (12) who reported that narrowing of the foramen magnum is associated with brainstem compression. The main reason is the high position of the dens in relation to the medulla oblongata (7, 16). The chief symptoms associated with assimilation of the atlas are headache, neck pain, abnormal posture of head and neck, restricted head and neck movements, numbness or pain in the extremities, weakness of lower limb, disturbances in balance and ataxia (7, 17). According to Hensinger

(1), a patient with occipitalization of the atlas will have a short neck and restricted neck movement. The vertebral artery may be compressed and symptoms—such as dizziness, seizure, mental deterioration and syncope—may occur.

Detection and treatment of this deformity are essential as this deformity often causes cervical spine instability. Special imaging, such as CT scan, three-dimensional CT scan, or MRI should be obtained before surgery. Tun et al. (12) reported a case in which CT images revealed not only a fusion between the posterior arch of the atlas and the occipital bone, but also hypertrophy of the occipital condyles and a reduction in the transverse diameter of the foramen magnum.

Spontaneous occipito-atlantal fusion, and anomalies of the occipital condyles (20) can cause changes in the biomechanics of the craniovertebral junction. In odontoid fracture or C1-C2 instability associated with rheumatoid arthritis, the occipito-atlantal fusion moves as a single unit, leading to more displacement of the odontoid process and more instability of the craniovertebral junction. The occipito-atlantal fusion must, therefore, be considered when operating on patients with C1-C2 instability—such as C1-C2 instability associated with odontoid fracture or rheumatoid arthritis. In these situations, preoperative X-rays, CT scan and MRI are recommended to determine the associated bone anomaly (21) and to ensure a complete preoperative evaluation (22). The instrumentation and arthrodesis must be fixed from the occiput to the C2, instead of the C1-C2 fixation, as is more common.

In previous studies done on Asians (3, 4, 9, 23), and including the present study, only two skulls were detected showing occipitalization of the atlas. The respective incidences were 2.04, 3.63, 1.59, 0.69 and 0.32 %. The relatively low frequency found in the current study was due to the higher total number of cases (633), while the others examined fewer cases (n=98, 55, 150 and 126, respectively).

Conclusion

Occipitalization of the atlas is the most common anomaly of the craniocervical junction, hence head and neck surgeons should be aware that such an anomaly may exist without any typical symptoms. Restriction or absence of movement in this articulation may be the first sign which attracts their attention regarding such assimilation. Knowledge of occipitalization of the atlas may be of substantial importance to orthopedists, neurosurgeons, physiotherapists and radiologists dealing with abnormalities of the cervical spine. Mistaken diagnoses have led to delayed treatment and at times adverse results.

Acknowledgements: We thank (a) the many Thais who donated their bodies to the Department of Anatomy, Faculty of Medicine and their families for granting permission (b) the staff of the Bone Museum in the Department of Anatomy and (c) Mr. Bryan Roderick Hamman and Mrs. Janice Loewen-Hamman for assistance with the English-language presentation of the manuscript.

Authors' contributions: Conception and design: KK; Acquisition, analysis and interpretation of data: RS, CW; Drafting the article: KK; Revising it critically for important intellectual content: WW, NM.

Conflict of interest: The authors declare that they have no conflict of interest.

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Acta Medica Academica 2013;42(1):46-54
DOI: 10.5644/ama2006-124.70

Musculoskeletal symptoms and job satisfaction among office-workers: A Cross- sectional study from Iran

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Received: 11 March 2013
Accepted: 10 May 2013

Objective. Office-work poses a high-risk for musculoskeletal disorders (MSDs), with consequences for workers, employers and society. The aims of this study were to determine the prevalence of musculoskeletal symptoms in a sample of Iranian office workers, to investigate the association between pain severity and job satisfaction and to investigate the association between MSDs and job satisfaction. **Materials and methods.** Iranian office workers from a university setting (n=91) were randomly selected and included in this cross-sectional study. The Nordic musculoskeletal questionnaire plus visual analogue scale of pain, and the Brayfield-Rothe Job Satisfaction Index were used to study the prevalence of MSDs, pain intensity and job satisfaction, respectively. Descriptive analysis, Pearson's correlation, and multiple regression analysis were performed for statistical assessment. **Results.** Eighty-nine percent of participants reported musculoskeletal symptoms during the past 12 months, most commonly in the neck (69.2 %), low back (58.2%), knees (41.8%), shoulders (35.2%), and upper back (34.1%). There was a significant negative correlation between pain intensity and job satisfaction. Pain intensity, low-back pain in the last week, wrist pain in the past 12 months and shoulder pain were significantly associated with job satisfaction ($p<0.05$). **Conclusion.** This study provides evidence that musculoskeletal symptoms are common in Iranian office workers, associated with low job satisfaction. These findings indicate the need for more attention to MSDs among office workers and designing effective preventive interventions.

Key words: Musculoskeletal pain, Occupational health, Job satisfaction.

Introduction

Musculoskeletal disorders (MSDs) are among the leading causes of occupational health problems, with consequences for workers, employers and society (1, 2). These disorders are widespread in different countries with substantial costs and impact on the quality of life (3). Prevalence data have indicated that more than 25% of the European working population have reported musculoskeletal symptoms (4). In the United States, MSDs represent 40% of compensated injuries and cause more work absenteeism than any other group of diseases (5). MSDs among office workers are receiving increas-

ing attention (6). Increased computer usage has been linked to a high prevalence of musculoskeletal symptoms and these disorders can have detrimental effects on workers' health and productivity (7, 8). Physical factors such as: repetitive movements, sustained postures, incorrect work positions, and prolonged sitting in incorrect fixed positions, should be considered (9, 10). On the other hand psychosocial factors such as: low job satisfaction, high job demands, low job control, and low workplace social support, have been associated with the onset of MSDs among office workers (11, 12). These factors may reinforce each other and their effects may be mediated by cultural or societal factors (13).

Studies on work related MSDs in Iran showed a high prevalence of musculoskeletal symptoms in different work settings, such as: automobile factories (14), rubber factories (15), carpet mending operations (16), the petrochemical industry (17) pharmaceutical industries (18) and health care settings (19, 20). Office workers are known to be at high risk of MSDs (21). The point prevalence of low back pain was reported as high as 60% among office workers in an Iranian university setting (22), but there has not been a comprehensive assessment of the prevalence of MSDs at multiple anatomical sites, and its association with job satisfaction in Iranian office workers.

The aims of this study were to determine the prevalence of musculoskeletal symptoms in a sample of Iranian office workers, to investigate the association between pain severity and job satisfaction, and to explore the association between MSDs and job satisfaction.

Material and methods

This was a cross-sectional study undertaken in the Medical and Pharmacy schools, of the Isfahan University of Medical Sciences, Isfahan, Iran. The target population were all administrative office-worker employees of these two schools. The inclusion criteria were people who work with computers for at least 3 hours per day, or have sedentary office-work for at least 6 hours per day, in either permanent or contract employment. The exclusion criteria were people who had had any previous illness and/or injuries that may have contributed to MSDs, or who had less than 1 year work experience. With 95% confidence interval (p=0.6, d=0.15) (20) and considering 10% attrition, we considered 95 office workers sufficient to examine the prevalence of MSDs and its association with job satisfaction. A cluster sampling was done. The departments of each school were clustered, and the sample was selected randomly according to the size of each cluster.

Tools

The main variables of this study were musculoskeletal symptoms, pain intensity and job satisfaction, which were measured using these tools:

The Nordic Musculoskeletal Questionnaire

The self-rating Nordic Musculoskeletal Questionnaire (NMQ) is a standardized questionnaire to assess the prevalence of musculoskeletal symptoms (23, 24). The validity and reliability of this questionnaire have been investigated and approved in different studies and several languages, including the Persian language (25).

The first part of the NMQ is a general questionnaire to collect information about the individual (height, weight, age, handedness, hours worked per week, period of time in present occupation, etc.) as well as work absence (one day or more) due to musculoskeletal problems. It has also 40 forced-choice items identifying areas of the body causing musculoskeletal problems. Comple-

tion is aided by a body map to indicate nine anatomical sites: neck, shoulders, upper back, elbows, low back, wrist/hands, hips/thighs, knees and ankles/feet. Respondents were asked if they had had any musculoskeletal trouble in the last 12 months and the last 7 days, which has prevented normal activity at home or away from home (i.e. loss of function).

The Visual Analogue Scale of Pain

A Visual Analogue Scale (VAS) is a measurement instrument designed to measure a characteristic or attitude that is believed to range across a continuum of values that cannot easily be directly measured. Operationally a VAS is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end, with no pain at one end (0) and maximum pain (100) at the other. The participant marks on the line the point that they feel represents their current state of pain. The VAS score was determined by measuring in millimeters from the left hand end of the line to the point that the participant marked, converted into a scale of 0 to 10.

The Job-Satisfaction Questionnaire

Job satisfaction was assessed using the Brayfield-Rothe Job-Satisfaction Index (BRJSI) (26). Respondents were instructed to indicate the extent of their agreement with each item using a five point Likert type scale from 1 to 5 as follows: 1= strongly disagree, 2= disagree, 3= neither disagree nor agree, 4= agree, and 5= strongly agree. The scale includes 10 positive and 8 negative statements. A scale is formed by calculating the mean score for all 18 items, ranging from 18-90 and a higher score indicates higher job satisfaction (25). A total score of 18 to 55 is interpreted as low job satisfaction, while 70 and over is represented high job satisfaction (27). Socio-demographic variables [age, gender, marital status, education and working experience] were collected using a self-rated questionnaire.

Statistical analysis

All descriptive statistics are presented as means and standard deviations for quantitative variables and as relative frequencies and percentages for categorical variables. The BRJSI score is presented as mean with its 95 % confidence interval. Pearson's correlation coefficient was used to measure the strength of the relationship between pain intensity and job satisfaction. Variables achieving bivariate significance were placed into a linear regression model. Multiple regression (stepwise) analysis was applied to assess the association of MSDs with job satisfaction. The stepwise regression analysis produced our regression model from a set of candidate independent variables, by entering and removing variables into our model. This method may build a single final model, although there are often several good models to describe the association. Variables were selected for inclusion in the stepwise regression model based on theoretical importance, as well as significance in bivariate analyses. Considering job satisfaction as the dependent variable, the independent variables were entered in blocks, starting from the background socio-demographic variables (age, gender, education, marital status, working experience and BMI) and followed by the pain intensity and musculoskeletal symptoms in different anatomical regions. The level of significance was set at $P<0.05$, and all tests were two-tailed. Collinearity diagnostics were performed by means of the variance inflation factor (VIF) for each independent variable entered in the regression equations. A VIF>10 was considered as positive multicollinearity (28). The analysis of data was performed by the Statistical Package for Social Sciences (SPSS version 20) for Mac.

Ethics statement

The design of the study was approved by the Ethics committee of Vice Chancellor for Research, Isfahan University of Medical Sciences (project no. 391264). All participants received study information and provided written informed consent. Also, the confidentiality of all information was managed carefully by researchers.

Results

Of the potential 118 participants, 103 participants responded to the questionnaire, giving a response rate of 87%. Of these, 12 were excluded because they did not meet the inclusion criteria of having at least 1-year work experience (n=9) or had previous musculoskeletal disorder (n=3), leaving 91 who were included in the study. The mean age of all participants was 39.4 years (SD=8.43) with a range of 25-58 years. Of these participants, 67 were female (73.6%) and 24 participants were male (26.4%) with a female to male ratio of 2.79:1. About 85% of the respondents worked full time (32-41 hours per week) (Table 1).

Table1 Demographic characteristics of office-workers studied (n=91)

Demographic characteristics	Results
Age (Mean ± SD)	39.42 (8.4)
Working experience (yrs.) (Mean ± SD)	13.69 (7.2)
BMI (Mean ± SD)	25.21 (2.9)
Gender (n; %)	
Female	67 (73.6)
Male	24 (26.4)
Marital status (n; %)	
Single	13 (14.3)
Married	78 (85.7)
Education (n; %)	
Diploma	14 (15.4)
Associate degree	12 (13.2)
BSc	36 (39.5)
MSc	22 (24.2)
PhD	6 (6.6)
Post-Doc	1 (1.1)

Prevalence of musculoskeletal symptoms

Eighty-one (89%) participants reported musculoskeletal symptoms during the previous 12 months. The body regions most commonly affected were: neck (69.2%), low back (58.2%), knee (41.8%), shoulders (35.2%), and upper back (34.1%). Respondents reported symptoms less commonly in the thighs (7.7%), arms (5.5%), and palms (4.3%) (Table 2). Fifty-five (60.4%) participants reported loss of function, and work absenteeism was reported in 36.3% of participants during the previous 12 months.

Pain intensity and job satisfaction

The results of the visual analogue scale showed a median symptom intensity of 5.29. The mean score of job satisfaction was 54.14 (95% confidence interval: 51.61 to 56.68). The majority of office workers belonged to the low (47.3%) and intermediate level of job satisfaction (47.3%). The high level of

Table 2 Prevalence rate of reported MSDs in different body regions during the 12 months prior to the study (n=91)

Body Region	Number (%)
Neck	63 (69.2)
Shoulders	32 (35.2)
Elbows	12 (13.2)
Wrists/hands	26 (28.5)
Upper back	31 (34.1)
Lower back	53 (58.2)
Thighs	7 (7.7)
Knees	38 (41.8)
Ankles/feet	12 (13.2)

job satisfaction was observed in 5.5% of our participants. Using Pearson's correlation analysis, the pain intensity was negatively correlated with job satisfaction score (r= -0.58, p<0.001).

Musculoskeletal symptoms and job satisfaction

In multiple linear regression analyses, after evaluating the correlations among the independent variables, no multicollinearity problem was detected. Stepwise linear regression was performed on the variables previously listed, to determine association with job satisfaction. Pain intensity had the strongest association with job satisfaction (R^2=0.39). To determine which musculoskeletal symptoms of the NMQ were most important in determining its association with the job satisfaction score, the job satisfaction was regressed onto the musculoskeletal symptom. Among these symptoms, low back pain in the last week, wrist pain in the previous 12 months and shoulder pain were associated with significantly worse job satisfaction (Table 3).

The final model (model 4) indicated that pain intensity, low back pain in the last week, wrist pain in the previous 12 months and shoulder pain were negatively associated with job satisfaction (p<0.05). This final model explained 61% of the variance of the job satisfaction. Demographic factors and musculoskeletal pain in other anatomical regions were not found to be significantly associated with job satisfaction in these participants.

Discussion

This study investigated the prevalence of musculoskeletal symptoms among office-workers and their association with job satisfaction. In our study, musculoskeletal symptoms were common among office workers in a university setting. Eighty-nine percent of our participants reported musculoskeletal symptoms during the previous 12 months. Loss of function and work absenteeism were

Table 3 Association of musculoskeletal symptoms and pain intensity with job satisfaction

Model*	Standardized beta	p-Value	Standard error of the estimate	R square
Model 1				
Pain intensity (VAS)**	-0.63	<0.001	9.96	0.39
Model 2				
Pain intensity (VAS)	-0.58	<0.001	9.59	0.48
Low back pain (last 7-days)	-0.32	0.003	-	-
Model 3				
Pain intensity (VAS)	-0.57	<0.001	9.33	0.55
Low back pain (last 7-days)	-0.29	0.008	-	-
Wrist pain (last 12-months)	-0.20	0.015	-	-
Model 4***				
Pain intensity (VAS)	-0.53	<0.01	-	-
Low back pain (last 7-days)	-0.27	0.005	9.17	0.61
Wrist pain (last 12-months)	-0.17	0.005	-	-
Shoulder pain (last 7-days)	-0.16	0.028	-	-

*Regression analysis was adjusted for age, gender, education, marital status, working experience and BMI; **VAS= Visual Analogue Scale; *** Model 4 is the final model.

reported in more than half the participants. This indicated that the prevalence of musculoskeletal symptoms is higher in the studied population in comparison to international studies (3, 7, 9, 29-31) and Iran (32).

Office workers were most likely to report musculoskeletal symptoms in their neck (69.2%), low back (58.2%), knees (41.8%), and shoulders (35.2%). This is line with the previous studies indicating the high prevalence of neck pain in office workers and pain in other regions of the body (33, 34). Likewise the prevalence of back pain was in the range of 7.4% to 59.6% in previous studies (21, 35-40) and upper extremity symptoms ranged from 18.6 to 62.7% (34, 41, 42). This wide range in different studies may be due to differences in the work settings and/or in the criteria used for ascertainment of symptoms.

MSDs were the main reasons for work-related consultations in general practice and medical costs (43, 44). Furthermore, musculoskeletal symptoms threaten the quality of life (45, 46) and job satisfaction of office workers (47).

Most of our participants reported low to medium job satisfaction. Job satisfaction is simply defined as the degree to which people like their jobs (48). Several studies indicated that the extent to which individuals feel satisfied with their work is associated with their physical and mental health (49, 50). A meta-analysis of almost 500 studies of job satisfaction, incorporating over 250,000 employees, found statistical correlations between job satisfaction and measures of mental health; and smaller relationships were detected for measures of physical health (51). In our study, pain intensity was significantly correlated with job satisfaction, and our results from the multiple regression analysis indicate that pain intensity, low back pain in the last week, wrist pain in the previous 12 months and shoulder pain were associated with job satisfaction.

However, previous studies indicated the association between low job satisfaction and musculoskeletal symptoms, such as low back pain (47, 52). It seems that there may be a bilateral relationship between job satisfaction and physical health. This implies the need for a holistic approach to improving the bio-psycho-social-environmental health of employees. An important aspect of the current study refers to assessing the prevalence of musculoskeletal symptoms in a developing country and its relationship with job satisfaction.

Lower job satisfaction in developing countries has been reported in several studies, which is in line with our findings (53-55). The proposed reasons for lower job satisfaction in developing countries include lack of employment security, poor salaries, benefits, work conditions, promotion and communication, as well as lower control over job, leadership behaviors, job stress, and mental and physical status (56-59). However, there are some issues that should be considered as limitations of this study. Job satisfaction is a multi-dimensional concept. Several factors, such as: mental health, working hours, economical issues, job security, supervisor support, and changes in job control levels, have also been related to individual job satisfaction levels (60) and are not addressed in this study. Furthermore, satisfaction levels can vary markedly between different job features (61). These all bring raise criticism of the concept of job satisfaction and its measurement. However, there is no 'gold standard' indicating the aspects that should be taken into account when job satisfaction is measured (62). Qualitative studies may be helpful to consider all aspects of job satisfaction in future studies.

The target population in our study was from two schools in a medical university. The higher prevalence of musculoskeletal symptoms in this sample may be related to their higher awareness of medical symptoms

since they were health care workers. Also, the cross-sectional design of this study limits its generalizability, and causation cannot be inferred. More research, particularly longitudinal, is warranted to direct the causation between musculoskeletal symptoms and job satisfaction. Despite these limitations, the current study appears to be unique in that it used standardized measures to quantitatively evaluate the prevalence of musculoskeletal symptoms and its association with job satisfaction among Iranian office workers.

Conclusion

In conclusion, our study provides evidence that musculoskeletal symptoms are common in Iranian office workers, which may impact negatively on job satisfaction. These findings indicate the need for more attention to MSDs among office workers and designing effective preventive interventions.

Acknowledgements: This manuscript is the first report of the dissertation project numbered 391264, funded by the Research Chancellor of Isfahan University of Medical Sciences. Our profound gratitude and deepest thanks are extended to all of the office-workers who so graciously agreed to participate in this study in spite of their high workload, and to S.A. Mostafavi PhD, the Dean of School of Pharmacy, Isfahan University of Medical Sciences, for providing us with an excellent atmosphere for accomplishment of this research. We would also like to thank all the staff of Community Medicine Department for their continued support throughout the project.

Authors' contributions: Conception and design: AL, PG, AZ; Acquisition, analysis and interpretation of data: AL, NJ; Drafting the article: AL, NJ; Revising it critically for important intellectual content: AL, NJ.

Conflict of interest: The authors declare that they have no conflict of interest.

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Acta Medica Academica 2013;42(1):55-60
DOI: 10.5644/ama2006-124.71

Palatal lifting prosthesis and velopharyngeal insufficiency: Preliminary report

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Received: 17 December 2012
Accepted: 2 April 2013

Objectives. Our study aimed to highlight the effectiveness of palatal lift prosthesis in patients with velopharyngeal insufficiency with previous operated cleft palate. **Methods.** This study was done undertaken January 2008 to December of 2009 in the Phoniatic unit of Alnoor Specialist Hospital, Makkah, Saudi Arabia. Ten patients of ≥ 8 years to ≤ 10 years of age, who had previously undergone surgery for cleft palate, with or without cleft lip, with no other systemic illness and normal intelligent quotient level, were selected and managed by palatal lift prosthesis. All the study subjects were subjected to auditory perceptual speech evaluation for assessment of the degree of hypernasality, compensatory articulator mechanisms, glottal and pharyngeal articulation, audible nasal emission, facial grimace and overall intelligibility of speech. Data were analyzed using SPSS version 16. **Results.** The study included 10 subjects whose mean ± standard deviation of age was (8.9±0.9). On auditory speech perceptual evaluation after prosthesis application, significant improvement was found in glottal articulation 6 (85.7%), p=0.04, facial grimace 6 (85.7%) p=0.04, hyper nasality 10 (10%) p=0.008, and speech intelligibility 9 (90%) p=0.008. **Conclusion.** Young patients with repaired palatal cleft have significant improvement after application of palatal lift prosthesis.

Key words: Velopharyngeal insufficiency, Cleft palate, Cleft palate prosthesis.

Introduction

Velopharyngeal closure (VPC) is an important part of speech. The causes of hypernasality and velopharyngeal dysfunction (VPD), i.e., velopharyngeal insufficiency (VPI) and velopharyngeal incompetence, are many and range from structural causes with the velum, e.g., submucous cleft palate, short velum relative to the depth of the posterior pharyngeal wall, overt cleft palate, to neuromuscular problems, e.g., those observed in velocardiofacial (VCF) syndrome. Overt cleft palate, either before or after repair, is by far the most common cause of VPD. This condition occurs in approximately 1 of 2,000 live births. VPD has been reported in as many as 30-50% of patients following palate repair (1).

Orofacial clefts have an approximate rate of 1:500-1:550 births. In a large popu-

lation-based study of 4,433 children born with orofacial cleft, the birth prevalence of nonsyndromic cleft lip, with or without cleft palate, was 0.77 per 1,000 births (cleft lip, 0.29/1,000; cleft palate, 0.48/1,000) and the prevalence of nonsyndromic cleft palate was 0.31 per 1,000 births. Children with orofacial cleft require surgical procedures and complex medical treatments (2). The data from the gulf region is deficient, but according to one systemic review of studies, in Saudi Arabia it ranged from 0.3-2.19 per 1,000 live births, in Oman1.5 per 1,000 live births, in Dubai, UAE 0.5 per 1,000 live and still births, while in Amman, Jordan 1.39-2.4 per 1,000 live births (3).

The end result is the passage of air into the nose during speech. In speech production, the audibility of air through the nose is termed as nasal escape, and the resulting speech is termed hypernasal or rhinolalia aperta (4). Severe VPI will often lead to compensatory speech behaviors, resulting in poor speech intelligibility (5). Diagnosis of VPI is made through taking a history and physical examination, perceptual speech assessment, nasoendoscopy and radiographic multiplanar videofluoroscopy (6). The use of prosthetic devices for correction of velopharyngeal insufficiency is an alternative treatment for patients with conditions that preclude surgery, and for those with hypo functional velopharynx. Prosthetic management requires close cooperation between the prosthodontist and a phoniatrician (speech pathologist) (7, 8).

Surgical repair of a cleft palate is performed by one year of age, in order to minimize speech articulation abnormalities. However, children develop VPI after cleft palate repair require active intervention, i.e., speech therapy, prosthetic management and/or surgery (9). Palatal lifts were used when adequate palatal length exists, and they physically reduce the distance the palate must traverse to produce adequate closure, acting as positioning device. Comprehensive management for these patients requires close interaction between the prosthodontist and the speech language therapist, to achieve the maximum benefit from the palatal lift prosthesis. Fluoroscopy and nasoendoscopy must be used in the design, placement and modification of the prosthesis, which provides a profound tool for diagnosis, the treatment plan and assessment of prognosis (10).

Our study aimed to highlight the effectiveness of palatal lift prosthesis in patients with velopharyngeal insufficiency who had previously undergone surgery for cleft palate, in order to measure the improvement of VPI.

Methods

This self controlled sequential experimental study was undertaken from January 2008 to December 2009, in the Phoniatic unit of Alnoor Specialist Hospital, Makkah, Saudi Arabia. Ten children aged 8 to 10 years, who had previously undergone surgery for cleft palate, with or without a cleft lip, no other systemic illness and normal intelligent quotient level, were selected as study subjects. Before the final selection of cases, the mouth mirror test was performed to decide if the case was a candidate for a palatal lift appliance or not.

Palatal lift prosthesis was placed in the following steps

Primary alginate impressions were undertaken and poured into a study cast, followed by a primary survey. The upper first and second deciduous molars or second deciduous molar and first permanent molar were prepared to receive casted bands, followed by secondary rubber-based impressions poured into master casts, which received alterations. The master cast was duplicated

in the investment cast and then a wax pattern was made, spewed and cast. A metal skeleton was tried out the patient's mouth for metal adjustment, after finishing and polishing. An impression of the oro-pharyngeal border was then taken using a green stick compound for border molding and a rubber-base as the impression material, on the posterior border of the chrome-cobalt skeleton. It was then converted into acrylic resin, followed by a trial seating in the patient's mouth. The final functional impression was completed using a resilient liner in order to elevate the soft palate and cement the appliance using bands and resin cement. The patient was given a follow-up appointment with instructions for proper oral hygiene measurements. Figure 1-3

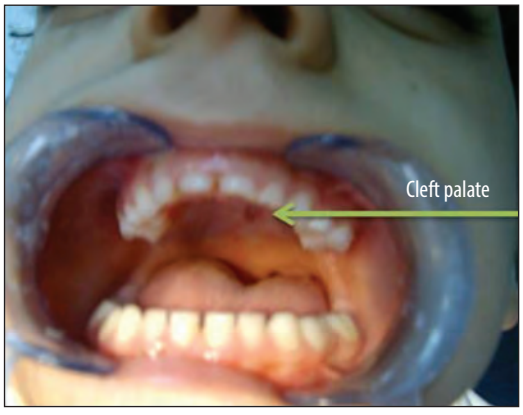

Figure 1 Case before appliance construction.

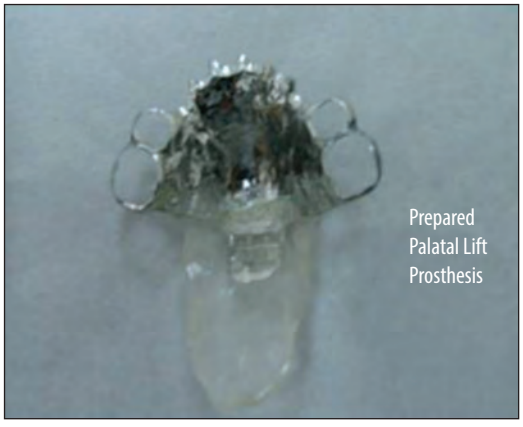

Figure 2 The finished palatal lift before relining.

Patients were evaluated pre-intervention and immediately post insertion, and given appointments for re-evaluation after 48-72 hours of appliance application. The final data of re-evaluation considered in this study was collected after an adaptation period of about two months of appliance insertion. All the study subjects were subjected to auditory perceptual speech evaluation, for assessment of the degree of hypernasality, compensatory articulatory mechanisms, glottal and pharyngeal articulation, audible nasal emission, facial grimace and overall intelligibility of speech. Two simple clinical tests were undertaken for patients i.e., Gutzman's (A/I) test and Czermak's (cold mirror) test. Videonasoendoscopic evaluation was performed for patients using a fiber optic nasofibroscope coupled with high intensity light and recorded using digital Atmos system. Topical anesthetic gel was applied to the nasofibrolaryngoscope before insertion through the nasal cavity, to reach superior to the velopharyngeal port in order to assess movement of the velum, and the lateral and the posterior pharyngeal walls were observed while the patient repeated an oral speech sample, loaded with phonemes, which needed increased oral airflow (plosives and fricatives). Videoendoscopy offers the advantage of a lack of ionizing radiation in videofluroscopy and the ability to help in

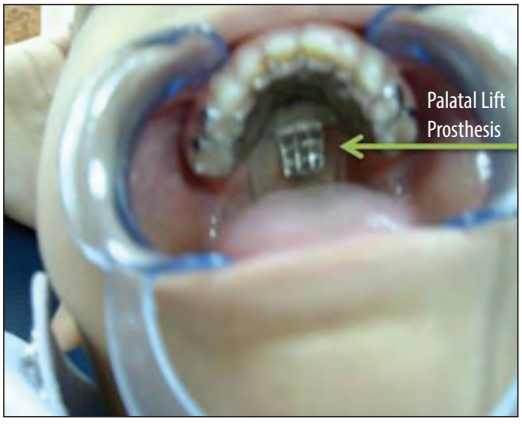

Figure 3 Palatal lift appliance in the patient's mouth.

assessment of all structures at the same time (11). We classified improvement in clinical features when they became absent after appliance application, except nasality and speech intelligibility, where we differentiated it according to the decrease in the severity of features i.e., from severe to moderate, moderate to mild and mild to absent.

Written informed consent was taken from all the subjects' guardians, and hospital research committee endorsement was given for this research.

Statistical analysis

Data were analyzed using SPSS version 16 (SPSS Inc., Chicago, IL, USA). The data was subjected to descriptive analysis. The McNemars test with continuity correction was applied to categorical data, to analyze the proportions in repeated measurements (12). One directional p-value of ≤0.05 was considered significant.

Results

The study included 10 subjects whose mean ± standard deviation of age was (8.9±0.9). By auditory speech perceptual evaluation before the application of appliance, abnormal pharyngeal articulation and audible nasal emission was positive in 6 (60%) subjects while facial grimace and abnormal glottal articulation was positive in 7 (70%) subjects. Following application of the appliance and intensive speech therapy for 3-6 months for each case, it was found that: 6 (85.7%) subjects improved their glottal articulation (p=0.04) and 6 (85.7%) had facial grimace improvement (p=0.04). On the other hand, the A/I test and cold mirror tests were found positive in all subjects, with insignificant improvement in 4 (40%) subjects after application of the appliance. Before the procedure, hypernasality was found mildly impaired in 3 (30%) subjects and in them it was completely improved, 5 (50%) subjects had improvement from moderate to mild and 2 (20%) from severe to moderate (p=0.004) with the appliance. Moreover, speech intelligibility was found to be improved from mild 3 (30%) to normal in two, from moderate 4 (40%) to mild and from severe 3 (30%) to moderate in all subjects (p=0.008). So the overall improvement in the last two features were (100%) and (90%) respectively.

Table 1 Speech evaluation before and after appliance insertion

Speech evaluation variables	Before (n=10)	After	Significance
	Abnormality/ Positivity	Improvement	p-value*
	n (%)	n (%)	
Glottal articulation	7 (70%)	6/7 (85.7)	χ^2=4.16; 0.04
Pharyngeal articulation	6 (60)	1/6 17)	NS**
Facial grimace	7 (70)	6/7 (85.7)	χ^2=4.16; 0.04
Audible nasal emission	6 (60)	3/6 (50)	NS
Gutzman's A/I test	10 (100)	4/10 (40)	NS
Cold mirror test	10 (100)	4/10 (40)	NS
Hyper nasality	10 (100)	10/10 (100)	χ^2=8.1; 0.008
Speech intelligibility	10 (100)	9/10 (90%)	χ^2=7.1; 0.008

*McNemars test with continuity correction. NS=**Non significant. A/I=It's test by Gutzman.

Discussion

Velopharyngeal (VP) incompetency occurs when the surgically repaired soft palate is of adequate length but of inadequate mobility to elevate to achieve velopharyngeal closure. Achieving VP closure, and thus optimal speech, is one of the primary goals of palatoplasty. The literature indicates that VP competence is achieved in only 70% to 90% of patients. This variability is most likely the result of the type of palatoplasty performed and differences in definitions and opinion regarding what constitutes VPI (13).

Palatal lift prosthesis covers the hard palate and extends posteriorly to engage the soft palate, and physically elevates and extends it to the proper position, to achieve closure. This prosthesis is most effective when the soft palate has little muscle tone and offers little resistance to elevation (14). Most patients with palatopharyngeal incompetency are treated surgically or with speech therapy, or both, but there are individuals who might benefit most from palatal lift prosthesis than from other treatments (10).

Before starting construction of palatal lifting appliance, the mouth mirror test was performed to determine the potential amount of force required to lift the soft palate to create the desired effect, prior to committing to lift fabrication. Usually, patients with little or no soft palate movement will present with flaccid paralysis of the soft palate muscles. The soft palate is easily displaced upward by pressing on it with a mouth mirror or tongue blade. If the soft palate resists displacement because of fibrosis or tonicity of the muscles, a palatal lift might not be successful. Too much force will be required to lift the palate and likely result in a lift that cannot be kept in place or in pressure irritation and ulceration of the soft palate mucosa, so the mouth mirror test is a quick indicator of the potential for success of the lift.

In our study there was highly significant improvement in hypernasality and speech intelligibility after application of a palatal lift prosthesis, and our results are somehow consistent with those of Sell et al, (15). Nevertheless, oral tone was achieved only in patients with mild hypernasality 3 (30%), while no subject with moderate 5 (50%) or severe 2 (20%) hypernasality obtained oral tone. However, they improved towards mild and moderate, respectively. Similarly, we found improvement in 3 (50%) in terms of audible nasal emission.

Pinto et al. (16) mentioned that speech intelligibility was significantly better after placement of the prosthesis for patients with VPI, after primary palatoplasty, and speech therapy was needed to eliminate any compensatory articulation production that had developed. In another study, seven patients with velopharyngeal dysfunction, secondary to a surgically corrected cleft palate, were subjected to palatal lift prosthesis. A significant decrease in nasal resonance and improvement in speech intelligibility was found (17).

The clinical effect of a speech appliance in improving velopharyngeal function during blowing may be caused by an increase in the reserve capacity of the levator muscle. An increased reserve capacity in levator activity may be effective in preventing fatigue of the muscles related to velopharyngeal function for speech (18).

Conclusions

Application of an appliance and intensive speech therapy gave significant benefit to the young subjects in improving their glottal articulation, facial grimace, hypernasality and speech intelligibility. To achieve maximum benefit from palatal lift prosthesis, the prosthodontist and the speech pathologist must co-operate, using the technology of fluoroscopy and nasoendoscopy in the design, placement and modification of the prosthesis. Ongoing intensive speech ther-

apy is frequently necessary for patients receiving palatal lifts for further improvement in speech intelligibility, achieving accepted comprehensive speech.

Authors' contributions: Conception and design: AIA, SG, MUF; Acquisition of data: AIA, SG; Analysis and interpretation of data: MUF; Drafting the article: AIA, SG; Revising it critically for important intellectual content: AIA, SG.

Conflict of interest: The authors declare that they have no conflict of interest.

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Review article

Acta Medica Academica 2013;42(1):61-70
DOI: 10.5644/ama2006-124.72

Doctoral degree in health professions: Professional needs and legal requirement*

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Received: 17 December 2012
Accepted: 2 April 2013

To respond to ever increasing complexity of health care professions, education of nurses, midwives, physiotherapists, radiology engineers, and medical laboratory workers, has been upgraded to pregraduate, graduate and postgraduate university levels. In Croatia, nursing was defined as a branch of clinical medical science in 1997. Croatia and Bosnia and Herzegovina have introduced first two levels, but there is a strong need for the third one (doctoral degree). It should last three years and contain 180 ECTS points. It includes acquisition of evidence-based advanced health care, and the ability for independent research and critical analysis. Doctoral degrees in health professions are instrumental for academic careers of faculty of health professions. Yet this will not separate them from their patients or make them administrators, as the majority of their work will still be spent alongside patients.

Key words: Education, Nursing, Postgraduate, Nurses, Health occupations.

Introduction

The last fifty years have seen dramatic changes in all aspects of biomedical science, including the health sciences: nursing, midwifery, radiologic technology, physiotherapy, and medical laboratory diagnostics. The importance of better education for all healthcare professionals has increased in order to address the increasing complexity of health care due to aging population, chronic disease management, numerous new technologies and expensive procedures,

It is generally accepted that the minimum level of education required for nursing practice and other health professions, is a bachelor's degree (1, 2). Formerly, most common nursing skills were very simple and few in number, such as: setting bed, changing patient position, cleaning of patient room and furniture and use of enema. Today, the description of nursing competencies and skills include many complex skills such as clinical reasoning, use of evidence-based practice, interdisciplinary collaboration and team-

*Translated by permission from Croatian version Marušić M, Mimica M, Mihanović F, Janković S. Doktorat iz zdravstvenih znanosti: stručne potrebe i zakonske zadanosti. Medix. 2012;18(103):169-74.

work, health promotion, participation in chronic disease management - for instance educating patients with diabetes, chronic obstructive pulmonary disease etc., and care for terminally ill patients, with complex skills like an open heart massage during cardiac surgery (3).

In physiotherapy, radiologic technology and medical laboratory diagnostics, as in nursing, complex skills development is very marked, and in some areas it is even more prominent.

The World Health Organization (WHO) has for decades included nurses and other health professionals (midwives, physical therapists, radiologic technologists, sanitary engineers) in the process of promoting and protecting health (4).

According to the instructions of the European Union, countries with no qualified nurses for teaching in the field of nursing may employ teachers from other countries (5).

University education for health professions: Three cycles

Outcome of Bologna process is the convergence of higher education in the European Union, which will facilitate mobility and employment opportunities, including those in regulated professions – nurses and midwives. Since the Republic of Croatia enters the European Union on 1 July 2013 it is necessary to harmonize nursing education with dominant European trends (6, 7). Understanding and acceptance of this need has resulted in establishment of university health studies. University studies enable system of continuing education, knowledge updating and adoption of the latest findings, as well as continuous monitoring and identification of health needs priorities in the state and the European environment. Education and practice are closely related and strongly influence each other (8).

In its basic principles The Bologna Declaration (9) emphasizes strengthening the transition between university studies. The Sorbonne Declaration (10) recommends that studies should be organized in two successive cycles - undergraduate and graduate master's or doctoral level programmes. Subsequent discussions led to Berlin document (11) which introduced so-called European model, with three basic education university degrees: undergraduate, graduate and postgraduate; this has created the European Higher Education Area, 2010, based on three educational cycles bachelor-master-doctor.

Undergraduate or baccalaureate degree

The first cycle (undergraduate study) is focused on basic education. According to the instructions of the World Health Organization (12) the training of nurses and other healthcare workers must be at university level. The goal of the first cycle of education is to equip nurses with the necessary skills for becoming autonomous practitioners. It comprises three-years of study with workload of 180 ECTS credits, after which the professional title of Bachelor is acquired.

Nurses responsible for general healthcare (care)

Directive 2005/36/EC of the European Parliament and of the Council of 7 September 2005 on the recognition of professional qualifications defined training programme for nurses responsible for general care (13). Admission to training for nurses responsible for general care requires completion of ten-year general education.

Education of nurses responsible for general care comprises at least three years of study or 4600 hours of theoretical and clinical training, the duration of the theoretical training representing at least one third and the duration of the clinical training at least one half of the minimum duration of the training. Training is given on a full time basis and includes the programme of theo-

retical and clinical (practical) training. By graduation, students should acquire the following knowledge and skills:

a) Adequate knowledge of the sciences on which general nursing is based, including sufficient understanding of the structure, physiological functions and behaviour of healthy and sick persons, and of the relationship between the state of health and the physical and social environment of the human being;
b) Sufficient knowledge of the nature and ethics of the profession and of the general principles of health and nursing;
c) Adequate clinical experience; such experience, which should be selected for its training value, should be gained under the supervision of qualified nursing staff and in places where the number of qualified staff and equipment are appropriate for the nursing care of the patient;
d) The ability to participate in the practical training of health personnel and experience of working with such personnel;
e) Experience of working with members of other professions in the health sector.

Midwives

Training for midwives should guarantee the acquisition of the following knowledge and skills:

a) Adequate knowledge of the sciences on which the activities of midwives are based, particularly obstetrics and gynaecology;
b) Adequate knowledge of the ethics of the profession and the professional legislation;
c) Detailed knowledge of biological functions, anatomy and physiology in the field of obstetrics and neonatology, and also a knowledge of the relationship between the state of health and the physical and social environment of the human being, and of his behaviour;
d) Adequate clinical experience gained in approved institutions under the supervision of trained staff qualified in midwifery and obstetric;
e) Adequate understanding of the training of health personnel and experience of working with such (13).

University programme in radiologic technology

The rapid development of radiology in the world prompted by development of radiologic devices and radiologic technology has led to the need for opening new studies in the field of radiologic technology. In the USA in 2005 the Joint Review Committee on Education in Radiologic Technology's (JRCERT) demanded that the directors and lecturers at the radiologic technology and imaging methods study complete the Master's degree level of education by 2009 (14). This requirement has led to the opening of several study programmes at universities in the USA, and among the first to recognize the need and develop a programme was Thomas Jefferson University in Philadelphia. The program is based on 3 + 2 model of study. A three-year baccalaureate degree completion is required to enrol in graduate university study programmes (15). Midwestern State University (MSU) has also introduced a master's (Engl. Master of Science) programme in radiologic technology (16). In most countries in Europe the studies in the field of radiologic technology are based on the Bologna Declaration stipulating the 3 + 2 model. University of Bradford in England provides Master's degree study programme in radiologic imaging studies (17), while a few European universities established inter-university Master's degree programme in the field of radiological imaging methods in 2009 (18).

University programme in physiotherapy

Development of physical therapy profession in Europe and the world is marked by a sig-

nificant increase in the range of knowledge and skills and therefore the programmes are adapted to the present needs of profession and the current needs of modern health care. The World Confederation for Physical Therapy devoted a special thematic conference to postgraduate and continuing education of physiotherapists in the European region (19). The programme is compliant with the European standards in physical therapy (20), and post-graduate training programmes in physical therapy as well (21).

European educational strategy considers undergraduate, graduate and post-graduate training (first, second and third cycle of education according to the Bologna process) to be a key prerequisite for successful work of physiotherapist as a professional.

Curricula in Split and Mostar are made and customized to curricula of the School of Physiotherapy and Performance Science University College Dublin, Queen Margaret University College Edinburgh and Faculty of Physiotherapy Wroclaw. There is a doctoral degree programme in physical therapy at the University of Wroclaw (22).

University programme in medical laboratory diagnostics

Medical Laboratory Diagnostics is a health and scientific field related to medical laboratories of various specialties and profiles in health care institutions and institutions that are not within health care system but are associated with the laboratory diagnostics. The rapid development of science and application of new technologies in the field of laboratory biomedicine requires constant professional and scientific education. Applying new knowledge is made possible only by an expert who is in touch with recent scientific advances, with competencies and skills based on them, harmonized with professional priorities and comparable to programmes at respectable universities in the European Union countries (Norway, Austria, and Slovenia). According to the principles of the Bologna declaration a bachelor should adopt basic practical and theoretical knowledge of the profession, work successfully in a team and perform less complex tasks independently (9).

Graduate or master megree programmes

According to current European views (23) graduate master degree programme represents further step in university education after completion of undergraduate study of nursing or other health professions (3 years, 180 ECTS credits). Admission to graduate programme requires completion of undergraduate studies at a recognized higher education institution. Educational goals for graduate two-year master's programme , with a total of 120 credits, are training students for teamwork, planning processes, projects, decision-making, acquiring leadership skills, with process assessment, as well as additional specialist skills and knowledge in chosen fields. Besides these skills, students at graduate level are trained for teaching and new training methods as well.

Postgraduate or doctoral studies

The third cycle, doctoral degree is organized for health professionals who intend to pursue academic career in health studies. It lasts three years and has 180 ECTS credits. It includes studying advanced evidence-based practice, with acquisition of skills for independent research that encourages abstract thinking and critical analysis, with understanding and adapting scientific knowledge. It is achieved by using analytical and conceptual skills, leading to improvement of the theoretical foundations of nursing practice and health care and application of research into practice by using scientific methods in

research and teaching (24, 25). The result of establishing postgraduate studies will be acquiring a degree that provides health professionals with academic certificates whose value is equal to the certificates of their colleagues at other universities upon completing post-doctoral studies (26).

Doctoral degree in health sciences is necessary for academic career of teachers at health studies. Namely, that health studies must have a qualified teaching staff and highly educated nurses, midwives, physical therapists, radiologic technologists and other health professions.

Teachers of health care should meet following requirements:

- Have master's and doctoral degree,
- Their teaching is based on research,
- Are qualified for teaching,
- Have at least 2 years of teaching experience in their field.

Postgraduate study is organized primarily with aim of enriching their own scientific potential by creating teachers trained at the highest academic level. The curriculum of postgraduate study is multidisciplinary, which allows mastering the methodology of scientific research and provides a competitive knowledge, skills and abilities in the field of nursing, physical therapy, radiologic technology, midwifery and medical laboratory diagnostics (27).

Graduate and postgraduate studies will not separate nurses, midwives, radiologic technologists and physiotherapists from patients and they will not become administrative officers; they will continue to perform most of their work with patients in health care institutions.

Croatian rule on the establishment of scientific fields

In Croatia, nursing as a branch of science was introduced in1997, in the area of biomedicine and health science, the field of clinical medical sciences (28), while in Europe, according to "Field of Science and Technology (FOS) Classification in the Frascati Manual", nursing as a branch of science is found in the area of Medical and Health Sciences, the field of Health Sciences (29). By 2011 in Croatia higher education in nursing and most of other health professions was not possible at the university level, which is a prerequisite for continuing higher education at the postgraduate university level. Establishment of postgraduate studies in the field of Health Science is a logical continuation of higher education of health professionals in order to create conditions for development of branches in Health Sciences and obtaining a doctoral degree, and ensuring scientific and academic staff in the field of Health Sciences.

General characteristics of doctoral studies in health professions

Curricula comprise compulsory courses (60 ECTS), elective courses (60 ECTS) and doctoral thesis work (60 ECTS). Elective courses are organized into modules related to individual health professions (e.g., nursing, midwifery, physiotherapy, radiologic technology, medical laboratory diagnostics, etc.). The model should be applied to all three levels of education.

The goals of the doctoral degree programme

The most important goals of the doctoral programme are to prepare students for clinical research, for participation in college work and pursuing teaching career at university, along with ability to create modern innovative concepts and approaches aimed at improving the quality of life of individuals, organizations and society (30-34).

The study takes a minimum of three academic years (6 semesters), ending with final examination after completion of all courses,

and preparing and defending a doctoral dissertation in the maximum period of seven years. After the thesis is defended students are awarded the title of Doctor of Health Sciences (30-32).

The main goals of doctoral study programme "Health Sciences" are (32-34):

c) Provide a critical understanding of the theoretical and methodological concepts
d) Enable students to pursue independent, interdisciplinary research,
e) Generate new and relevant knowledge by verifying existing and creating new solutions,
f) Develop critical thinking based on evidence-based research,
g) Involve international organizations in research and quality control studies.

The most important objectives of the doctoral programme "Health Sciences" are to enable students to pursue clinical research, to participate in teaching and creating modern innovative concepts, approaches and attitudes. Scientific work should be focused on health science and changing health practices (8).

Competences acquired during studies

Wider and relatively general list of competencies (32-35) would include:

a) Contribution to the health profession through independent scientific research and creation of new knowledge,
b) Identifying, analysing and solving problems by finding, understanding, and evaluating evidence-based information,
c) Planning and conducting original scientific research in the field of health studies, using the results of evidence-based practice in a format suitable for publication in international journals,
d) Understanding, evaluation and application of modern analytical methods in research, with continuous improvement in health care and acceptance (adoption) of attitudes in response to the constant changes in health care and more complex types of health care,
e) Ability to identify and promote ethical and legal principles in conducting research,
f) Theoretical, methodological, analytical and critical approach by testing scientific discoveries in health practice, through debates, conference presentations, and research workshops,
g) Evaluating clinical practice through scientific research,
h) Using research results in clinical decision making
i) Continuous clinical judgment, evaluation and self-evaluation aiming at ensuring quality and excellence,
j) Communicating by different techniques of informing, educating, motivating and improving the quality of life of healthy individuals, patients, families and larger populations,
k) Establishing a respectful relationship with patients, their families and colleagues,
l) Participating in interdisciplinary research teams and their management,
m) Promoting health in vulnerable and multicultural populations,
n) Understanding "philosophy" of medical science.

Jobs the students are trained for

Jobs of a health professional with doctoral degree include:

a) Academic researcher with emphasis on evidence-based research, along with teaching younger colleagues,
b) Jobs in practice with high-quality patient care;
c) Conducting research in healthcare systems (organizations);
d) Management positions in health care institutions and systems.

Curriculum

Postgraduate degree programme "Health Sciences" (third cycle) shall be organized and conducted according to the curriculum, lasting at least three years (six semesters). Since 60 ECTS represent the workload of one academic year, a three-year programme is worth 180 ECTS credits.

a) Structured courses (mandatory and optional),
b) Work with a mentor and thesis writing,
c) Mandatory and optional extracurricular activities.

Students

We believe that number of enrolled students should be relatively small, so that teachers can be committed to them as much as possible within a given program, especially in the individual work, so that most of them actually get a doctoral degree. It needs emphasizing because the number of PhD candidates has never exceeded 20% and most often it is less than 10%. 704 participants were enrolled in postgraduate studies in the field of biomedicine and health care in the academic year 2010-2011 while 10 PhD candidates submitted doctoral dissertation in the same academic year (35).

Mastery of the English language should be mandatory condition of enrolment since it is universal language of science and no teaching can make a scientist from a person that does not master English well. Students should be determined to carry out the part of their education abroad and in English language.

Knowledge of English is required at a level enabling oral and written communication, following scientific and teaching materials and use of computer programs. Students' working places must have potential, opportunity and support so that they are able to conduct research on which they will base their doctoral dissertation. Students should not cover the costs of studying abroad themselves (36). Moreover, small, objective, informed and fair board will, when the time comes, assess how much the institution can help students financially to complete their dissertation. On the other hand, students must pay the full amount of tuition fee for each new academic year, until they defend dissertation. After defending thesis, a college should pay back half of tuition for the first three years of study.

Doctoral dissertation

Based on the Guidelines for organization of doctoral programs in biomedicine and health studies (37), reached by consensus, a doctoral dissertation should be equivalent to at least three *in extenso* papers published in internationally indexed peer-reviewed journals. They must display independent intellectual contribution of bachelor (for example, a PhD candidate should be the first author). According to the Guidelines courses should occupy no more than 20% of the candidates' workload.

Special features of doctoral studies in health professions

Today there is virtually no teacher of health professions in Bosnia and Herzegovina and Croatia at the Assistant professor level - a person who has an MA and PhD degree and has relevant scientific publications. Actually this is about a decisive interruption of the "vicious circle" of falling behind the world: unless we have teachers, we cannot have universities, and unless we have schools (including doctoral studies), we cannot have teachers. So far students of health studies who have completed university graduate study due to various reasons, on average lag behind the students of medicine and dental medicine in scientific education, and

this should be borne in mind when organizing postgraduate studies for them. Postgraduate courses in health professions should rest on three basic principles:

a) Focus on research and developing a doctoral dissertation, formal ex cathedra teaching should be reduced to a minimum. This principle applies to postgraduate courses of all other professions as well.
b) Teaching should be tailored to the individual needs; therefore, it should be flexible, individualized, relying on elective courses and courses held outside home colleges and universities, and always aiming directly at developing each individual doctoral dissertation.
c) All forms of learning should be based on principles and techniques of evidence-based medicine.

Teachers should be selected according to their expertise, flexibility and commitment to adapting to the individual needs of students. Therefore most of the classes should be delivered in tutorials, directly or via electronic media. For all these reasons the first task of the institution which considers launching doctoral studies in health science is to choose three teams: 1) a team for making rational decision to start doctoral studies, 2) an operational team for implementing the decision, and 3) a team for objective and careful monitoring the implementation of the decision.

Conclusion

Establishment of postgraduate studies in the field of health science is the achievement of modern Europe and the developed world. It is a logical continuation of higher education for health professionals because it creates conditions for development of branches in health sciences and obtaining a doctorate which would ensure scientific and academic staff in the field of health sciences. These doctoral studies should a) focus on research and developing a doctoral dissertation and formal ex cathedra teaching should be reduced to a minimum b) teaching should be tailored to the individual needs and therefore should be flexible and individualized, relying on elective courses and courses outside home colleges and universities as well, and c) all forms of learning should be based on principles and techniques of evidence-based medicine.

Conflict of interest: The authors declare that they have no conflict of interest.

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Rewiev article

Acta Medica Academica 2013;42(1):71-79
DOI: 10.5644/ama2006-124.73

A proposal for enhancement of research capacities in Croatian general practice

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Received: 26 March 2013
Accepted: 23 April 2013

Research in family medicine contributes to the increase of knowledge, and its practical application improves the work of family physicians. Although research in family medicine in the Republic of Croatia has a long tradition, no sustainable research network exists as yet. Enhancing such a network is essential to efficaciously conduct research that is specific and important for family practice. This article describes the experiences of other countries and offers a proposal for a conceptual model for the development of a permanent research network in family medicine through three key elements: recognition of research as an indicator of quality of care that is specifically funded, introducing a continuing cycle of education for family physicians/researchers in the field of scientific research and building the capacity of academic family medicine and the success of their applications for domestic and international projects and funding sources. **Conclusion**. The application of the conceptual model from Australian primary health care research, adjusted to our circumstances, could further enhance research capacity building in Croatian family medicine.

Key words: Research capacities, Family medicine.

Introduction

If you keep on doing what you've always done,
you'll keep on getting what you've always got.
W.L. Bateman

In countries with well-developed family medicine, patients have better health outcomes and health systems cost less than in countries where family medicine is poorly developed (1). Quality health care for the population at the primary level reduces waiting time, the unnecessary and excessive use of diagnostic tests ("hyper-diagnostics"), and possible inappropriate treatment, and is one of the most powerful means of advancing health care (2, 3). The General Practitioner's (GP's) office is the first place of contact between patients and the health care system, where about 90% of all contacts between doctors and patients take place (4), and most health problems are solved. Scientific research in family medicine practices, in real-life situations, with a variety of patients, burdened by a wide range of diseases, conditions, comorbidities and problems (in a so-called "unselected" sample of health care users), is useful for patients, doctors and the

health system as a whole. Just such research and its results could contribute to an increase in the system's effectiveness and the improvement of the population's health (5, 6).

The aim of this article was to observe the current situation in the field of family medicine research in European countries, and in Croatia, and offer some enhancement proposals.

Methods

We searched the PubMed/MEDLINE database for articles using the keywords: general practice and research. The inclusion criteria were: observational studies or reviews published in the last 15 years. Out of 1453 articles, 37 met the inclusion criteria, two reviewers read them independently and 28 were included in the study. One additional reference was added for its historical importance, although it did not meet the publishing year inclusion criterion. A synthesis of the main results of studies included is presented in this overview.

Results

The tradition of research in the family medicine setting

Research in family medicine has a long historical tradition. Many family physicians in the past were excellent individual researchers, such as Edward Jenner and James Parkinson, whose discoveries changed the history of medicine (7). However, compared to other clinical specialties, family medicine is relatively young, it has only recently been recognized as an academic discipline, and it is still developing as a research discipline. At its centre is the patient, as a complete biopsychosocial being, approached holistically and provided with continuing care over time, with the focus on the family and community. The framework for research topics is shown in the detailed document: "Research Agenda for General Practice / Family Medicine and Primary Health Care in Europe," in the form of a manual for GP-researchers in family medicine and health policymakers, written by a group of experts from the organization, the European General Practice Research Network (EGPRN), of the World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians (WONCA) for Europe (8). The Agenda complements the European Academy of Teachers in General Practice/Family Medicine (EURACT) Educational Teaching Agenda, which addresses academic and vocational training (9).

Research in family medicine in Croatia

The Republic of Croatia was the first country in the world to introduce specialization in family medicine, in 1960. Currently there are four departments of family medicine at four Medical schools in Zagreb, Rijeka, Osijek and Split. The Department of Family Medicine at the School of Medicine in Zagreb was the first among them, established in 1980 and has a long tradition of quality education, research, and domestic as well as, more recently, international research projects. In 1996, the Department of Family Medicine of the Medical School, University of Zagreb and the Croatian Association of Family Medicine established the Family Medicine Research Club, which represented this network formally. It was also a valuable effort to motivate family physicians/practitioners to undertake research, relying on the academic family medicine department (10, 11).

After the reform of the curriculum of the Faculty of Medicine, which was adopted in 2010, the new reformed curriculum became a reality in the Republic of Croatia, starting from the academic year 2010/11. The Department of Family Medicine at the University of Split, School of Medicine saw the

new curriculum as a chance to improve and modernize its own organization and work. The new innovative approach included two aims: to improve patient-student communication through writing letters to patients, and to introduce an evidence-based medicine (EBM) concept, not only to the curriculum, but also to family medicine practice (12-15). The Department also founded its own Journal Club for GPs to critically read papers and to encourage and help less-experienced GPs to develop research questions and conduct their own studies.

But despite all those activities, a permanent and stable network of GP/researchers has not yet been created. There is still no optimum "critical mass" of GPs, who would be able to conduct systematic quality studies in the field. The "culture of research" as an integral part of the daily work of family physicians has never become a reality, except for some enthusiastic individuals within family medicine departments. There has always been a gap between the "family physicians/researchers" and "family physicians/practitioners" and we can only seldom speak of family physicians' research practices, where research and practice are permanently intertwined, as for example in the Netherlands, Great Britain and Australia (3, 6, 16-18). An average family physician in Croatia does not experience research as an integral part of their clinical work, more often it is perceived as "extra work reserved for colleagues, who want to thrive academically and to participate in science" (19).

Some research into issues important for GPs, such as primary care management, person-centred care, specific problem solving, the holistic approach and community orientation, has been conducted in the Croatian family medicine setting, doctoral theses on those topics have been written and papers published. However, overall, GPs are (with the exception of rare individuals) seldom independent researchers and are much more often the passive recipients of complete information and the results of research carried out "by others, elsewhere". Unfortunately, these are mostly clinical studies conducted in secondary care, in which the influence of pharmaceutical companies and other funding agencies (either through visible sponsorships or those that are "invisible" at first sight) is often worrying. Despite the great research potential of family medicine, GPs themselves seldom manage to create and conduct high quality research, focused at the peak of the hierarchical pyramid of studies and based on the strength of evidence provided.

The number of studies, in which family medicine specialists were the principal investigators and which were conducted fully precisely in GP practices , from recruiting participants to collecting data, is praiseworthy, but still too small (20). In contrast, trials in family medicine done by "someone else", from "outside", usually with a project manager or principal investigator from a field of clinical medicine, are not so rare, and family physicians usually play a minor role in the process. It is highly questionable whether the results of clinical trials done elsewhere, with a selected sample of patients can be unconditionally and directly applied to the current population in GP care. Additional training, especially in searching and finding the best "trustworthy" evidence, as well as in critical reading and evaluation of the published results, is of crucial importance for the provision of quality care in GP offices (21-23).

Teaching research in the Croatian Medical School system

In recent years at Croatian medical schools, students have been systematically taught about the importance of evidence-based medicine and the basics of scientific research, in a variety of undergraduate courses. At the Department of Research in Biomedicine and Health, of the University of Split, School of Medicine, an integrated manda-

tory course in research methodology and evidence-based medicine (EBM) has been introduced very early on in the curriculum and spread in smaller courses throughout 6 curriculum years (24). The Department of Family Medicine of the University of Split, School of Medicine also teaches EBM in the sixth year of the undergraduate curriculum. The latter was founded on the fact that the School of Medicine in Split nourishes an active Croatian branch of the Italian Cochrane Centre, and some teachers in the family medicine department are active members of the branch (13). Scientific research in family medicine has also been incorporated into the curriculum for the family medicine specialization course, as part of its postgraduate studies. In fact, creating an individual research plan, conducting a small research project and writing it up as a postgraduate thesis are set as an obligatory condition for GP graduation (10). All undergraduate and postgraduate forms of training are aimed at conveying to undergraduate and postgraduate students the basic knowledge and skills needed for research, and motivating them for continuous research activities later as integral part of their practice. However, a significant number of physicians employed in Croatian family medicine nowadays are middle-aged or older and did not have the opportunity to attend such an undergraduate program or postgraduate program either. Among those who did, only a minority has the motivation to initiate research and/or participate in it. What are the reasons for this? The growing demands of various health care organizations for administrative work have become a time-consuming burden for family physicians, not leaving them enough space for medical work, prevention, and particularly, for research. In such a busy schedule in the GP's office, curative work and compulsory administration inevitably take priority over the GP's prevention and research activities: they are regularly "sacrificed" or "left for better times" (25).

A protected time, as a part of the working day, intended for research activities, exists in many countries of the world (26), but not in Croatia. Health policies in our country have never recognized research as an important element in improving the quality of the work of GPs and have not validated it in any way. Even GPs, who are trained for research and who have an intrinsic drive for it, alongside the lack of time mentioned, are also faced with an additional obstacle when trying to answer questions arising from their practice: the inability to search their own database with ease! Namely, the electronic health records (e-records), compulsory in the fully computerized family medicine system in Croatia, are not standardized, and have very poor usability for research purposes (27). Therefore, their standardization at state level is a priority and a fundamental prerequisite for the future development and enhancement of the capacities of family medicine research, especially because the systematic investigation of their own daily work through the information accessible in the e-records, is usually the first crucial step in planning a GP's future research.

For all of these reasons there have not been enough quality studies undertaken so far in family medicine in Croatia, they are not systematized, and only a small number of creative enthusiasts have tried to implement them (mostly permanent members of Departments of Family Medicine, or their associates).

Experience from other countries

Many countries with well-developed family medicine have elaborated systems and established practices in research, with their own research capacities in family medicine, and, as study groups, systematically publish the results of their research in international

journals. Their studies are normally based on the existence, constant maintenance and strengthening of organized networks of researchers working together.

What makes those countries different from us and why are they more successful in research? In this overview, we chose the examples of the UK, the Netherlands and Australia, which are traditionally used as role models for other countries, both in the development of general practice and research networking. In the UK, the National Health Service (NHS) and the Ministry of Health fund research development and allocate substantial funds to research networks in primary health care (PHC). A prototype of such a functioning network is The West London Research Network (WeLReN), covering 979 GPs, with about two million people in their care (6). The Royal College of General Practice (RCGP) involves family physicians/practitioners through the Research Ready Program in research and projects, which are additionally financed (18). In Norway, by participating in research, practices obtain points for re-licensing, which is required every five years (16).

In the Netherlands, the networks of researchers (the best known is in Nijmegen) traditionally "rely" on academic departments and departments of family medicine at medical schools, as centres of excellence, that provide continuous education, mentoring and support (3). The Australian government, from 2000 to 2004, supported the strategy to develop research networks in primary health care (the Primary Care Research, Evaluation and Development Strategy, PHC-RED) with $A 50 million. From 2000 to 2005, every department of family medicine at Australian universities received $A 200,000 a year to build their research capacities, according to their own strategic plans (17). So the financial support that Flinders University in South Australia received through the PHCRED program (bursaries, writing grants and research fellowship) resulted in the strengthening of research skills, confidence, outcomes and family physicians' interest in research (28).

Strengthening research capacity is one of the most powerful and cost-effective ways of improving the health of the community. Therefore, the governments and health politicians of these countries recognized the importance of creating quality research capacities in family medicine, and have allocated and still allocate significant funds for that purpose. Designing and planning and / or GP participation in research is evaluated as one of the criteria for quality of care, and it is specifically funded. Each year GP practices are assessed and characterized as "research practices".

Challenges in building family medicine research capacities - the Australian model

The conceptual model of research capacity building in primary health care (2, 29) is also applicable to the situation in Croatia. According to this model, there are four different groups of GPs:

1. Physicians who do not participate in research (nonparticipants),
2. Physicians who participate to some extent (participants),
3. Physicians who manage their own research and educate others (managing/training),
4. The academic segment of family medicine that conducts research aimed at gaining a doctor of science degree and the scientific advancement of its members, prepares applications for research projects and funds, initiates studies, publishes results in journals, and teaches students and academics.

In order to create research capacities in family medicine, the awareness must be raised of the first group of the importance of research for improving their work, their motivation strengthened, and their basic knowledge and needed skills increased. The

second group, already included in research, should improve their research skills and be encouraged to set their own hypotheses, and design, develop and ultimately implement the research results. The third group, which has already conducted research, should be given further training in new techniques and methods and encouraged to find funding for research through projects (instead of self-financing, which is often rather overpriced and unacceptable over a long period). Finally, academic family medicine as a centre of excellence and a "learning organization" has a key role in the oversight, support and encouragement of less experienced researchers from all three groups, as well as providing on-going mentoring support (Figure 1).

Eventually, the gradual shift of some of the researchers from "left to right" might occur (Figure 2), i.e., from the first to the second group, from the second to the third and from the third to the fourth group. Research capacity building in family medicine is not an easy process. In Croatia it is further aggravated by the lack of funding for the creation of a national network of researchers in family medicine. There are numerous obsta-

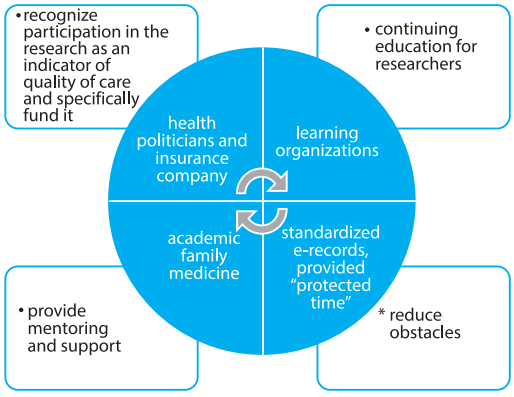

Figure 1 A conceptual model of creating a network of researchers in family medicine applied to Croatia.

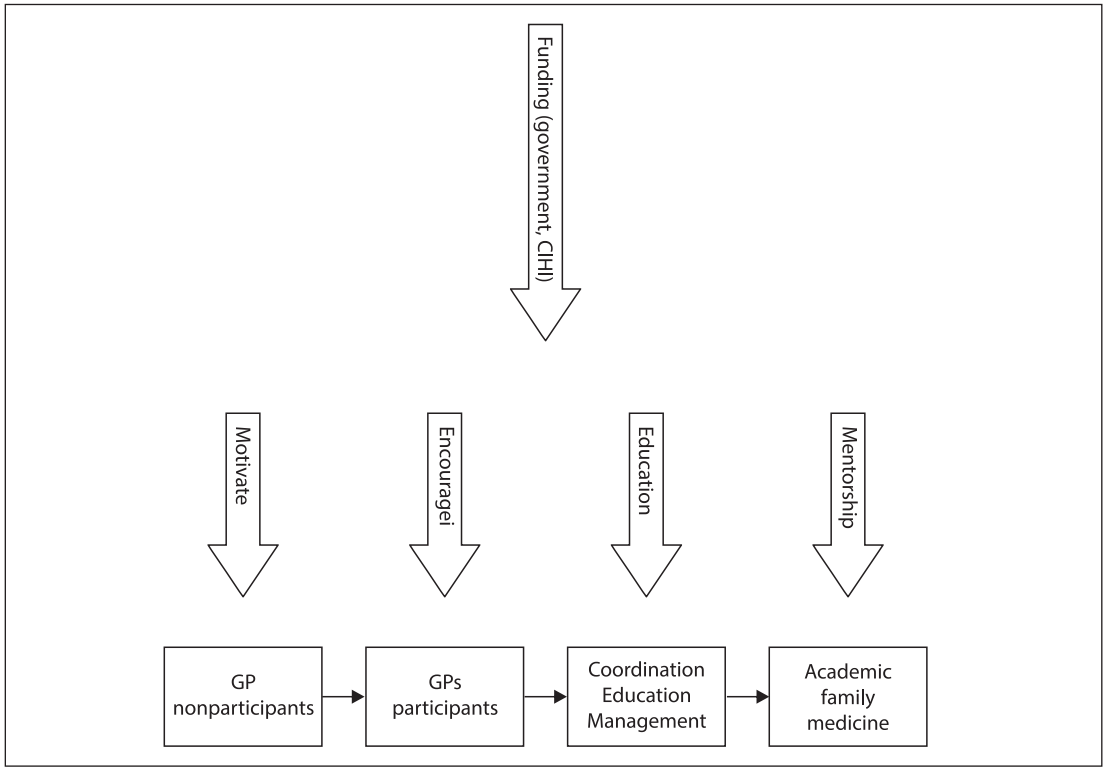

Figure 2 Four groups of researchers in family medicine and their flow through the process of education and additional education (lifelong learning). GPs – family physicians, CIHI – Croatian Institute for Health Insurance.

Table 1 Summary of obstacles to research in Croatian GP offices

Type of obstacles	Content
From the system	- There is no allocation of funding for the development and maintenance of research networks.
	- The insurance company (CIHI) does not include research in GP practices among its "quality of care" indicators nor does it specifically fund them.
	- Researchers have no "protected time" for research during working hours in the office.
	- If they want to investigate, they must do it in their own time and at their own expense.
From physicians	- Lack of time for research due to the excessive number of daily visits (free and uncritical "access" to the PHC system).
	- Often wrong attitudes towards research and EBM.
	- Lack of education, knowledge, skills and competencies for research.
	- Dedicated to earning money, do not recognize and appreciate the value of research.
From academic family medicine	- There are few qualified and experienced scientists/mentors.
	- Lack of skills in writing applications for research projects.
	- Low efficiency in getting national and international projects funded.
	- Overloaded by regular teaching.
	- In science as in healthcare, clinical and basic research have advantage over "applied" science, not being recognized even in medical schools.

cles to establishing a network of researchers in Croatia (Table 1).

Although research in PHC, including family medicine, has a relatively long historical tradition in Croatia, it does not exist as a continuous and permanent "current" activity based on a stable network of researchers. The small academic community in Croatian family medicine works persistently to support giving research a worthy place in the organization and funding of family medicine. A rather small number of teaching practices has been recognized (though not paid, but at least GPs can formally have fewer patients, 80% of the average list, to be able to teach). The process of research in family medicine should be systematic and planned long-term, permanently financed and encouraged, and not occasional or in spurts. Several preconditions should be met in order to create a network of researchers that would undoubtedly strengthen research in family medicine:

– Health policies and the system overall need to recognize the creation of research and/or participation in it as a valid and verifiable indicator of quality of care, which is specifically funded, and thereby provide "protected time" for research.

– Continuous education courses for GP/researchers (potential and existing ones) should be introduced, through basic and advanced workshops and courses in the field of scientific research.

– The number of qualified scientists and mentors should be increased in order to strengthen the capacities of academic family medicine and increase application performance, for both domestic and international projects and funds, which the upcoming accession of Croatia to the European Union makes highly topical.

Such a model could create, continuously maintain and strengthen the network of researchers in family medicine in Croatia, which undoubtedly have great research potential but it has so far been underused.

Research in the family medicine setting could have many advantages. Studies conducted in family medicine practice could perhaps represent "real clinical practice" and reflect everyday practice better than

artificial clinical studies. Also recruiting a large sample of patients (especially those with comorbidities) can be much easier in primary health care.

The Australian model includes motivating, recruiting and training GPs to become part of the permanent research network, and health policies there recognize the importance of research in family medicine as a basis for everyday quality care provision. Although this model demands constant funding through health policies, it significantly improves the clinical excellence important for patients in GP care.

Conclusion

Research is a critical element in the further development and improvement of the quality of all branches of medicine, including family medicine. On the basis of the results and experiences of other countries, we propose the application of the Australian model for further enhancement of research capacities in Croatia.

Authors' contributions: Conception and design: DV; Acquisition, analysis and interpretation of data: DV; Drafting the article: DV; Revising it critically for important intellectual content: DP.

Conflict of interest: The authors declare that they have no conflict of interest.

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Short communication

Acta Medica Academica 2013;42(1):80-82
DOI: 10.5644/ama2006-124.74

An unusual renal accessory artery originating from the thoracic aorta and its potential clinical implications

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We report a case of an unsual anatomical vascular blood supply to the right kidney. In an analysis of kidneys, by dissection of 39 foetuses, additional renal arteries were found in 18 cases (46.15%). In only one case (2.5%) was it noticed that the right kidney was supplied with blood by three renal arteries, one main and two additional arteries. One of the additional arteries, marked as the upper pole artery of aortic origin, separated from the thoracic aorta at the level of T11 (the eleventh thoracic rib), 1.5 cm above the truncus coeliacus. This artery, after passing through the diaphragm, entered the renal hilus at its upper part and served to vasculate that part of the kidney. **Conclusion**. The importance of this study is seen in the fact that anatomic knowledge of variations in the vascularization of the kidneys is of exceptional practical importance. Also, this information may concern transplant surgeons involved in living donor nephrectomies.

Key words: Additional renal arteries, Anatomy, Dissection method.

Introduction

The long-held opinion, that there is usually only one renal artery in the vascularization of a kidney, has been replaced with a new one which holds that in 9-76% of cases vascularization of the kidneys is by additional arteries from various sources (1). With the increase in the number of kidney transplants indicated, vascular reconstruction, surgical procedures on the kidneys and the development of new digital radiological methods, the knowledge of variations in renal vascularization is becoming increasingly important from day to day.

Material and methods

Using anatomical dissection, an analysis of kidneys was carried out on 39 human fetuses. Legal and ethical considerations were consistent with the Helsinki Declaration and the approval of the Ethics Committee of the Medical Faculty in Sarajevo.

Results

Additional renal arteries were found in 18 cases of 39 human fetuses (46.15%). In only one case (2.5%) was it noticed that the right kidney was supplied with blood by three renal arteries, one main and two additional arteries. One of the additional arteries, marked as the upper pole artery of aortic origin, separated from the thoracic aorta at the level of T 11 (the eleventh thoracic rib), 1.5 cm above the truncus coeliacus. This artery, after passing through the diaphragm,

Figure Supernumerary artery (1 – Aorta abdominalis, 2– Arteria renalis dextra, 3 – Arteria renalis poleis superior dextra, 4 – Arteria renalis poleis inferior dextra, 5 – Arteria renalis sinistra, 6 – Ureter).

entered the renal hilus at its upper part and served to vasculate that part of the kidney. The other extra artery, the lower pole artery, separated from the abdominal aorta a little above the site of where it forked into two common iliac arteries, and after briefly passing behind the urethra, it entered the hilus of the kidney in the lower part and served to vasculate its lower pole (Figure). By observation it was noticed that the diameters of the main and the additional renal arteries were approximately the same, but no detailed morphometric measurements of these arteries were made.

Discussion

There is no unified opinion amongst researchers about the percentage of and where additional renal arteries appear. Double blood supplies, according to data in the literature, occur in a range from 10% (2) to 23.2% (3) of cases. One of these arteries is the main one and the other is additional. Goscicka et al. (4), in their analysis of renal arteries in foetuses, found double blood supplies in 19.2 % of cases. The authors mentioned give differing data on the incidence of triple blood supply to the kidneys. Triple blood supply to the kidneys, according to data in the literature, occurs in a range from 1.2% (2) to 4.5% (3) of cases. In their analysis of 140 human foetuses, Goscicka et al. (4) recorded triple renal arteries in 2.1% of cases. Satyapal et al. (3) point out that the kidney may be vascularized by three or more blood vessels, which is recorded in the literature in sporadic cases.

Through an analysis of the material presented in our study, we recorded one unilateral triple renal artery. One of these blood vessels was the main renal artery, whilst the other two were additional arteries, marked as the upper pole artery, originating from the thoracic aorta, and the lower pole artery originating from the abdominal aorta. The case presented corresponds to the presentation given by Norman (5) in his study.

Practice so far has shown that additional renal arteries have major practical importance, because overlooking them during the pre-operative preparation of patients for surgical procedures may be fatal for the patients, especially if laparoscopic methods are used for the procedure. The increasing number of kidney transplants has led in recent times to an increase in the use of laparoscopic surgical techniques, which, with all their advantages, also have failings. That is to say, using these methods reduces the operative field, whereby the risk is increased that variations in the vascularization of the kidneys may lead to a fatal outcome.

Conclusion

The importance of this study is seen in the fact that anatomic knowledge of variations in the vascularization of the kidneys is of exceptional practical importance. In surgical terms, the upper pole artery represents a major risk because it is frequently located high up, meaning that in most cases the surgeons mistake it for surrounding connective tissue, and unknowingly cut through it, causing thereby massive bleeding, which most often leads to a fatal outcome (6).

Authors' contributions: Conception and design: ET, AV; Acquisition, analysis and interpretation of data: ET; Drafting the manuscript: AV; Revising it critically for important intellectual content: ET, AV.

Conflict of interest: The authors declare that they have no conflict of interest.

Received: 14 January 2013; Accepted: 11 April 2013

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Acta Medica Academica 2013;42(1):83-84
DOI: 10.5644/ama2006-124.75

Brachytherapy dose received by bladder and rectum in patients with inoperable cervical cancer: CT-based 3D view

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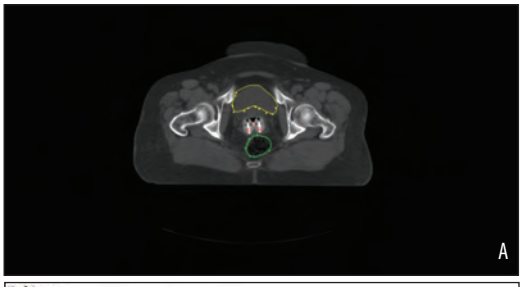
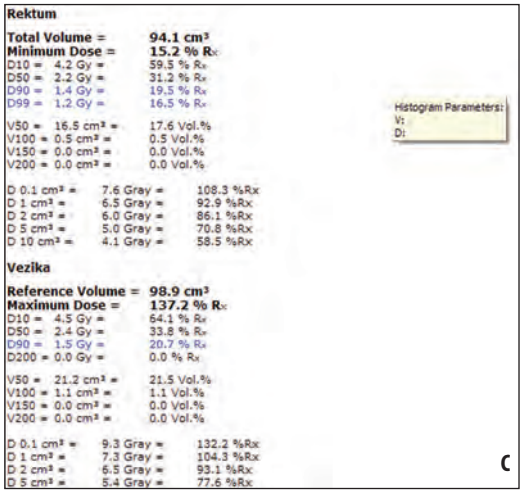
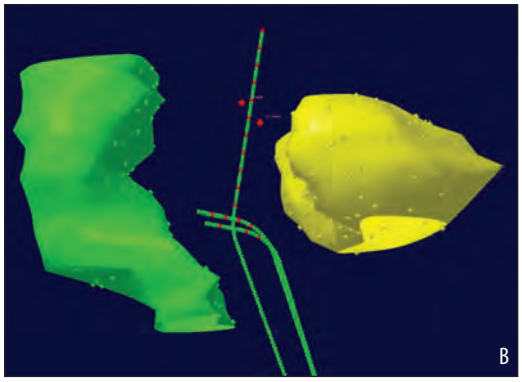
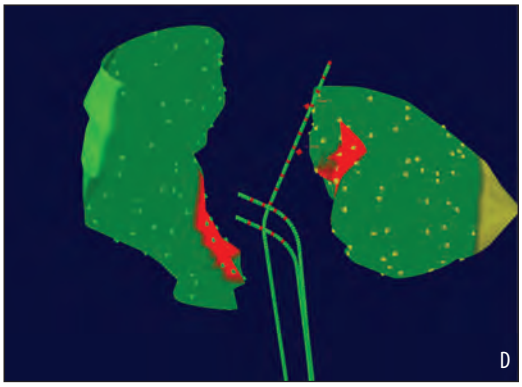
As recommended by the GEC-ESTRO work group, it is important for the 3D image guided CT, or MRI based brachytherapy of cervical cancer to verify what dose is received by 0.1 cm^3, 1 cm^3 and 2 cm^3 ($D_{0,1cc}$, D_{1cc} and D_{2cc}, respectively) of the bladder and rectum volume (1). Intracavitary brachytherapy was applied with applicators type Fletcher tandem and ovoids, once a week on a HDR regime (high dose rate). Delineation of organs at risk (bladder and rectum) was made after each computer tomography (Panel A). The bladder and rectum were delineated on each









CT slice: the rectum was delineated at 1 cm from the anus to the recto-sigmoid transition through the entire thickness of the organ wall, and the bladder was delineated following the outer contour of the entire organ volume (Panel B). The therapy dose of (5 x 7 Gy) was prescribed according to the Manchester system, to the A point. Brachytherapy $D_{0,1cc}$, D_{1cc} and D_{2cc} doses for the bladder and rectum were established for each application (Panel C). The EQD_2 (total biologically equivalent dose in 2 Gy) for bladder and rectum were 76.7 Gy and 81 Gy, respectively. Also, we could see the position (three – dimensional view) of the brachytherapy dose received by bladder and rectum (Panel D).
In planning brachytherapy, CT does not give us the possibility to precisely delineate the tumor and plan the distribution of the therapy dose to the tumor (as is the case with MR planning). However, it is possible to obtain precise data on the contribution of the brachytherapy dose to the organs at risk (2).

Key words: D2cc, Brachytherapy, Cervical cancer.

Authors' contributions: Conception and design: GM; Acquisition, analysis and interpretation of data: GM and SF; Drafting the article: GM and HO; Revising it critically for important intellectual content: JB and DM.

Conflict of interest: The authors declare that they have no conflict of interest.

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Received: 11 November 2012; Accepted: 11 April 2013

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Acta Medica Academica 2013;42(1):85-86
DOI: 10.5644/ama2006-124.76

Solitary extramedullary plasmocytoma of the liver

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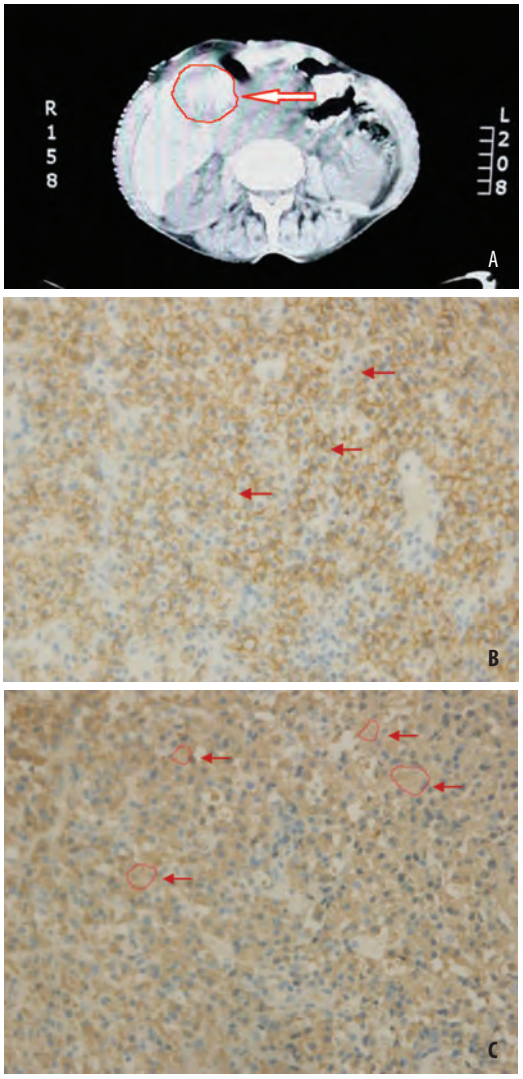

Solitary extrameduallary plasmacytomas represent approximately 3% of all plasma cell neoplasms. Extramedullary plasmacytoma of the liver is a very rare tumor, although a few cases of extramedullary plasmacytoma of the liver have been reported. We report an unusual case of liver plasmacytoma without systemic disease, diagnosed by percutaneous needle biopsy of the hepatic lesion. The patient was a 67 year old female who exhibited a solitary liver mass on dynamic computed tomography (Panel A). We performed percutaneous needle biopsy of the hepatic lesion. Histologically, the tumor was composed of CD 138 positive plasma cells with mild atypia (Panel B: H&Ex40 black arrow), and 80% of them demonstrated Kappa light chain (Panel C: H&Ex40 red circle – white arrow). There was no evidence of a monoclonal protein in the serum and urine, lytic bone lesions, anemia, renal insufficiency, or hypercalcemia. The bone marrow examination revealed no abnormalities. The patient was treated with local radiation and is doing well without further evidence of disease after one year of follow-up. Primary extramedullary plasmacytoma (EMP) is defined as an extraosseous proliferation of neoplastic plasma cells, without evidence of bone or bone marrow involvement, as evidenced by morphological bone marrow examination and radiographic studies. EMP accounts for

about 3% of plasma cell tumors, and more than 80% occur in the upper aerodigestive tract. Among the plasmacell dyscrasias, a rare form is the extramedullary plasmacytoma requiring, for diagnosis, histological evidence of monoclonal plasmacell infiltration localized in the lesion, in the absence of a marrow plasmacytosis. This peculiar presentation of a plasmacell neoplasia is rarely observed in the liver, while it is most frequently seen in the mucosa of the upper airway. Generally, the presence of plasmacells in the liver, spleen and lymphonodes, is associated with a more aggressive form of multiple myeloma (1). The diagnosis of solitary extramedullary plasmacytoma requires the demonstration of a monoclonal plasma cell infiltrate without any evidence of multiple myeloma elsewhere. Only a few cases of primary hepatic extramedually plasmacytoma have been reported (2). The patient described here is a woman who presented with a solitary hepatic extramedullary plasmacytoma without evidence of myeloma elsewhere, including no monoclonal protein in the serum or urine.

Key words: Plasmocitoma, Extramedullare, Liver.

Authors' contributions: Conception and design: SH; Acquisition, analysis and interpretation of data's: SH and JP; Drafting the article: EA and MK; Revising it critically for important intellectual content: SH and MK.

Conflict of interest: The authors declare that they have no conflict of interest.

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Received: 11 May 2013; Accepted: 30 May 2013

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Acta Medica Academica 2013;42(1):87-96
DOI: 10.5644/ama2006-124.77

International publications of authors from Bosnia and Herzegovina in Current Contents indexed publications in the second half of 2012*

Alagić-Smailbegović J, Kučukalić-Selimović E, Šetić I, Bećirović M, Begović L. Importance of measurement of thyroglobulin and anti-thyroglobulin antibodies in differentiated thyroid cancer. Coll Antropol. 2012 Nov;36 Suppl 2:33-8.

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Differentiated thyroid cancers include papillary and follicular carcinomas, both originating from follicular epithelium. Treatment of choice is usually total or near total thyroidectomy, followed by ablative radioiodine 131I treatment, and by the long-term administration of thyroid hormone. Despite its excellent prognosis, recurrent disease does occur in approximately 20-40% of patients. Guidelines for the follow-up management of differentiated thyroid cancer are commonly based on circulating thyrogobulin measurement in the complete absence of eutopic thyroid tissue. A retrospective review was conducted on 116 patients (66 papillary and 50 follicular carcinoma, mean age 51.2 years) who had undergone total or near total thyroidectomy and radioactive iodine remnant ablation. Serum thyroglobulin (Tg) and anti-thyroglobulin antibodies (TgAb) levels were measured preoperatively, 1 month after thyroidectomy (before 131I treatment) and 6 and 12 months after ablation therapy (Tg1, TgAb1 and Tg2, TgAb2, respectively). During one year of follow-up, in a total of 24 patients (21%) recurrent disease were confirmed by ultrasonography and whole-body-scanning, mostly. It was found significant correlation between serum Tg levels (measured preoperatively and postoperatively) and recurrent diseases ($p < 0.05$), while serum TgAb levels did not have any statistical significance. However, in multivariate regression analysis only Tg levels measured 12 months after the therapy (Tg2) remained a significant predictor of recurrent disease ($p = 0.008$). Although a high Tg level before surgery does not indicate that tumor is present, in the postoperative period and after ablative therapy Tg has proven predictive value because stimulated Tg levels above 10 ng/ml confirmed that indicate residual or recurrent cancer, and its periodically measurements is recommended.

Bišćević M, Bišćević S, Ljuca F, Smrke BU, Kapur E, Tezer M, Smrke D. Clinical and radiological morphometry of posterior parts of thoracic and lumbal vertebras. Coll Antropol. 2012 Dec;36(4):1313-7.

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The aim of this work is to measure clinically important dimensions of thoracic and lumbal vertebras. Charts of one-hundred and seventeen patients with implanted internal fixateur on the thoracic and lumbal spine between 01.01. 2008. and 31.3.2010. at the Department for Orthopedics and Traumatology, of the Sarajevo Clinical center were retrieved, and only 14 patients, with 46 vetrtebras and 89 pedicles have had complete documentation (clearly visible measured

*Data for this survey were collected from PubMed database using the keywords Bosnia and Herzegovina and 2012.

structures on X-ray and CT scans). Digitalized anteroposterior and latero-lateral X-ray, and transversal and sagital CT scans were basic inputs for measurement of height and width of the pedicle--PH, PW, axial and vertical cortico-cortical transpedicular distances--AL, VL, and interpedicular distance--IP. The correction of enlargement on X-ray pictures was performed according to known dimensions of implants and length scale on CT scans. Enlargement of those parameters, from T1 to L5 level was from 50 to 150%. This increasing was not always linear, sometimes there was even decreasing. For instance, the IP on second and third thoracic vertebra was shorter compared to the first thoracic vertebra. Pedicles from the third to the eighth thoracic vertebra were narrower compared to the second thoracic vertebra. The importance of this work is in to analyze the mentioned dimensions by methods available to the clinician. Every other in vivo measurement is impossible because of the excessive surgical approach, while preoperative CT scanning with a great number of slices per one millimeter for this purpose is not ethical.

Bjelanović V, Babić D, Orešković S, Tomić V, Martinac M, Juras J. Pathological pregnancy and psychological symptoms in women. Coll Antropol. 2012 Sep;36(3):847-52.

Mostar University Hospital Centre, Department of Gynecology and Obstetrics, Mostar, Bosnia and Herzegovina.

Pregnancy is followed by many physiologic, organic and psychological changes and disorders, which can become more serious in pregnancy followed by complications, especially in women with pathological conditions during pregnancy. The purpose of this study was to find out and analyze the prevalence and intensity of psychological disorders in women with pathological conditions during pregnancy and compare it with conditions in pregnant women who had normal development of pregnancy. The research is approved by the Ethical committee of the Mostar University Hospital Center, and it was made in accordance with Helsinki declaration and good clinical practices. The research conducted section for pathology of pregnancy of Department for gynecology and obstetrics of the Mostar University Hospital Center. It included 82 pregnant women with disorders in pregnancy developement and control group consisted of pregnant women who had normal development of pregnancy. The research work was conducted from September 2007 to August 2008 in Mostar University Hospital Center. Pregnant women had Standard and laboratory tests, Ultrasound. CTG examinations were done for all pregnant women and additional tests for those women with complications during pregnancy. Pregnant women completed sociobiographical, obstetrical-clinical and psychological SCL 90-R questionnaire. Pregnant women with pathological pregnancy exibited significantly more psychological symptoms in comparison to pregnant women with normal pregnancy ($p < 0.001$ to $p = 0.004$). Frequency and intensity of psychical symptoms and disorders statisticly are more characteristic in pathological pregnancy (61%/40.6%). The statistical data indicate a significantly higher score of psychological disorders in those pregnant women with primary school education ($p = 0.050$), those who take more than 60% carbohydrates ($p = 0.001$), those with pathological CTG records ($p < 0.001$), those with pathological ultrasound results ($p < 0.001$ to 0.216) and those pregnant women with medium obesity and obesity ($p = 0.046$). Body mass index (BMI) during normal pregnancy development is lower ($p = 0.002$) but the levels of glucose, triglycerides, cholesterol, HDL and LDL in blood are higher Blood pressure in pregnant women with pathological pregnancy was statistically significantly higher ($p < 0.001$). Diagnostic criteria for the metabolic syndrome were found in 19 pregnant women with the pathological pregnancy. Statistically, in those women, a significantly higher appearance of psychological symptoms and disorders was observed in comparison to the pregnant women without metabolic syndrome ($p < 0.001$). The research has shown that 87.8% from all pregnant women included in this study have been hospitalized due to premature birth, hypertensive disorders, and diabetes in pregnancy, and also due to bleeding in the second and third trimester of pregnancy.

Busuladžić M, Hasović E, Becker W, Milošević DB. Application of the dressed-bound-state molecular strong-field approximation to above-threshold ionization of heteronuclear molecules: NO vs. CO. J Chem Phys. 2012 Oct 7;137(13):134307. doi: 10.1063/1.4757255.

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We theoretically investigate high-order above-threshold ionization (HATI) of heteronuclear diatomic molecules applying the molecular strong-field approximation which includes dressing of the molecular bound state. We consider HATI of nitrogen monoxide molecules, which are characterized by the π symmetry of their highest occupied molecular orbital. We show that the HATI spectra of NO exhibit characteristic interference structures. We analyze the differences and similarities of the HATI spectra of NO molecules and the spectra of CO (σ symmetry) and O(2) (π(g) symmetry) molecules. The symmetry properties of the molecular HATI spectra governed by linearly and elliptically polarized fields are considered in detail. The

yields of high-energy electrons, contributing to the plateau region of the photoelectron spectra, strongly depend on the employed ellipticity.

Ćavar S, Vidic D, Maksimović M. Volatile constituents, phenolic compounds, and antioxidant activity of Calamintha glandulosa (Req.) Bentham. J Sci Food Agric. 2013 May;93(7):1758-64. doi: 10.1002/jsfa.5967. Epub 2012 Nov 26.

University of Sarajevo, Faculty of Science, Department of Chemistry, Zmaja od Bosne 33-35, Sarajevo, Bosnia and Herzegovina.

BACKGROUND: Calamintha glandulosa (Req.) Bentham is an aromatic perennial plant belonging to the family Lamiaceae, mostly found on rocky pastures, dry meadows, and abandoned places of the Mediterranean area. Plants belonging to this genus are known as highly aromatic and to possess significant antimicrobial and antifungal properties. The aim of this study was to provide clear picture of the volatiles of this plant species, and, for the first time, to present C. glandulosa from Croatia in terms of its antioxidant activity. RESULTS: The essential oil and headspace obtained from odorous parts of C. glandulosa were subjected to capillary gas chromatography-mass spectrometry analysis. More than 50 volatile compounds were identified in six samples obtained using different extraction techniques. The most abundant components in all the samples examined were oxygenated monoterpenes, with piperitone (19.9-59.5%) and piperitenone (7.1-42.6%) as the main representatives. The total phenolic content of extracts obtained by successive Soxhlet extraction was measured, and the scavenging potency of the samples, indicated as IC50 values, were examined using four different spectrophotometric and spectrofluorimetric methods. In all cases the essential oil showed the lowest antioxidant activity, while the aqueous extract showed the highest. This can be explained by the levels of the phenolic compounds in the samples examined. CONCLUSIONS: A clear picture of aroma profile of C. glandulosa is presented, and the results obtained differ from those published previously. The high antioxidant potential of C. glandulosa from Croatia was established for the first time. Results from the present study suggest further analysis on this plant species in order to define its medicinal properties.

Erić J, Stančić I, Tihaček-Šojić L, Kulić L, Popovac A, Tsakos G. Prevalence, severity, and clinical determinants of oral impacts in older people in Bosnia and Herzegovina. Eur J Oral Sci. 2012 Oct;120(5):438-43. doi: 10.1111/j.1600-0722.2012.00994.x. Epub 2012 Aug 24.

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This study aimed to assess the prevalence and the severity of oral impacts and the relationships between oral health-related quality of life (OHRQoL) and clinical measures of oral function in a sample of older adults in Bosnia. The sample comprised 261 community-dwelling adults of ≥65 yr of age. Participants were randomly drawn from three senior day-centres for elderly people. Data were collected using clinical examination and a questionnaire. The OHRQoL was assessed through the Oral Impacts on Daily Performances (OIDP) measure, in terms of the prevalence, intensity, and extent of oral impacts. Overall, 55.2% reported at least one oral impact in the last 6 months. Difficulty eating (43.3%) and difficulty speaking (34.1%) were the most common impacts. These were also the most severely affected performances, while 'going out' and 'enjoying the contact of other people' were the least severe. A higher number of natural teeth, natural occluding pairs, and anterior and posterior occluding pairs were all significantly associated with a lower prevalence of oral impacts and correlated with the OIDP score, even after adjusting for sociodemographic factors. The prevalence of oral impacts was high and there was a strong and consistent association between OHRQoL and clinical dental indicators of function.

Fočo F, Bilalović N, Vranić S, Serdarević F, Ramović I, Imamović E. Peritumoral p53 expression in oral carcinoma. Coll Antropol. 2012 Nov;36 Suppl 2:129-32.

Clinical Center of the University of Sarajevo, Department of Maxillofacial Surgery, Sarajevo, Bosnia and Herzegovina.

p53 is one of the most frequently mutated genes in human tumors including head and neck tumors like oral squamous cell carcinoma. It might be responsible for more than 50% of all relapses in patients with surgically treated oral carcinoma and clean margins. The aim of the present study was to explore p53 protein expression in peritumoral tissue and correlate it with relapse of the disease. The study included 25 patients (17 males and 8 females) with oral squamous cell carcinoma in the period August 2006 till August 2008. For immunohistochemical assay, a monoclonal antibody against p53 protein was applied (clone DO-7, DAKO Glostrup, Denmark). Peritumoral expression of p53 was as follows: 10 out of 25 cases (40%) were negative, 2 cases (8%) showed weak, 5 cases (20%) moderate and 8 cases (32%) strong p53 positivity. No significant correlation between peritumoral expres-

sion of p53 protein and patient's relapse was found. In contrast, we found a trend toward association between intratumoral p53 expression and patient's relapse (p = 0.07). There was also trend toward higher peritumoral p53 expression in females comparing with p53 expression in males (52.9% of males did not have p53 expression while 87.5% females had mild, moderate or high p53 expression, p = 0.088). Peritumoral expression of p53 protein is frequently seen in oral squamous cell carcinoma and merits further research.

Hasanović M, Pajević I. Religious Moral Beliefs Inversely Related to Trauma Experiences Severity and Depression Severity among War Veterans in Bosnia and Herzegovina. J Relig Health. 2012 Sep 1. [Epub ahead of print]

Department of Psychiatry, University Clinical Center Tuzla, Rate Dugonjića bb, Tuzla, Bosnia and Herzegovina.

The aim of this study is to determine the association of religious moral beliefs and depression severity of war veterans in Bosnia and Herzegovina. The sample consists of male war veterans who were inpatients with clinically presented depression and those who were observed as healthy, regarding results of previous psychological testing (n = 65 both). The Bosnia-Herzegovina versions of Hopkins Symptom Checklist and Harvard Trauma Questionnaire with questionnaire for religious moral beliefs were applied. The religious moral belief index was inversely correlated to depression severity. The religious moral beliefs may help protection of the war veterans' mental health stability after surviving multiple war traumas.

Hasukić ŠI, Iljazović ES, Odobašić AH, Matović EA. A rare case of primary rectal adenocarcinoma metastatic to the breast. Saudi Med J. 2012 Sep;33(9):1014-7.

Department of Surgery, Polyclinic for Laboratory Diagnostics, University Clinical Center Tuzla, Faculty of Medicine, University of Tuzla, Tuzla, Bosnia and Herzegovina.

Primary rectal adenocarcinoma metastatic to the breast is an exceedingly rare event. Its management differs from that of primary breast cancer, as illustrated by this case. A 63-year-old woman presented with a breast lump 30 months after abdominoperineal resection for rectal adenocarcinoma, stage $T_3N_1M_0$ (stage III), followed by standard postoperative radiochemotherapy. The patient underwent a mammography and ultrasonography. A CT scan of the abdomen showed metastatic disease. An excisional biopsy of the breast lump was performed; morphological features were identical to the original rectal cancer. Immunohistochemical results were negative for estrogen and progesterone receptors and gross cystic disease fluid protein-15, and intensity positive for cytokeratin 20 and carcinoembryonic antigen. The patient died after treatment with palliative chemotherapy. Metastatic disease from rectal carcinoma to the breast is a marker for disseminated metastatic spread with poor prognosis.

Hudić I, Bujold E, Fatušić Z, Skokić F, Latifagić A, Kapidžić M, Fatušić J. The Misgav-Ladach method of cesarean section: a step forward in operative technique in obstetrics. Arch Gynecol Obstet. 2012 Nov;286(5):1141-6. doi: 10.1007/s00404-012-2448-6. Epub 2012 Jul 3.

Clinic for Gynecology and Obstetrics, University Clinical Center Tuzla, Trnovac bb, Tuzla, Bosnia and Herzegovina.

OBJECTIVE: The objective of this study is to compare the intraoperative and short-term outcomes of two cesarean techniques: the modified Misgav-Ladach and the Pfannenstiel-Kerr.
METHODS: We performed a prospective observational cohort study of women undergoing a primary cesarean at the Clinic for Obstetric and Gynecology Tuzla, Bosnia and Herzegovina, between January 2003 and December 2011. The two cesarean techniques were compared for intraoperative and short terms outcomes. RESULTS: A total of 4,944 women were included in this study, 4,336 allocated to the modified Misgav-Ladach and 608 to the Pfannenstiel-Kerr techniques. The rate of modified Misgav-Ladach increased from 74 % in 2003 to 99 % in 2011. The modified Misgav-Ladach technique was associated with a shorter operative time (13.3 min ± 7.4 vs. 19.1 min ± 6.8, $p < 0.05$), as well as significantly less surgical material (3.5 ± 2.5 vs. 7.9 ± 2.1, $p < 0.05$). The modified Misgav-Ladach technique was also associated with lower analgesic requirements, lower rates of febrile morbidity and wound infection compared to the Pfannenstiel-Kerr technique ($p < 0.05$). No significant differences were observed in the incidence of endometritis, wound dehiscence, bowel restitution, postoperative antibiotic use, and hospital stay. CONCLUSION: The modified Misgav-Ladach technique is associated with a shorter operative time than Pfannenstiel-Kerr and might lead to better postoperative outcomes.

Kučukalić-Selimović E, Alagić J, Valjevac A, Hadžović-Džuvo A, Begić A, Bešlić N. The value of serum thyreoglobulin levels and whole body (I-131) scintigraphy in the follow-up of the thyroid cancer patients after thyroidectomy. Coll Antropol. 2012 Nov;36 Suppl 2:67-71.

Clinical Center University of Sarajevo, Clinic for Nuclear Medicine, Sarajevo, Bosnia and Herzegovina.

Serum thyreoglobulin (Tg) and whole body scintigraphy (I-131 WBS) have been used to detect recurrent and metastatic thyroid cancers postoperatively. However, discordant results of Tg measurement and 131I WBS have been reported. Negative 131I WBS and a positive Tg test are usually found, but less common occurrence of positive 131I WBS and a negative Tg test has also been demonstrated in a small but significant number of cases. Therefore, the aim of the study was to retrospectively analyse patients with positive 131I WBS after total thyreoidectomy and again 1 year after the radioactive iodine. There were 52 patients included in the study. Four weeks after surgery, during which thyroid hormone treatment was not introduced, each patient received an ablative dose of 131I. The evaluation of the WBS was qualitative and considered positive if thyroid remnant, lymphatic node or metastasis were detected. WBS and serum Tg was measured 12 months after 131I ablation with thyroid hormone suppression. We considered positive any Tg level above the sensitivity values and negative if lower than this level. Tg levels were related to the existence of a positive scan or a negative one. In our 52 WBS positive patients concordant positive Tg levels were observed in 42 patients while in 10 patients we found a negative Tg levels after the surgery. After 1-year follow-up, out of initially 42 concordant patients 8 patients showed remaining concordant positive Tg and WBS values. Discordant results were observed in 13 patients (4 patients were Tg- and WBS+ while 9 patients were Tg+ and WBS-). In the majority of patients (50%) remained with concordant results but changed from Tg+ and WBS+ to Tg- and WBS-. Diagnostic WBS is an additional valuable tool, besides Tg levels, in the follow up of patients after total thyreoidectomy.

Kukavica BM, Veljović-Jovanović SD, Menckhoff L, Lüthje S. Cell wall-bound cationic and anionic class III isoperoxidases of pea root: biochemical characterization and function in root growth. J Exp Bot. 2012 Jul;63(12):4631-45. doi: 10.1093/jxb/ers139. Epub 2012 Jul 3.

University of Banja Luka, Faculty of Science and Mathematics Mladena Stojanovića 2, Banja Luka, Bosnia and Herzegovina.

Cell wall isolated from pea roots was used to separate and characterize two fractions possessing class III peroxidase activity: (i) ionically bound proteins and (ii) covalently bound proteins. Modified SDS-PAGE separated peroxidase isoforms by their apparent molecular weights: four bands of 56, 46, 44, and 41kDa were found in the ionically bound fraction (iPOD) and one band (70kDa) was resolved after treatment of the cell wall with cellulase and pectinase (cPOD). Isoelectric focusing (IEF) patterns for iPODs and cPODs were significantly different: five iPODs with highly cationic pI (9.5-9.2) were detected, whereas the nine cPODs were anionic with pI values between pH 3.7 and 5. iPODs and cPODs showed rather specific substrate affinity and different sensitivity to inhibitors, heat, and deglycosylation treatments. Peroxidase and oxidase activities and their IEF patterns for both fractions were determined in different zones along the root and in roots of different ages. New iPODs with pI 9.34 and 9.5 were induced with root growth, while the activity of cPODs was more related to the formation of the cell wall in non-elongating tissue. Treatment with auxin that inhibits root growth led to suppression of iPOD and induction of cPOD. A similar effect was obtained with the widely used elicitor, chitosan, which also induced cPODs with pI 5.3 and 5.7, which may be specifically related to pathogen defence. The differences reported here between biochemical properties of cPOD and iPOD and their differential induction during development and under specific treatments implicate that they are involved in specific and different physiological processes.

Maksimović A, Maksimović Z, Filipović S, Beširović H, Rifatbegović M. Vaginal and uterine bacteria of healthy bitches during different stages of their reproductive cycle. Vet Rec. 2012 Oct 13;171(15):375. doi: 10.1136/vr.100886. Epub 2012 Aug 17.

Department of Surgery, Veterinary Faculty, Zmaja od Bosne 90, Sarajevo, Bosnia and Herzegovina.

No abstract available.

Mandić A, Tomić M, Petrov B, Romić Z. Atrial fibrillation, atrioventricular blocks and bundle branch blocks in hemodialysis patients. Coll Antropol. 2012 Dec;36(4):1395-9.

Health Center Široki Brijeg, Široki Brijeg, Bosnia and Herzegovina.

Atrial fibrillation is one of the most frequent arrhythmias diagnosed in clinical practice and it is also relatively common in dialysis patients. Atrioventricular and intraventricular conduction disturbances are less investigated in hemodialysis patients and data about their prevalence are insufficient. The objective of this study was to determine the prevalence of atrial fibrillation, atrioventricular blocks and bundle branch blocks in hemodialysis patients and to analyze different clinical risk factors. The study included 140 patients on long-term hemodialysis treatment. The pres-

ence of atrial fibrillation, atrioventricular blocks and bundle branch blocks was determined by electrocardiogram. Patients were divided into groups depending on the presence or absence of atrial fibrillation/ bundle branch blocks and investigated variables were compared. Atrial fibrillation was present in 11 (7.9%) of the 140 patients. In multivariate analysis, age and higher concentration of uric acid were associated with atrial fibrillation. Prevalence of first-degree atrioventricular block was 2.9% (4 patients) and second- and third-degree atrioventricular blocks were not found. Prevalence of bundle branch blocks was 17.1% (24 patients): 5% of patients had a complete right bundle branch block, 6.4% had an incomplete right bundle branch block, 3.6% had a complete left bundle branch block and 2.1% of patients had an incomplete left bundle branch block. The prevalence of atrial fibrillation and bundle branch blocks in this study was relatively high in patients on hemodialysis and greater than that observed in general population. Presence of atrial fibrillation was associated with older age and higher concentration of uric acid.

Marković-Peković V, Škrbić R, Godman B, Gustafsson LL. Ongoing initiatives in the Republic of Srpska to enhance prescribing efficiency: influence and future directions. Expert Rev Pharmacoecon Outcomes Res. 2012 Oct;12(5):661-71. doi: 10.1586/erp.12.48.

Faculty of Medicine, University of Banja Luka, Banja Luka, Republic of Srpska, Bosnia and Herzegovina.

BACKGROUND: Multiple reforms have been introduced in the Republic of Srpska to enhance prescribing efficiency. OBJECTIVES: First, assess their influence on utilization and expenditure on proton-pump inhibitors, statins and renin-angiotensin inhibitor drugs. Second, assess whether the Republic can obtain low prices for generics. Third, suggest additional reforms that could be introduced. METHODS: Observational study of all ambulatory care patients between 2003 and 2010. Defined daily doses (DDDs) and DDDs per 1000 inhabitants per day used for measuring changes in utilization. Reimbursed expenditure used as health insurance perspective. RESULTS: Increasing utilization in all three classes. Utilization of angiotensin-receptor blockers principally limited by prescribing restrictions. Reimbursed expenditure/ DDD in all three classes decreased by up to 82% in 2010 versus 2004, appreciably improving prescribing efficiency for the statins. Increased utilization of esomeprazole at higher reimbursed expenditure/ DDD, and similarly angiotensin-converting enzyme-inhibitor combinations at higher expenditure versus single drugs, limited the ability to fully capitalise on these reductions. CONCLUSION: Multiple measures helped lower expenditure/ DDD, providing hope to countries with small populations. Additional measures are planned to further improve prescribing efficiency in the Republic of Srpska.

Memišević H, Sinanović O. Predictors of visual-motor integration in children with intellectual disability. Int J Rehabil Res. 2012 Dec;35(4):372-4. doi: 10.1097/MRR.0b013e32835a23d0.

Center for Education and Rehabilitation of Children with Intellectual Disability, Sarajevo, Bosnia and Herzegovina.

The aim of this study was to assess the influence of sex, age, level and etiology of intellectual disability on visual-motor integration in children with intellectual disability. The sample consisted of 90 children with intellectual disability between 7 and15 years of age. Visual-motor integration was measured using the Acadia test of visual-motor integration. A multiple regression analysis was used for data analysis. The results of this study showed that sex, level of intellectual disability, and age were significant predictors of visual-motor integration. The etiology of intellectual disability did not play a significant role in predicting visual-motor integration. Visual-motor integration skills are very important for a child's overall level of functioning. Individualized programs for the remediation of visual-motor integration skills should be a part of the curriculum for children with intellectual disability.

Miljko M, Grle M, Kožul S, Kolobarić M, Djak I. Intercondylar notch width and inner angle of lateral femoral condyle as the risk factors for anterior cruciate ligament injury in female handball players in Herzegovina. Coll Antropol. 2012 Mar;36(1):195-200.

Mostar University Hospital, Institute of Radiology, Mostar, Bosnia and Herzegovina.

The principal purpose of this prospective study was to examine intercondylar notch size and the value of inner angle of lateral femoral condyle as the risk factors for noncontact anterior cruciate ligament ACL injury and than to correlate them to the physical values of the athletes such as body mass index (BMI), hight, wight, etc. There are indentified two type of risk factors, external include shoes-surface interaction, type of playing surface, weather conditions and internal include anatomic, neuromuscular, biomechanical and hormonal factors that may predispose female athlets to noncontact injury of ACL. Among anatomic factors, intercondylar notch stenosis and larger inner angle of lateral condyle of femur as the factors which can cause

impigement of ACL, were related to an increased risk of injury of ACL. In this study were included 51 female athlete. In the study group there were 24 female handball players with ACL tear and in control group there were 27 female handball players without any type of injury of the knee, who are practicing handball on a daily basis for at least for two years. In the first step, were gathered clinical data performed by orthopaedic surgeon. In the second step, the femoral notch width and the inner angle of lateral condyle of femur were measured on coronal MR-images. Study has shown that value of inner angle of lateral condyle of femur was significantly higher in athletes with ACL tear compared to those without. Value of width of intercondylar notch was statisticaly smaller in athletes with ACL tear, compared to those without. In the conclusion the inner angle of lateral femoral condyle is better predicting factor for ACL tear in young female handball players compared to intercondylar notch width.

Pranjić N, Nuhbegović S, Brekalo-Lazarević S, Kurtić A. Is adrenal exhaustion synonym of syndrome burnout at workplace? Coll Antropol. 2012 Sep;36(3):911-9.

Service of Occupational Health Tuzla in Tuzla Canton, Department of Occupational Pathology and Toxicology, Tuzla, Bosnia and Herzegovina.

The objective of this study is the assessment of the association of burnout syndrome with adrenal exhaustion specific symptoms and signs among 116 patients who were exposed to violence or mobbing at workplace and who were treated during 2005 to 2008 in Department of Occupational Pathology and Toxicology Tuzla; to detect symptoms and signs of adrenal exhaustion differences between patients who were exposed to act of violence as acute catastrophic event and patients who were long-term exposed to mobbing or chronic distress at workplace. MATERIAL AND METHODS: Data of 86 employees who were exposed to mobbing > 1 years (chronic distress syndrome) and data of 30 employees who were exposed to act of violence as acute traumatic crisis situation (evaluation in first week after acute stress situation and post control observation 6 months later). TOOLS FOR ASSESSMENT WERE CLINICAL EXAMINATION AND QUESTIONNAIRES: Occupational stress questionnaire (OSQ short version), self-constructed Questionnaire about symptoms and signs of Adrenal exhaustion; self-constructed mobbing questionnaire; and Maslach--Burnout Inventory. RESULTS: The patients expressed their traumatic experiences during exposure to stress more than 1 year (long-term exposure) which were compared with acute stress experiences (mostly high level of stress intensity. CONCLUSION: when workers constant expose to repeat mobbing behavior or have perception of extended distress reaction after act of violence at workplace they are suffering of Syndrome burnout and clinical picture of adrenal fatigue.

Prodanović N, Špirić Z, Trninić G, Erić M. Digital clubbing as an unusual complication of the secondary hyperparathyroidism associated with atypical neutrophils: a case report. Eur Rev Med Pharmacol Sci. 2012 Oct;16 Suppl 4:98-102.

Department of Rheumatology and Clinical Immunology, Clinical Center Banja Luka, Republic of Srpska, Bosnia and Herzegovina.

Digital clubbing is a rare clinical finding and usually represents a sign of underlying disease.There are only few cases of digital clubbing in patients with primary hyperparathyroidism or with secondary hyperparathyroidism (SHPT) during long-term hemodialysis. We haven't come across papers dealing with the relation of digital clubbing and SHPT caused by vitamin D deficiency. In this article, we report a case of 43 year-old female patient with prominent clubbing of the fingers and toes, and 22 year history of SHPT caused by vitamin D deficiency. Current radiographic findings of the hands and feet are actually uncommon, and they show massive osteolytic lesions of numerous phalanges, which is the consequence of long-time untreated SHPT. Besides, our patient has a rare case of neutrophils with bilobed nuclei and decreased cytoplasmic granularity. This paper for the first time describes digital clubbing as an unusual complication of the SHPT caused by vitamin D deficiency associated with atypical neutrophils.

Radošević B, Bukara-Radujković G, Miljković V, Pejičić S, Bratina N, Battelino T. The incidence of type 1 diabetes in Republic of Srpska (Bosnia and Herzegovina) and Slovenia in the period 1998-2010. Pediatr Diabetes. 2012 Aug 28. doi: 10.1111/j.1399-5448.2012.00898.x. [Epub ahead of print]

Clinic for Endocrinology, Diabetes and Metabolic diseases, Clinical Centre Banja Luka, and School of Medicine, University of Banja Luka, Banja Luka, Republic of Srpska, Bosnia and Herzegovina.

OBJECTIVE: To establish and compare the incidence and trends of type 1 diabetes mellitus (T1DM) in Republic of Srpska and Slovenia in age group 0-18 yr from 1998 to 2010. METHODS: The subjects (413 newly diagnosed T1DM patients in the Republic of Srpska and 664 in Slovenia) were grouped into the age groups: 0-4, 5-9, 10-14, and 15-18 yr. Confidence intervals (CI) for crude incidence rates were estimated assuming numbers of cases were counts from the

Poisson distribution. Gender and age-specific standardization was done according to the EURODIAB criteria. Statistical analysis used Poisson-regression models to analyze difference rate between countries and to investigate the incidence trend. RESULTS: Case ascertainment was estimated to be 99.95% for the Republic of Srpska and 100% for Slovenia by using the capture-recapture method. The standardized incidence of T1DM for age group 0-18 yr in the Republic of Srpska was 7.5/100 000/yr (95% CI: 6.8-8.3). For the same period and the same age group incidence in Slovenia was 12.5/100 000/yr (95% CI: 11.5-13.5). Annual increase in the incidence in the Republic of Srpska was 2.3% (95% CI: -0.3 to 5.0%), whereas in Slovenia 4.3% (95% CI: 2.2-6.5%). CONCLUSION: The incidence for age group 0-18 yr standardized to the world population is remarkably higher in Slovenia than in the Republic of Srpska. Further follow-up and investigations are needed to explain the high difference in incidence of T1DM between the two geographically related countries.

Ravlija J, Vasilj I. Communication in crisis situations in the process of immunization. Coll Antropol. 2012 Sep;36(3):1069-73.

Public Health Institute of Federation of BIH, Mostar, Bosnia and Herzegovina.

Immunization is one of the most effective medical interventions in the prevention of the disease and represents the easiest and most cost-effective investment in health. The strategy of controlling contagious diseases that can be prevented through immunization has a long tradition in B&H. Mandatory immunizations are administered against ten diseases. Although the development of new technologies, the efforts of the pharmaceutical industry, the development of new vaccines provides better vaccines in terms of greater safety and effectiveness it should be pointed out that no vaccine is "absolutely effective and safe", and it will not achieve the immune response in 100% vaccinated, also there are possible side effects and unexpected reactions that could occur. Vaccination is often a media issue because previously unnoticed local, isolated events-side effects and complications of vaccination are now accompanied by media attention as there are now numerous and fast communication channels (internet, e-mail, TV1 etc.) and media evolved from being less "controlled" to more "commercial". Doubt in benefit of vaccination is growing even among health professionals who are expected to provide up-to-date, understandable information, and issue information about immunization benefits and potential risks. It is therefore important for health professionals to be well informed, to be a good source of authoritative, scientific and reasonable advice, and to speak openly about the benefits and risks of vaccination so that consumers fully understand both possible outcomes of vaccination. This takes communication skills, particularly in crisis situations connected with vaccination. Health professionals are thus faced with a changing attitude toward importance of immunization in the social climate where risk is less tolerated than ever before.

Salkić A, Brkić F, Čičkušić A, Čičkušić E, Altumbabić H. Thyroid cancer in Tuzla region of Bosnia and Herzegovina: a 10-year study (1999-2008). Coll Antropol. 2012 Nov;36 Suppl 2:53-7.

University Clinical Centre Tuzla, Department of ENT Surgery, Tuzla, Bosnia and Herzegovina.

Bosnia and Herzegovina (B&H) is one of the Eastern European countries with lacking data on thyroid cancer (TC) epidemiology. We aimed to assess the incidence of TC in Tuzla Canton of B&H during a 10-year period (1999-2008). We retrospectively evaluated 65000 hospital records of both inpatients and outpatients with possible thyroid symptoms residing in Tuzla Canton of B&H (total of 496280 inhabitants) between 1999 and 2008. Patients with histological proof of TC were included in study. Incidence rates were calculated with age standardisation using European standard population. Trends in incidence were evaluated as moving three-year averages. During observed period 117 patients met the diagnostic criteria for TC with male to female ratio of 1:4.85. Median age of all cases was 51 years (interquartile range: 41 to 60) with men in average 9 years older than women at the time of diagnosis. The mean annual standardized incidence was found to be 2.30/10(5) (% 95 CI = 1.38-3.22) inhabitants ranging from 1.0 to 3.2 per 10(5). The average crude incidence in men was 0.82/10(5) and 3.83/10(5) in women. The prevalence of TC, at the end of the observed period was found to be 23.58/10(5) (% 95 CI = 19.3-27.58). There is a slight decline of incidence in our region during the observed period, but with the increase in the latest years of the study. This increase is probably the result of combination of various factors, mainly the better detection of new cases due to wider availability of diagnostics. Based on depicted trends, we believe that in the future years, TC incidence in our region will continue to rise.

Subasi A. Medical decision support system for diagnosis of neuromuscular disorders using DWT and fuzzy support vector machines. Comput Biol Med. 2012 Aug;42(8):806-15. doi: 10.1016/j.compbiomed.2012.06.004. Epub 2012 Jul 2.

International Burch University, Faculty of Engineering and Information Technologies, Sarajevo, Bosnia and Herzegovina.

The motor unit action potentials (MUAPs) in an electromyographic (EMG) signal provide a significant source of information for the assessment of neuromuscular disorders. In this work, different types of machine learning methods were used to classify EMG signals and compared in relation to their accuracy in classification of EMG signals. The models automatically classify the EMG signals into normal, neurogenic or myopathic. The best averaged performance over 10 runs of randomized cross-validation is also obtained by different classification models. Some conclusions concerning the impacts of features on the EMG signal classification were obtained through analysis of the classification techniques. The comparative analysis suggests that the fuzzy support vector machines (FSVM) modelling is superior to the other machine learning methods in at least three points: slightly higher recognition rate; insensitivity to overtraining; and consistent outputs demonstrating higher reliability. The combined model with discrete wavelet transform (DWT) and FSVM achieves the better performance for internal cross validation (External cross validation) with the area under the receiver operating characteristic (ROC) curve (AUC) and accuracy equal to 0.996 (0.970) and 97.67% (93.5%), respectively. These results show that the proposed model have the potential to obtain a reliable classification of EMG signals, and to assist the clinicians for making a correct diagnosis of neuromuscular disorders.

Šoljić V, Perak RB, Vukojević K, Saraga-Babić M, Bubalo P, Karan D, Todorović J, Batinić D. ZAP-70 expression and proliferative activity in chronic lymphocytic leukemia. Leuk Lymphoma. 2012 Nov 19. [Epub ahead of print]

Department of Histology and Embryology, School of Medicine, University of Mostar, Mostar, Bosnia and Herzegovina.

The expression of 70 kDa protein zeta-associated protein (ZAP-70) in chronic lymphocytic leukemia (CLL) has been used to detect those patients with more aggressive disease. The aim of this study was to determine the proliferative activity of ZAP-70(+) leukemic cells by immunocytochemical methods. The study was undertaken on native blood marrow (BM) and peripheral blood (PB) smears from 65 patients with CLL. ZAP-70 was expressed in leukemic cells of 35 patients (54%). We demonstrated that ZAP-70 immunoreactivity correlated with Rai 0-IV ($p = 0.002$) and Binet A-C stages ($p < 0.001$), total tumor mass (TTM score) ($p < 0.001$), $\beta(2)$-microglobulin ($p = 0.006$), atypical lymphocytes ($p < 0.001$) and proliferative activity in bone marrow and peripheral blood ($p = 0.014$, $p = 0.002$, respectively) using $\chi(2)$ test and Mann-Whitney test. ZAP-70 protein expression is in direct correlation with the poorer prognostic parameters, which additionally confirms the successful method of detection of ZAP-70 expression. Higher Ki-67 expression in BM and PB smears of patients with ZAP-70(+) disease indicates higher proliferating compartments, which may contribute to poorer prognosis.

Tahirović H, Toromanović A. Adhesion of the labia minora in girls: a common disorder that is rarely considered. J Pediatr Endocrinol Metab. 2012;25(7-8):631-2.

Department of Pediatrics, University Clinical Center, Tuzla, Bosnia and Herzegovina.

No abstract available.

Vukojević M, Dizdarević A, Novaković D. Early detection and recognition of children with ADHD (attention deficit hiperactivity disorder) symptoms. Coll Antropol. 2012 Dec;36(4):1183-8.

University of Mostar, School of Medicine, Mostar, Bosnia and Herzegovina.

Aim of this study was to determine the probability of occurrence of Attention Deficit/Hyperactivity Disorder- ADHD in children of preschool age and early school age, and to identify differences in the assessment of children identified with high probability for the disorder with regard to assessment by parents and teachers, and with respect on age and sex of children. Total of 107 children were included in the study: 51 girls and 56 boys. The study employed two questionnaires: Questionnaire for Analysis at School for teachers and Questionnaire for Analysis at Home for parents. Both questionnaires contained 39 statements which covered three dimensions of child's behavior needed for ADHD diagnosis. Raw data in each questionnaire were converted according to the standard norms of Guide to Standard Scores (SS) and Total Standard Scores (TSS) and as such were used for statistical analysis. It was found that a considerable number of children demonstrated high probability for ADHD disorder in assessments done by both parents and teachers. Parents recognize probability of ADHD presence more frequently among male children, while teachers recognize this probability more often among female children. Research shows that a significant percentage of children from the entire sample have been labeled with significant ADHD symptoms. Given the age of the child both parents and teachers recognize similar levels of high ADHD probability. Future studies should be directed toward early detection and recognition of children with ADHD syndrome, and clinical evaluation as a first step toward successful treatment and prevention of additional psychological and other problems in an adult.

Zerem E, Imamović G, Latić F, Mavija Z. Prognostic value of acute fluid collections diagnosed by ultrasound in the early assessment of severity of acute pancreatitis. J Clin Ultrasound. 2013 May;41(4):203-9. doi: 10.1002/jcu.21995. Epub 2012 Sep 18.

Department of Gastroenterology, University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina.

PURPOSE: To evaluate the prognostic value of acute fluid collections (AFC) diagnosed by conventional transabdominal ultrasound in the early assessment of severity acute pancreatitis (AP). METHODS: We studied 128 consecutive patients with AP between March 2006 and March 2011. The predictor was the number of AFC. Outcome measure was the occurrence of complications. Abdominal sonogram, contrast-enhanced CT, and pancreatitis-specific clinical and laboratory findings were performed. RESULTS: AFC were associated with complications ($p < 0.0001$), Balthazar grade ($p = 0.004$), Ranson score ($p < 0.0001$), and the majority of clinical, radiologic, and biochemical parameters for predicting complications of AP ($p < 0.05$). Univariate logistic regression also revealed significant association between the number of AFC and the occurrence of complications (OR 4.4; 95% CI 2.5-7.6). After the adjustment for covariates, AFC remained prognostic for complications and a cutoff point of >1 AFC was prognostic of their occurrence with 88% sensitivity and 82% specificity. CONCLUSIONS: AFC are related to the clinical course of AP and can predict its severity.

Zulčić-Nakić V, Pajević I, Hasanović M, Pavlović S, Ljuca D. Psychological problems sequalae in adolescents after artificial abortion. J Pediatr Adolesc Gynecol. 2012 Aug;25(4):241-7. doi: 10.1016/j.jpag.2011.12.072.

Department of Gynecology and Obstetrics, University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina.

STUDY AND OBJECTIVES: Controversy exists over psychological risks associated with unwanted pregnancy and consecutive abortion. The aim of this study was to assess the psychological health of female adolescents following artificial abortion up to 12(th) week of pregnancy. DESIGN: The control case study. SETTING: The study was carried out in the Department of Gynecology and Obstetrics, University Clinical Center Tuzla, in Bosnia-Herzegovina. PARTICIPANTS: We assessed 120 female adolescents. The mean (SD) age of the patients was 17.7 (1.5) years experiencing sexual intercourse in the age of 14-19 years for trauma experiences, presence of posttraumatic stress symptoms, depression and anxiety as state, and anxiety as trait. Sixty adolescents had intentional artificial abortion and 60 had sexual intercourse but did not become pregnant. MAIN OUTCOME MEASURES: We used the PTSD Questionnaire, the Beck Depression Inventory, and the Spielberger State Trait Anxiety Inventory (Form Y) for assessment of anxiety in adolescents. Basic socio-demographic data were also collected. RESULTS: PTSD presented significantly more often in adolescents who aborted pregnancy (30%), than in adolescents who did not abort (13.3%) (odds ratio = 4.91 (95%CI 0.142-0.907) $P = 0.03$). Anxiety as state and as trait were significantly higher in the abortion group, as the mean (SD) anxiety score of patients was 59.8 (8.9), 57.9 (9.7) respectively, than in non-abortion group 49.5 (8.8), 47.3 (9.9) respectively ($t = 6.392$, $P < 0.001$; $t = 5.914$, $P < 0.001$, respectively). Adolescents who aborted pregnancy had significantly higher depression symptoms severity 29.2 (5.6) than controls 15.2 (3.3) ($t = 8.322$, $P < 0.001$), and they presented significantly more often depression (75%), than adolescents who did not abort (10%) ($\chi(2) = 53.279$, $P < 0.001$). Logistic regression showed that only experience of life threatening(s) and injury of other person(s) reliably predicted PTSD, whereas abortion and experience of life threatening(s) reliably predicted depression. CONCLUSION: Adolescents who aborted pregnancy presented significantly greater prevalence of PTSD and depression, and significantly greater depression severity and anxiety as state and trait than those who did not abort. Abortion predicted depression only, and did not predict PTSD.

by Nerma Tanović

Instructions to authors

Scope

Acta Medica Academica is a biannual, peer-reviewed journal that publishes: (1) reports of original research, (2) original clinical observations accompanied by analysis and discussion, (3) analysis of philosophical, ethical, or social aspects of the health profession or biomedical sciences, (4) critical reviews, (5) statistical compilations, (6) descriptions of evaluation of methods or procedures, (7) case reports, and (8) images in clinical medicine. The fields covered include basic biomedical research, clinical and laboratory medicine, veterinary medicine, clinical research, epidemiology, phramacology, public health, oral health, and medical information.

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Acknowledge. Anyone who contributed towards the study by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. List the source(s) of funding for the study and for the manuscript preparation in the acknowledgements section.

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Sample references

Articles in journals

Standard journal article (*List the first six authors followed by et al.*):

> Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002;347(4):284-7.

More than six authors:

> Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6.

Organization as author:

> Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension. 2002;40(5):679-86.

No author given:

21st century heart solution may have a sting in the tail. BMJ. 2002;325(7357):184.

Volume with supplement:

Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache. 2002;42(Suppl 2):S93-9.

Issue with supplement:

Glauser TA. Integrating clinical trial data into clinical practice. Neurology. 2002;58(12 Suppl 7):S6-12.

Issue with no volume:

Banit DM, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. Clin Orthop. 2002;(401):230-8.

Letters or abstracts:

Tor M, Turker H. International approaches to the prescription of long-term oxygen therapy [letter]. Eur Respir J. 2002;20(1):242.;
Lofwall MR, Strain EC, Brooner RK, Kindbom KA, Bigelow GE. Characteristics of older methadone maintenance (MM) patients [abstract]. Drug Alcohol Depend. 2002;66 Suppl 1:S105.

Article republished with corrections:

Mansharamani M, Chilton BS. The reproductive importance of P-type ATPases. Mol Cell Endocrinol. 2002;188(1-2):22-5. Corrected and republished from: Mol Cell Endocrinol. 2001;183(1-2):123-6.

Article with published erratum:

Malinowski JM, Bolesta S. Rosiglitazone in the treatment of type 2 diabetes mellitus: a critical review. Clin Ther. 2000;22(10):1151-68; discussion 1149-50. Erratum in: Clin Ther. 2001;23(2):309.

Article published electronically ahead of the print version:

Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sacderived precursor cells. Blood. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

Books and other monographs

Personal author(s):

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

Editor(s), compiler(s) as author:

Gilstrap LC 3rd, Cunningham FG, VanDorsten JP, editors. Operative obstetrics. 2nd ed. New York: McGraw-Hill; 2002.

Organization(s) as author:

Royal Adelaide Hospital; University of Adelaide, Department of Clinical Nursing. Compendium of nursing research and practice development, 1999-2000. Adelaide (Australia): Adelaide University; 2001.

Chapter in a book:

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

Conference paper:

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

Dissertation:

Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

Other published material

Newspaper article:

Tynan T. Medical improvements lower homicide rate: study sees drop in assault rate. The Washington Post. 2002 Aug 12;Sect. A:2 (col. 4).

Dictionary and similar references:

Dorland's illustrated medical dictionary. 29th ed. Philadelphia: W.B. Saunders; 2000. Filamin; p. 675.

Electronic material

CD-ROM:

Anderson SC, Poulsen KB. Anderson's electronic atlas of hematology [CD-ROM]. Philadelphia: Lippincott Williams & Wilkins; 2002.

Audiovisual material:

Chason KW, Sallustio S. Hospital preparedness for bioterrorism [videocassette]. Secaucus (NJ): Network for Continuing Medical Education; 2002.

Journal article on the Internet:

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [serial on the Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 3 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htm.

Monograph on the Internet:

Foley KM, Gelband H, editors. Improving palliative care for cancer [monograph on the Internet]. Washington: National Academy Press; 2001 [cited 2002 Jul 9]. Available from: http://www.nap. edu/books/0309074029/html/.

Homepage/Web site:

Cancer-Pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources, Inc.; c2000-01 [updated 2002 May 16; cited 2002 Jul 9]. Available from: http://www.cancer-pain.org/.

Part of a homepage/Web site:

American Medical Association [homepage on the Internet]. Chicago: The Association; c1995-2002 [updated 2001 Aug 23; cited 2002 Aug 12]. AMA Office of Group Practice Liaison; [about 2 screens]. Available from: http://www.ama-assn.org/ama/pub/category/1736.html.

Database on the Internet:

Who's Certified [database on the Internet]. Evanston (IL): The American Board of Medical Specialists. c2000 – [cited 2001 Mar 8]. Available from: http://www.abms.org/newsearch.as.

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