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Use of colposcopy for detection of squamous intraepithelial lesions

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ABSTRACT

Introduction: Pap smear, the main tool of cervical cancer screening is not always available, but some patients are in urgent need for proper diagnostic. Aim of this article was to investigate accuracy of colposcopy for detection of squamous intraepithelial lesions of low or high grade (LGSIL, HGSIL) and to promote colposcopy as useful tool for detection of patients in need for immediate further diagnostics.

Methods: Prospective multicentric study performed in B&H in 2012-2014 included 87 patients with colposcopic images related to squamous intraepithelial lesion (SIL) who formed experimental group: 56 patients with colposcopic images related to LGSIL and 31 patients related to HGSIL. Control group included 50 patients without colposcopic abnormalities. To test accuracy of colposcopy, PAP smear and histology were used. For statistical analysis $\chi^2$ was used.

Results: 94.5% patients in experimental group had abnormal PAP test: 64.3% correlated to LGSIL ($\chi^2 = 60.48 \ P < 0.0001$), while 64.5% correlated to HGSIL ($\chi^2 = 54.23 \ P < 0.0001$) Odds Ratio = 490; 95% CI = 42.024 to 5713.304. HGSIL was confirmed in 27 (87%) cases by histology (CIN II/CIN III). There were no statistically significant differences between colposcopic finding and histology results (Yates-corrected $\chi^2 = 0.33 \ P = .5637$).

Conclusions: This study showed high level of correlation between colposcopy and PAP results (63-64%) and to histology for HGSIL (87%). In absence of PAP test colposcopy could be used to select patients in need for biopsy.

Keywords: Papanicolaou test; cervical intraepithelial neoplasia; colposcopic surgical procedures

INTRODUCTION

Squamous intraepithelial lesion (SIL) starts at the cellular level as transformation and abnormal growth of squamous cells on the surface of the cervix. In the cervical channel intraepithelial lesion
starts as squamous metaplasia, which includes proliferation of undifferentiated reserve cells, columnar cells and their transformation into the squamous cells. SIL begin as cellular change at low grade level (LGSIL) and during the time could advance to high grade lesion (HGSIL) and cervical cancer. When detected, SIL can be successfully treated at any stage. It is well known and scientifically proven fact that cervical cancer screening program decreases incidence of cervical cancer by detecting early stages of intraepithelial changes (SIL) using PAP test as main tool (1). For the patients with abnormal PAP smear, colposcopy is usually the next step. However, what happens if the cervical cancer screening is not available and there is lack of information about disease prevention possibility? What happens if PAP control depends only on patients’ awareness of disease? In such circumstances usually, incidence of inoperable cervical cancer is very high. Where does Bosnia and Herzegovina stand in this respect?

Health system in Bosnia and Herzegovina does not provide cervical cancer screening at any level (State level, Entity level, Cantonal level). System for education of patients does not exist. Even more, there is no cancer database. First official reports about cancer incidence including cervical cancer were published by Public Health Institute of Federation Bosnia and Herzegovina (PBIFB&H) in 2007. According to that report cervical cancer is second most common cancer in females in the Federation Bosnia and Herzegovina (FB&H). Furthermore in the period 1996-2007 there were 20-25/100.000 newly detected cervical cancers in Tuzla Canton. Only 20.3% of those cases were in operable stages (2).

If we do not have cervical cancer screening program and if we cannot provide a PAP test as frequently as needed (due to lack of means), could we use colposcopy to select patients who are in need for a kind of “immediate” PAP smear or even biopsy? The aim of this article was to investigate accuracy of colposcopy for detection of squamous intraepithelial lesions (SIL) and to promote colposcopy as tool for detection of patients in need for immediate PAP smear in the health systems without screening program.

METHODS

Study design

This was prospective multi-centric study that took a place in Obstetrics and Gynecology practice Omeragić, Tuzla, Health Centre of Tuzla, Health Centre Tešanj, Cantonal Hospitals of Mostar and Clinical Centre Banjaluka, during the period January 2012 to January 2014.

Patients

The patients in the study were selected in accordance to colposcopic criteria for squamous intraepithelial lesions.

Experimental group marked as Group A was formed by 87 patients. They were selected by means of colposcopy which showed one or more coploscopic images (markers) related to squamous intraepithelial lesion (SIL).

Colposcopic assessment of lesions was based on the following characteristics: location of the lesion related to Transformation zone (within or outside of the Transformation zone), reaction to 3-5% solution of acetic acid, color intensity, surface and borders, vascularization (inter-capillary distance), speed of emergence and time of duration.

Group A was divided in two subgroups: A1 and A2. Subgroup A1 included 56 patients with colposcopic images that are clearly defined as characteristics of LGSIL. Subgroup A2 included 31 patients with colposcopy images that are clearly defined as characteristics of HGSIL. Extensive lesion that was spread over the broad area of surface of the cervix, in the same time, was indication for biopsy.

A group of 50 patients without any colposcopic changes related to SIL formed Control group marked as Group B.

To test accuracy of colposcopy

1. PAP smear that was taken from all patients including experimental and control group was analyzed. Results were interpreted using Bethesda system: BCC - Benign Cellular Changes, ASCUS-atypical squamous cells undetermined significance, ASC H- atypical squamous cell which does not exclude HGSIL, LGSIL-low grade squamous cell intraepithelial
lesion, HGSIL-high grade squamous cell intraepithelial lesion (3).

2. Colposcopy directed biopsy was done in all patients from Subgroup A2. Histological results were analyzed as well.

Previous colposcopy and/or PAP smear were without any abnormality and were not taken 24 months prior to the beginning of the study. Cancers of any stage were not included in the study. Patients with unclear finding were not included in study.

Statistical analysis
Results were analyzed by descriptive and analytical statistics. Chi square test with or without Yates correction, Odds ratio, Fischer exact test were used. The level of significance was defined as p<0.05. For statistical analysis software GrahPad Prism 6 for Windows, version 6 was used.

RESULTS
Experimental group and control group were homogenous. There were:
1. similar participation of nulliparous Group A 31 or 35%, Group B 16 or 32%,
2. similar distribution within the age groups 20-50 year
3. similar participation of those who previously did not have PAP smear and colposcopy Group A 31 or 35% and Group B 19 or 38%.

In experimental group (Group A) there were 87 patients with single or multiply markers for SIL. Out of all 82 (94.2%) had abnormal PAP test results including all varieties of Bethesda nomenclature.

In control group (Group B) out of all, 17 (34%) patients had abnormal PAP test. Difference is statistically significant ($\chi^2 = 18.91 \ P < 0.0001$: Odds Ratio = 3.027; 95% CI = 1.851 to 4.951) According to statistical analysis it means that patient with positive colposcopic markers for SIL have 3 times higher chances to have abnormal PAP test (Figure 1).

Out of all patients in experimental group there were 56 patients with colposcopic images defined as markers for LGSIL. They formed Subgroup A1. Those patients had markers located within the transformation zone (100%). Aceto-white (AW) epithelium was the most frequently seen (53 or 94.6%) as a single marker (50 or 89.3%) or associated with vascular changes, mosaic (M) or/and punctuation (P) (3 or 5.35%).

When detected outside of Transformation zone (31 patients) more than one markers were seen most often. Aceto-white epithelium (AW) is most frequently seen, but only in two cases as a single marker (6.4%). Vascular changes (Mosaic, Punctuations) associated with AW epithelium were present in 29 (93.5%) cases. These images (markers) are defined as colposcopic criteria for HGSIL. Patients with such images formed Subgroup A2 (Table 1).

PAP smear was performed in all patients including control group. Distribution of PAP diagnosis (Bethesda categories) per groups was shown in Table 2.

In control group there were 17 (34%) PAP results marked as abnormal. In 12 (24%) cases it was ASC-US, atypical cells were related to inflammation or lack of hormonal activity, while only 8% had SIL.
ASCUS was also seen in subgroups A1 (7.1%) and A2 (3.2%).

Analysis of LGSIL and HGSIL results showed significant differences compared to control group LGSIL ($\chi^2 = 60.48$ P < 0.0001; Odds Ratio = 141; 95% CI = 29.670 to 670.067), HGSIL ($\chi^2 = 54.23$ P < 0.0001 Odds Ratio = 490; 95% CI = 42.024 to 5713.304) which means that chances for LGSIL or HGSIL in PAP test are very high if colposcopy result are positive too.

All thirty-one (31) patients with extensive cervical tissue deterioration diagnosed by colposcopy as HGSIL (Subgroup A2) had biopsy. The following correlation between colposcopy and histopathology diagnosis was noticed (Table 3).

There are no statistically significant differences between colposcopic finding and histology results (Yates-corrected $\chi^2 = 0.33$ P = .5637) but there is a four times higher possibility that histology will show cervical intraepithelial lesion of medium grade (CIN II) and two times higher possibility that histology will show high grade dysplasia (CIN III) [Odds Ratio = 2.086; 95% CI (logit method)= 0.627202 to 6.940587] if colposcopic images related to HGSIL are present [Odds Ratio = 4; 95% CI (logit method) = 0.362 to 44.112].

**DISCUSSION**

Correlation between colposcopy and PAP, including all varieties of Bethesda nomenclature is high. Out of all 94.2% patient had both colposcopy and PAP results abnormal. According to statistical analyses patient with present colposcopic images (markers) for SIL have 3 times higher chances to have abnormal PAP test. Such results show that colposcopy markers have high accuracy in detection of cellular pathology. High level of correlation is reported by other researches (3-6). PAP test results correlate with colposcopic staging, too: 64.3% for LGSIL ($\chi^2 = 60.48$ P < 0.0001), 64.5% for HGSIL ($\chi^2 = 54.23$ P < 0.0001). In literature similar results are shown. Parvin at all reported correlation in 76.1% patients. Koigi-Kamau R at all reported correlation in 59-65% cases (7-9).

Biopsy or Loop excision of transformation zone (LETZ) was performed in 31 patients from subgroup A2/HGSIL. Medium and high grade intraepithelial dysplasia (CIN II/CIN III) were found by histology in 87% cases. There are no statistically significant differences between colposcopic finding and histology results (Yates-corrected $\chi^2 = 0.33$ P = .5637). Correlation between colposcopic findings and histology studied by many researchers showed high level of correlation. Savage EW at all reported accuracy of directed biopsies in 96% cases (10). Boelter WC 3rd at all found 96 - 98% correlation between the colposcopic findings, biopsies and cone specimens (11). Recent study by Boicea A at all showed correlation of 78.5% in the CIN I category, 84% in the CIN II category, 88.6% in the CIN III category (12).

ASC-H was detected in 12% patients in Group A. However, ASC-H does not exclude LG or HG SIL (13-17). In the same time 34% abnormal PAP smear results in control group additionally confirm hypothesis that the tissue architecture is not necessarily deteriorated from the beginning, particularly in cases of HPV infection.

Those patients were selected for intense follow-up. Same protocol were reported by other researchers (14,18,19).
CONCLUSIONS

Colposcopy is useful method for detection of early stages of SIL. This study showed high level of correlation between colposcopy and both, PAP test and histology. In the absence of cancer screening program and regular frequency of PAP smear diagnostics or if PAP test is not available, it can be used as a non-invasive, inexpensive and accurate tool.

CONFLICT OF INTEREST

The authors declare no conflict of interest. No specific funding was received for this study.

REFERENCES


The evaluation of B-type Natriuretic Peptide and Troponin I in acute myocardial infarction and unstable angina

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ABSTRACT

Introduction: The diagnostic utility of B-type natriuretic peptide (BNP) has prompted interest in its use as an aid in the detection of early heart failure and assessment of diseases. The first objective of this study was measurement of BNP and troponin I (TnI) blood levels in patients with acute myocardial infarction (AMI) and unstable angina. The second objective of this study was to find a correlation between TnI and BNP in blood.

Methods: The concentrations of BNP and TnI in 150 blood levels were determined using CMIA (chemiluminescent microparticle immunoassay) Architect and 2000 (Abbott diagnostics). The retrospective study included 100 patients who were hospitalized at the Department of Internal Medicine of the University Clinical Center Sarajevo and 50 healthy control. The reference blood range of BNP is 0-100 pg/mL and TnI is 0.00-0.4 ng/mL.

Results: In the patients with AMI the mean value of BNP is 764.48 ± 639.52 pg/mL and TnI is 2.50 ± 2.28 ng/mL. The patients with unstable angina have BNP 287.18 ± 593.20 pg/mL and TnI 0.10 ± 0.23 ng/mL. Our studies have shown that the correlation between BNP and TnI was statistically significant for p < 0.05 using Student t test with correlation coefficient r = 0.36.

Conclusions: BNP and TnI levels can help to identify the patients with a high risk for cardiovascular diseases.

Keywords: BNP; TnI; acute myocardial infarction; unstable angina

INTRODUCTION

Since the discovery of the natriuretic peptides in the 1980s and their subsequent introduction into clinical laboratory testing in the 2000s, assays of B-type Natriuretic peptides (BNP) have gained widespread acceptance as important tools for diagnosis and risk stratification in the acute-care setting (1,2). BNP was first isolated from porcine brain tissue, but heart has been determined to be the major source. It is synthesized and released in the blood in response to volume overload or conditions that cause ventricular stretch, to control fluid and electrolyte homeostasis by interaction with
renin-angiotensin-aldosterone system. Pre-proBNP (134 amino acids) is synthesized in the cardiac myocytes and it is processed to a proBNP (108 amino acids) precursor molecule.

BNP is realized from cardiac myocytes due to their stretching, volume overload and high filling pressure (3-5). It is a neurohormone produced in the ventricular myocardium in response to dilatation and pressure overload, and its plasma concentration correlates with the magnitude of pressure and/or volume overload. As markers of neurohormonal activation, BNP and NT-proBNP were subsequently studied within clinical trials of acute coronary syndrome (ACS) as adjuncts to risk stratification and have been associated with short and long term mortality in (ACS) patients, even after adjusting for the presence of congestive heart failure (6,7). The levels of BNP increase with decreasing functional capacities and elevated levels in the patients with heart failure (HF) indicate disease progression. BNP levels are very high in the patients with HF, but remain low in the patients with acute dyspnea due to other causes such as chronic obstructive pulmonary disease, asthma or obesity. Plasma BNP values increase with increasing age and are higher in women than in men (2).

Unstable angina, for example is a common transitory phase of coronary ischemia, bordering on myocardial infarction (MI). It is a strong relationship with BNP and outcomes in ACS patients (8).

It has been previously reported that 21% of ambulatory patients with established chronic heart failure who are stable may have plasma BNP levels less than 100 pg/mL. All commercially available BNP assays incorporate the value 100 pg/mL as the diagnostic cut off (9). If BNP level is 100-500 pg/mL that requires further diagnostic evaluation ("grey zone"). If BNP is higher than 500 pg/mL there is probability of the heart failure (10).

Troponins I, T and C are structural proteins bound to the thin filaments (actin) in striated muscle. A small amount (5-8%) of troponin exists free in the cytosol. Elevated levels of cTnI (above the values established for non-MI specimens) are detectable in serum within 4 to 6 hours after the onset of chest pain, reach peak concentration in approximately after 8 to 28 hours, and remain elevated for 3 to 10 days following MI. Cardiac troponin is the preferred biomarker for the detection of myocardial injury based on improved sensitivity and superior tissue-specificity compared to other available biomarkers of necrosis, including CK-MB, myoglobin, lactate dehydrogenase, and others. The high specificity of cTnI measurements is beneficial in identify cardiac injury for clinical conditions involving skeletal muscle injury resulting from surgery, trauma or muscular disease (11). The Joint European Society of Cardiology/American College of Cardiology/American Heart Association/World Heart Federation Task Force redefinition of acute myocardial infarction (AMI) is predicated on the detection of increase or decrease of cardiac troponin (cTn), with at least 1 concentration above the 99th presence reference value in patients with evidence of myocardial ischemia. Blood samples for measurement of cTn are recommended to be drawn at presentation and 6-9 h later to optimize clinical sensitivity for ruling in AMI (12,13). The reference range for troponin I (TnI) in serum is 0.00-0.032 μg/mL.

In our study we have measured BNP and TnI blood levels in the patients with ACS in a first 12 hours and investigate correlation with peak value of TnI.

METHODS

Patients

Our research included patients (n = 100) and 50 healthy control group in period from January till September 2011. The retrospective study included patients who were hospitalized at the Heart Disease Department at the University Clinical Center Sarajevo. In our study we included patients with acute myocardial infarction (AMI) and unstable angina. The clinical spectrum of ACS consists of ST elevated myocardial infarction (STEMI) and non-ST elevated myocardial infarction (NSTEMI)/or unstable angina (UA), which are classified using electrocardiography (ECG) changes. The study included patients who had a level of BNP more than 100 pg/mL and level of TnI more than 0.032 μg/mL. Our research included determination of BNP and TnI in blood of patients in a first 12 hours of ACS symptoms.

The healthy control group included patients without AMI and unstable angina using electrocardiography (ECG), BNP level < 100 pg/mL and TnI level <0.032 μg/mL. The patients with history of
pulmonary thromboembolism, acute and chronic renal failure, end stage renal disease, sepsis, liver cirrhosis, chronic obstructive lung disease, hyperthyroidism and adult respiratory distress syndrome were excluded from the study. The research was done respecting ethical standards in the Helsinki Declaration.

Specimen preparation
Na-EDTA plasma should be used for the Architect BNP assay. Samples should be collected in plastic collection tubes, because the BNP molecule has proven to be unstable in glass containers. Specimens containing blood cells or particle matters may give inconsistent results and must be clarified by centrifugation prior to testing. Specimens with BNP assay value exceeding 5000.0 pg/mL are flagged with the code “>5000.0 pg/mL” and may be diluted using the Automated Dilution Protocol. The samples for determination of TnI should be collected in the tubes with gel. The TnI assay concentration greater than 50 ng/mL may be diluted using the Automated Dilution Protocol. The patients’ samples of blood were collected in Na-EDTA and gel Vacutainer test tubes (Becton Dickinson, Rutherford, NJ 07,070 U.S.) in volume of 3.5 mL.

Assays
All immunoassays require the use of labeled material in order to measure the amount of antigen or antibody. A label is a molecule that will react as a part of the assay, so that a change in signal can be measured in the blood after added reagent solution. CMIA is a noncompetitive sandwich assay technology to measure analytes. The amount of signal is directly proportional to the amount of analyte present in the sample.

Chemiluminescent microparticle immunoassay – CMIA
Architect BNP or TnI assay is a two-step immunoassay to determine the presence of BNP and TnI in human blood using CMIA technology. As a first step, sample, assay diluent and anti-antibody-coated paramagnetic particles are combined. BNP or TnI present in the sample binds to the anti-coated microparticles. After incubation and wash, anti-acridinium-labeled conjugate is added in the second step. Following another incubation and wash, pre-trigger and trigger solutions are then added to the reaction mixture. The pre-trigger solution (hydrogen peroxide) creates an acidic environment to prevent early release of energy (light emission), helps to keep microparticles from clumping and splits acridinium dye off the conjugate bound to the microparticle complex (this action prepares the acridinium dye for the next step). The trigger solution (sodium hydroxide) dispenses to the reaction mixture. The acridinium undergoes an oxidative reaction when it is exposed to peroxide and an alkaline solution. This reaction causes the occurrence of chemiluminescent reaction. N-methylacridone forms and releases energy (light emission) as it returns to its ground state. The resulting chemiluminescent reaction is measured as relative light units (RLU). A direct relationship exists between the amount of BNP in the sample and RLU detected by Architect System optics. The concentration of BNP or TnI will be read relative to a standard curve established with calibrators of known BNP and TnI concentration.

Statistical analysis
The results were statistically analyzed using NCSS and statistical software SPSS version 12.0 software, determined by the average value (x̄), standard deviation (SD) or median and interval. The date were not distributed normally we use Mann Whitney U-test. Pearson correlation test was used to assess association between measured parameters. P – Values less than <0.05 was considered as statistically significant.

RESULTS
The serum concentrations of BNP and TnI in the patients with AMI (acute myocardial infarction) and unstable angina are shown in Table 1. The study included 100 patients (53 men and 57 women), they were classified depending on their diagnosis and healthy control group without ACS. The average age was 64 years for the AMI patients, and 61 years for the patients with unstable angina. The value of BNP and TnI was higher in the group with AMI than the group with unstable angina. The healthy control group had a lower concentration of BNP and TnI than the patient groups.

Using Mann Whitney U test we made comparison of BNP and TnI levels among the groups including the
patients with AMI, unstable angina and the healthy control group. According to Mann-Whitney U test for $\alpha = 5\%$ the difference between concentrations of BNP in the patients with AMI and the patients with unstable angina were significant. The same test for $\alpha = 5\%$ has shown a significant difference between concentrations of BNP in patients with AMI and healthy control group. The results between the groups were statistically significant for $P<0.05$. The same test has shown a significant difference between concentrations of TnI in the patients with AMI and the patients with unstable angina for $P<0.05$.

In our study we found a significant correlation between the average concentrations of TnI and BNP with Pearson correlation coefficient ($r = 0.36$). Regression equation revealed a slope of 344.09 and a y axis intercept of 457.83. The results between average concentrations of TnI and BNP were statistically significant for $P<0.05$ using Student t test, the results are shown in Figure 1.

**DISCUSSION**

Natriuretic peptides elevations have shown the correlation with wall stress, and thus provided functional information. The level of plasma BNP depends on the equilibrium between myocardial secretion as compensatory response to injury or wall stress and an amount and activity of expressed guanylyl cyclase-type BNP receptors and also peripheral degradation rate of BNP through neutral endopeptidases. The ischemia induced by increase in ventricular wall stress that induced release of BNP. The TnI elevations are seen in multiple chronic cardiac and noncardiac conditions, a rise or fall in serial measurement of TnI levels strongly supports an acutely evolving cardiac injury such as, most commonly, acute myocardial infarction (14). In our study we found significant elevated levels of plasma BNP and TnI in acute myocardial infarction. In our study we determined the value of BNP $764.48 \pm 639.52$ pg/mL ($260-4441$ pg/mL) in the patients with AMI. The level of TnI in the group with AMI was $2.50 \pm 2.28$ ng/mL ($0.31-7.07$ ng/mL). Grybauskiene R. and al. (15) have got the mean concentration of TnI $0.499$ ng/mL ($0.07-2.89$ ng/mL) and BNP level $758$ pg/mL ($206-2158$ pg/mL). In our study patients with unstable angina had the concentration of BNP $287.18 \pm 593.20$ pg/mL ($18-2514$ pg/mL) and TnI level $0.10 \pm 0.23$ ng/mL ($0.00-1.10$ ng/mL) and healthy control group has concentration of BNP $18.74 \pm 7.64$ pg/mL ($10-33.10$ pg/mL) and TnI level $0.01 \pm 0.024$ ng/mL ($0.00-0.09$ ng/mL). It is a lower concentration of BNP and TnI than in the patients with AMI, the results are shown in Table 1. The other researchers have got results of BNP $70.2 \pm 53.3$ pg/mL in the patients with unstable angina (16). In the present study, we have shown significantly higher BNP plasma level by patients with AMI in compare BNP level in healthy group results are shown in Table 1. The similarly results have got Morita and al. (17) and Richards and al. (18). Patients with elevated plasma BNP levels (>80 pg/mL) had a significantly higher incidence of new heart failure and all-cause
mortality than those with a normal plasma BNP level (<or = 80 pg/mL) (19). In our study, patients with BNP level 80 pg/mL have stayed longer in the Department of Heart Diseases and had a higher incidence of new heart failure. The data of While HD and al. (14) have shown that BNP concentration is increased during AMI and occurring after the first AMI. BNP concentration in plasma during AMI is strongly related to the marker of myocardial necrosis reflecting the extent of injured myocardium, and to degree of acute heart failure. During AMI BNP levels correlated strongly with TnI. In our study we have got good correlation of BNP and TnI in patients with AMI. In correlation between BNP and troponin we got correlation coeffi cient r = 0.36 with statistical signifi cance for p<0.05. The results are shown in Figure 1. The other researchers have got results of BNP and troponin correlation with correlation coeffi cient r = 0.273-0.70 (15, 19). Necrosis and apoptosis of myocytes in AMI are contributions of progressive left ventricle dysfunction. Therefore we have done a correlation between BNP and TnI to contribute that BNP as TnI could be a marker of myocytes necrosis in patients with AMI. The results of Karcaiauskaite have shown a correlation coeffi cient r = 0.72 indicating strongly correlation between BNP and TnI. The reason why we got lower correlation coeffi cient is a fact that BNP gene transcription is increased both in infarcted tissue and it surrounding ischemic but viable myocardium whose extent differs (20). Studies have shown that BNP secretion and BNP mRNA expression are increased mainly in the borderline region between the infarcted and non-infarcted regions. The stimulus for this appears to be increased all stress directly related to the infarction. The clinical ischemia is result of extensive necrosis is associated with release of BNP. Ischemia itself rather than changes in wall stress secondary to ischemia might promote BNP release (21,22). Our study show that BNP can predict high risk features in ACS such as more severe underlying atherosclerosis, left ventricular hypertrophy and burden of ischemic insult. The patients with higher BNP have worse prognosis of AMI even with normal value of TnI. Therefore BNP could be used as a marker of myocardial necrosis as well as marker of risk for myocardium ischemic viable.

CONCLUSION

In our study BNP plasma levels are significant higher in AMI in compared with unstable angina group and healthy control group. Plasma level BNP was elevated in patients with left ventricular (LV) dysfunction. Serial measurements of plasma BNP and TnI concentrations might be a useful tool for identifi cation of patients at risk of developing AMI and unstable angina. In patients with ACS BNP
adds important prognostic information to clinical and laboratory variables as well as levels of troponin. Determination of BNP rise could be used for quick and easy estimation of infarction size. BNP together with TnI levels in acute phase of myocardial infarction might be useful in predicting subsequent cardiac function.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

REFERENCES


Prevalence of behavioral risk factors of non-communicable diseases among urban and rural population in the Federation of Bosnia and Herzegovina

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ABSTRACT

Introduction: The objective of the paper is to analyze and to assess prevalence of the major behavioral risk factors among adult population (25-64 years of age) in the rural and urban areas in the Federation of Bosnia and Herzegovina (FBiH).

Methods: Data were taken from cross-sectional population survey on the health status population in the FBiH. To ensure a sample representative for the adult population in the FBiH it was applied the two-stage stratified systematic sample. The survey covered a total of 2735 adult population aged 25-64 years, of which 1087 in the urban areas and 1648 in rural areas.

Results: The prevalence of smoking among men in rural areas is significantly higher than among men in urban areas (69% vs. 55%), while the prevalence of smoking among women is higher in urban than in rural areas (45% vs. 31%). There is no statistically significant difference in prevalence of obesity and physical activity according to the age groups among men and women in the urban and rural areas. The frequency of changes in behavior related to acquiring healthy living habits in the rural areas is statistically significant among men and women, while in the urban areas there is no statistical significance among the sexes.

Conclusions: The results indicate that there are no significant differences in prevalence of factor risks in urban and rural areas. Prevalence of unhealthy lifestyles is high, and the results should be used to improve standard planning of health promotion-prevention programs.

Keywords: smoking; obesity; urban-rural differences

INTRODUCTION

The health care systems of countries are facing challenges of ensuring comprehensive protection aimed at reducing burden of diseases and early death from the non-communicable diseases (NCDs) through
integrative approaches from health promotion and disease prevention to the management of NCDs at strategic level (1).

Smoking, unhealthy eating habits and lack of physical activity with consequent obesity are proven major risk factors for NCDs, especially diseases of the cardiovascular system (CVDs), as well as for subsequent events; hypertension, glucose intolerance and hyperlipidemia. These risk factors are also indicators of major preventable health problems and their regular monitoring within the population makes a good basis for setting and implementing evidence-based preventive and promotional programs (1,2).

In the last decades the health care systems of countries with clear and strong recommendations of the World Health Organization (WHO) implement activities to reduce prevalence of these risk factors that are proven to be preventable. These are not activities of health care sector only, but also activities of other government bodies, which represents the base of the new WHO European policy “Health 2020” (3,4).

The increase in emergence of NCDs is recorded in the Federation of Bosnia and Herzegovina (FBIH) through the figures from the regular health-statistical data, including mortality and morbidity data (5,6). Prevalence of the risk factors is assessed from periodic cross-sectional population surveys.

The first cross-sectional study population and risk factors for NCDs in a representative sample of the population in the FBIH was conducted in the autumn of 2002. The survey conducted in FBIH in 2002 was taken as a baseline survey, when significant prevalence of smoking habits, physical inactivity and obesity, as critical risk factors for emergence of NCDs, was assessed among adult population in the FBIH (7).

Ten years later, in 2012, a cross-sectional survey was conducted on the sample of adult population aimed at evaluating state of health of population and assessing prevalence of risk factors in the FBIH. The survey was conducted in line with internationally established standards and protocols (8-10).

The paper shows analyses and assessment of prevalence of main behavioral risk factors among adult population (25-64 years of age) in urban and rural areas in the FBIH in order to examine possibilities of existence of differences, which is necessary for designing evidence-based population programs and interventions.

METHODS

Data were taken from cross-sectional population surveys on the health status population in the FBIH. Population surveys were carried out by the Federal Ministry of Health (FMoH) and the Federal Public Health Institute (FPHI) in the period from November 2012 to January 2013, as a part of primary health care reform process in the FBIH with purpose to measure performance in the health care system and public health.

To ensure a sample representative for the adult population in the FBIH it was applied the two-stage stratified systematic sample. Sample frame is a master sample of visiting sites and households from 2009, which was prepared by the Federal Institute of Statistics (FIS).

The first sampling strata were visiting sites stratified by type of settlement - urban and rural, and by the cantons in the FBIH (ten cantons). The second sampling strata were households. The visiting sites were selected by Lahiri method of sampling, which means the selection probabilities are not equal, but the probability of selection is proportional to the size of the primary unit, wherein the size of the primary unit is represented by the number of secondary sampling units, or households within the primary unit. Households were selected by systematic method, which means that the choice probabilities were the same. Stratification of units was made according to the type of settlement (urban/rural). The allocation of households was made proportionally to size of settlement types, taking care to include all cantons in the FBIH. In this population were not included collective households such as student hostels, residential colleges, nursing homes, prisons etc. Out of 1752 households that made the pattern in the FBIH, the survey was conducted in 1402 households (RR 80%). From this number, 40% of households were in urban areas and 60% in rural areas. Respondents were all adult members of the household aged 18 years and older. For the purpose of comparison with the results of a cross-sectional
survey that was conducted in the FBIH in 2002, the document analyzed the results of the adult population aged 25-64 years. The survey covered a total of 2735 adult population aged 25-64 years, of which 1087 in the urban areas and 1648 in rural areas.

The study was conducted in accordance with the Helsinki Declaration, which defines the ethical principles of biomedical research on humans. All participants were informed of the purpose of research, and were explained that use of data is needed solely for research purposes. The study included a standardized questionnaire and anthropometric measurements.

The questionnaire included questions about behavioral risk factors (smoking, physical activity, nutrition habits), while anthropometric measurements included measurements of height, weight, blood pressure and biochemical analysis of capillary blood samples (blood sugar, cholesterol and triglycerides). Information on smoking was obtained from a set of questions that were set to respondents. Daily smokers were respondents who currently smoke or who have smoked in the previous month prior to the survey.

Physical activity was estimated from a set of questions about the frequency of physical activity in leisure time. Respondents who identified themselves to exercise two or more times a week (issue related to the intensity of exercise that accelerates breathing or sweating), were all categorized as having moderate physical activity.

Increased awareness of risk factors and the change in eating habits, were both estimated by set of questions about habit changes in the past year. Physical measurements, among others things, included the measurements of height and weight. Height was measured by an stadiometer that was attached to the wall or to a special holder. Weight was measured in light clothing using digital scales. Obesity has been described in terms of BMI (body mass index) and was expressed in kg/m².

Fieldwork was carried out by ten trained teams.

**Statistical analysis**

The data were analyzed using SPSS for Windows, version 17.0. Descriptive statistics was used to represent the data – index of structure and relative relations. Statistical significance was tested by $\chi^2$ test. Frequency of each observed variable relative to the place of residence (urban/rural), sex and age subgroup was examined by descriptive statistical analysis.

**RESULTS**

**Smoking**

In the total sample in FBIH 37% of women and 63% of men are every day smokers. Prevalence of smokers among men in rural areas is significantly higher than among men in urban areas (69% vs. 55%), while the prevalence of smoking among women is significantly higher in urban than in rural areas (45% vs. 31%).

Prevalence of daily cigarette smokers in urban areas is increased by the respondents’ age among both sexes, especially among women. In the group of respondents between 55-64 years of age the prevalence is equal both among men and women (18%). There is no statistically significant difference in prevalence of smoking according to the age groups among respondents of both sexes in the urban areas ($\chi^2=3.2 \text{ df}=2 \text{ p}=0.358$) (Table 1).

In the rural areas prevalence of smoking habits is higher among men and lower among women and it also increases with age of respondents of both sexes, especially among women. In the group of respondents between 45-54 years of age prevalence

| TABLE 1. Prevalence of smoking according to age and sex, urban/rural differences |
|------------------|---------|------------------|---------|----------|---------|<p value> |
|                  | Urban areas | Rural areas | p value |
|                  | Daily smokers | Daily smokers |          |          |          |          |
| Men              | 197 55 | 329 69 | p<0.01 | |
| Women            | 163 45 | 148 31 | p<0.01 | |
| Age (years)      |          |          |         |          |          |          |
| Men 25-34 y      | 53 27 | 66 20 | p>0.1 | |
| Women 25-34 y    | 36 22 | 33 22 | p>0.1 | |
| Men 35-44 y      | 53 27 | 104 32 | p>0.1 | |
| Women 35-44 y    | 38 23 | 41 28 | p>0.1 | |
| Men 45-54 y      | 55 28 | 87 26 | p>0.1 | |
| Women 45-54 y    | 59 36 | 53 36 | p>0.1 | |
| Men 55-64 y      | 36 18 | 72 22 | p>0.1 | |
| Women 55-64 y    | 30 19 | 21 14 | p>0.1 | |
is higher among women than among men (36% vs. 26%). There is no statistically significant difference in prevalence of smoking according to the age groups among respondents of both sexes in the rural areas ($\chi^2=6.91 \text{ df}=2 \text{ p}=0.075$) (Table 1).

**Obesity**

In total 22% of respondents in the FBIH is obese (BMI $\geq 30$ kg/m$^2$). Prevalence of obesity in urban areas is 20%, while the prevalence of obesity in rural areas is 24%. In the urban areas prevalence of obesity is higher among men than among women (18% vs. 17%), while in the rural areas prevalence of obesity is higher among women than among men (37% vs. 28%). There is no statistically significant difference in prevalence of obesity among men and women in the rural areas ($\chi^2=6.91 \text{ df}=2 \text{ p}=0.075$) (Table 1).

Prevalence of obesity in the urban areas increases by the respondent’s age among both sexes. There is no statistically significant difference in prevalence of obesity according to the age groups among men and women in the urban areas ($\chi^2=5.50 \text{ df}=3 \text{ p}=0.138$) (Table 2).

Prevalence of obesity in the rural areas increases by the respondent’s age among both sexes, and among both sexes aged between 35-54 years it grows much faster than in the urban areas. Prevalence of obesity is lower among both sexes between 55-64 years in the rural areas than among respondents in the urban areas. There is no statistically significant difference in prevalence of obesity according to the age groups among men and women in the rural areas ($\chi^2=4.41 \text{ df}=3 \text{ p}=0.250$) (Table 2).

**Physical activity**

Physical activity was measured as a physical activity lasting 30 minutes where the respondent would be out of breath or sweat, but in different intervals during seven days. 2-3 times a week as the recommended frequency of the physical activity. Total of 36% of respondents in the FBIH is physical inactive, while 14% of respondents is physically active 2-3 times a week, whereof 45% are women and 55% are men.

The percent of physically active women and men aged between 25-34 years is the same in urban areas. Generally, there is no significant difference in the recommended physical activity among men and women in the urban areas ($\chi^2=3.43 \text{ df}=3 \text{ p}=0.330$) (Table 3). The percent of physically active women and men, especially in younger age groups, is the same in urban areas. Generally, there is no significant difference in the recommended physical activity among men and women in the rural areas ($\chi^2=2.66 \text{ df}=3 \text{ p}=0.446$) (Table 3).

**Healthy behaviors**

The respondents were asked whether, in the last

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**TABLE 2.** Prevalence of obesity according to age and sex, urban/rural differences

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Urban areas BMI $\geq 30$</th>
<th>N</th>
<th>%</th>
<th>Rural areas BMI $\geq 30$</th>
<th>N</th>
<th>%</th>
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<td>55-64 y</td>
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**TABLE 3.** Physical activity according to age and sex, urban/rural differences

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Urban areas Physical activity 2–3 times a week</th>
<th>N</th>
<th>%</th>
<th>Rural areas Physical activity 2–3 times a week</th>
<th>N</th>
<th>%</th>
<th>p value</th>
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12 month, they have changed their behavior related to the diet, increase in physical activity, giving up smoking and alcohol consumption.

The changes in behavior are more frequent in the older age groups, between 45-64 years of age. Generally, the most frequently changed habits relate to increase in fruit and vegetable consumption, as well as reduction of fat intake, while the reduction of smoking habits was recorded only in small percent.

The frequency of changes in behavior related to acquiring healthy living habits in the rural areas is statistically significant among men and women, because women in rural areas change living habits rather more frequently than men, while in the urban areas there is no statistical significance among the sexes (Figure 1).

**FIGURE 1.** Prevalence of changes in behavior according to the area, age and sex, urban/rural difference.
DISCUSSION

The prevalence of risk factors for NCDs in the FBIH in the last decade was evaluated through a few isolated studies on risk factors and health behavior in different samples of the population.

The first cross-sectional study population and risk factors for NCDs in a representative sample of the population in the FBIH was conducted in 2002. The prevalence of risk factors related to the health behavior of the population in the study from 2002 year was relatively high and there were significant differences in the level of the main risk factors - smoking, physical activity and obesity in urban and rural areas (11).

Ten years later it was conducted a follow-up study in order to monitor trends in preventable risk factors and in getting real information about the profile of risk factors for NVDs among the adult population in the FBIH. Great significance of this research lies in representation of FBIH in both urban and rural areas, and the high response rate.

Data from routine health statistics in the FBIH show a slight increase in circulatory system diseases, particularly CVDs, followed by malignant diseases. Therefore, monitoring and control of risk factors are necessary measures to protect the health of the population. Conducting periodic surveys enables monitoring of trends and creation of evidences for development of public health activities and algorithms for clinical work within primary health care.

Results of cross-sectional studies identify smoking as the most important risk factor in the occurrence of NCDs among the adult population in the FBIH. Despite the existence of clear legislation in the FBIH regarding the limited use of tobacco products, the prevalence of smoking in the FBIH is still very high, what, among other things, speak in favor of an inconsistent implementation of the Law. Consistent implementation of the Law on the limited use of tobacco products in the FBIH, promotion of non-smoking places and work environment free of tobacco smoke should be basic measures. In accordance with the practice in EU countries and in the region, part of the revenue from excise taxes on tobacco products would be redirected to funding for preventive and promotional programs related to reducing smoking prevalence, what would treat causes and not consequences of the problem. As important actors in both prevention and promotional activities, apart from the health system, seems to be definitely local communities where people live. At the same time it is necessary to increase the knowledge and skills of healthcare workers in primary health care (PHC), especially for nurses, in treatments of smoking cessation, considering that the strengthening of PHC through continuous improvement of family medicine teams is a fundamental commitment to the reform of the health sector in the FBIH. These treatments should become standard practice in teams of family medicine in PHC, given the very high prevalence of smoking in the FBIH, which is significantly higher than in neighboring countries (12-13).

Obesity is one of major public health challenges in the 21st century. The prevalence of obesity from the 1980s nearly tripled in many countries of the European region, and consequently led to an increase in various physical disabilities and development of non-communicable diseases, especially diabetes mellitus. In the FBIH, the prevalence of obesity increases with age in both sexes. If we add this to an increasing prevalence of other risk factors in middle and old age, this creates an additional burden in the accumulation of unhealthy habits within the population. Enhancing public awareness about healthy eating and increasing knowledge about influences of obesity on health must be a method of everyday work in primary health care, in collaboration with the local community. Increasing prevalence of obesity in rural areas is significant and this should be given special attention in the future.

Prevalence of physical activity is insufficient and there is certainly a space for public health improvements. In recent population surveys conducted in Serbia, the prevalence of physical activity of the adult population was similar to those in the FBIH, indicating that the lack of physical activity in leisure time is almost culturally adopted a pattern of behavior in both the FBIH and the neighboring countries (14).

It is especially necessary to improve awareness of population about the importance of physical activity in all age groups. At the same time, it is necessary to create conditions for the massification of physical activity. The role of local communities in these
activities is also necessary to be strengthened, as the creation of conditions for the implementation of physical activity in leisure time lies precisely within the places of residence of the population.

Changing behavior related to the acquisition healthy habits in the last year prior to the survey was low in both men and women, and there are no significant differences between urban and rural areas. Enhancing awareness of healthy habits is a long process and requires very lengthy preventive work. This is work that needs to be strengthened intensively in the coming period through individual and group counsellings, work within the local community, particularly through the work of nurses in primary health care. The advantage of the FBIH can be continuous strengthening of family medicine teams in PHC, and obtained matrix with several important indicators which should serve as proof for posting prevention programs and increasing awareness of the risk factors. Experiences in many countries show that a well-planned health intervention programs at the community level in order to promote health and health behavior changes have good results (15-16).

The results of surveys showed no significant differences in the prevalence of risk factors for NCDs in both urban and rural areas. The prevalence of unhealthy lifestyles in the FBIH is quite high and it is necessary to conduct vigorous public health action to reduce risk factors, as well as individual access to high-risk individuals.

CONCLUSIONS

Social responsibility for health in the local community includes the creation of preventive health programs and proposed measures for improving and enhancing the health of the population. This is particularly important for rural areas, where the impacts of local communities can be significant. Active involvement of all actors in the social system and the coordination of all government sectors, from the health sector to the education sector, the inspectorate, finance and other sectors, as well as active cooperation with non-governmental sectors in the implementation of the current legislation, can all create a favorable environment for reducing these risk factors. Intersectoral cooperation is the main principle of the WHO European policy “Health 2020” and is reflected in the approach “Health in all policies” and is necessary to follow in strategic and operational approaches in the FBIH.

ACKNOWLEDGEMENTS

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REFERENCES

Nurses’ knowledge and responsibility toward nutritional assessment for patients in intensive care units

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ABSTRACT

Introduction: Nutritional assessment is a prerequisite for nutritional delivery. Patients in intensive care suffer from under-nutrition and nutritional failure due to poor assessment. Nursing ability to early detect nutritional failure is the key for minimizing imparities in practice and attaining nutritional goals. Aim of this article is to examine the ability of Jordanian ICU nurses to assess the nutritional status of critically ill patients, considering biophysical and biochemical measures.

Methods: This cross sectional study recruited nurses from different health sectors in Jordan. ICU nurses from the governmental sector (two hospitals) and private sectors (two hospitals) were surveyed using a self-administered questionnaire. Nurses’ knowledge and responsibility towards nutritional assessment were examined.

Results: A total of 220 nurses from both sectors have completed the questionnaire. Nurses were consistent in regard to knowledge, responsibility, and documentation of nutritional assessment. Nurses in the governmental hospitals inappropriately perceived the application of aspiration reduction measures. However, they scored higher in applying physical examination and anthropometric assessment. Although both nurses claimed higher use of biochemical measurements, biophysical measurements were less frequently used. Older nurses with longer clinical experience exhibited better adherence to biophysical measurement than younger nurses.

Conclusion: Nursing nutritional assessment is still suboptimal to attain nutritional goals. Assessment of body weight, history of nutrition intake, severity of illness, and function of gastrointestinal tract should be considered over measuring albumin and pre-albumin levels. A well-defined evidence-based protocol as well as a multidisciplinary nutritional team for nutritional assessment is the best to minimize episodes of under-nutrition.

Keywords: assessment; nutritional status; nurse

INTRODUCTION

Critical illness is associated with many complications such as anorexia, hyper metabolism, malabsorption; atrophy of muscles, liver, kidney, gastrointestinal tract & heart; impaired cell mediated immunity,
susceptibility to infections, poor wound healing, anemia, death (1,2). Enteral nutrition (EN) is the preferred nutritional method whenever is possible to feed critically ill patients (3,4). When gut is used for nutrition, bacterial translocation and septicemia are prevented.

Malnutrition is a term used frequently in healthcare system which is the analogy of under-nutrition or inadequate energy intake less than the metabolic demands (5,6). Under-nutrition can also be resulted from abnormal digestion or absorption of protein and calories (5,6). It is also acknowledged that malnutrition in the critically ill is associated with impaired immune functions; impaired ventilator drive, and weakened respiratory muscles, leading to prolonged ventilator dependence and increased infectious morbidity and mortality (7,8).

Proper nutritional assessment is strongly linked to successful nutritional plans for critically ill patients (4,9,10). The current focus on nutrition in critical care settings is that carefully selecting patient’s parameters that would highly reflect patient’s outcome (11-13). In order to design an appropriate and effective strategy for nutritional assessment in the intensive care, a crucial guidelines have to be applied systematically for all critically ill patients (14,15).

Nurses in intensive care are in a key position to maintain patients’ nutritional status at an optimal level and closer to the nutritional goals (16,17). While most of the critical care nurses are responsible for establishing nutritional access and initiating feeding, in some instances, they calculate the caloric needs according to the body requirements and measure the daily calories delivered (16,17). However, disparity in nursing practices contributes to developing serious deficiencies and complications due lack of unified guidelines (18,19). When adherence to evidence-based guidelines is assured, the discrepancy inherent in nursing practice can be curtailed and the effectiveness of nutritional practices are maintained (20,21).

In Jordan, critical care nurses have no obvious role regarding nutritional care (22). While dietitians are available in the most of Jordanian hospitals, nurses often hold the responsibility for early detecting the sings of under-nutrition and assessing the outcomes of the delivered feeding although lack of expertise and training is sometime evident (23,24). Unfortunately, a limited number of tools for nutritional assessment are available in the Jordanian hospitals; in addition to poor academic preparations that suffice this domain (22).

The most recommended nutritional assessment tools are as follows: (a) biophysical assessment and anthropometric measurement which include body mass index (BMI), mid-arm muscle circumference, triceps skin fold thickness, in addition to measuring Gastric Residual Volume (GRV) and detecting tube placement for enteral fed patients (16,17). However, the ratio of subcutaneous layer to total body fat may vary from 20% to 70% in the normal individuals; so they are not recommended in extreme weight change due to the risk for overestimating body fat in malnourished patients (16). (b) Physical examination which includes history of weight loss, alcohol abuse, dietary habits, skin, mouth, and neurological system monitoring (25,26). Body temperature is also a part of the physical examination (27,28). (c) Biochemical assessment includes serum albumin, transferrin, transthyretin (prealbumin), retinol-binding protein, somatolin C and fibronectin (29,30). However, changes in fluid distribution may result in pseudo rise or fall in the value of albumin level causing false medical interpretation (31). (d) Dietary assessment which includes 24 hours recall, food records (diaries), diet history and food frequency questionnaires (32). These methods may however be impractical for critically ill patients who are unable to communicate effectively with practitioners (18,33).

The purpose of this study was to assess Jordanian nurses’ knowledge and responsibility of nutritional assessment in the critical care, considering biophysical and biochemical measures.

**METHODS**

This descriptive cross sectional study employed nurses from four hospitals in Jordan; two governmental hospitals and two private hospitals. It is assumed that there are many differences between heath care sectors in Jordan in terms of medical protocols and nursing practice (22). For that reason, nurses in different heath care sectors may exhibit
various level of adherence to nutritional assessment tools. Nurses working in any intensive care units and had at least one year of clinical experience and hold the bachelors or diploma degree in nursing was eligible for participation. Convenient sampling technique was used to select participants from each involved hospital. The estimation of sample size was based on the medium effect size, power of 0.80, and \( \alpha = 0.05 \) (34). All selected hospitals are located in Amman, the capital of Jordan, and all are considered as major and referral hospitals that operate well occupied intensive care units.

Study instrument included a self-administered questionnaire developed to assess nurses’ ability to assess patients’ nutritional status while staying in the intensive care. This questionnaire consisted of five demographic questions; six questions related to the attitudes towards nutritional assessment including aspiration-reduction measures; and five questions related to using different bio-physical and biochemical measures. The scoring system ranged from 1 (to a very small extent) to 5 (very great extent). A pilot study was carried out by 10 nurses from the same study target to test the clarity, applicability, and feasibility of the questionnaire. Minor modifications were done after piloting and those nurses participated in the pilot study were excluded from the study sample. The content validity was also assessed by a panel of experts in this field, including a physician, a dietitian, and two expert nurses.

Ethical approvals were anticipated from each hospital’s authority prior to data collection. A written permission (informed consent) for participation was obtained from each participant after providing complete information about the study and its significance. Anonymous participations and confidentiality of data were also assured. Data were collected in collaboration with the head nurses of the unit in which they contributed in selecting the eligible participants, handing, and returning the completed questionnaires in a sealed envelope within one week.

**Statistical analysis**

After returning all completed questionnaires, data were entered the statistical package for social sciences (SPSS) software, version 17. Descriptive statistics including number, percent, mean, Standard Deviation (SD) were used and followed by comparing differences between study groups using Chi-square and Kruskal-Wallis test.

**RESULTS**

**Participants’ demographics**

A total of two hundred and twenty intensive care nurse participated in the study and returned the completed questionnaires. As shown in Table 1, the majority of the study participants were female accounting 65% while 34% were male. Regarding the ages, around 38% were aged less than 25 years old and the second majority age group was between 25-45 years old. About the half of the sample had a clinical experience of less than five years and very few had an experience of more than 20 years. While the majority of participants (71.4%) hold the bachelors degree of nursing, the vast majority (82.3%) claimed no previous clinical training received with the respect of nutritional assessment (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Participants’ demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Gender</td>
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<td></td>
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<td></td>
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<td>Age</td>
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<td>Years of experience</td>
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<td>Level of Education</td>
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<td></td>
</tr>
<tr>
<td>Attending Nutrition Course</td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>
Attitudes to nutritional assessment

As shown in Table 2, the nurses showed a consistent adherence to the use of nutritional assessment in the ordinary nursing process. There were no any significant differences between nurses from both groups in relation to the importance of assessment in acquiring knowledge, having responsibility, and documenting nutritional changes. Scores were mainly above the midpoint of 2.5, indicating that nurses perceived the importance of assessment through their nursing process. Regarding some nutritional assessment tools, nurses in the private sectors claimed measuring gastric aspirate more frequently than nurses in governmental sectors. Similarly, detecting tube placement was also scored higher among nurses in the private sectors than governmental nurses. In addition, nurses in the private hospitals claimed using other aspiration reduction measures such as degree of head of the bed, controlling feeding rates, and using of promotility agents more frequently than nurses in the governmental hospitals.

Adherence to various nutrition assessment tools

This section shows nurses’ attitudes towards adherence to various nutritional assessment tasks while providing EN care for critically ill patients. There were a statistical significant differences between governmental and private sector nurses in regard to adherence to these nutritional assessment provisions. Nurses in the governmental hospitals scored significantly higher in undertaking assessment using physical examination, anthropometric assessment, and dietary assessment than nurses working in the private sector. However, both groups had equally showed the extent of using biomedical assessment and screening for nutritional risks as main tools for assessing the nutritional status (Table 3).

Variations in nutritional assessment between demographic groups

While no significant differences between male and female nurses in regard to the adherence to nutritional assessment, older nurses with longer clinical experience scored higher in applying a nutritional assessment using biophysical measurements ($x^2 = 24.261$, df=3, $p=0.043$). However, younger nurses with shorter clinical experience scored higher in having a nutritional assessment using biochemical measurements ($x^2=35.171$, df=3, $p<0.001$). Although bachelor and diploma degree holders did not differ significantly in term of nutritional assessment, nurses who received previous nutritional training were more likely to adhere to different assessment measures than those who did not ($x^2=76.184$, df=1, $p<0.001$).

DISCUSSION

It was evident that nurses well perceived the knowledge and responsibility for nutritional assessment and claimed competency in undertaking nutritional assessment while examining the effectiveness of delivered feeding. This premise is supported by other researchers who reinforced the importance of nutritional assessment as the first step of nutritional care (14,35,36).

Aspiration is the most common dangerous side effect resulting from EN. Aspiration-reduction measures can be applied individually; however, most of them are combined into one protocol especially in patients with mechanical ventilation. For instance, Bowman et al. (2005) established and implemented a new ‘evidence-based feeding protocol’ and an

### TABLE 2. Attitude to nutritional assessment

<table>
<thead>
<tr>
<th></th>
<th>Governmental (n=129)</th>
<th>Private (n=91)</th>
<th>Total (n=220)</th>
<th>Kruskal-Wallis test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M SD</td>
<td>M SD</td>
<td>M SD</td>
<td>$\chi^2$ test</td>
</tr>
<tr>
<td>Knowledge of assessment</td>
<td>2.79 1.28</td>
<td>3.22 1.22</td>
<td>2.97 1.21</td>
<td>5.782</td>
</tr>
<tr>
<td>Responsibility of assessment</td>
<td>2.87 1.19</td>
<td>3.26 1.11</td>
<td>3.03 1.13</td>
<td>5.696</td>
</tr>
<tr>
<td>Documentation of assessment</td>
<td>3.13 1.32</td>
<td>3.00 1.08</td>
<td>3.01 1.17</td>
<td>1.598</td>
</tr>
<tr>
<td>Measuring gastric aspirates</td>
<td>3.14 1.36</td>
<td>4.05 1.29</td>
<td>3.70 1.33</td>
<td>25.909</td>
</tr>
<tr>
<td>Detecting tube placement</td>
<td>3.88 1.31</td>
<td>4.31 0.93</td>
<td>4.00 1.14</td>
<td>10.176</td>
</tr>
<tr>
<td>Other aspiration reduction measures</td>
<td>3.06 1.19</td>
<td>3.59 0.99</td>
<td>3.27 1.14</td>
<td>9.249</td>
</tr>
</tbody>
</table>

Scores range from 1 (to a very small extent) to 5 (very great extent) * M: Mean, * SD: Standard deviation
‘aspiration reduction algorithm’ for enteral fed, mechanically ventilated patients in the ICUs. Also, Metheny et al. (2010) evaluated the effectiveness of using ‘Aspiration Risk-Reduction Protocol’ (ARRP) for enteral fed patients with mechanical ventilation. The importance of controlling GRVs was adequately perceived by nurses as a protective measure to prevent higher GRV limits (28, 37). This conforms to the evidence-based recommendations that measuring GRVs is an essential element in EN and should be maintained under the universal threshold of 200-500 ml (10). It is also accepted to define GRV as the cutoff point of 30% of the last given feeding amount which is remaining in the stomach (38,39). However, previous studies addressed that GRVs should not be taken into account for all potential risks for pulmonary aspiration, the evidence showed that many other factors should be considered along with GRVs to reduce the risk of aspiration such as trauma, head injury, using of sedation, and mental instability (40). A number of other recommendations are helpful to accomplish nutritional goals such as avoiding inappropriate feeding cessation, using prokinetic agents with EN, keeping the head of the bed elevated at 35-45°, increasing feeding rate in a constant manner and using pre-prepared feeding packs (10,41,42).

Studies stressed on the regular checking for tube position which is strongly associated with low complication incidences. Feeding tube should be checked regularly before each feeding administration or at least every day using a reliable indicator such as radiographic confirmation (X-ray) which is still considered as a ‘gold standard’ (43-45). Measuring pH of gastric aspirate is another reliable indicator for tube placement. However, studies have confirmed that radiography is superior to other technique despite the risk of radiation exposure, but if not available, pH method can be applied (10,38,46-50).

The use of bio-physiological and bio-chemical parameters such as body weight, abdominal girth, bowel exam, skin integrity, and urine and stool analysis in addition to serum protein level in the blood were assessed in this study. The nurses showed a higher reliance on the bio-chemical indicator than bio-physical measurement. Previous studies revealed that not all patients in intensive care have a regular nutritional assessment and the essential aspects of nutritional documentation are missing(23,51). Also, it is unlikely to have entire screening tool for evaluating nutritional outcomes (52, 53). Evidence-based guidelines stressed on investigating weight, history of nutrition intake, severity of illness, and function of gastrointestinal tract prior to admission instead of measuring albumin and pre-albumin (10,54). The frequent assessment of BMI should also be measured by dividing weight in kilograms by the square of the height in meters (Normal range 19-25) (55). In general, all studies confirmed the significance of using evidence-based guidelines for nutritional assessment as the majority of nurses showed inconsistency in having the systematic tools for measuring nutritional outcomes (52).

Although the study recruited sample from two health care sectors in Jordan, involving the other health sectors such as the military health sector would enhance the external validity of the study. In addition, including other hospitals from different geographical location, away from the capital, would provide further understanding about the phenomenon and enhance generalizability.

Nurses require understanding factors associated with under-nutrition and hypo-caloric feeding through undertaking such nutritional assessment

<table>
<thead>
<tr>
<th>TABLE 3. Adherence to nutritional assessment</th>
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<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Physical examination</td>
</tr>
<tr>
<td>Governmental Mean (SD) (n=129)</td>
</tr>
<tr>
<td>2.28 (1.03)</td>
</tr>
<tr>
<td>Private Mean (SD) (n=91)</td>
</tr>
<tr>
<td>1.48 (0.87)</td>
</tr>
<tr>
<td>Kruskal-Wallis test</td>
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<tr>
<td>χ² test</td>
</tr>
<tr>
<td>22.43</td>
</tr>
<tr>
<td>p-value</td>
</tr>
<tr>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anthropometric assessment</td>
</tr>
<tr>
<td>Governmental Mean (SD) (n=129)</td>
</tr>
<tr>
<td>2.56 (1.35)</td>
</tr>
<tr>
<td>Private Mean (SD) (n=91)</td>
</tr>
<tr>
<td>1.74 (1.08)</td>
</tr>
<tr>
<td>Kruskal-Wallis test</td>
</tr>
<tr>
<td>χ² test</td>
</tr>
<tr>
<td>19.65</td>
</tr>
<tr>
<td>p-value</td>
</tr>
<tr>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dietary assessment</td>
</tr>
<tr>
<td>Governmental Mean (SD) (n=129)</td>
</tr>
<tr>
<td>4.31 (0.93)</td>
</tr>
<tr>
<td>Private Mean (SD) (n=91)</td>
</tr>
<tr>
<td>3.79 (1.09)</td>
</tr>
<tr>
<td>Kruskal-Wallis test</td>
</tr>
<tr>
<td>χ² test</td>
</tr>
<tr>
<td>24.09</td>
</tr>
<tr>
<td>p-value</td>
</tr>
<tr>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Biochemical assessment</td>
</tr>
<tr>
<td>Governmental Mean (SD) (n=129)</td>
</tr>
<tr>
<td>3.51 (1.33)</td>
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<tr>
<td>Private Mean (SD) (n=91)</td>
</tr>
<tr>
<td>3.69 (1.09)</td>
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<tr>
<td>Kruskal-Wallis test</td>
</tr>
<tr>
<td>χ² test</td>
</tr>
<tr>
<td>5.54</td>
</tr>
<tr>
<td>p-value</td>
</tr>
<tr>
<td>0.590</td>
</tr>
<tr>
<td>Screening for nutritional risks</td>
</tr>
<tr>
<td>Governmental Mean (SD) (n=129)</td>
</tr>
<tr>
<td>3.27 (1.64)</td>
</tr>
<tr>
<td>Private Mean (SD) (n=91)</td>
</tr>
<tr>
<td>3.46 (1.23)</td>
</tr>
<tr>
<td>Kruskal-Wallis test</td>
</tr>
<tr>
<td>χ² test</td>
</tr>
<tr>
<td>8.17</td>
</tr>
<tr>
<td>p-value</td>
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<tr>
<td>0.360</td>
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</tbody>
</table>

Scores range from 1 (to a very small extent) to 5 (very great extent)
measures that assist to early detecting the risk for these episodes. The application of bio-physical measurements in the intensive care is still deficient so further insight about the usefulness of these measures should practically be applied.

Future researchers are invited to conduct other extensive research works that involve more aspects about nutritional care. Investigating the role of multidisciplinary work is also a priority to provide further understanding about the role of physicians and dietitians in assessing patients’ nutritional status while being in the intensive care.

CONCLUSION

Nursing nutritional assessment is still suboptimal to promote patients’ successful nutrition. The impact of nutritional assessment on determining the patients’ status and detecting some complications such as aspiration pneumonia is well-known, but nurses need to underpin their practice with some evidence-based guidelines to manage these issues effectively.

This study provides overview to the body of knowledge about the role of intensive care nurses in maintaining optimal nutritional therapy in Jordan. Awareness about the current feature of nutritional assessment sheds the light on the future development strategies. In eventual, nurses’ practitioners would emphasize the role of training to improve their professional competency in the light of nutritional delivery in the critically ill.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

ACKNOWLEDGMENT

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The effects of education and training on self-esteem of nurse leaders

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1Faculty of Health Sciences, University of Ljubljana, Ljubljana, Slovenia, 2Faculty of Administration, University of Ljubljana, Ljubljana, Slovenia

ABSTRACT

Introduction: A successful leader must have high self-esteem. The main aims of this study were to identify changes in the self-esteem of nurse leaders in Slovenia from 2001 to 2011 and to determine homogeneous groups of leaders with similar personal characteristics.

Methods: The study used a version of a personal characteristics questionnaire with 16 self-descriptive statements. Two surveys were conducted among nurse leaders in Slovenian public hospitals, one in 2001 and the other in 2011. Relationships between variables were analysed using chi-square tests for categorical variables and the one-way analysis of variance for quantifiable variables. Factor analysis was used to determine groups of leaders with similar personal characteristics.

Results: A total of 327 nurse leaders participated in the survey in 2001 and 296 filled in questionnaires in 2011. The analysis showed that the level of self-assessment of personal characteristics among nurse leaders in Slovenian public hospitals was significantly higher in 2011 than in 2001, and that differences among individual leaders decreased in most areas. Based on the assessments of personal characteristics, four groups of nurse leaders were established: task-oriented, knowledge and creativity oriented, relationship oriented and extroverted nurse leaders. In the 2011 data, the groups of personal characteristics were much more clearly defined. These groups were established in accordance with leadership theory and research from other fields.

Conclusions: The positive effects of better education and training are visible in nurse leaders in terms of both their higher self-esteem and in the establishment of more homogeneous groups of leaders.

Keywords: education; nursing; leadership; self-esteem; Slovenia

INTRODUCTION

Only a leader with high self-esteem can be a good leader as high self-esteem is the foundation on which...
accordingly. The autocratic style of leadership, which prevailed in nursing in the past, needs to be replaced with more democratic leadership styles: transformational, sharing, authentic, servant, etc. (5,6). In addition to high integrity, all these leadership styles call for leaders with high self-esteem as only such leaders are capable of sharing leadership with their subordinates and patients. Because only secure leaders, which have a strong sense of self-worth are able to give themselves away (7).

Defining self-esteem is beyond the scope of this article. Our study used the concept of self-esteem in its broadest sense: ‘Positive self-concept can be equated with a positive self-evaluation, self-respect, self-esteem, self-acceptance, while a negative self-concept becomes synonymous with a negative self-evaluation, self-hatred, inferiority and a lack of feelings of personal worthiness and self-acceptance’ (8). In this way, concepts like ‘self-concept’, ‘self-perception’, ‘self-attitude’ and ‘self-esteem’ become synonymous and, if considered attitudes toward self, can be seen to exist on a positive—negative continuum, or scale (9).

Leaders with low self-esteem who doubt their abilities, knowledge and views do not get respect and appreciation and are not satisfied with themselves (10). Insecure leaders are dangerous – to themselves, their followers, and the organizations they lead – because a leadership position amplifies personal flaws (11). If a leader cannot rely on his or her own abilities, he or she will doubt others’ abilities, and in turn cause mistrust in them as well (12).

Individuals’ self-esteem is shaped gradually through their psychological development and interaction with their environment from early childhood, through adolescence and maturity (13). An individual’s self-esteem is the basis for the development of professional self-confidence and the two influence each other throughout one’s professional career (14). Therefore, the creation of a professional group of self-confident and balanced leaders is a process influenced by many factors the results of which only become apparent over a longer period of time. However, appropriate education and training are key factors in this process.

The development of professions has been most pronounced within the health care system (15). An important characteristic of professionalism is the integrity of systematic and generalized knowledge which must be used by professionals to solve different problems (16,17). The basis for the nursing profession and nurses’ knowledge is a good educational system that must be supplemented with continuing education following graduation and should be provided by professional associations and health care organisations (18). The significance of continuing education and development after graduation has been emphasized since the beginning of the nursing profession (19), including among others, within international nursing organisations (20).

The health care system in Slovenia employs 16,783 nurses, or 36.6% of all employees in health care (21). The field of education in nursing in Slovenia has changed significantly since 2000. In 2000 Slovenia had two nursing colleges with 974 students, while in 2010 there were three faculties and three nursing colleges with 2,435 students (bachelor of science in nursing, master of nursing) (21,22). The higher number of colleges and faculties also resulted in an increased scope of research into leadership in nursing.

Leadership training programmes within professional organisations have also undergone significant changes resulting in a greater awareness of the importance of good leadership. In 2000, the Professional Group of Nurses in Management was established as part of the Nurses and Midwives Association of Slovenia (23). Its aim is to provide nursing leaders with modern knowledge, attitudes and skills relating to the management of organisations and human resources. Nurse leaders now have more opportunities to meet and exchange leadership experiences and ideas. Such meetings are intended both for training and for shaping and reinforcing their professional self-confidence and the homogeneity of their professional group.

These changes will undoubtedly lead to significant improvement in leaders’ self-esteem. We were interested in (research questions):

- whether there were significant changes in the self-assessment of personal characteristics between 2001 and 2011 that would indicate changes in leaders’ self-esteem?
• whether it was possible to determine homogeneous groups of leaders with similar characteristics based on self-assessments of personal characteristics?

METHODS

Study design
This study was part of a larger research project entitled ‘Leaders in Nursing’ conducted between the autumn of 2010 and the spring of 2011. The authors of the study had previously obtained approval from the Management Board of the Nurses and Midwives Association of Slovenia and the managements of individual hospitals. The survey was conducted at the 15 largest Slovenian public hospitals: two university medical centers, six general hospitals, and seven specialized hospitals. These institutions employ 87% of all hospital nurses in Slovenia. The participating institutions employ 526 nurse leaders, 296 of whom (56% the sample) answered the questionnaire (Table 1).

A comparative study (13) entitled ‘Nurses in Slovenia’ was conducted on a representative sample of nurses in 2001. A sample of 2,450 nurses in Slovenia was established based on the National Register of Nurses and Midwives. A total of 1,067 nurses (44% of the sample) participated in the survey. A secondary data analysis was used to include in Sample 2 only 327 nurse leaders who were employed in public hospitals in 2001.

Statistically significant differences between the samples were recorded at the leadership level ($\chi^2=7.32$, $p=0.039$). The larger share of team leaders in the 2011 sample was the consequence of a reorganisation of nursing care in hospitals aimed at increasing the importance of team work.

The greatest changes in the population of nurses in Slovenia occurred in the area of formal education. The difference is even more pronounced in the group of nurse leaders, which is also reflected in the sample (statistically significant differences at $\chi^2=287.0$, $p=0.0001$). In 2001, 17.5% of nurse leaders had at least a university education, while in 2011 their share rose to 85.2%.

In terms of gender ($\chi^2=0.22; p=0.638$) and age ($\chi^2=3.1, p=0.379$), there were no statistically significant differences between the samples.

**TABLE 1. Demographic data on the sample of nurse leaders**

<table>
<thead>
<tr>
<th>Leadership level</th>
<th>Sample 1 – nurse leaders in 2011</th>
<th>Sample 2 – nurse leaders in 2001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head nurse and heads of departments</td>
<td>19</td>
<td>30</td>
</tr>
<tr>
<td>Ward head nurses and nurses supervising several teams</td>
<td>111</td>
<td>149</td>
</tr>
<tr>
<td>Team leader nurse</td>
<td>166</td>
<td>148</td>
</tr>
<tr>
<td>Gender</td>
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<td></td>
</tr>
<tr>
<td>Female</td>
<td>273</td>
<td>302</td>
</tr>
<tr>
<td>Male</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>N/A</td>
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<td>3</td>
</tr>
<tr>
<td>Education</td>
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<td></td>
</tr>
<tr>
<td>Secondary school</td>
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<td>95</td>
</tr>
<tr>
<td>Professional college degree</td>
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<td>172</td>
</tr>
<tr>
<td>University degree</td>
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<td>45</td>
</tr>
<tr>
<td>Specialisation, master’s degree, doctorate</td>
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<td>12</td>
</tr>
<tr>
<td>N/A</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Age</td>
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<td></td>
</tr>
<tr>
<td>Under 30</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>30 to 40</td>
<td>93</td>
<td>102</td>
</tr>
<tr>
<td>41 to 50</td>
<td>101</td>
<td>110</td>
</tr>
<tr>
<td>Over 50</td>
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<td>55</td>
</tr>
<tr>
<td>N/A</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>296</td>
<td>327</td>
</tr>
</tbody>
</table>

Measurement instrument
To enable direct comparison, in 2011 the study used the same group of statements that were used in 2001 and other studies of the population of nurses in Slovenia (13, 24). The study focused on personal characteristics relating to:

• leaders’ self-image (self-satisfaction and personal-self (25), personal self-esteem (26), self-image and self-values (27), self-mastery (28), agreeableness/neuroticism/conscientiousness (29, 30) – item number 1-9 (Table 2),
• leaders’ opinion about their relationships with others: social self (25), social self-esteem (26), interpersonal values (27), people skills (28), extraversion/openness (29, 30) – item number 10-16 (Table 2).
The study used a version of a personal characteristics questionnaire with 16 self-descriptive statements (Table 2). The statements were formulated so that they expressed positive self-esteem. The respondents used a three-grade scale to answer the following question: “To what degree, in your opinion, are you…” (1 - Not at all, 2 - Moderately, 3 – Very).

**Statistical analysis**

The data was analysed using SPSS 19.0. Descriptive statistics were used to describe the sample. Internal consistency was examined using the Cronbach’s alpha. Factor analysis was used to determine groups of leaders with similar personal characteristics. In the factor analysis, principal component analysis with varimax rotations was used to examine which factors of the scale comprised coherent groups of items (31,32). The Kaiser-Meyer-Olkin (KMO) test and Bartlett’s test of sphericity was applied to measure sampling adequacy (33). Relationships between variables were analysed using chi-square tests for categorical variables and the one-way analysis of variance for quantifiable variables (ANOVA). A significance level of alpha = 0.05 was used for all statistical tests.

**Reliability and validity of measurement instrument**

First, we verified the degree of reliability of the measurement instrument. Cronbach’s Alpha was 0.79 in 2011 and 0.81 in 2001. The value indicated a high level of reliability of the measuring instrument. A similar degree of reliability was produced by the questionnaire in studies on nursing students and nurses conducted in previous years (13,24).

Factor Analysis was applied to determine the construct validity of the measurement instrument. The KMO measure of sampling adequacy was 0.822 in 2001 and 0.793 in 2011 and indicated that factor analysis was appropriate. Bartlett’s test was significant (p-value less than 0.005). This indicates good construct validity.
Ethical consideration
The study was approved by the Honorary Court of Arbitration of the Nurses and Midwives Association of Slovenia. Participants were assured that there was no risk from participating in the study and that their responses would be treated confidentially.

RESULTS
Changes in the self-esteem of nurse leaders
The average ratings of the detected personal characteristics increased in 2011 as compared to 2001 in all areas (Table 2). Nurse leaders in 2011 were significantly more interested in social issues, and they saw themselves as more creative and intelligent and more willing to put their ideas into practice. The results of the analysis clearly show that the self-esteem of the observed leaders increased significantly.

The order of importance of individual personal characteristics did not change in any significant way. Most nurse leaders in both years believed they were responsible, reliable and, at least, sufficiently educated and willing to put their ideas into practice.

A comparison of standard deviations in 2001 and 2011 shows in which areas the differences between nurse leaders increased and in which they decreased. The variability of assessment results decreased, which indicates a higher homogeneity of the observed group. The greatest decreases were recorded in the areas of responsibility (38.2%) and reliability (35.9%) (Column H in Table 2). Differences between the results of the self-assessments of personal characteristics among nurse leaders increased in the areas of education (32.0%) and intelligence (30.0%).

We examined whether the self-assessments of personal characteristics had been influenced by the level of leadership, gender, education or age. Statistically significant differences were evident in the following areas (year 2011):

- Nurse leaders at the highest leadership levels said they were more practical and educated, but less understanding.
- Nurse leaders with the highest education said they were more educated, practical and more interested in new areas of work, but less interested in social issues.
- Older nurse leaders assessed they were more critical and more interested in social issues, but less articulate.
- No differences between genders were apparent in any of the areas.

The differences between the genders were greater in 2001: the women said they were more educated, responsible and diligent, but less independent and sociable than men.

Statistically significant differences between the results of the self-assessments of personal characteristics between groups defined according to the level of leadership, gender, education and age were evident only in a small number of areas. Therefore, differences between these groups cannot be seen as the reason for such a pronounced increase in self-esteem between 2001 and 2011.

Homogeneous groups of nurse leaders with similar characteristics
By using factor analysis we were able to define groups of personal characteristics, and each of these groups was characteristic of one of the groups of nurse leaders. The Principal Component Analysis (PCA) method was applied to the extraction of components. According to Kaiser criterion, only the factors that have eigenvalues greater than one are retained. Four factors were extracted that accounted for 49.5% (2011) and 50.4% (2001) of total variability. Varimax rotation was applied in order to optimize the loading factor of each item on the extracted components.

In the 2011 data, we defined four groups of nurse leaders. The first group comprised leaders who believed they were reliable, responsible, practical and independent. This group was oriented towards the management of tasks, work, procedures, but less so towards the leadership of people. They are believed to be conscientious and precise.

The second group comprised leaders who believed they were intelligent, educated, creative and reasonable. These leaders are defined by knowledge, on which they also base their actions. They are supposed to be characteristically self-restrained and emotionally stable.
The third group comprised leaders who believed they were understanding and sociable. Their primary leadership style is people-oriented and inclusive. They are open and kind to people around them. Their actions are defined by empathy.

The fourth group comprised leaders who were willing to put their ideas into practice, interested in social issues and critical, as well as interested in new areas of work and articulate. Leaders in this group are characteristically outward-oriented and tend to shape and influence relationships with other people. Their actions are supposedly defined by their extroverted nature.

The results of the factor analysis for 2001 data paint a slightly different picture (Table 3). Here, four factors stand out as well. The first factor, which could arguably be linked to extraverted nature and intelligence, clearly stands out. The groups of characteristics defined on the basis of the remaining factors would be difficult to relate to the personal characteristics of a leader. In the 2011 data, the groups of characteristics were much more clearly defined and in accordance with the theory of leadership in other fields.

**DISCUSSION**

The analysis shows that the self-assessments of personal characteristics, on the basis of which the self-esteem of a group of nurse leaders was evaluated, improved between 2001 and 2011 (first research question). In both observed periods (2001 and 2011) the highest ratings were assigned to personal characteristics related to the nature of work in nursing (reliability and responsibility). Other research also shows personal characteristics related to work be the most important for workers in nursing care (34,35).

The greatest increase was recorded in characteristics indicating leaders’ high self-esteem: the share of nurse leaders who believed they were intelligent, creative and interested in social issues increased from 2001 to 2011. Differences between assessment results were smaller than in 2001. This is indicative of the creation of a more homogenous and successful group of leaders as a solid and realistic self-image is one of the key characteristics of a good leader (36). Professional identity, which is shaped by the educational process (37) can only be preserved through appropriate organized continuing

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**TABLE 3. Rotated component matrix**

<table>
<thead>
<tr>
<th></th>
<th>Component – 2011*</th>
<th>Component – 2001*</th>
</tr>
</thead>
<tbody>
<tr>
<td>To what degree, in your opinion, are you…</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Reliable</td>
<td>0.74</td>
<td>0.55</td>
</tr>
<tr>
<td>Diligent</td>
<td>0.63</td>
<td>0.74</td>
</tr>
<tr>
<td>Responsible</td>
<td>0.61</td>
<td>0.58</td>
</tr>
<tr>
<td>Practical</td>
<td>0.56</td>
<td>0.40</td>
</tr>
<tr>
<td>Independent</td>
<td>0.55</td>
<td>0.48</td>
</tr>
<tr>
<td>Intelligent</td>
<td>0.84</td>
<td>0.63</td>
</tr>
<tr>
<td>Educated</td>
<td>0.77</td>
<td>0.46</td>
</tr>
<tr>
<td>Reasonable</td>
<td>0.38</td>
<td>0.49</td>
</tr>
<tr>
<td>Creative</td>
<td>0.37</td>
<td>0.61</td>
</tr>
<tr>
<td>Understanding</td>
<td>0.71</td>
<td>0.64</td>
</tr>
<tr>
<td>Sociable</td>
<td>0.64</td>
<td>0.74</td>
</tr>
<tr>
<td>Willing to put your ideas into practice</td>
<td>0.70</td>
<td>0.70</td>
</tr>
<tr>
<td>Interested in social issues</td>
<td>0.58</td>
<td>0.51</td>
</tr>
<tr>
<td>Critical</td>
<td>0.50</td>
<td>0.76</td>
</tr>
<tr>
<td>Interested in new fields of study</td>
<td>0.44</td>
<td>0.55</td>
</tr>
<tr>
<td>Articulate</td>
<td>0.41</td>
<td>0.75</td>
</tr>
<tr>
<td>Total variance explained</td>
<td>49.5%</td>
<td>50.4%</td>
</tr>
<tr>
<td>Cronbach’s Alpha</td>
<td>0.79</td>
<td>0.81</td>
</tr>
</tbody>
</table>

*Extraction Method: Principal Component Analysis; Rotation Method: Varimax with Kaiser Normalization.
education programs (38). A nurse’s career path from graduation to the highest leadership position takes 10-15 years (39). The positive dimensions of improved self-esteem and better training and education will only start to show results after a few years, which needs to be confirmed through additional research.

By using the factor analysis of the 2011 data, we defined four groups of nurse leaders with similar personal characteristics (second research question). The data shows three groups that are most often defined as positive for leadership in the Big Five model (10,40,41): extraversion (fourth factor), conscientiousness (first factor) and openness (third factor). Other studies also confirm that those factors are most directly linked to leadership (29,30,40).

The main limitation of our study was that it included only nurse leaders in hospitals. Therefore, a similar method should be employed to study the self-esteem of all nurses and compare it to that of nurse leaders. Furthermore, the study does not answer the question whether the higher self-esteem of leaders resulted in better leadership in health care. Studies in other areas show that high self-esteem has a positive impact on the quality of leadership, but there are many other factors influencing leadership (10,11).

CONCLUSIONS

Our analysis shows that in the period between the two studies (2001 and 2011) a group of leaders with high self-esteem was formed within the nursing profession in Slovenia. This was undoubtedly partly due to the activities of professional associations and the expansion of the network of colleges and faculties. There were 3,209 nurses with a university degree, specialisation and masters’ or doctoral degrees in Slovenia in 2001 compared to 5,576 in 2011 (21,22). Since 2005, increasing numbers of nurses have been coming out of faculties with a university education and are gradually assuming important leadership positions in health care organisations. Better support from professional organisations, leadership and management oriented training and higher formal education have all contributed to the higher self-esteem of nurse leaders. Clearly, the key part of responsibility now falls on health care organisations, which need to ensure that this potential is realised in the form of a higher quality of nursing care.

COMPETING INTERESTS

There was no funding source. The authors declare that there is no conflict of interest.

REFERENCES

Influence of coffee consumption on bone mineral density in postmenopausal women with estrogen deficiency in menstrual history

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ABSTRACT

Introduction: Complex etiology of osteoporosis include genetic, hormonal, environmental and nutritional factors. The aim of this study was to examine influence of coffee consumption on bone mineral density in postmenopausal women with estrogen deficiency in menstrual history.

Methods: This prospective study included 100 postmenopausal women, aged 50-65 years living in Sarajevo area, with estrogen deficiency in their menstrual history. The controlled clinical trials were conducted. Two groups were formed (based on bone mineral density values). The examination group included 50 women who had osteoporosis, while the control group included 50 women without osteoporosis (osteopenia, normal bone mineral density). The lumbar spine and proximal femur bone mineral density was measured by Dual–Energy X–ray Absorptiometry using Hologic QDR-4000 scanner. Coffee drinking habits were assessed for each subject.

Results: The average daily intake of coffee in women with estrogen deficiency in menstrual history was at 267.6 ml in the examination group and in the control group 111.6 ml. The difference in the average daily intake of coffee between the two groups was statistically significant (p < 0.001). There was registered significant correlation between intake of coffee and bone mineral density in examination (p < 0.01) and in control group (p < 0.05).

Conclusion: This study indicates that coffee consumption is a risk factor for osteoporosis in postmenopausal women, aged 50-65 years living in Sarajevo area, with estrogen deficiency in their menstrual history. It was shown that the effects of coffee on bone mineral density are dose-dependent.

Keywords: coffee consumption; osteoporosis

INTRODUCTION

The female reproductive system plays a major role in regulating the acquisition and loss of bone by the skeleton from menarche through senescence (1). Longer exposure to estrogen, either through natural menstruation or postmenopausal Estrogen Replacement Therapy, have protective effects.
on bone mineral density (2). The loss of ovarian function, whether premature or not, lead to an increased risk of bone mineral loss and developing of osteoporosis because of the lengthened time of exposure to reduced estrogen (3).

Osteoporosis has a complex etiology and is considered as a multifactorial polygenic disease in which genetic determinants are modulated by hormonal, environmental, and nutritional factors (4). Determination of osteoporosis risk factors related to habits (lifestyle) is important for both, prevention as well as disease treatment, as these factors can be modified. Caffeine for years is under discussion, whether has positive or adverse impact on health (5). Opinions about impact of coffee consumption on bone metabolism are still controversial. Study of Hasling C. et al. found that a coffee intake in excess of 1000 ml could induce an extra calcium loss of 1.6 mmol calcium/d, whereas intakes of 1-2 cups of coffee per day would have little impact on calcium balance in postmenopausal osteoporotic women, age 48 to 77 years, with postmenopausal crush fracture (6). Barger-Lux MJ et al. analyzed data from 560 calcium balance studies carried out on women aged from 34.8 to 69.3 years. The authors found a caffeine relationship such that for every 177.5 ml serving of caffeine-containing coffee, calcium balance was more negative by 0.114 mmol/day (4.6 mg/day). There was no evidence that the putative caffeine effect is confined to, or is greater among, subjects with low calcium intakes or those who are older or estrogen-deprived (7). Heaney RP found no evidence that caffeine has any harmful effect on bone status or on the calcium economy in individuals who ingest the currently recommended daily allowances of calcium (8). Study of Lacerda et al. examining effects of coffee on bone metabolism of mouses, indicated that coffee consumption has an effect on metabolism of calcium (including increased level of calcium in urine and plasma, decreased bone mineral density and lower bone volume) (9). Study of Sakamoto et al. haven’t found that coffee stimulates loss of bone tissue in mouses (10). That intakes of caffeine in amounts >300 mg/d accelerate bone loss at the spine in elderly postmenopausal women and that women with the genetic variant of vitamin D receptor appear to be at a greater risk for this deleterious effect of caffeine on bone was indicated in the study of Rapuri PB et al. (11). Direct negative effects of caffeine on osteoblastic cells (deleterious effect on the osteoblasts viability) was suggested in the study of Tsuang YH et al. (12). Goto et al. have found that plasma concentration sex hormone-binding globulin (SHBG) that binds estrogen (lower bioavailability of sex hormones) was higher in women who consumed four or more cups than women who did not consume coffee (13). The results of Wedick NM et al. study do not indicate a consistent effect of caffeine consumption on SHBG in men or women (14).

The data about the effects of coffee on bone are inconsistent. The aim of this study was to examine influence of coffee consumption on bone mineral density in postmenopausal women with estrogen deficiency in menstrual history.

**METHODS**

**Study design**

This prospective study included 100 postmenopausal women, aged 50-65 years living in Sarajevo area, with estrogen deficiency in their menstrual history. The controlled clinical trials were conducted. Two groups were formed (based on bone mineral density values, according to the WHO criteria). The examination group included 50 women who had osteoporosis, while the control group included 50 women without osteoporosis (osteopenia, normal bone mineral density). The lumbar spine and proximal femur bone mineral density was measured by Dual-Energy X-ray Absorptiometry using Hologic QDR-4000 scanner. Coffee drinking habits were assessed for each subject.

The women who met the following criteria were included in the study: postmenopausal women with estrogen deficiency in menstrual history (fewer than 30 years menstruation, menopause before age of 45 years), women aged 50-65 years, women who live in the Sarajevo area, women with osteoporosis, women without osteoporosis (osteopenia or normal bone mineral density), women who do not use hormone replacement therapy. The exclusion criteria were postmenopausal women without estrogen deficiency in menstrual history, women younger than
and older than 65 years, women who do not live in the Sarajevo area, women who are not postmenopausal, women who use hormone replacement therapy, women who have a disease that can cause osteoporosis, women who use drugs that may cause osteoporosis.

**Statistical analysis**

Statistical significance between examination and control group in intake of coffee was tested by Student’s t-test. The coefficient of linear correlation between intake of coffee and bone mineral density was calculated. P values less than 0.05 was considered as statistically significant. Data is presented in graphical and tabular forms.

**RESULTS**

The average age of women with estrogen deficiency in their menstrual history in the examination group was 58.48 years, and in the control group was 57.30 years (Figure 1). There was no statistically significant differences between these two groups, t = 1.169.

The average daily intake of coffee in women with estrogen deficiency in menstrual history was 267.6 ml in the examination group and in the control group 111.6 ml (Figure 2). The difference in the average daily intake of coffee between the two groups was statistically significant, t = 8.697; p < 0.001.

The coefficient of linear correlation between T scores and the average daily intake of coffee among women with estrogen deficiency in menstrual history in the examination group was statistically significant, r = −0.491; p < 0.01. The coefficient of linear correlation between T scores (Table 1) and the daily intake of coffee among women with estrogen deficiency in menstrual history in the control group was statistically significant, r = −0.356; p < 0.05.

**DISCUSSION**

The peak bone mass in the young can be increased and the rate of bone loss in the elderly possibly be reduced by dietary manipulation, which would be important and beneficial in the prevention of osteoporosis (15).

Coffee, a beverage used worldwide, includes a wide array of components that can have potential implication on health (16). Results of the studies on influence of coffee consumption on calcium metabolism, bone mineral density and fracture risk are contradicting. (6-8, 17–22). Potential of coffee intake as an osteoporosis risk factor is under debate (16). Lloyd T. et al. found no association between dietary caffeine intake and total body or femoral neck bone density or bone mass and found no associations between caffeine consumption and longitudinal changes in total body or femoral neck bone measurements (with and without statistical adjustment for calcium intake) (17). In the study of Choi EJ et al. coffee consumption showed no
significant association with bone mineral density of either femoral neck or lumbar spine in Korean premenopausal women (18). Ilich JZ et al. found that caffeine is negatively associated with bone mineral density of different skeletal sites in elderly women (19). Hallström H. et al. studied the relation between coffee intake and bone mineral density, taking into account, genotypes for cytochrome P450 1A2 (CYP1A2) associated with metabolism of caffeine. Men consuming 4 cups of coffee or more per day had 4% lower bone mineral density at the proximal femur compared with low or non-consumers of coffee. This difference was not present in women. High consumers of coffee with C/C genotype, rapid metabolism of caffeine, had lower bone mineral density than slow metabolizers (T/T and C/T genotypes). Calcium intake did not modify the relation between coffee and bone mineral density (20). In their study Tavani A. et al. found no association between hip fractures among women and consumption of regular or decaffeinated coffee, tea, and cola (21). Hallstrom H. et al. found that a high coffee consumption significantly increased the risk of osteoporotic fractures. The results of the study indicate that a daily intake of 330 mg of caffeine, equivalent to 4 cups (600 ml) of coffee, or more, may be associated with a modestly increased risk of osteoporotic fractures, especially in women with a low intake of calcium (22).

Data from animal studies are also inconsistent (9,10). In animal studies the influence of individual constituents of coffee on bone tissue was examined (23,24). The aim of Folwarczna J. et al. study was to investigate the effects of trigonelline, an alkaloid present in coffee, on bone mechanical properties of rats with normal estrogen level and estrogen deficiency. Administration of trigonelline did not affect the bone turnover markers, bone mineralization and mechanical properties of the tibial metaphysis, femoral diaphysis, and femoral neck in non-ovariectomized rats, but it worsened the mineralization and mechanical properties of cancellous bone in ovariectomized rats (estrogen-deficient rats) (23). The results of Folwarczna J. et al. study showed that caffeine has favorably affected on the skeletal system of ovariectomized rats, slightly inhibiting the development of bone changes induced by estrogen deficiency. Study found no significant caffeine effects on the bone in non-ovariectomized rats (normal estrogen levels) (24).

In this study influence of coffee consumption on bone mineral density in postmenopausal women, aged 50-65 years living in Sarajevo area with estrogen deficiency in their menstrual history was examined. The difference in the average daily intake of coffee between the group of women with osteoporosis and group of women without osteoporosis was statistically significant (p < 0.001). The coefficient of linear correlation between T scores and the average daily intake of coffee was statistically significant in both, group of women with osteoporosis (p < 0.01) and group of women without osteoporosis (p < 0.05). Results of this study showed that intake of coffee has an impact on bone mineral density in postmenopausal women, aged 50-65 years living in the Sarajevo area, with estrogen deficiency in their menstrual history. The effect of coffee on bone mineral density was dose-dependent. The average amount of consumed coffee in women with osteoporosis was 267.7 ml, and in women without osteoporosis 116.6 ml.

**CONCLUSION**

This study indicates that coffee consumption is a risk factor for osteoporosis in postmenopausal women, aged 50-65 years living in Sarajevo area, with estrogen deficiency in their menstrual history. It was shown that the effects of coffee on bone mineral density are dose-dependent. Based on the results of this research, it recommended that daily consumption of coffee be limited in order to preserve bone health of postmenopausal women with estrogen deficiency in their menstrual history (the average amount of consumed coffee in women without osteoporosis was 116.6 ml).

**CONFLICT OF INTEREST**

The authors declare that they have no competing interests.

**REFERENCES**


Evaluation of the treatment efficacy of patients with multiple sclerosis using Barthel index and expanded disability status scale

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ABSTRACT

Introduction: Multiple sclerosis (MS) is a chronic, autoimmune and progressive multifocal demyelinating disease of the central nervous system. The aim of this study was to evaluate rehabilitation of patients with multiple sclerosis using BI (Barthel index) and EDSS (Expanded Disability Status Scale).

Methods: A clinical observational study was made at the clinic for physical medicine and rehabilitation in Sarajevo. We analyzed 49 patients with MS in relation of gender, age and level of disability at admission and discharge, patient disability were estimated using EDSS scale. The ability of patients in their activities of daily living were also analyzed according to the BI at admission and discharge.

Results: Of the total number of patients (n=49) there were 15 men and 34 women. The average age of female patient was 42.38±13.48 and male patient 46.06±9.56. EDSS values were significantly different at the beginning and at the end of the therapy (p=0.001) as was the value of BI (p=0.001).

Conclusion: MS patients, after the rehabilitation in hospital conditions show significant recovery and a reduced level of disability; they show higher independence in activities but rehabilitation demands individual approach and adjustment with what patients are currently capable of achieving.

Keywords: rehabilitation; MS (Multiple Sclerosis); EDSS (Expanded Disability Status Scale); BI (Barthel Index)

INTRODUCTION

Multiple sclerosis (MS) is a chronic, demyelinating and progressive multi-focal disease which affects the auto-immunity of the central nervous system. When a certain part of the myelin sheath is inflamed and damaged, transfer of impulses through neurons is disturbed, slow or intermittent (1-3). Clinical symptoms of MS include nystagmus, tremors and dysarthria, eye disorder, movement disorders, sensibility problems with the coordination and balance of movement, problems with urination and defecation, sexual dysfunction, disturbances in cognition, fatigue, pain etc. (4,5).
Symptomatic treatment includes a full range of procedures that aim to alleviate the existing symptoms, in order to maintain active mobility for as long as possible and reduce the degree of disability of these patients (6,7).

The plan of rehabilitation of these patients is made to the status of disability by EDSS scale. The minimum value of the EDSS scale is 0 (normal neurological examination result) and the highest 10 (death due to complications of MS).

Activities of daily living were assessed by the Barthel Index with the lowest value of 0 (total dependence on others for care and assistance) to 20 (independent in activities of daily living) (8,9).

MS is often diagnosed in people between the ages of 25 and 50, but rarely in children and persons above age of 60. Women are 2 to 3 times more prone than man in contracting MS (6,7).

The aim of this study was to evaluate rehabilitation of patients with multiple sclerosis using BI (Barthel index) and EDSS (Expanded Disability Status Scale).

METHODS
A clinical observational study was made at the Clinic for physiology and rehabilitation, University Clinical center Sarajevo. The study included 49 patients with MS of both genders aged between 18 and 65 who were diagnosed with MS and who have undergone the recommended physical therapy as per the protocol. The study excluded patients who have not undergone physical therapy as per the protocol or had their treatment continued at the Neurological clinic in Sarajevo due to the worsening of the underlying disease. Level of disability of patients at admission and discharge in accordance with the EDSS (Expanded Disability Status Scale) is used as a measure of disease progression. This scale ranges from 0 to 10, with lower scores indicating lower level of disability. We have also analyzed the abilities of the patients in their activities of daily living according to the Barthel index at admission and discharge. This scale ranges from 0 to 20. A patient is fully dependent when the sum of point was 0-4, 5-12 shows high level of dependence, 13-18 shows moderate level, 19 shows low level and 20 shows total independence.

Statistical analysis
All the analytical data are presented in tables with an absolute number of cases, the arithmetic mean, standard deviation and range of value $\chi^2$ - square test. We also used ANOVA and Wilcoxon nonparametric test. All the tests with p<0.05 were considered statistically significant.

RESULTS
Of the total number of patients (n=49) there were 15 men and 34 women. The average age was 43.51±12.43, the average age of female patients was 42.38±13.48 years, and the average age of male patients was 46.06±9.56 years (Table 1).

By using a nonparametric Wilcoxon test, there was a statistically significant difference in the EDSS value before and after therapy (Table 2). The EDSS value before therapy was 6.04±1.52 (required regular or occasional assistance to walk up to 100 m with or without rest), whereas after therapy, the value fell to 5.46±1.51 (mobile without aid or rest, but with restrictions in daily activities), $Z$=-0.514; p=0.001.

By analyzing activities of daily living of the patients—before and after the therapy—based on the Barthel index and by implementing the Wilcoxon test, we have established a statistically significant difference in the clinical status. Before the therapy and after reception, based on the Barthel index, the patients were classified in the heavily dependent category (12.89±5.52), while after therapy their clinical

<table>
<thead>
<tr>
<th>TABLE 1. Gender and age of patients</th>
</tr>
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<tbody>
<tr>
<td><strong>N</strong></td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
condition improved and they were classified, according to the Barthel index, with moderate dependence (14.48±5.37), Z=-4.843; p=0.001 (Table 3).

DISCUSSION

Multiple sclerosis (MS) is a chronic disease of the central nervous system. It was named after lesions where histopathological samples of brain tissue appear as indurated areas-plaques (6). These plaques are “disseminated” in different areas of the central nervous system and appear at irregular intervals. With the development of neuro-radiological techniques, especially MRI (magnetic resonance imaging) of the brain, the number of diagnosed and newly diagnosed patients with MS has dramatically increased. It was found that in patients with MS, typically only one clinical manifestation of the disease occurs for each new 8 to 10 new lesions in the brain, that were confirmed by MRI (7).

Clinical features of patients with MS is actually very diverse with different symptoms that vary in severity. These patients, after diagnosis and neurological therapy, register for the rehabilitation mainly because of the problems with their motor skills and their inability to control their sphincters (8,9).

Study results show statistically significant difference in the gender representation of the respondents, and in the examined sample women dominated (p=0.007). These figures correspond to data from the literature; female patients suffer from MS, 2 to 3 times more than men.

Analysis of the age structure of patients shows that the average age was 43.51±12.43, the average age of female patients was 42.38±13.48 years, and for male patients, it was 46.06±9.56 years. This data indicates that there is no statistically significant difference in age structure of the respondents in relation to their gender (p=0.344). Research conducted earlier show that the average age of patients with MS in rehabilitation was lower. We think that reason for this difference is better diagnosis and the earlier involvement of patients in the rehabilitation process, but it is also possible that other studies involved younger patients (10,11).

The assessment of the degree of disability is shown through EDSS and used as a measure of the progression of the disease and severity of neurological disorder in these patients (12). During the process of rehabilitation, patients tried to increase their mobility by kinesiotherapy (13). Also, all patients underwent occupational therapy to gain competence in day to day activities. The analysis of the EDSS values before and after the therapy showed statistically significant differences. The EDSS value before therapy was V6.04±1.52 which means that patients needed permanent or temporary orthopedic aid such as the use of canes, crutches or walking frame to walk up to 100 m, with or without rest; while after the therapy, the value dropped to 5.46±1.51, which means that the patient is mobile without assistance or rest, but is limited in daily activities (p=0.001). Our research shows that patients with a greater degree of disability were registered for the rehabilitation then what other studies have shown (14,15). Research conducted in France and England have shown that inpatient rehabsilizations is carried out for small disabilities and in the earlier phases of the disease when they expect the effects of the treatment to be better (16-18).

By analyzing the activities of daily living according to the Barthel index, significant statistical difference in clinical conditions was established (p=0.001) before and after physical therapy. Upon reception, the patients were classified as being heavily dependent (12.89±5.52), while after the treatment, their clinical condition improved and they were, according to the Barthel index, classified as being moderately dependent (14.48±5.37). These
data confirm that physical therapy (kinesiotherapy and occupational therapy) is of great importance in enabling patients in carrying out day to day activities. Research done in the last three years also gives similar results. It is recommended that the evaluation of different possibilities and aspects of physical therapy should be tailored to each patient and to respect current possibilities of these patients in each therapeutic procedure (19,20). An important prognostic factor is the movement in the Barthel index at the beginning, during and after physical therapy which will, if stagnant, show that the best clinical recovery in day to day life activities has been reached (20).

CONCLUSION

Patients with the MS, after rehabilitation in hospital conditions, show significant recovery and reduced degrees of disability. In activities of daily living they were more independent, but the rehabilitation demands an individual approach and adaptation to the current capacities of the patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

Adherence to oral anticoagulation therapy

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ABSTRACT

Introduction: Warfarin is the most frequently prescribed anticoagulant. Clinical treatment is demanding because of the narrow therapeutic range and considerable differences between the patients. The aim of this survey is to establish adherence to warfarin in subjects who have been prescribed warfarin as a long-term therapy.

Methods: The survey included 30 subjects, and was conducted at local pharmacy store. Statistical processing was carried out using the SPSS (ver. 21.) software. Used for qualitative variables was the Chi-square test, and for quantitative ones the ANOVA test. Data were provided in the form of tables and charts. Level of significance was p=0.05.

Results: The survey included 30 subjects, 14 men and 16 women. Of the total number of polled subjects, 15 were informed by a health care professional about the specifics of warfarin use, 7 said they were not informed, while 8 said they did not know. Most compliant in terms of regularly taking their medicines were pensioners, followed by the unemployed, χ²=13.231; p<0.05. The number of subjects within the expected therapeutic INR range was 22 (p<0.05).

Conclusion: Strict compliance with the warfarin regimen is important in order to increase its effectiveness, extend the time and strengthen the intensity of anticoagulant action in the body. That is why the target groups of patients, who use warfarin, need additional information before and during therapy, in order to avoid side effects, and at the same time maintain therapeutic efficacy of the medicine throughout the treatment.

Keywords: adherence; compliance; anticoagulation therapy

INTRODUCTION

Warfarin is the most frequently prescribed anticoagulant; it is prescribed to more than 2 million new patients every year. Warfarin is often used as a permanent therapy for prevention of embolism in patients with atrial fibrillation, heart valve disease, and for primary and secondary prevention of venous thromboembolism (1). Warfarin is also used to prevent thromboembolic attacks in patients with acute myocardial infarction and angina pectoris, in patients with biological heart valves, and after certain orthopedic surgeries. Clinical treatment is demanding because of the
narrow therapeutic range and considerable differences between the patients. In the absence of data obtained by genetic research or clinical information to predict the necessary dose of warfarin for each individual patient (2), initial prescribed doses may be too low, which increases the risk of thrombosis, or too high, which leads to the risk of excessive anticoagulation and heavy bleeding. In the United States, there are annually up to 800 adverse events related to the use of warfarin that are encompassed by the reporting rule (3). The risk of serious warfarin-related side-effects, its narrow therapeutic range and large inter-individual dosing differences require a preparation of algorithms in order to be able to predict, as closely as possible, the dose necessary at the initial stage(s) of treatment. Because proper administration of therapy remains a clinically significant problem despite years of research (4), a new assessment of basic issues, such as the terms used in the field, may be necessary to be able to identify innovative strategies of clinical interventions and investigations (5). Adherence is defined as: “the extent to which patients follow the instructions they are given for prescribed treatments” (6). Adherence to warfarin treatment, as well to that of other medicines (7), is essential for a good health condition of elderly patients and is thus a critical health care component. Non-compliance with the recommendations for the therapy at old age has been proven to increase the likelihood of therapeutic failure (8) and is responsible for unnecessary complications leading to increased health protection costs, early functional disability and premature death (9). Poor adherence to therapy was reported in all age groups. However, a larger prevalence of cognitive and functional disorders in elderly persons increases the risk of poor adherence. Multiple concomitant diseases and a complex medical treatment may further compromise warfarin adherence. Age-related changes in pharmacokinetics and pharmacodynamics render this population even more sensitive to the problems caused by poor adherence to therapy (10). The aim of the study was to determine the adherence to warfarin in patient’s whom warfarin is a long-term therapy and to evaluate the factors that directly or indirectly reduce or increase the level of adherence.

METHODS
The survey included 30 subjects, who were undergoing an anticoagulant therapy. The survey was conducted at local pharmacy store in Sarajevo in 2013. The main inclusion criterion was continuous warfarin therapy through at least 12 months. Within the group of subjects who met inclusion criteria, 30 patients were randomly chosen. The subjects were polled, and the answers received were statistically processed. Modified Morisky questionnaire on chronic therapy adherence has been used. Subjects have had 4 measurements of INR values during the therapy course.

Statistical analysis
Statistical processing was carried out using the SPSS (ver. 21.) software. Used for qualitative variables was the Chi-square test, and for quantitative ones the ANOVA test. Data were provided in the form of tables and charts. Level of significance was p=0.05.

RESULTS
The survey included 30 subjects, 14 men and 16 women. An analysis of average age of the subjects, by applying the ANOVA test, did not find a statistically significant difference (Table 1). The average age of male subjects was 55.14±16.96 years, and that of female subjects 54.43±15.48 years, F=0.014; p=0.906.

An analysis of marital status of the subjects included in the survey found that the majority of the subjects were married (n=22), while three subjects from each group have never been married or have the status of a widow(er). One of the subjects was divorced (Figure 1).

Figure 2 shows INR values during measurement. Established with the use of the Chi-square test, there was a statistically significant difference in the frequency of findings within the expected therapeutic range (p<0.05). On first measurement, in 12 subjects the INR values were within the expected therapeutic range, on the second measurement 14, on the third measurement 17, and finally on the ultimate, fourth, measurement the number of subjects whose results were within the expected INR therapeutic range was 22.
Of the total number of polled subjects, 15 were informed by a health care professional about the specificities of warfarin use, 7 said they were not informed, while 8 said they did not know (Table 2). Answers to the question about the frequency of forgetting to take the medicine have produced statistically significant difference (Table 3). Most compliant in terms of regularly taking their medicines were pensioners, followed by the unemployed, $\chi^2=13.231; p<0.05$.

Over the past two weeks, the frequency of forgetting to take medicine was the lowest in pensioners and the unemployed (Table 4), while those employed and students tend to forget to take their medicines more often, so there is a statistically significant difference in relation to the employment status, $\chi^2=14.948; p<0.05$.

Based on the answers to the question on adherence, the subjects mostly said they did not forget to take medicines while traveling; also they never stop using medicines without prior consultation with the relevant doctor. When asked whether they feel under pressure because daily administration of medicines might be impractical, they mostly said they never felt that way, while 5 subjects said they sometimes do feel under pressure (Table 5).

**DISCUSSION**

Coumarine derivatives (warfarin and acenocoumarol) are vitamin K antagonists (VKA) and are used for long-term treatment of patients with venous thrombo-embolism (VTE). Warfarin therapy usually starts within 24-72 hours of the onset of parenteral heparin treatment. The usual initial dose is 5-10 mg, while lower doses are recommended to elderly patients, or those with lower body weight, or underweight patients. Warfarin doses and their monitoring have been adjusted to the INR (international normalized ratio) values (11). The survey polled 30 patients on warfarin. The average age of the subjects was 55. Most of the subjects were married. While measuring INR values during the treatment statistically significant difference in terms of the number of subjects with referent

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**TABLE 1.** Age and gender of subjects

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Std. Error</th>
<th>95% confidence interval for mean Lower bound</th>
<th>Upper bound</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>14</td>
<td>55.14</td>
<td>16.96</td>
<td>4.53</td>
<td>45.3473</td>
<td>64.9384</td>
<td>23.00</td>
<td>75.00</td>
</tr>
<tr>
<td>Female</td>
<td>16</td>
<td>54.43</td>
<td>15.48</td>
<td>3.87</td>
<td>46.1848</td>
<td>62.6902</td>
<td>30.00</td>
<td>75.00</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>54.76</td>
<td>15.91</td>
<td>2.90</td>
<td>48.8247</td>
<td>60.7086</td>
<td>23.00</td>
<td>75.00</td>
</tr>
</tbody>
</table>

**TABLE 2.** Level of information concerning the specificities of warfarin use, provided by health care professional

<table>
<thead>
<tr>
<th>Answer</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>15</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
</tr>
<tr>
<td>No</td>
<td>7</td>
<td>23.3</td>
<td>23.3</td>
<td>73.3</td>
</tr>
<tr>
<td>Do not know</td>
<td>8</td>
<td>26.7</td>
<td>26.7</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

**FIGURE 1.** Marital status of subjects.

**FIGURE 2.** INR values during measurement period.
values during 4 measurements was discovered. On first measurement, the figure was 12, and after the fourth measurement the number of subjects within the expected therapeutic INR range was 22 (p<0.05) (Chart 2). Randomized clinical studies during which the patients indicated for anticoagulant therapy were randomly prescribed warfarin or some other alternative anticoagulant were rather helpful by showing the risk of warfarin-related non-compliance (5,12), independently from the potentially confounding factors affecting the validity of observational studies. When it comes to patients who were prescribed warfarin or an alternative medicine, it is necessary to analyze additional factors affecting the treatment outcome due to non-compliance or improper drug administration (6,8). In such studies, regular INR testing was carried out mostly on randomized patients using warfarin. In these studies, both the side-effects and the monitoring may be factors affecting poor adherence (13). Some trials have shown that subjects using oral anticoagulants tend to discontinue their therapy more often, while some have shown no difference in terms of non-compliance with the prescribed therapy in relation to placebo (13). In the polled group, only 50% of the subjects were informed by a health care professional about the specificities of warfarin administration. The frequency of forgetting to take medicines was most often reported in those employed, while pensioners were most regular in taking their therapy. The subjects polled mostly said they did not forget to take warfarin even when they traveled. Of the total number of subjects (n=30), 28 said they never stopped taking warfarin without consulting a physician, despite good clinical picture of primary disease for which warfarin has been administered. Most of the subjects never feel pressure on account of the medicine administration regimen, while 5 subjects said they sometimes felt pressure, and 4 subjects feel pressure more often. Unemployed subjects are the ones who have most difficulties remembering to take warfarin. A study conducted in Japan analyzed warfarin adherence in subjects who took therapy for atrial fibrillation (14). Of the total number of subjects (n=330), as many as 52% did not know the therapeutic significance of warfarin. A questionnaire found that only 51% of the subjects had a basic preliminary knowledge of warfarin, atrial fibrillation and heart attack (14).

**TABLE 3. Frequency of forgetting to take medicine**

<table>
<thead>
<tr>
<th>Employment status</th>
<th>Unemployed</th>
<th>Employed</th>
<th>Student</th>
<th>Pensioner</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I never forget to take medicine</td>
<td>9</td>
<td>5</td>
<td>0</td>
<td>11</td>
<td>25</td>
</tr>
<tr>
<td>I forget to take medicine once a week</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>I forget to take medicine 2 to 3 times a week</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>11</td>
<td>30</td>
</tr>
</tbody>
</table>

**TABLE 4. Frequency of forgetting to take medicine over the past two weeks**

<table>
<thead>
<tr>
<th>Employment status</th>
<th>Unemployed</th>
<th>Employed</th>
<th>Student</th>
<th>Pensioner</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not once</td>
<td>11</td>
<td>5</td>
<td>0</td>
<td>11</td>
<td>27</td>
</tr>
<tr>
<td>Once or twice</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>3 to 5 times</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>11</td>
<td>30</td>
</tr>
</tbody>
</table>

**CONCLUSION**

Strict compliance with the warfarin regimen is important in order to increase its effectiveness, extend the time and strengthen the intensity of anticoagulant action in the body. That is why the target groups of patients, who use warfarin, need additional information before and during therapy, and a quality interaction between the health care professional and the patient, in order to avoid side effects, and at the same time maintain therapeutic efficacy of the medicine throughout the treatment. Adherence to warfarin can be successfully monitored by determining the value of INR, however adherence itself is directly affected by patient’s knowledge on warfarin’s mode of action, patient’s...
daily and professional activities as well as form of the drug and therapy regimen.

**COMPETING INTERESTS**

Lana Lekić works as a medical representative for Boehringer Ingelheim RCV GmbH&Co.KG. Alen Lekić works as a medical representative for Sanofi Aventis groupe.

**REFERENCES**

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<table>
<thead>
<tr>
<th>TABLE 5. Answers to questions on compliance</th>
<th>Employment status</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>When you travel, do you forget to take your medicines with you?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I do not travel</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>Never</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>$\chi^2=1.197$; $p=0.754$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>When you feel your health is under control, do you sometimes stop taking medicines on your own, without consulting a doctor?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I never do it alone</td>
<td>11</td>
<td>28</td>
</tr>
<tr>
<td>I sometimes do it alone</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>I always do it alone</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>$\chi^2=11.727$; $p=0.068$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taking medicines every day is impractical for many people. Do you feel under pressure because you need to follow recommendations for your treatment?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I never feel that way</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>I sometimes feel that way</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>I often feel that way</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>I always feel that way</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>$\chi^2=12.006$; $p=0.213$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>How often do you have difficulties remembering to take your medicine?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>8</td>
<td>24</td>
</tr>
<tr>
<td>Sometimes</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Often</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>$\chi^2=0.249$; $p=0.168$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Knowledge, perception, practices and barriers of healthcare professionals in Bosnia and Herzegovina towards adverse drug reaction reporting

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ABSTRACT

Introduction: Pharmacovigilance is an arm of patient care. No one wants to harm patients, but unfortunately any medicine will sometimes do just this. Underreporting of adverse drug reactions by healthcare professionals is a major problem in many countries. In order to determine whether our pharmacovigilance system could be improved, and identify reasons for under-reporting, a study to investigate the role of health care professionals in adverse drug reaction (ADR) reporting was performed.

Methods: A pretested questionnaire comprising of 20 questions was designed for assessment of knowledge, perceptions, practice and barriers toward ADR reporting on a random sample of 1000 healthcare professionals in Bosnia and Herzegovina.

Results: Of the 1000 respondents, 870 (87%) completed the questionnaire. The survey showed that 62.9% health care professionals would report ADR to the Agency for Medicinal Products and Medical Device of Bosnia and Herzegovina (ALMBIH). Most of surveyed respondents has a positive perception towards ADR reporting, and believes that this is part of their professional and legal obligation, and they also recognize the importance of reporting adverse drug reactions. Only small percent (15.4%) of surveyed health care professionals reported adverse drug reaction.

Conclusions: The knowledge of ADRs and how to report them is inadequate among health care professionals. Perception toward ADR reporting was positive, but it is not reflected in the actual practice of ADRs, probably because of little experience and knowledge regarding pharmacovigilance. Interventions such as education and training, focusing on the aims of pharmacovigilance, completing the ADR form and clarifying the reporting criteria are strongly recommended.

Keywords: knowledge; health care professionals; adverse drug reaction (ADR); pharmacovigilance; Bosnia and Herzegovina

INTRODUCTION

Any drug/medicine during its normal therapeutic use has a potential to produce adverse drug reaction(s) (ADRs). ADRs contribute to a significant number of morbidity and mortality all over the world (1). It has been estimated that around...
2.9-5.6% of all hospital admissions are due to ADRs and as many as 35% of hospitalized patients experience an ADR during their hospitalization (2). The economic burden of ADRs is also considerable; for example in the United States, annual total cost of $47.4 billion for 8.7 million drug related admissions were reported (3).

Many developed countries have strong and efficient pharmacovigilance systems. Good pharmacovigilance system will identify the risks and the risk factors in the shortest possible time so that harm can be avoided or minimized (4). These systems among other use spontaneous reporting to collect and analyze adverse events associated with the use of drugs. Though this process is not perfect, it can provide evidence that can be used to establish regulatory action to protect public health, and in addition it is fast and cost-efficient method.

Several studies (5) have indicated a variety of obstacles to the spontaneous reporting of ADRs, such as lack of time (6,7) different care priorities (7), uncertainty about the drug causing the ADR (7-10), difficulty in accessing reporting forms (6), lack of awareness of the requirements for reporting (7,10) and lack of understanding of the purpose of spontaneous reporting systems (6).

Physicians, pharmacists, dentists and nurses are in a position to play a major key role in pharmacovigilance programs (11,12) but underreporting is very common, with an estimated median underreporting rate (defined as percentage of ADRs detected from intensive data collection that were not reported to relevant spontaneous reporting systems) of 94% (5).

Pharmacovigilance is still in its infancy in Bosnia and Herzegovina (BiH) and there exists very limited knowledge about this discipline. In the period after the war, until the establishment of the Agency for Medicinal Products and Medical Devices of Bosnia and Herzegovina (ALMBiH) there were two regional centers where health care professionals (HCP) were able to report ADR. In the Federation of Bosnia and Herzegovina (FBiH), this was a Center for Medicine at the Institute of Pharmacology, Faculty of Medicine in Sarajevo, while in the Republic of Srpska (RS) this was Drug Agency RS.

The ALMBiH was established in accordance with the Medicinal Products and Medical Devices Act of Bosnia and Herzegovina as the competent body responsible for the field of medicinal products and medical devices manufactured and used in BiH. It began operating on May 1 2009. (13). ADR reporting in BiH is closely linked to economic problems in the local healthcare system, which is still being developed. The level of ADR reporting is inadequate despite the fact that information on the safety of medicinal products is of vital importance and despite the fact that reporting on adverse effects to the ALMBiH is a legal obligation. This obligation is defined in the Book of rules on the manner of reporting, collecting and following adverse effects of the medicinal product, in Article 11 (14) “medicinal product manufacturers, health care institutions and health care professionals (medicinal doctors, dentists, pharmacists, health technicians, nurses) are under the obligation to report to the Agency any suspicion about the adverse effects of a medicinal product”.

The objective of this study was to gain insight into the perceptions, practices and barriers of HCP with respect to the reporting of ADRs and pharmacovigilance.

**METHODS**

Knowledge, perceptions, practices and barriers of healthcare professionals about terms related to pharmacovigilance and reporting of adverse drug reactions have been tested with the help of a structured questionnaire that was distributed in person (the response to the survey was either obtained at the same time or collected at a later time) or via e-mail. A random sample of healthcare professionals (doctors of different specialties, pharmacist, dentists, technicians and nurses) were randomly selected from different hospitals and health centers, distributed over all regions of BiH. As there is no common database of HCP in BiH there is no guarantee they represent country profile. The questionnaire included issues addressed in previous studies examining the same problem (6-8,15-20), but was modified by taking into account local features and simplified to exclude non relevant questions. A draft questionnaire was pretested by administering it to 6 healthcare professionals, which consisted of three pharmacists, two physicians and two dentists. Based on their comments and suggestions a final questionnaire was
prepared for conducting the survey. The final version consisted of five sections containing 20 questions. Among these questions, 5 items were related to the demographical and professional profiles, 3 to the knowledge, 3 to the perception, 2 were related to practice aspects and the remaining 7 items were related to the barriers. Except questions related to demographical and professional profile, questions were worded as a series of statements and the healthcare professionals were asked to indicate their agreement or disagreement on a 4-point Likert scale from ‘strongly agree’ to ‘strongly disagree’.

This questionnaire survey was conducted during January 2012 to September 2012.

Statistical analysis
The collected data were entered into the Excel table and then analyzed using the IBM Statistical Package for Social Sciences (SPSS) version 20.0.

RESULTS
A total of 1000 questionnaires were distributed/sent and 870 were returned completed, so all analyses were therefore made based on the 870 filled in questionnaires. The demographic and professional details of the respondents are shown in Table 1.

Most respondents were in Sarajevo (36.9%), Tuzla (22.8%) and Banja Luka (21.5%). The remaining 18.8% of respondents were interviewed in other cities.

The majority of respondents (84.6%, i.e. 736 respondents) provided a negative response to the question “Have you ever reported an adverse drug reaction?” and only 15.4% (133 respondents) gave a positive response. 17.1% of them were physicians, 25.2% pharmacists, 6.6% dentists, 10.7% nurses and 13.8% technicians.

62.9% of respondents recognize the Agency for Medicinal Products and Medical Devices of Bosnia and Herzegovina as the institution to which ADR of a medicinal product are to be reported. A further question we used to establish how informed the respondents are on the issue pharmacovigilance was whether they agreed with the assertion that ADR reporting forms are available. Pharmacists in many cases (43.4%) claimed that the reporting forms are available, while not even a fifth of the respondents from the other categories agreed that this was the case.

Asked about their experience in filling out the ADR reporting form, 46.6% of the respondents from our sample stated that they do not have enough experience.

Almost three quarters (79.1%) of respondents report ADR only if they are certain that it is linked to a specific medicinal product, 80.5% of respondents would consult with a physician/pharmacist/dentist before reporting an ADR and only 4.1% do not share such a view.

It was found out from the result that almost all health providers agree towards the fact that reporting about ADR is part of their ethical (83.2%) and legal (82.2%) duty and that the science of pharmacovigilance is important (92.6%).

Several factors were reported that negatively affected health care professionals’ willingness to report. Table 2 lists factors that may act as deterrents to reporting by HCP.

DISCUSSION
This is the first survey, which we are aware of, to explore healthcare professionals knowledge, attitude,
perceptions and their barriers towards ADR reporting and pharmacovigilance in BiH. The survey response rate was good (87%).

Although the majority of healthcare professionals correctly responded to whom they should report adverse reactions, it needs to be noted that almost a third gave a wrong answer to this question. This is a relatively high percentage of healthcare professionals who failed to provide a correct answer. This also indicates that although more than 4 years have passed since the establishment of ALMBIH, not enough publicity has been given to this. Results of the survey in one of Istanbul’s districts show that only 6.7% of pharmacists would send their reports to the national pharmacovigilance center (TUFAM), i.e. the correct address (21).

It has transpired that the unavailability of ADR reporting forms is significantly impacting the informedness of healthcare professionals, despite the fact that the forms are also on the ALMBIH website, as well as in the Register of Medicinal Products. The Rhode Island survey (22) provided similar results with 38% of physicians stating that they do not know where to find the forms and that this is why they were not reporting adverse reactions.

Asked about their experience in filling in the ADR reporting form, just under 50% of healthcare professionals included in the survey stated that they do not have enough experience.

The majority of healthcare professionals in our survey have never reported an adverse reaction.

The percentage of reported adverse reactions is very low when compared to the number of adverse reactions reported by physicians in Great Britain (23), the Netherlands (24), Spain (25) and China (26). Differences in the number of reported ADRs can be attributed to the priority, care and commitment to pharmacovigilance on the part of the national governments of those countries. Regulatory bodies in BiH should also adopt such an approach. It is evident that pharmacovigilance activities in BiH are not adequately presented or advertised.

Questions concerning perception focused on the general perception of healthcare professionals regarding the standard aspects of ADR reporting. The survey has shown that healthcare professionals have a positive attitude towards ADR reporting. The vast majority consider reporting a part of their professional obligations, as well as an integral part of the code of ethics. These results are largely similar to the results of surveys carried out among pharmacists working in pharmacies in cities in the Netherlands (27) and Great Britain (28).

Although the majority of healthcare professionals covered by the survey expressed a proper and positive attitude towards ADR reporting, actual hands-on experience in reporting is still lacking. Similar responses were obtained through three surveys conducted in India (29-31) where both the knowledge and a positive attitude exist, but adverse reactions are still not being reported.

Even though the Book of Rules on Adverse Effects (14) stipulates that all adverse effects are to be reported, even when a link has not been established, healthcare professionals have stressed that they must be certain that a link between a medicinal product and an adverse effect does exist. This is in line with the conclusions from earlier surveys conducted among pharmacists and physicians in other countries (10,32,33) who expressed concern over showing a lack of knowledge because they are uncertain whether a medicinal product has caused an adverse reaction or not. This problem needs to be approached carefully and educational programs need to be organized to alleviate the anxiety of healthcare professionals and strengthen their confidence in reporting adverse reactions.

| TABLE 2. Barriers to spontaneous reporting of ADRs |
|---------------------------------------------------|-------------------------------------------------|---------------------------------|---------------------------------|-----------------------------|
| Barriers                                          | Agree                                           | Partially Agree                  | Partially disagree              | Disagree                    |
| Reporting form too complicated                    | 19.9                                           | 31.3                            | 10.8                            | 37.0                         |
| Reporting ADRs is time consuming                   | 20.2                                           | 29.5                            | 10.6                            | 38.6                         |
| Difficult to admit harm to patient                 | 26.6                                           | 27.7                            | 9.2                             | 36.4                         |
| Fear of liability                                 | 10.6                                           | 14.9                            | 12.3                            | 62.1                         |
| Insufficient clinical knowledge                    | 13.1                                           | 19.2                            | 10.3                            | 57.2                         |
| Patient confidence                                | 11.3                                           | 26.4                            | 14.4                            | 47.5                         |
| No motivation                                     | 9.2                                            | 18.4                            | 11.4                            | 60.9                         |
A large percentage of healthcare professionals have indicated that they would consult a colleague (physician/pharmacist/dentist) before reporting an adverse effect even though they are not under an obligation to do so. This could indicate a lack of confidence in their own knowledge, and perhaps even fear of legal consequences. Similar results came out of previous surveys (27, 28). Colleagues should not be consulted in relation to reporting an adverse effect because that could be an obstacle to reporting and lead to a situation where the person reporting the adverse effect is dependent on someone else’s opinion.

It is widely accepted that reporting on adverse effects is linked to a high degree of side effects not being reported, however, it is difficult to assess the scope of this problem. It is estimated that 90-95% of adverse effects go unreported (34). To identify the reasons for underreporting, several studies were conducted where different authors investigated the knowledge, attitudes and practices of healthcare professionals toward the ADR reporting. According to the findings of the studies (1, 5, 26, 32) healthcare professionals mentioned different factors that have contributed towards their underreporting: lack of awareness of the requirement for reporting, lack of resources for surveillance and reporting, time-consuming reporting process, well-known reactions, an uncertain association, what is similar to our results. Of all obstacles mentioned in the survey, respondents have identified two as being the dominant reasons for the failure to report adverse effects, including lack of experience in filling out the ADR reporting forms (71.4%) and unavailability of ADR reporting forms (72.7%). Other reasons mentioned in the survey include: the ADR reporting form is too complicated (51.6%), reporting requires a lot of time (50.2%), reporting could show a lack of knowledge (32.3%), reporting requires the use of my own resources and I am not motivated to do that (27.6%), fear of responsibility (25.6%) and the position that one case that goes unreported does not make a difference (18.1%).

According to responses provided by healthcare professionals covered by the survey, non-reporting of adverse effects in BiH appears to be linked with a lack of knowledge concerning the ADR reporting process and not with the personal and professional characteristics reported in other surveys. The ADR reporting rate can therefore be increased by overcoming the abovementioned obstacles as has been confirmed by certain studies. Some of these obstacles can be addressed by proper management and the promotion of a pharmacovigilance program, and with relevant guidelines that would be available to all. Also there is an urgent need for postgraduate educational programs to emphasize the role and responsibility of the HCP in pharmacovigilance practices, to underline the importance of pharmacovigilance and ADR reporting. In conclusion, it is necessary to offer continuous educational programs until we reach the point that voluntary reporting of ADRs become customary and habitual among all HCP.

The limitation of this study is the fact that surveyed HCP as well as related institutions and cities, which are randomly selected, do not represent HCP in all BiH. Another limitation of this study is the answer reliability - inherent problem with surveys and interviews, and whether the responses of HCP are truly representative. Third limitation of study is small number of questions in the survey which evaluated knowledge and perception of PV. Although this study has certain limitations and it would be inappropriate to plan interventions based on the findings of this study alone, however, it does provide an insight into the possible interventions that could be planned in future.

CONCLUSION

Under-reporting of adverse reactions is a phenomenon present in all parts of the world, this has been confirmed by surveys already conducted, and it can be attributed to all healthcare professionals.

The results of this survey have shown that even though the majority of healthcare professionals have never reported an ADR, although they do have a positive perspective towards pharmacovigilance. The results suggest that ADR under-reporting is a result of unfamiliarity with the existing reporting system. Regulatory bodies need to improve the management and promotion of the reporting system in BiH in order to address the issue of healthcare professionals lacking the necessary knowledge on ways to report. It could take a while before healthcare professionals accept ADR reporting as part of their everyday
practice, but on the long run, this is definitely worth the effort.

COMPETING INTERESTS
The authors declare no conflict of interest.

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Mental foramen mimicking as periapical pathology - A case report

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ABSTRACT
The radiographic recognition of any disease requires a thorough knowledge of the radiographic appearance of normal structure. Intelligent diagnosis mandates an appreciation of the wide range of variation in the appearance of normal anatomical structures. The mental foramen is usually the anterior limit of the inferior dental canal that is apparent on radiographs. It opens on the facial aspect of the mandible in the region of the premolars. It can pose diagnostic dilemma radiographically because of its anatomical variation which can mimic as a periapical pathosis. Hereby we are reporting a rare case of superimposed mental foramen over the apex of right mandibular second premolar mimicking as periapical pathology.

Keywords: mental foramen; periapical radiolucency; mandibular premolars

INTRODUCTION
Many articles have been reported about various conditions that may mimic periapical inflammatory lesion such as carcinoma (1), odontogenic cyst (2) and periapical cemental dysplasia (3) etc. Film processing errors has also been reported to mimic the appearance of periapical infection (4), while normal anatomies such as the mental foramen or incisive foramina are familiar as radioluencies that may overlie teeth and cause diagnostic confusion. This case report enlightens an anatomical variation of mental foramen (MF) manifesting as well defined periapical radiolucency in relation to the roots of lower right second premolar, which was suggestive of periapical pathology.

CASE REPORT
A 30 year old male patient reported to the Department of Oral Medicine and Radiology with the complaint of tooth decay in the lower right back tooth jaw region since six months. It was associated with dull, intermittent, non-radiating type of pain. Medical, family and dental histories were non-contributory. On intra oral examination, deep class II cavity with respect to right second premolar, first and second molar was observed. Provisional diagnosis of chronic irreversible pulpitis was considered for right mandibular first and second molar and deep dental caries with respect to right mandibular second premolar.

Periapical radiograph of right mandibular posterior region revealed diffuse coronal radiolucency.
involving pulp with no periapical changes noticed with respect to mandibular molars. The mandibular second premolar revealed diffuse coronal radiolucency approximating the pulp with intact lamina dura in the periapical region. Hazy periapical radiolucency (Figure 1) noticed at the apex of mandibular second premolar with poor defined borders mimicking as periapical pathology. To rule out, a second radiograph (Figure 2) was taken at different angulation which revealed the same finding but the radiolucency had moved mesially with an intact the lamina dura around the tooth, hence we arrived at a provisional diagnosis of mental foramen which was mimicking as periapical pathology. We also noticed increased in the width of root at the apical one third of the second premolar suggestive of hypercementosis. The patient was referred to the Department of Conservative Dentistry and Endodontics for the further treatment.

**DISCUSSION**

The MF is an opening on the anterolateral surface of the mandible, which is generally seen to be oval or circular in shape from where the mental neurovascular bundle exits. After passing through the mandibular foramen, the inferior alveolar nerve and artery, exit at the mental foramen as the mental nerves and vessels which innervate the lower teeth, lip, gingiva and soft tissues of chin area. The foramen opens directed posteriorly, outward and upwards. There are variations in the position of mental foramen. Frequent position is in between and below the apices of first and second premolars (5).

The mental nerve is a somatic afferent sensory nerve and corresponds to the terminal branch of the mandibular nerve, which is the third division of the trigeminal nerve. In the premolar region, the inferior alveolar nerve, a branch of the mandibular nerve, usually splits into two branches, the mental nerve and the incisive nerve. The incisive nerve runs intra-osseously along with veins and innervates the anterior mandibular teeth (incisors, canines, and premolars) (6). The mental nerve emerges at the mental foramen and divides into four branches: angular (innervations of the angle of the mouth region), medial and lateral inferior labial (skin of the lower lip, oral mucosa, and gingiva as far posterior as the second premolar), and mental branch (skin of the mental region) (7).

It is usually the anterior limit of the inferior dental canal that is apparent on radiographs. Its image is quite variable and it may be identified only about half the time because the opening of the mental canal is directed superiorly and posteriorly. Because of this, the usual view of the premolars is not projected through the long axis of the canal opening. This circumstance is responsible for the variable appearance of the mental foramen (8).

Mental foramen variations are often encountered, ranging from difference in position of foramen
on anterolateral surface of mandible or presence of accessory foramina or even complete absence in some rare cases. The location of mental foramen also changes along with the age changes (9). Usually the MF is seen to be closer to the alveolar ridge in children before tooth eruption; as the teeth start to erupt the MF starts descending to the midway between the upper margin and lower border and in adults with the teeth present for long time, the MF moves somewhat closer to the inferior border comparatively. In old age eventually with the loss of teeth and bone resorption of the edentulous ridge the MF moves relatively up towards the alveolar ridge. In extreme cases of resorption, the MF and the adjacent part of the mandibular canal are open at the alveolar margin. According to the degree of resorption, in severe cases, the mental nerve and the final part of the inferior alveolar nerve may be found directly under the oral mucosa (10).

Radiographically, this foramen appears as small, ovoid or round radiolucent area located in the apical region of the mandibular premolars (11). The absence of a MF (12) and the presence of multiple MF (13) are rarely reported. The presence of more than one MF, referred to as accessory mental foramina, has been noted on dissection, surgical findings, conventional radiographs, spiral computed tomography (CT), and cone beam CT.

When it is projected over one of the premolar apices, it may mimics periapical disease as seen in our case. In such cases, evidence of the mandibular canal extending to the suspected radiolucency or a lamina dura traceable around the root apex would suggest the true nature of the radiolucency. In the case presented here, there was intact lamina dura around the root. However, the lamina dura superimposed on the radiolucent foramen may be of too low a density to be recognized in the image (‘burn out’) (14). Nevertheless, a second radiograph from another angle is likely to show the lamina dura clearly, as well as some shift in position of the radiolucent foramen relative to the apex (8). Similarly, the second radiograph was taken in the present case which showed intact lamina dura with slight mesial shift in the periapical radiolucency. Thus, confirming our diagnosis of mental foramen mimicking as periapical pathology.

However, radiography is not a perfect diagnostic tool, partly because radiographs are two-dimensional representations of three-dimensional structures, and partly because particular clinical and biological features may not be reflected in radiographic changes. The presence of a lesion may not be directly evident and its real extent and the spatial relationships to important anatomical landmarks are not always easily visualized. The diagnosis and management of periapical pathosis requires a thorough clinical and radiographic examination. As chronic apical periodontitis often develops without subjective symptoms, the radiological diagnosis is particularly important and should not be confused with the variations of the normal anatomical landmarks.

CONCLUSION
A basic knowledge of the variations of the normal anatomical landmarks of jaw bones is mandatory for all the dental physicians, so that we can avoid misdiagnosing as any periapical pathology. In this paper, we have highlighted about the variations of mental foramen which was mimicking as periapical pathology. As the routine dental intraoral radiographs are the two dimensional representation of the three dimensional object, the newer radiographic methods has to be implemented to overcome this limitation.

CONFLICT OF INTEREST
The authors declare that they have no competing interests.

REFERENCES


Gastric antral vascular ectasia: a case report

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ABSTRACT
Gastric antral vascular ectasia (GAVE) is a vascular gastric malformation which represents a rare cause of upper gastrointestinal system bleeding, mostly in elderly. It is usually presented with a significant anemia and it is diagnosed with an endoscopic examination of the upper gastrointestinal system. The disease is often associated with other chronic illnesses such as liver cirrhosis, scleroderma, diabetes mellitus and arterial hypertension. It is treated symptomatically in terms of anemia correction with blood transfusions and iron supplements, proton pump inhibitors, beta-blockers and endoscopic procedures such as argon plasma coagulation which currently represents the treatment of choice in Sy. GAVE cases. We report a case of a 76 years old female patient who was admitted to the hospital because of general weakness, exhaustion and abdominal pain. Laboratory analysis of blood went in favor of anemia. Proximal endoscopy showed no changes on the esophagus, the stomach had a normal volume with pale mucosa and signs of antral vascular ectasia which is presented typically as a “watermelon” stomach due to the longitudinal creases oriented toward pylorus. The patient was treated symptomatically in terms of anemia correction with blood transfusions and iron supplements, proton pump inhibitors, beta-blockers. Five months later control proximal endoscopy findings were identical to those found in the previous hospitalization.

Keywords: endoscopy; GAVE; gastric antral vascular ectasia; gastrointestinal bleeding

INTRODUCTION
Gastric antral vascular ectasia, scientifically identified also as Sy. GAVE is a rare and usually undiagnosed cause of the occult gastrointestinal bleeding, mostly in elderly. Proximal endoscopy usually reveals longitudinal creases oriented towards pylorus. It is also known as a “watermelon stomach” due to the longitudinal “stripes”. It is histologically characterized with dilated and thrombosed capillaries as well as with fibro muscular hyperplasia of lamina propria. The treatment includes conservative procedures such as blood transfusions and endoscopic therapy with argon plasma coagulation. Recent reports suggest that Endoscopic Band Ligation (EBL) is a regular and efficient alternative treatment.

A study by Irish authors reported an overall treatment of 23 Sy. GAVE cases. Eight patients were treated with EBL, with a mean number of 2.5 treatments. Six (75%) of those eight patients had previously failed APC (argon plasma coagulation treatment) despite having a mean of 4.7 sessions. Band ligation was not associated with any complications. EBL treatment resulted with the significant improvement of endoscopic finding and the need
for blood transfusions was periodical (1). Antral vascular ectasia is considered as a cause of nonvariceal upper gastrointestinal system bleeding in 4% of cases (2).

The disease can be presented with occult bleeding which demands blood transfusions or as acute gastrointestinal bleeding. It is often associated with a significant mortality and morbidity rate and following comorbidities: scleroderma, diabetes mellitus and arterial hypertension. Sy. GAVE may also be developed as a complication after haematopoetic stem cell transplantation or after per oral or intravenous application of busulfan (3). An average of 30% of Sy GAVE cases is associated with liver cirrhosis (4). The treatment of the syndrome is divided into three categories: pharmacological, endoscopic and surgical. A few studies compared the efficiency and complications of endoscopic and medicamen- tous treatment of Sy. GAVE. Current evidence of endoscopic Sy. GAVE treatment are insufficient. Sy. GAVE diagnosis is often based on endoscopic examination according to its caracteristical appearance, thus it can be easily misinterpreted with mild to severe form of gastritis. Radiofrequency ablation represents an alternative therapeutic option for Sy. GAVE. It is considered a secure and effec- tive method (5). Among the most frequent illnesses associated with Sy GAVE is a chronic renal insuffi- ciency (6).

CASE REPORT

A female patient, 76 years old, was admitted to the Department of Internal Medicine, General hospital “Prim.dr. Abdulah Nakaš”, Sarajevo in December, 2012. The symptoms on the day of the admission were general weakness, exhaustion and abdominal pain. Laboratory findings on the admission reported signs of anemia: RBC 3.71 × 10¹², Hemoglobin 87.4 g/L, Hematocrit 0.28, MCV 74.8 fl, MCH 23.6 pg, MCHC 315 g/L, Reticulocytes 8 × 10⁹/E. Plt 103 × 10⁹/L, WBC 4.1 × 10⁹/L. Serum iron level 3.7 umol/L, TIBC 66.0 umol/L, UIBC 62.3 umol/L. The abdominal ultrasound showed signs of chronic calculous cholecystitis, with a bended gallbladder and a slightly larger spleen - craniocaudal diame- ter of 15.5 cm. Proximal endoscopy - showed no changes on the esophagus, the stomach had a nor- mal volume with pale mucosa and antral vascular ectasia – typical watermelon finding (Figure 1). Duodenal bulb showed no changes, D1 and D2 were neat.

During hospitalization, the patient was treated with deplasmatized erythrocytes transfusions (a total of 300 ml), parenteral iron supplements, primarily intravenously administered proton pump inhibitors followed with peroral administration of the same. The patient was discharged with a recommendation of per oral use of proton pump inhibitors in a single dose of 40 mg per day with non-selective beta blockers, Propranolol in a single dose of 40 mg per day. On April, 2013 the patient was readmitted to the Department because of severe anemia signs: RBC 2.54 × 10¹², Hemoglobin 51.0 g/L, Hematocrit 0.17 I, MCV 65.7 fl, MCH 20.1 pg, MCHC 305 g/L, Plt 171 × 10⁹/L, WBC 5.6 × 10⁹/L, RDW 18%. Follow up proximal endoscopy findings were identical to those found in previous hospitalization – antral vascular ectasia was still present (Figure 2).
DISCUSSION

Gastric antral vascular ectasia represents a vascular malformation of gastrointestinal system and a rare cause of upper gastrointestinal tract bleeding. Hemorrhage within Sy GAVE may be profound as well as occult with signs of mild, moderate or severe anemia. The disease may be treated conservatively by anemia correction with blood transfusion and iron supplements as well as with proton pump inhibitors and beta blockers. Well-designed controlled randomized studies will be necessary to prove the efficacy and complications of conservative and endoscopic treatment of Sy GAVE (7). According to some authors capsule endoscopy is superior in GAVE syndrome cases, compared to classic endoscopic examination. The diagnosis may be established with an endoscopic examination only, although it may be misdiagnosed with moderate to severe form of gastritis. Classic endoscopic examination is considered to be physiological without need for air insufflations and consequent vascular compression and therefore misdiagnosis of the same (8). Current model of invasive treatment is proximal endoscopy with argon plasma coagulation. Proximal endoscopy with APC is in general more acceptable way of treatment for Sy GAVE patients, although many of them continue to bleed and demand continuous blood transfusions after the treatment and show a low level of endoscopic improvement. Endoscopic band ligation (EBL) according to mentioned studies proved to be a safe and effective treatment of GAVE. Radiofrequency ablation may serve as an alternative therapeutic method. Endoscopic laser photoocoagulation or diathermia are proved to be efficient in stopping hemorrhage. Antrectomia represents the final and only definitive therapeutic solution specially in patients with severe symptoms such as severe anemia and recurrent profuse bleeding (9).

CONCLUSION

Gastric antral vascular ectasia or Sy. GAVE represents a group of vascular gastric malformations and is a rare cause of upper gastrointestinal system bleeding. The diagnosis is set throughout a proximal endoscopy exclusively. It may be treated conservatively with proton pump inhibitors and beta blockers or using invasive methods such as argon plasma coagulation, radiofrequency ablation or endoscopic band ligation.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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An extremely rare case of testicular malign neoplasm; alveolar subtype of rhabdomyosarcoma with long term follow-up

Dear Editor,

We would like to draw readers attention to testis tumours, notably rare ones in this letter. Yue et al. recently reported rare tumours in testis (1). However, subtypes of testicular tumours with their incidences are well-defined in published literature, some rare types of them could be reported by pathology (2). Overcome these issues, we would like to affix an extremely case of paratesticular alveolar rhabdomyosarcoma. A handful of cases were published in literature and also most of them were including childhood series. A 23-year-old man was admitted to our urology outpatient clinic with main symptoms of right scrotum. In detailed physical examinations, there was a nodular mass with 6 cm diameter in upper part of right testis. Ultrasonography (US) revealed 6 × 5 × 4 cm and computed tomography (CT) showed an 11 × 9 mm parailiac lymph node. Radical orchiectomy was performed and pathology reported paratesticular alveolar rhabdomyosarcoma (Figure 1). He has no metastasis after 6 cycles of chemotherapy with vincristine, actinomycin, and cyclophosphamide. However, rare tumour can occur in testis, early diagnosis and adequate treatments can provide long-term survival without metastasis.

Paratesticular and testicular tumours usually occur in childhood and most of these have benign characteristics (3). They are originated from mesenchymal tissue of testis and spermatic cord. Besides these, paratesticular tumours may be felt like arising from testis during physical examinations, US is useful for differential diagnosis. Nevertheless, the exact diagnosis can be made by histopathology examinations. There were hyperchromatic nucleuses and spindle cytoplasmic cells with haematoxylin–eosin (Figure 1). Additionally actin, desmin, and myoglobin were positive (Figure 1). Alveolar subtype was reported by pathology, in the present case.

Sarcomas consist of 1% of all malign tumours, and they are originated from embryonic tissues. The common sites of sarcomas are skeletal system. However, paratesticular rhabdomyosarcom is an extremely rare. Specifically, embryonic subtype of rhabdomyosarcoma were reported in literature (4). Subtypes can be diagnosed by pathology examinations. Alveolar subtype of rhabdomyosarcoma is an extremely entity for paratesticular tumours, as in our case. The main clinical sign of this tumour is painless scrotal mass. Weakness and tiredness with palpable lymph nodes in inguinal and abdominal area may come into question, in advanced stages. Radical orchiectomy, chemotherapy, and radiotherapy are the main parts of treatment. Our case had clinical stage 1 tumour with intermediate risk (5). Thus, he underwent chemotherapy for 6 cycles, after operation. He did not need radiotherapy. Chest x-ray, abdominal and pelvic CT has been used for follow-up. He has been in follow-up period for 7 years and he had no metastasis.

Differential diagnosis is an important entity for testicular and paratesticular masses. Surgery with adjuvant therapy options are used for contemporary
treatment. Long-survival can be provided by suitable treatment options with close follow-up.

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