Health MED

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Visual acuity in end stage renal disease patients undergoing hemodialysis versus those not undergoing hemodialysis

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Abstract

Background: The prevalence of end-stage renal disease (ESRD) is growing probably due to increasing prevalence of its underlying diseases such as diabetes mellitus and systemic hypertension. Not only ESRD but also hemodialysis and its consequences impose heavy social and financial burden on patients and societies. Since underlying causes of ESRD, ESRD itself and hemodialysis process may result in visual problems, it is important to evaluate patient's visual condition.

Objective: This study aimed to evaluate whether hemodialysis process leads to or affects visual problems in ESRD patients.

Methods: In this case control study, ESRD patients undergoing hemodialysis were considered as case group(n=47) and ESRD patients without the history of hemodialysis and ocular problems before ESRD were considered as control group(n=41). Demographic data were recorded. Best corrected visual acuity (BCVA), automated visual field were assessed. Slit lamp and dilated funduscopic exam and applanation tonometry were performed. BCVA, visual field indices, intra-ocular pressure (IOP), glaucoma and fundus changes were determined and compared in case and control groups. Data were analyzed using SPSS version 16 for windows. In order to compare the means, Independent student t test and Chi-square test were performed.

Results: Difference between visual acuity and IOP in case and control was not statistically significant, with normal examination. After omission of confounders, visual acuity difference became significant by being less in the case group. Mean deviation of right eye perimetry was significantly lesser in both groups (p<0.05) in compare to normal examination. The difference between glaucoma within case and control was significant by being more in the case group (p=0.019). Difference of diabetic retinopathy, scotoma and cataract was statistically insignificant between case and control groups. Duration of hypertension significantly correlated with right eye perimetry (p=0.007).

Conclusion: Hemodialysis worsened visual acuity and probably visual field, but has no effect on intraocular pressure. The frequency of glaucoma was significantly higher in hemodialysis patients. Also Duration of hypertension can affect visual field.

Key words: End-stage renal disease; Hemodialysis; Visual acuity; Visual field

Introduction

Diabetes mellitus (DM) and systemic hypertension (HTN) are among the most common diseases which can lead to severe and irreversible end-organ damage including renal damage [1]. The prevalence of end-stage renal disease (ESRD) is growing, for example there has been a remarkable increase in the number of ESRD patients in the United States, [1, 2] probably due to increasing prevalence of its underlying diseases such as diabetes mellitus [3, 4] and systemic hypertension[5]. Not only ESRD but also hemodialysis and its consequences impose heavy social and financial burden on patients and societies [6,7]. Although in the past decades, patients with ESRD died soon; but nowadays they survive longer. Survival without good quality of life is not pleasant for these patients.

Since underlying causes of ESRD, ESRD itself and hemodialysis process may result in visual problems, it is important to evaluate patient's visual condition. In Iran, chronic hemodialysis patients are the main portion of ESRD patients, but there is no survey about prevalence or frequency of visual problems in these patients. The present study is to evaluate whether hemodialysis process leads to or affects clinically significant visual problems in ESRD patients; and visual conditions that need emergency intervention which in turn promotes patients' quality of life.

Methods and Materials

Study population:

This case-control study was conducted at hemodialysis ward of Shahid-Mohammadi (Bandar Abbas University of Medical Science, Bandar Abbas, Iran) during 2006-2007. Subjects who met the following criteria were considered as "case group": all patients who were referred to hemodialysis ward of Shahid Mohammdi hospital in Bandar Abbas (n=47). Subjects who met the following criteria were allocated to " control group ": ESRD patients with negative history of hemodialysis, affected by DM or HTN, who were referred from specialists' offices or renal specialty clinics with a certified cause of ESRD (n=41). There were a total 100 patients in case and control groups, but 12 patients were excluded for data missing or lack of cooperation. Demographic data including gender, age, presence of DM and HTN, medication history and medical history were recorded for all subjects, and control subjects were matched to the case subjects for age and sex. Chronic hemodialysis was defined as a patient with ESRD who needs both repeated and regular hemodialysis. Diabetes mellitus was defined as fasting plasma glucose $\geq$ 126 mg/dL or 2-hour postprandial glucose $\geq$ 200 mg/dL [1, 9]. Non diabetics were defined as fasting plasma glucose < 100 mg/dL without history of DM. Hypertension was defined as systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg, at least in two different sessions [9]. All patients were examined by a single ophthalmologist and single devices. Visual acuity was evaluated by Snellen chart for each eye and central 24 degrees of visual field was evaluated

by Humphrey analyzer (Carl Zeiss Meditec Inc., Germany) with SITA strategy and mean deviation and pattern standard deviation indices were recorded. Presence of relative afferent pupillary defect was examined for each eye. Intraocular pressure was measured twice with Goldman applanation tonometer and pressure more than 24 mmHg was considered abnormal. After administration of Tropicamide drop three times, each eye was examined by 78 diopter lens and slit lamp (Topcon, Japan). Hypertensive retinopathy was recorded by modified *Scheie* Classification [10] and diabetic retinopathy was recorded as proliferative or non-proliferation if present by ETDRS classification [11, 12]. Every other remarkable abnormal funduscopic findings were recorded. We compared BCVA, visual field indices, frequency of cataract, glaucoma, IOP, and retinopathy in case and control groups. In addition, we assessed correlation of BCVA and visual field indices with hypertensive and/or diabetic retinopathic changes of the same class in case and control group. Every subject read and signed an "informed consent" form, approved by Ethics Committee of Bandar Abbas University of medical Sciences, before entrance to the study.

Statistical analysis

Statistical analysis was done with SPSS 16. We used "independent sample t test" for comparison of significant difference of quantitative data and Chi-square test for descriptive data. P value < 0.05 was considered significant.

Results

Patient's characteristics are shown in table 1. There was no significant difference between mean age of cases and controls (p=0.99).

The results of ocular examination are shown in table 2. No significant difference was found between visual acuity of right and left eye between case and control groups, while ophthalmoscopic examination were almost normal. P value for right and left eye was 0.07 and 0.17, respectively. Statistical analysis showed no significant difference between right and left intraocular pressure within case and control groups (p=0.65 and p=0.99, respectively). Also, we found no significant discrepancy between mean of foveal threshold of right

Table 1. Patients' characteristics within case and control

	Age (yrs) (mean± SD)	Gender		DM n(%)*	HTN¶ n(%)
		Male n(%)	Female n(%)		
Case	48.3 ±15.7	25 (53.2%)	22 (46.8%)	9 (19.1%)	38 (80.9%)
Control	51.7 ±16.7	18 (43.9%)	23 (56.1%)	7 (17.1%)	41 (100%)
Total	49.9 ±16.2	43 (48.9%)	45 (51.1%)	16 (18.3%)	79 (89.9%)

DM, diabetes mellitus; ¶ HTN, systemic hypertension; all values are shown as value (%) except for mean age which is shown as value (± standard deviation)

Table 2. Results of ocular examination

	IOP (mmHg)*		MFT¶		MDP†		BCVA§	
	Right	Left	Right	Left	Right	Left	Right	Left
Case	13.3	12.8	27.9	25.2	-6.5	-.38	7.66/10	7.12/10
Control	13.6	12.8	28.8	26.8	-2.8	-0.9	8.64/10	7.95/10

IOP, intraocular pressure in terms of millimeter of mercury; ¶ MFT, mean of foveal threshold; † MD, mean deviation; § BCVA; mean of Best corrected visual acuity

Table 3. Clinically significant ocular pathologies

	Glaucoma n(%)	Cataract n(%)	DM ret* n(%)	PSD¶		Con. Calc n(%)
				OD† (%)	OS§ (%)	
Case	2 (4.3)	22 (46.8)	3 (6.3)	3.80	3.88	11 (23.4)
Control	8 (19.5)	24 (58.5)	5 (12.2)	3.67	2.66	8 (19.5)

* DM ret, diabetes mellitus retinopathy; ¶ PSD, pattern of standard deviation; † OD, right eye; § OS, left eye; Con. Calc., conjunctival calcification; all values are shown as value (%)*

and left eye in case and control groups (p=0.19 and p=0.33 respectively). Analysis of mean deviation of perimetry indicated that only mean of right eye was significantly lesser in both groups (p<0.05), but ophthalmoscopic examinations were almost normal. Several clinically significant ocular pathologies were seen (table 3). There were 10 patients (11.4%) with glaucoma whose problem had started after renal involvement including: 5 patients with primary open angle glaucoma, 3 patients with normal tension glaucoma, 1 patient with primary close angle glaucoma and 1 patient with pseudoexfoliative glaucoma. The difference between glaucoma within case and control was significant (p=0.019). Meanwhile, 19 patients (21.6%) had conjunctival calcification (table 3) but difference between case and control was insignificant (p=0.95). Presence of diabetic retinopathy, scotoma and cataract was insignificantly different between case and control. We analyzed pattern of standard deviation (PSD) and resulted that difference of mean of PSD was insignificant within case (p=0.83) and control (p=0.19).

We studied correlation between duration of hemodialysis, HTN and chronic renal failure with ocular pathologies. Duration of hemodialysis (mean 3.25 years) significantly correlated with PSD of right and left eye (p=0.014 and p=0.045 respectively); but showed no significant correlation with scotoma, foveal threshold of right and left eyes, and mean deviation of perimetry. Duration of HTN only significantly correlated with right eye PSD (p=0.007). Time span of chronic renal failure had no significant correlation with any ocular pathology.

Regarding several confounding factors including glaucoma, cataract, ocular vessels pathologies, macular edema and diabetic retinopathy that can affect visual acuity and visual field; we excluded those subjects, and repeated analysis to eliminate known confounders. The results show that visual acuity of right and left eye within control was significantly better than case (p=0.024 and p=0.046 respectively). In addition, mean deviation of right eye perimetry was significantly better in control group (p=0.05).

Discussion

Care of chronic disease patients now predominates in medical practice and accounts for more than 75% of U.S. $ 2.1 trillion medical care costs[6]. The chronic kidney disease is growing and it carries a heavy burden of other health problems [7]. End-stage renal disease (ESRD) is complex, costly and affects more than 500,000 patients in the United States [7] and its prevalence is growing, for example there has been a remarkable increase in the number of ESRD patients in the United States, [1, 2] probably due to increasing prevalence of its underlying diseases like diabetes mellitus [3, 4, 14] and systemic hypertension [5].

Not only ESRD but also hemodialysis and its consequences impose heavy social and financial burden on societies [6,7]. In past decades, patients with ESRD died soon; but they survive longer today. This issue emphasizes on researches for improving the patient's quality of life.

Since underlying causes of ESRD, the ESRD itself and hemodialysis process may result in visual problems, it is important to evaluate patient's visual condition. In Iran there has been no survey about frequency or prevalence of visual problems in these patients.

ESRD and its underlying diseases like DM and HTN, and hemodialysis itself can produce visual problems including: diabetic retinopathy (a progressive microangipathy), retinal detachment, lens disease (cataract), iris diseases (decrease of pupil reflex due to neuropathy and aggregation of glycogen), increase or decrease of intraocular pressure (open angle glaucoma), red eye, and etc. The study of ischemic consequences of hemodialysis in visual system was described from the middle of 1980s. [14] Although it is difficult to distinct between impact of underlying diseases, confounders, comorbidities and hemodialysis itself, but some acute consequences indicate hemodialysis side effects [15].

In the present study, we compared visual acuity in hemodialysis patients with ESRD patients who do not need hemodialysis. There was no difference between case and control in this regard, and mean of corrected visual acuity was approximately 7/10 in case and 8/10 in control. A cross sectional study by Vrabec et al suggested that most of hemodialysis patients had visual acuity of at least 6/10[16]. In this step, our study supports the finding of Tomazzoli et al that proposed visual acuity did not differ before and after hemodialysis; [17] but after omission of confounders, the difference became significant and visual acuity was lower in the patients undergoing hemodialysis.

We investigated that there was no significant difference between visual field of case and control, except for better visual field of right eye in both groups. Pelit et al did not find any significant difference too [18]. In a case control survey, Pahor investigated that visual field was not correlated with hemodialysis duration [19]. Study of intraocular pressure showed insignificant difference between case and controls. Changes of intraocular pressure are well described [20]. There are two main reasons for its change during hemodialysis: ultrafiltration and clearance of toxic materials [20]. A cross sectional survey by Erol and colleagues suggested that even the type of hemodialysis filter affects this pressure [21]. Since we adjusted patients for confounding factors like age, DM and HTN, we might have seen no difference between intraocular pressure in case and control.

Our study indicates significant difference concerning glaucoma between case and control. However the true prevalence of glaucoma is unknown, but there are several case reports about exacerbation of glaucoma through hemodialysis. Based on those reports, clinicians administer beta-blockers, α2-agonists, prostaglandin agonists, meiotics, acetazolamide or hypertonic solutions (such as mannitol or saline 3%), or prolong the time of hemodialysis session [22]. Another finding of the present study was conjunctival calcification that leads to red eye, an inflammatory response to metastatic calcification, which is well described. It is recommended to lower serum calcium level < 5mg/dL for avoiding such problem [23], [24]. Although there are no data about prevalence of this problem, we concluded that conjunctival calcification was insignificantly more common in hemodialysis patients.

Retinopathy in hemodialysis patients is a broad spectrum from macular edema (secondary to DM) to retinal detachment (probably due to uremia); [25, 26] moreover HTN can result in retinopathy too. Retinopathy leads to a progressive visual loss. The only prospective study by Tokuyama et al concluded that hemodialysis for 4 weeks cannot save the

patients vision [26] Retinal hemorrhage is a subgroup of retinopathy. However "American College of Cardiology" endorsed administration of low-dose heparin in hemodialysis [27] but there are studies neither compare hemodialysis with and without heparin nor evaluate risk of retinal hemorrhage with heparin administration. A prospective survey compared hemo- and peritoneal dialysis and showed that although heparin administration is safe during hemodialysis but control of HTN more effectively avoids retinal hemorrhage [28] Optic neuropathy, ischemic and mostly permanent, is another category of retinopathy. Hemodialysis patients suffer from anterior ischemic optic neuropathy (AION) because of repeated hypotension during hemodialysis and anemia [15, 29]. Its hallmark is painless visual loss. Korzets et al reported cases of ESRD and chronic hemodialysis with AION [30]. In another case report by Buono et al, optic neuropathy occurred while ophthalmoscopic examinations were normal [31]. Cataract is a common but idiopathic problem in ESRD. It is claimed that DM, steroid administration, HTN, uremia and hypocalcemia are among probable causes. Tomazzoli and colleagues' study failed to find any difference between occurrence of cataract before and after hemodialysis [17]. As seen in the present study, we found that difference of retinopathy (diabetic, hypertensive, uremic, ischemic and optic neuropathy), cataract and scotoma were insignificant between case and control. Since medication toxicity of some drugs like desferrioxamine confounds the results, we excluded patients with current drug history of such medications.

Regarding notable frequency of visual and ocular diseases in hemodialysis patients including cataract, scotoma and conjunctival calcification in the present study, it is recommended that patients should undergo visual and ocular examination after hemodialysis; the differences between patients who need and do not need hemodialysis, however, are insignificant. These findings also support Vrabec et al, [16] Pelit and colleagues, [18] Pahor [19] and Pavlovic [32] who proposed regular ocular examination with short periods and assessment of visual field, because prevalence of ocular problems was higher in hemodialysis. On the other hand, incompatibility between ocular examination and patients' complaint (especially about visual field) in Pahor's survey [19] and in the present study (about visual acuity and visual field) emphasizes on more exact and careful examination.

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Enteroviral Meningitis in adults

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Abstract

Background: Enteroviruses (EVs) are the main cause of viral meningitis in children. Role of EVs in adult meningitis is less clear especially in developing countries. The aim of this study is to clear the burden of EV meningitis in adults in Mashhad, Iran.

Method: In this descriptive study from May 5, 2007 up to November 6, 2007, all consecutive CSF samples obtained from patients older than 18 years in Imam Reza Hospital were evaluated with RT-PCR for EV. Clinical data was retrospectively extracted from the hospital files.

Result: There were 33 CSF samples during 6 months. The mean age of patients was 36.07 years. EV PCR and bacterial culture were positive in 39.3% and 12.1% of specimens respectively. Concomitant EV and bacterial meningitis was found in one patient (3%). Herpes simplex PCR was positive in one of the CSF sample. The WBC of CSF was normal in 23% of EV positive samples, and 23.07% of them had PMN dominancy in CSF cell count. The mean PMN percentage in the peripheral blood of EV positive patients was 76.45%. Hyponatremia was seen in 38.4 % of patients with pure EV meningitis.

Conclusion: The frequency of EV meningitis is more than two times of bacterial meningitis in people older than 18 years in Mashhad. Concomitant enteroviral and bacterial meningitis is not a rare finding.

Key words: Meningitis, Enterovirus, Enteroviral meningitis, adult.

Introduction

Viral meningitis is the leading type of central nervous system infections in children and young adults. EVs are the most common cause for viral meningitis, they are responsible for almost 90% childhood meningitis (1-4). Herpes simplex type 2 and the varicella-zoster virus are other common causes of viral meningitis in adults (5). The importance of EV meningitis in adults is underestimated because of mild symptoms and lack of routine virological evaluation of CSF in most hospitals (5). Many patients with EV meningitis are hospitalized and treated with parenteral antibiotics. Early diagnosis of EV meningitis can reduce antibiotic overuse and the length of admission (2). The current study aimed to find the frequency of EV meningitis among adults who were admitted in Imam Reza hospital and underwent Lumbar puncture during spring and summer 2007.

Method

This descriptive study was carried out in Imam Reza educational hospital (Mashhad, Iran) during 6 months period (May 5, 2007 up to November 6, 2007). During this time all consecutive CSF samples obtained from patients older than 18 years were collected and saved in -20°ᶜ (after primary analyses including Gram Stain, Culture, Sugar and Protein measurement). At the end of the six months RT-PCR for EV, by a pan-enteroviral primer, was done for all CSF samples. The clinical data was extracted retrospectively from the hospital files.

Result

We had 33 CSF samples during 6 months. The mean age of patients was 36.07 years (range:18-75y). Female to male ratio was 18/15. An infectious etiology was found in 51.4% of the samples, including pure EV: 36.3%, pure bacterial: 12.1%(meningococcus 2 cases, pneumococcus and group

A streptococcus each one case), concomitant EV and bacterial: 3% and herpes simplex virus: 3% (Table1).

Table 1. The causes of CNS infections among adults in Mashad, Iran

Variable	No(%)
Total Number of CSFs	33
Pure EV meningitis (EVM)	12(36.3%)
Bacterial meningitis(BM)	4(12.1%)
Concomitant EVM and BM	1(3%)
Concomitant EVM and Bacterial sepsis	0(0)
Encephalitis	1(3%)
Total identified causes	18(54.5%)

Table 2. Clinical and laboratory findings of EV meningitis among adults in Mashad, Iran

Variable	Result
Total CSF specimens (No)	13
Fever (%)	92.3
Headach (%)	100
Rash (%)	7.6
Seizure (%)	0
CSFs without pleocytosis (%)*	27.2
PMN% of CSF (Mean)	40.8
PMN >50% in CSF (%)	37.5
CSF Sugar,mg/dl (Mean)	59.6(65.0**)
CSF Protein,mg/dl (Mean)	160.0(55.1**)
Serum CRP =Negative(%)	10.0
Serum CRP =One plus(%)	80.0
Serum CRP =Two plus(%)	10.0
ESR,mm/h (Mean)	30.2
WBC of peripheral blood /mm3×10³ (Mean)	11.5
PMN≥75% in peripheral blood (%)	90.9
Hyponatremia (%)	46.1(38.4**)

*WBC<5/mm3(%),**results of pure EV positive patients

Mean age of EV positive group was 39.2 years, female to male ratio was 5/8. Table 2 shows the summery of clinical findings of the patients. Pleocytosis and PMN dominancy of CSF were seen in 76.9% and 23.07% of EV positive patients respectively. The mean of sugar, protein, WBC and PMN cells in the CSF of pure EV positive patients was 65.0mg/dl (range:48-87), 55.1mg/dl (range:10-183), 115/mm³ (range:7.8-16.4) and 40.87% (range:0-92%) respectively. The mean of ESR was 21.6 mm/hour (range:4-104) in all patients and 30.25 mm/hour (range:5-104) in pure EV positive patients. Qualitative serum CRP was negative in 10%, one plus in 80% and two plus in 10% of EV positive patients. The mean of white blood cell count and PMN percentage in peripheral blood of EV positive patients were 11581/µl (5500-16400) and 76.45%(52%-85%). Hyponatremia (serum sodium<135meq/L) was seen in 38.4 %(5 of 12) of patients with pure EV meningitis (Table2).

Discussion

There is little information about adults EV meningitis in developing countries. The findings of the present study clarify the importance of EV meningitis in adults in Mashhad ; a city with more than 2000000 population. In this study we could find the etiology of 51.4% of CNS infections and EVs were responsible for 66.6% of these cases.

In a study by Taylor (from a tertiary referral hospital in Hanoi, Vietnam), CSF samples from 352 adults (median age 34 years) with suspected meningitis or encephalitis were evaluated for viral and bacterial pathogens. In result the cause of CNS infection was found by culture and PCR in 27.3% of cases (versus 54.5% in our study), bacterial pathogens were 2.7 times of viral causes (vs. 0.33 in our study) and herpes simplex virus was the most common virus (12/19) followed by varicella virus (5/19) and enterovirus (2/19). PMN dominancy of CSF (PMN> 50%) and peripheral blood (PMN> 75%) was seen in 7.7% (vs. 37.5% in our cases) and 62.5% (vs. 90.9% in our patients) of aseptic meningitis cases (6).

Nahdi (from Tunisia) investigated the viral causes of 126 immunocompetent patients with neuromeningeal disorders. Viral genome was detected in 46% (58/126) of the CSF samples in comparison to 36.3% in our group , EVs (53.4%) and CMV(34.5%) were the most common viruses followed by HSV(15.5%) (7). In another study from Tunisia, Sghaier could find a viral cause in 17.5% of 1071 patients hospitalized for CNS infections. In this study West Nile virus (34.5%) and EVs (23.5%) were the leading causes (8).

Mechai (from Paris, France) has reported 59 cases of adults EV meningitis. Leukocytosis of peripheral blood , elevated serum CRP and PMN dominancy of CSF was seen in 20% (vs. 90.9% in our cases), 39% (vs. 37.5% in our series) and 47% (vs. 37.5% in our series) of these cases (9).

Ihekwaba (from 2004 to 2007 in Sheffield Hospital, UK) has reported 38 cases of viral meningitis among immunocompetent adults, of whom 57%(22 pateints) were caused by enteroviruses. HSV type 2 and VZV each caused 21% of the cases. Mean CSF PMN percentage and protein level was 9 %(0-95) and 64 mg/100cc respectively. Mean serum CRP was 15mg/100cc (2.1-112) (10).

CRP of serum has a sensitivity of 69% to 99% and specificity from 28% to 99% for differentiating bacterial from viral meningitis. The negative predictive value of serum CRP for Gram stain–negative bacterial meningitis can be 99% (11).

In our study qualitative serum CRP was negative in just 10% of EV meningitis cases, while 80% of cases had one plus positive CRP. There was no case of EV meningitis with serum CRP more than two plus. In a case series of 103 children with meningitis (bacterial and viral) from Nepal, serum CRP was positive (>6mg/lit) in 90% of bacterial and 64% of viral meningitis , showing that positive CRP is not useful for clinical decision making in meningitis, although CRP titer was significantly higher in bacterial meningitis (12).

The two main limitations of this study are lack of CSF test for other viruses specially HSV2 and VZV and insufficient clinical data from patients.

Conclusion

The frequency of enteroviral meningitis is 2.6 times of bacterial meningitis among adults in our study. Simultaneous EV and bacterial meningitis is not rare. Hyponatremia, neutrophilia in peripheral blood and absence of CSF pleocytosis is common in enteroviral meningitis.

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Head and neck cancer; a clinicopathologic review of nasopharynx tumors in northern Iran descent from 1990 to 2011

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Abstract

Objective; Neoplasm of the head and neck are usually a challenging issue, both from the diagnostic and from the curative perspective. In this research, we tried to elucidate the various clinical modes of presentation of nasopharynx malignancies and their association with last histopathological diagnosis.

Method; Clinical records of the patients were retrieved from the files of the university hospital from1990 to 2011 (August).

Result; Study populations included 14 patients involving 9 (64.28%) male and 5 (35.71%) female aged from 20 to 74 years old. Mandible angle enlargement (Lymphadenopathy)(28.57%), pain and effusionof ear (28.57%), odynophagia (28.57%), dysphagia (28.57%) were the most common clinical modes of presentation. lymphoepithelioma (50%) and Squamous cell carcinoma (28.5%) were the most frequent histologic type of malignancy in our study.

Conclusion; In conclusion, nasopharyngeal malignancies are seldom in north of Iran like other part of the world. Analysis of this data revealed nasopharynx cancers are manifested in variety of ways. Clinicians need to establish those characteristics associate with suspicion of malignancy.

Key words; Cancer, Nasopharynx, Squamous Cell Carcinoma, Lymphoepithelioma

Introduction

Head and neck cancers consist of malignant tumors deriving from different places in the upper respiratory tract. Investigations about these cancers indicate various neoplastic process including many sites with unique features of epidemiologic, pathologic, and treatment considerations. The most common histologic type of head and neck cancer is squamous cell carcinoma (SCC), which is most commonly seen in the oral cavity, oropharynx, hypopharynx, and larynx (1).

In 2000, head and neck cancer was the eighth common cause of cancer –associated death. Almost 481,100 new patients developed, and 320,000 subjects died since of this disease (2).

Three factors are thought to be involved nasopharynx carcinoma (NPC) that are included the ubiquitous Epstein-Barr virus, a genetically determined susceptibility and an environmental factor which may vary from one populations group to another (3).

In this research, we attempted to study the different clinical modes of presentation of nasopharynx malignancies and their relation with final histopathological diagnosis and to clarify these conditions from other benign situations.

Methods

In total, study population included 14 subjects pathologically proved with nasopharynx malignancy. Approvals for our study were obtained from the research committee of the university.

All cases ofnasopharynx cancer were retrieved from the files of the university hospitals from1990 (January) to 2011 (August).

The clinical information closely connected with the lesions was documented involving age, sex, presenting symptoms, and associated malignancy.

Statistics

For statistical analysis, data were entered to MS-excel spread sheets. The procedures included were transcription, preliminary data inspection, content analysis and finally interpretation. Investigators used percentages (SPSS software, Version 15, Chicago, IL, USA) to clarify epidemiological variables.

Results

There were 14 patients including 9 (64.28%) male and 5 (35.71%) female aged from 20 to 74 years old. Mandible angle enlargement (Lymphadenopathy) (28.57%), pain and effusion of ear (28.57%), odynophagia (28.57%), dysphagia (28.57%) were the most common clinical modes of presentation (table 1).

Table 1. Clinical features of patients in this series

	Number of patients
Mandible angle enlargement (Lymphadenopathy)	4(28.57%)
Pain and effusion of ear	4(28.57%)
Nasal airway collapse	2(14.28%)
Epistaxis	3(21.42%)
Headache	1(7.14%)
Odynophagia	4(28.57%)
Dysphagia	4(28.57%)
Runny nose	1(7.14%)
Rhinophoxiaclausa	1(7.14%)
Smoking	1(7.14%)
Opium addict	1(7.14%)

Lymphoepithelioma (50%) and Squamous cell carcinoma (28.5%) were the commonest histologic type of cancer in our series . Adenoid cystcarcinoma was the rarest, that were seen in 3 patients; 2 women (a 20 years old with chief complain of chronic epistaxis, and a 56 years old with chief complain of chronic foreign body sensation in her throat) and a 70 year old man with chief complain of bilateral mandible angle lymphadenopathy(table 2).

Table 2. Pathological characteristic of study population

Pathology	Number of patients
Squamous cell carcinoma	4 (28.5 %)
lymphoepithelioma (WHO type III)	7 (50 %)
Adenoid cystcarcinoma	3 (21.4 %)

Discussion

This investigation was done to establish the clinicopathologic information on nasopharynx cancer over a period of 21 years in our descents and compare the results with other ethnic background of the world. This study was done in a referral hospital in north of Iran that has 600 patients with head and neck tumors were diagnosed and treatedduring 10 years.

Nasopharyngeal cancer (NPC) is a well defined neoplasm and its etiology may relate to ethnic and geographic distributions (4, 5) Epstein-Barr virus infection (6), lifestyle like consuming pickled food (7) and history of hazardous inhalants (8). This NPC epidemic indicates familial aggregation; in this regard,first-degree relatives of the patient are more susceptible to NPC than first degree relatives of the spouse (9).

The incidences of age standardized rates (ASR) for NPC are below 1 per 100,000 person-years (4,5). But there are more cases of NPC in some part of the world including natives of southern China, Southeast Asia, the Arctic and the Middle East/North Africa (4,5,10).

Most of oral and oropharyngeal cancer patients seen to have a history of tobacco or alcohol use, but some researchers like Llewellyn et al showed that 25% of their study population didn't have any exposure to tobacco or alcohol. (11).

Some other investigations indicated that there might be a distinction between the cancer growth in smoker/drinkers patients in comparison to non-smokers/ non-drinkers (12,13). Wiseman et al (13) reported most patients with no history of tobacco or alcohol use were female (mean age of 60 years old). In the same way Koch et al (12) showed in their study that 46 cases were non-smokers, 233 smokers, and 29 former smokers. In our study one patient had history of smoking and majority of them didn't have any exposure to tobacco. On the other hand, all of these patients had no history of alcohol use.

Kimura Y et al studied nasopharyngeal carcinoma features in the central area of Japan during the period from 1996 to 2005. They reported neck mass was observed in 52% of the patients, ear symptoms in 48%, nasal symptoms in 27%, headaches in 10%, pharyngeal symptoms in 9%, ophthalmologic symptoms in 9%, and cranial neurological symptoms in 9% (14).

In contrast, most of our study patients presented with Mandible angle enlargement (Lymphadenopathy) (28.57%), pain and effusion of ear (28.57%), odynophagia (28.57%), dysphagia (28.57%). Although other symptoms and signs like nasal airway collapse, epistaxis, headache, runny nose, rhinophoxiaclausa were observed.

Lymphoepithelioma were the commonest histologic type in these cases in contrast to other studies (1) which reported SCC is the commonest type.

In conclusion, nasopharyngeal malignancies are rare in this region like other part of the world. Analysis of this information revealed head and neck cancers are manifested in variety of ways. Clinicians need to find those characteristic associated with suspicion of malignancy.

Generally, in our series, the patients were presented with Mandible angle enlargement (Lymphadenopathy), pain and effusion of ear, odynophagia, dysphagia.

Acknowledgment

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The Effects of COREPOWER Machine Training versus Home-Based Core Training on Recreational Golf Players' Physical Fitness

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Abstract

Purpose: This study investigated the effects of COREPOWER machine training versus home-based core training on recreational golf players' physical fitness.

Methods: Participants were randomly divided into a machine group (M: n = 51), home group (H: n = 50) and control group (C: n = 22). Lower back flexibility, muscle endurance, muscle strength, cardio respiratory fitness and balance were measured. Pre- and post-intervention measurements within and between each group with significance set at p < 0.05, were analyzed.

Results: With the exception of cardio respiratory fitness, all variables in group M and H showed significant improvement. Group C revealed no significant changes. Push-ups (p = 0.000; ↑17.03%; d = 0.92) showed the greatest percentage improvement within group M, while sit-ups (p = 0.000; ↑14.41%; d = 0.77) and push-ups (p = 0.000; ↑12.52%; d = 0.90) showed the greatest percentage improvement within group H.

Conclusion: Both modalities were equally effective in improving selected fitness components.

Key words: functional fitness, core muscles, training, golf players

Introduction

In order to improve fitness, training should be based on the demands of the specific sport (1, 2, 3). To this end and within golf, evidence suggests that optimal training should include sufficient core training (4, 5, 6, 7, 8). The term "core" commonly refers to the mid-section of the body and thus involves many structures that form the "center" of the body, an area which is also known as the "torso" or the "power zone" (9, 10). The structures comprising the core are networked, creating an integrated system which functions as an entity of support and operates as a unit. When functioning optimally, the core provides appropriate support to the body during daily activities, during sport and even in the absence of movement (11, 12). Many athletes undertake core stability and core strength training as part of their training programs, despite contradictory findings as to their efficacy (11). The COREPOWER machine was designed to specifically target the core musculature and involves users performing a simultaneous upper body row and lower body step action.

No documented literature is available on the COREPOWER machine and the closest comparison to this machine would arguably be a health walker or elliptical trainer. These machines require the individual to stand and train, shifting the body weight from one side to the other, whereas the COREPOWER machine provides the individual with an adjustable seat with back support and requires the left and right sides of the body to work independently of each other. The COREPOWER machine uses an adjustable setting to determine the resistance level of the workout. The resistance increases from setting one (easiest) to setting ten (hardest) and can be altered manually by the individual. This setting can furthermore be altered in such a way that the arms and the legs of the participants are exposed to different levels of resistance. When training on the machine (Figure 1), the athlete is required to stretch one arm in a forward movement while simultaneously flexing the same side's knee. The contra lateral leg is extended and the same side's arm is flexed. Thus, the major muscle groups that are activated in the process of performing this action include the pectorals, the abdominals, the erector spinae, the quadriceps, the hamstrings and the gluteus muscle groups. These muscle groups form part of the core muscle group

along with several other deep rooted and superficial muscles (13).

The COREPOWER was designed by a general practitioner with a specific interest in golf and as the name implies the focus underlying the design was the enhancement of core muscle strength. The aim of this study was to investigate the effects of a 36 session intervention training program on the COREPOWER machine and a 36 session home-based manual core training program on golf players' physical fitness [body mass index (BMI), fat percentage, lower back flexibility, muscle endurance (sit-ups, push-ups), muscle strength (lower back strength, wall squats), cardio respiratory fitness] and functional fitness (static balance).

Figure 1. Athlete using COREPOWER Machine

Methods

Measurements

The participants' body mass and stature were recorded to establish the BMI (15). Four skinfold measurements were taken to determine body fat percentage (15). The sit-and-reach test (flexibility) (15) was then performed, the shoulder/arm-strength/endurance (push-ups) test, abdominal strength/endurance (sit-ups) test, wall squats (16), lower back strength (17, 18, 19, 20) cardio respiratory fitness (15) and static balance test (17, 20) were also performed in this order. Participants were instructed not to use their hands for support and the static balance of each participant was measured by 3 static balance recordings of 20 seconds each.

Following the 12 week intervention all dependent variables were reassessed in all three groups.

Intervention Program

The intervention program of group M consisted of two three-minute sessions at level 2 of the COREPOWER machine with a 1 minute rest between sets. The short duration of this program was based on feedback from the pilot study indicating that participants were unable to perform more than two three-minute sets at a given level. Borg's rating of perceived exertion (RPE) scale was used to ensure all the participants trained at the desired intensity between level 12 and 14 ("somewhat hard") (15). The intensity of the intervention program was increased by one level every fourth week as illustrated in Table 1.

Table 1. Program Progression of Group M.

Weeks	Level of Training on COREPOWER	Exercise Sessions
1 - 4:	2	12
5 - 8:	3	12
9 - 12:	4	12
Total Sessions: 36		

The exercises for group H mirrored those of group M regarding frequency, intensity and duration and were based on core exercises selected by means of a combination of the experience of registered biokineticists, the Gary Player Fitness Centre (14) as well as published literature (7). All exercises were demonstrated to the participants 2 to 5 days prior to the start of the intervention. They followed the program in their own time and each participant received a log book in order to document their training sessions. Each participant also received an exercise card with a drawing of the specific exercises, as well as an explanation regarding the execution of the exercises, their intensity (level 12 to 14 on RPE scale), and the desired duration (6 minutes). The exercises involved a circuit program consisting of 2 sets of core exercises which were performed for a duration of 3 minutes with a 1 minute rest between sets. The exercises were adjusted every fourth week in order to ensure that the program remained challenging and that the participants maintained their training at the desired intensity on the RPE scale. Participants in this group were also prohibited from engaging in additional or new physical activities and exercise routines or from changing their pre-existing activities/exercise routines during the intervention.

The amount of time spent playing golf during the intervention period did not change, as evidenced by each participant's physical activity feedback questionnaire. Thus, during the intervention period, the participants performed only the prescribed intervention program and continued with their normal golfing routine.

Participants from group C were also refrained from participating in any sporting activities or change their normal activity routine. Participants from group C were allowed to continue with their normal golfing routine, without any changes or adjustments for the 12 week intervention period.

Selection and Description of Participants

All of the participants recruited for the study had been playing golf for at least two years on a regular basis. "Regular golf playing" is regarded as playing golf 25 or more times per year (14). The participants' were all male, aged between 13 - 71 years. All participants read and signed and informed consent form explaining the research study. In the event of minors, parents/guardians signed the informed consent form. To ensure that participants did not change their pre-existing activity/exercise routine for the duration of the intervention, they had to monitor their physical activity by completing a physical activity questionnaire. The participants were recruited from local golf clubs through poster and newspaper based advertising as well as through the local Pro Shop. All tests and procedures were performed under the supervision of qualified biokineticists (exercise therapists) and/or trained fieldworkers. To reduce the risk of researcher bias, participants performed the post-test under the supervision of a different assistant/fieldworker. Ethical approval for the study was granted by the institutions' Faculty of Science & Agriculture Ethics Committee.

Technical Information

A standard, calibrated Seca Robusta 813 weight scale and stadiometer were used to determine each participant's body mass and stature with the aim to determine their BMI (15). A calibrated, metal Lange skinfold caliber was used to determine their body fat percentage. The hamstring-lower-back flexibility was performed using a sit-and-reach box (15). To determine the cardio respiratory fitness of each participant, the 3 minute YMCA step-test was applied, using the appropriate step box (15). All the above tests were performed according to the protocols as prescribed by the ACSM (15). To determine lower back strength, a calibrated Takei Physical Fitness BACK-D back strength dynamometer (17, 18, 20) was used according to the prescribed protocol for measuring lower back strength (18). Static balance was determined using the Biodex balance system (21, 22) by selecting the option for static balance testing.

The design was a prospective, experimental study. Participants were randomly assigned to either the machine group (Group M; n=51), the group performing a home-based manual core training program (Group H; n=50) or the control group (Group C; n =22) who did not partake in any form of physical activity apart from their normal golfing routines. All the participants trained for 12 weeks, 3 times a week for 6 minutes at a time. Group M trained 3 minutes on the COREPOWER machine with a 1 minute rest followed by a further 3 minutes on the machine. Group H followed a home-based core training circuit for 3 minutes with a 1 minute rest which, too, was followed by a further 3 minutes of training. As a result of observations and participant feedback from the pilot study, the duration of the session was set at 6 minutes for this study. In addition to the results of the pilot study, one of the aims was to investigate whether short bouts of exercise, which are convenient and practical to complete, could have an effect on dependent variables. The home-based manual core training program mirrored that of group M with regards to intensity, duration, and frequency. Group C, the control group performed no form of sporting activity apart from their normal golfing routine.

We can thus express the central experimental approach of the study in terms of this question: will the outcome of this study benefit golf players over and above their normal golfing activities? Moreover, which modality shows the greatest improvement and benefit - COREPOWER machine training or home-based core training? Finally, can either of these two programs be used in addition to normal golfing activities, thereby enhancing selected aspects of golf related fitness?

Table 2. Pre-and Post-Intervention Values for Group M and Group H [Mean $\pm$ SD (95 % CI)].

Variables	Group M Pre (n=51)	Group H Pre (n=50)	Group C Pre (n=22)	Group M and H Pre P-Value	% change Group M (n=51)	Group M Pre/Post P-Value	Group M Pre/Post Cohen's d	Group M Post (n=51)	Group H Post (n=50)	Group C Post (n=22)	Group M and H Post P-Value	% change Group H (n=50)	Group H Pre/Post P-value	Group H Pre/Post Cohen's d
Fat Percentage	16.4 ± 5.66 (14.68 - 18.12)	16.81 ± 6.98 (14.71 - 18.91)	18.34 ± 5.10	0.847	4.27 %	0.003*	0.49	14.7 ± 5.46 (14.04 -17.36)	15.81 ± 6.61 (13.82 - 17.79)	17.25 ± 5.45	0.961	5.95 %	0.000*	0.60
BMI (kg/m²)	26.58 ± 4.71 (25.15 -28.01)	27.63 ± 6.56 (25.66 - 29.6)	28.24 ±4.60	0.602	0.23 %	0.182	0.13	26.52 ± 4.53 (25.14 -27.89)	27.4 ± 6.42 (25.47 - 29.3)	28.12 ± 4.56	0.821	0.83 %	0.017*	0.29
Lower Back Flexibility (cm)	41.34 ± 9.01 (38.6 - 44.08)	40 ± 10.56 (36.82 - 43.17)	36.80 ±14.71	0.940	2.41 %	0.041*	0.39	42.36 ± 9.20 (39.56 - 45.16)	41.18 ± 11.08 (37.86 - 44.51)	38.55 ± 12.40	0.987	2.87 %	0.021*	0.40
Sit-Ups (per minute)	39.19 ± 10.09 (36.08 - 42.29)	35.98 ± 9.34 (33.17 - 38.87)	34.27 ± 11.46	0.100	11.77 %	0.000*	0.80	44.42 ± 10.46 (41.2 - 47.64)	42.04 ± 10.37 (38.93 - 45.16)	40.59±11.68	0.233	14.41 %	0.000*	0.77
Push-Ups (per minute)	24.8 ± 11.76 (21.22 - 28.37)	27.18 ± 11.12 (23.84 - 30.52)	22.00 ±11.83	0.369	17.03 %	0.000*	0.92	29.89 ± 12.19 (26.18 - 33.59)	31.01 ± 11.95 (27.48 - 34.66)	25.95±12.34	0.774	12.52 %	0.000*	0.90
Wall Squats (per minute)	33.95 ± 11.3 (30.52 - 37.39)	35.16 ± 8.21 (32.66 - 37.65)	31.45 ± 8.25	0.822	9.95 %	0.000*	0.63	38.58 ± 11.48 (35.05 - 42.12)	39.34 ± 8.36 (36.8 - 41.88)	32.77±9.06	0.750	10.63 %	0.000*	0.84
Lower Back Strength (kg)	143.4 ± 33.18 (133.3 - 153.5)	144.4 ± 44.98 (130.8 - 157.9)	149.41 ± 35.55	0.533	6.23 %	0.000*	0.86	156.5 ± 32.25 (146.5 - 166.4)	152.7 ± 49.09 (137.4 - 168)	160.00±37.15	0.916	-1.28 %	0.000*	0.65
3 Minute Step Test (HR)	125.3 ± 19.67 (119.3 - 131.3)	127.7 ± 20.26 (121.6 - 133.8)	127.82 ± 19.02	0.480	-0.02 %	0.824	0.00	125.3 ± 21.24 (118.8 - 131.8)	123.3 ± 23.12 (116.3 - 130.2)	127.82±19.50	0.928	3.46 %	0.057	0.30
Balance	2.92 ± 1.88 (2.35 - 3.50)	3.24 ± 2.617 (2.458 - 4.031)	3.49 ± 1.78	0.598	6.64 %	0.131	0.33	2.73 ± 1.67 (2.22 - 3.24)	2.85 ± 2.236 (2.175 - 3.518)	3.34 ± 1.83	0.625	12.04 %	0.008*	0.33

(* = $p \leq 0.05$)

Statistics

Results are expressed as means, standard deviations, percentage changes, 95% confidence intervals and effect sizes. A non-parametric Wilcoxon test was used to determine statistical significance ($p \leq .05$). Cohen's *d* test was used to determine the practical significance by way of effect sizes. Differences between groups were computed using a non-parametric Mann-Whitney test and ANCOVA.

Results

The intervention program was successfully completed by 45 participants in the home group and 44 participants in the machine group. All 22 participants from the control group performed the re-assessment. The resulting data (Table 2) suggests that in groups M and H, almost all physical fitness and functional fitness parameters showed significant improvement. Push-ups (p=0.000; 17.03%) showed the most pronounced changes in the machine group (group M), while in the home group (group H), the greatest percentage improvements were observed for sit-ups (p=0.000; 14.41%) and push-ups (p=0.000; 12.52%). The 3 min step-test however failed to show significant improvement in either group M or group H. For Group M, BMI and balance values did not show a significant improvement post intervention. Group C, revealed no significant change post intervention.

Discussion

Physical Fitness

At the baseline assessment there were no significant differences between the physical fitness parameters of all three groups (Table 2). Post intervention improvements were observed for fat percentage in both groups, whereas only group H showed significant post intervention change in the BMI ($p = 0.017$; $d = 0.29$). This result may indicate that core focused training (whether on the CORE-POWER machine or home-based) improves body composition by decreasing fat percentage and BMI. The finding that core training improves body composition is supported by previous research (23, 24) in which it was found that only a single set of core exercises, 3 times a week for 3 months, improves

body composition significantly (25). It is however speculative to conclude that muscle mass changed in the current study as this was not measured.

Lower back flexibility showed significant post intervention improvement in both groups (Table 2). No significant changes were observed between the two groups with regards to flexibility. Although no flexibility exercises were included in the programs, the improvement in the flexibility of group M ($p = 0.041$; $d = 0.39$) could be attributed to the stretch and step mechanism required while training on the machine. A possible explanation as to group H's significant improvement in flexibility ($p = 0.021$; $d = 0.040$) is offered by two published studies regarding the influence of golf specific resistance training on flexibility (23, 26). In the first study (23), participants showed significant improvement after only 8 weeks of training, 3 times a week. The training consisted of 8 core exercises of 20 seconds for each exercise, giving a total of 8 minutes of exercise a week (23). In the second study, flexibility showed significant improvement following a golf specific resistance training program and the training sessions of this study consisted of 3 sets of 10 repetitions 3 times a week for 11 weeks. The findings of this study are supported by the results in the present study, indicating that flexibility measurements may improve significantly in response to core training.

Sit-ups and push-ups (muscle endurance), wall squats and lower back strength (muscle strength) all showed significant improvements in both groups (Table 2), with sit-ups showing a 14.4% improvement in group H and push-ups a 17.03% improvement in group M. These significant improvements indicate that both machine training and home-based manual core training target the strength and endurance of the major muscle groups, including the quadriceps, the gluteus, the pectorals, the abdominals and the erector spinea. Improvements in these muscle groups were also documented in other core muscle intervention studies, using physical fitness and golf performance test protocols (23, 26). There were however, no significant post intervention differences between group M and group H with regards to muscle strength and muscle endurance (Table 2), indicating that both these groups improved post intervention and neither of the intervention's was su-

perior with regard to improving muscle strength and muscle endurance. Re-assessment differences between the Group M versus Group C, the control group, reveals a significant difference in sit-ups (p = 0.016), iron CD (p = 0.028) and iron CHS (p = 0.001). The re-assessment differences between the home group and the control group show no significant differences.

The 3 minute step-test showed no significant post intervention change (M: p = 0.824; H: p = 0.057) in either one of the groups (Table 2). This is not unexpected as previous findings have concluded that cardio respiratory fitness improves with aerobic training sessions of 30 minutes or more on a regular basis at a moderate intensity (15, 27). Nevertheless, group H approached significance (p = 0.057; d = 0.30) and this change has been reported (28) where it is shown that a home-based core training program involving a circuit format significantly improved cardio respiratory fitness (28). The participants of this study were exposed to a high-volume circuit resistance training protocol where the intensity of the training sessions was increased and the duration of the training sessions was 16 minutes per session (28). In the current study, the 6 minute duration of each session might not be a strong enough stimulus to elicit sufficient improvements in the cardio respiratory fitness. No significant changes were observed between the two interventions with regard to fitness parameters. Both modalities proved to be equally effective and none is superior to the other with regards to physical fitness parameters.

The re-assessment minus baseline data for the machine group versus the control group reveals significant differences except for BMI (p = 0.121), step-test (p = 0.946) and balance (0.094). The re-assessment minus baseline data for the home group versus the control group shows all significant differences except for the step-test (p = 0.280).

Functional Fitness

Balance is the only functional fitness variable tested in this study. Balance showed significant post intervention improvement in group H (p = 0.008; d = 0.33) (Table 2). Similar results have been reported by published literature (29). In one study, core training resulted in significant improvement in static and dynamic posture control and balance (29). In a second study, significant improvement in static balance was also documented (30) reporting that home-based core training results in significant improvement in static balance without any loss of potential core muscle training benefits (30). Group M did not show significant improvement in balance (M: p = 0.131; d = 0.33) and this would tend to suggest that the COREPOWER training is not specific enough to impart favorable changes in balance.

Significant improvements in balance are thus documented within the home group and not in the machine group in comparison to the control group. Significant improvements in static balance were previously documented. In this regard Hosseinimehr and Norasteh (2010) and Willardson et al. (2009) (29, 30) reported that a home-based core training program results in significant improvement in static balance without any loss of potential core muscle training benefits. Group M does not show significant improvement in balance (M: p = 0.131; d = 0.33) and this would tend to suggest that the COREPOWER machine training is not specific enough to impart satisfactory changes in balance.

Based on the findings above, no statistically significant difference is noted with the control group, when compared to the machine and the home group. From the results, it is clear that both interventions improved selected physical and functional fitness parameters. The broad range of fitness and sport specific aspects addressed during this study suggest that both methods of training can be applied to numerous if not all types of sport. Some would argue that training to develop the core is crucial as it forms the cornerstone of all athletic movement (26). To this end the interventions investigated in this study should not be advocated solely for golf players.

In addition, the interventions have shown that short duration training can indeed yield positive outcomes. The results of the home-based manual core training group indicate that individuals can obtain improvements in selected health and fitness parameters without having to purchase costly equipment. This may have practical application for athletes and non-athletes alike who are restricted in terms of time and/or access to facilities and equipment. These modalities are not time consuming and are also applicable to all age groups.

Any one of these two modalities can be applied as an addition to a comprehensive golf program as this study solely addressed questions relating to the core musculature within such a program. Furthermore, the benefits of using any one of these two training modalities can be applied to other sport populations as well, as this study established a good foundation for core training. Thus, this type of intervention can therefore also be applied to various settings as the benefits of core training have been documented in the clinical population (diabetes (9, 19), hypertension (10, 19), obesity (9, 10)) the fields of physical rehabilitation (back injuries (9, 10))), and health promotion (corporate/industrial) (9, 10, 19). It is consequently safe to say that both these intervention modalities can be applied outside the golf and sporting environment within the clinical population, rehabilitation as well as health and wellness.

In conclusion, short duration (6 minutes) core specific training sessions are effective in improving general physical fitness components in recreational golf players and both modalities (COREPOWER machine training and home-based core training) are equally effective in eliciting these benefits.

Acknowledgement

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Epidemiologic features of gastrointestinal infectious diseases in the region of the Herzegovina-Neretva Canton, Bosnia and Herzegovina

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Abstract

Introduction: *Gastrointestinal infectious diseases* are the most common infectious diseases in the world. Each year about one billion of people worldwide are diagnosed including five million of children under age of five who die from infectious intestinal diseases. Acute *gastrointestinal infectious diseases* are usually caused by bacteria and viruses while those chronic infectious intestinal diseases are caused by protozoa and helminths. These diseases have public health significance due to the large number of patients. *Gastrointestinal infectious diseases* often occur in developing countries because of poor hygiene and sanitary conditions, but also in highly developed countries due to changes in eating habits and an increase in industrial production of food.

The aim of the paper is to show the development of *gastrointestinal infectious diseases* in the region of the Herzegovina-Neretva Canton.

Materials and Methods: As the materials were used reported cases of *gastrointestinal infectious diseases* that are subject to mandatory reporting, which were accessed from the Institute of Public Health of the Herzegovina-Neretva Canton.

This paper is a retrospective descriptive-analytical epidemiological study for the period of observation from January 2008 - December 2013. There was shown the analyzed age-specific incidence of *gastrointestinal infectious diseases* and its individual rates in structure.

The *chi-square test (X²)* test is used to determine whether there are significant statistical differences.

Results: *Gastrointestinal infectious diseases* occur with different proportion from 2.95% to 35.9% in total structure of registered infectious diseases. The highest incidence rate was in 2008 and it was 2.09 / 000, and the lowest was in 2013 with 1.2 / 000. The most common disease was entercolitis acuta with proportion of 66.9% and the rarest one was ascariasis and viral hepatitis type A with proportion of 0.4%.

Conclusion: *Gastrointestinal infectious diseases* are common in Herzegovina-Neretva Canton. The most common disease is enterocolitis acuta.

Key words: *Gastrointestinal infectious diseases,* the Herzegovina-Neretva Canton.

Introduction

A significant part of modern infectious diseases epidemiology studies epidemiology of *gastrointestinal infectious diseases*. (1) Epidemiology of these diseases is changing greatly due to environmental changes and pathogen adaptation to the new living conditions. (2) *Gastrointestinal infectious diseases* are considered to be the most common infectious diseases in the world. Each year about one billion people are diagnosed with these diseases and five million children under the age of five years die from them. (3) Most of these diseases are transmitted through food. They have public health significance due to the large number of patients. (4) The etiology of *gastrointestinal infectious diseases* is different. Acute *gastrointestinal infectious diseases* are usually caused by bacteria and viruses while those chronic ones by protozoa and helminths. These diseases sources and reservoirs are people and animals which are patients and viral carriers. They spread via food, water, personal contact and contaminated objects which were used. The most significant *gastrointestinal infectious diseases* are typhoid fever, paratyphoid fever, infectious gastroenteritis, salmonellosis, alimentary toxic infections, brucellosis, amoebiasis. They occur as a sporadic disease in an epidemic form.(5)

To accurately track the number of people affected by *gastrointestinal infectious diseases*, it is necessary to establish a good surveillance system at all levels starting with local to national and even international.(6)

Gastrointestinal infectious diseases are significant diseases in Bosnia and Herzegovina. According to the law on the Protection of Population against Infectious Diseases Threat of the Federation of Bosnia and Herzegovina, these diseases must be reported: enterocolitis acuta, salmonellosis, alimentary toxic infections, viral hepatitis type A, amebiasis.

Factors that influence the emergence and spread of *gastrointestinal infectious diseases* are present in the area of the Herzegovina-Neretva Canton such as inadequate water supply and lack of food control, as well as facilities and staff in facilities involved in the production, transport and distribution of food. This paper will analyze the *gastrointestinal infectious diseases* registered in the Herzegovina-Neretva Canton in the period from 2008 - 2013.

The aim of the paper

To determine the proportion of *gastrointestinal infectious diseases* within all registered infectious diseases, to determine the age-specific incidence rate of the most common infectious intestinal disease and its individual rates in infectious intestinal diseases age group in the region of the Herzegovina-Neretva Canton.

Material and methods

Reported cases of *gastrointestinal infectious diseases* are used which reported according to the law and accessed from the Institute of Public Health of the Herzegovina-Neretva Canton in the Epidemiology Service, the Infectious Diseases Institute. This paper is a retrospective descriptive-analytical epidemiological study for the period of observation from January 2008 - December 2013. All the data were statistically analyzed including calculated incidence rates and percentage of certain diseases, also the *chi-square test (*X^2*)* test is used to determine whether there are statistically significant differences between the incidence of certain diseases.

Results of the research

In the observation period, there were 2,257 of *gastrointestinal infectious diseases* in a total of 22,821 infectious diseases which registered. (Table 1)

Table 1. *The proportion of total registered infectious diseases to gastrointestinal infectious diseases in the Herzegovina-Neretva Canton.*

Year	Total number of registered infectious diseases	Gastrointestinal infectious diseases - the number (N)	Gastrointestinal infectious diseases - proportion (%)
2008	2918	470	16,10
2009	2621	460	17,55
2010	**1139**	**409**	**35,90**
2011	11799	346	2,93
2012	1761	301	17,09
2013	2583	271	10,49
TOTAL	22821	2257	9,89

Table 2. *The number and incidence rate of people affected from infectious intestinal diseases per year*

Year	Gastrointestinal infectious diseases - the number (N)	Population Number	Incidence (promille)
2008.	470	224024	2,09
2009.	460	225158	2,04
2010.	409	225268	1,82
2011.	346	224902	1,54
2012.	301	224652	1,34
2013.	271	225178	1,20
TOTAL	2257	The average population number of 224863	Mean 1,67

The table shows that the proportion of gastrointestinal infectious diseases - in total number of diseases has been changing so the highest was in 2010 which was even 35.9%.
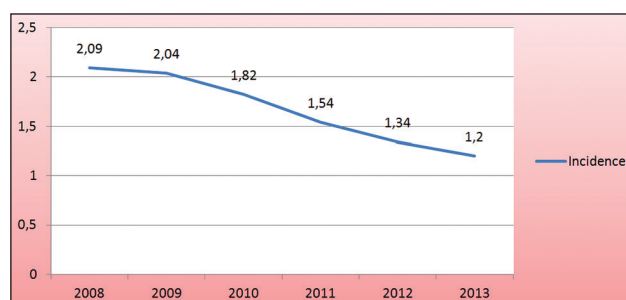

Graph 1. The incidence of gastrointestinal infectious diseases per year /100 000 inhabitants

The incidence of these diseases is linearly decreased from 2.09 / 000 promille in 2008 to 1.2 / 000 in 2013.

Table 3. The summary of incidence rates of certain gastrointestinal infectious diseases in total analyzed sample (2008 - 2013)

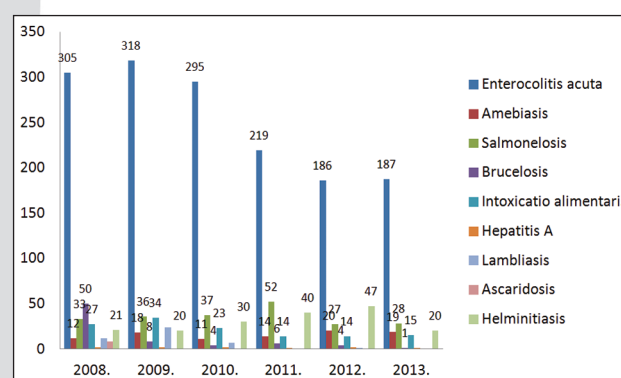| Diseases	Total	
	N	%
Enterocolitis acuta	1510	66,9
Amebiasis	94	4,2
Salmonelosis	213	9,4
Brucelosis	73	3,2
Intoxicatio alimentaris	127	5,6
Hepatitis A	10	0,4
Lambliasis	44	1,9
Ascaridosis	8	0,4
Helminitiasis	178	7,9
Total	2257	100,0
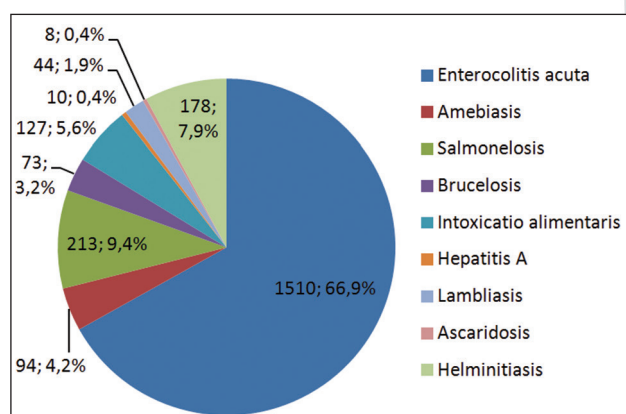
Graph 2. Percentage of proportion of certain gastrointestinal infectious diseases in total analyzed sample (2008 - 2013)

The analysis of the frequency of certain types of infectious diseases shows the total sample to have the highest levels of acute enterocolitis (66,9%), followed by *salmonelloses (213)*, *helminthiases (178)*, and toxic infections (127).

The percentage of other diseases was low, comprising less than 5% of the total sample makeup.

The analysis indicates significant statistical differences as for the occurrence of certain diseases according to the respective years of research.

Throughout the years of the survey the acute enterocolitis prevailed, immediately followed by brucellosis in the years 2008 – 2009 and *salmonellosis* or *helminthiasies (p<0,05)* over the remaining period of time.

Graph 3. Total number of reported intestinal infectious disease cases by year of research

Discussion

Gastrointestinal infectious diseases represent a common public health issue – both domestic as well as worldwide. Millions of people throughout the world every year fall ill due to different diseases spread through food and beverages and by fecal-oral route.(1) The situation has been alike in the region of the Herzegovina-Neretva Canton, with total 22821 recorded infectious disease cases in the years 2008 – 2013 which were subject to mandatory legal registration, counting 2257 intestinal infectious disease cases. The incidence of the disease shows a linear decrease from 2,09 promille in 2008 to 1,2 promille in 2013.

The analysis of the frequency of certain types of infectious diseases by their cause shows the total sample to have the highest levels of acute enterocolitis with registered 1510 cases, i.e. 66,9%. Acute enterocolitis is the common gastrointestinal

Table 4. Frequency of intestinal infectious diseases by year of research

Diseases	2008.		2009.		2010.		2011.		2012.		2013.		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Enterocolitis acuta	305	64,9	318	64,9	295	72,1	219	63,3	186	61,8	187	69,0	1510	66,9
Amebiasis	12	2,6	18	2,6	11	2,7	14	4,0	20	6,6	19	7,0	94	4,2
Salmonelosis	33	7,0	36	7,0	37	9,0	52	15,0	27	9,0	28	10,3	213	9,4
Brucelosis	50	10,6	8	10,6	4	1,0	6	1,7	4	1,3	1	0,4	73	3,2
Intoxicatio alimentaris	27	5,7	34	5,7	23	5,6	14	4,0	14	4,7	15	5,5	127	5,6
Hepatitis A	2	0,4	2	0,4	2	0,5	1	0,3	2	0,7	1	0,4	10	0,4
Lambliasis	12	2,6	24	2,6	7	1,7	0	0,0	1	0,3	0	0,0	44	1,9
Ascaridosis	8	1,7	0	1,7	0	0,0	0	0,0	0	0,0	0	0,0	8	0,4
Helmintiasis	21	4,5	20	4,5	30	7,3	40	11,6	47	15,6	20	7,4	178	7,9
Total	470	20,8	460	20,4	409	18,1	346	15,3	301	13,3	271	12,0	2257	100,0

$\chi 2=158,22; p=0,0001$

infectious disease, ranking first or second in every country in the world.(7) This is in particular true of the countries with underdeveloped diagnostic capacities.(8)

This study is based upon passive surveillance data, making the true number of the affected persons uncertain, as all were not admitted to hospital, therefore remaining unregistered.

In Japan, the percentage of people seeking medical aid due to acute gastroenteritis is 32%, fecal samples being taken in only 10,9% cases.(9) In the Una-Sana Canton, a total number of 35.014 gastrointestinal infectious disease cases was recorded in the period 1996 – 2008.

During this particular period 64 reported outbreaks of intestinal infectious diseases struck the Una-Sana Canton, also taking the form of an epidemic.(10)

In the Sarajevo Canton, gastrointestinal infectious diseases make up an average of 21% of the total number of registered infectious diseases, ranging from 16% in 2007 to 24% in 2008.(4)

Owing to lack of laboratory capacity it was impossible to isolate Rota- and Noro-viruses as the causes of the diseases, albeit Rota-virus has been known as the leading cause of diarrheal diseases in children up to 5 years and Noro-virus in adults. It has been estimated that Noro-virus causes up to 21 million diarrheal illnesses in the USA each year, with 5,5 million resulting from food contamination.(11)

According to our research, the second most frequent diseases were salmonelloses, affecting 213 persons or 9,4%. In Bosnia and Herzegovina, outbreaks of salmonellosis continue to be reported nearly every year, being primarily of local character and associated with fast-food restaurants. The largest epidemic was reported in Sarajevo in 2007. It was caused by Salmonella Enteritidis, affecting 700 people.(12)

In the countries which are highly dedicated to establishing etiological diagnosis, salmonelloses have been found as the leading cause of foodborne acute illnesses, predominantly of animal origin.(13)

The percentage of other reported diseases is as follows: different helminthiases affecting 178 people (7.9%), then alimentary toxic infections affecting 127 people (5.6%). There was also a relatively small number of additional diseases with less then 5% of the total number of registered gastrointestinal infectious diseases.

Amebiasis was rare – it was reported in 94 cases only. Amebiasis is estimated to infect about 50 million people worldwide per year, causing up to 100.000 deaths. It is considered to be the third leading parasite cause of death, after malaria and schistomiasis. In the USA, 1 – 3% of the population is infected with amoeba.(14) Lambliasis was also rare, with only 44 people reportedly affected. Lamblia was detected in 20% of children in Tuzla in 2001. Lamblia is the common cause of Traveller`s diarrhea. In certain parts of the world it is the leading cause of waterborne gastroenteritises.(15)

Hepatitis A and ascaridosis were reported in 10 and 8 cases respectively. The occurrence of virus A hepatitis is primarily attributed to the drinking of contaminated water; however, new viruses should also be taken into consideration, along with their presence in different types of food. There was an outbreak of virus hepatitis in the Netherlands related to tomatoes in oil.(16) Hepatitis A outbreaks recur almost every 7 – 10 years, depending on the number of susceptible individuals. In Bosnia and Herzegovina, hepatitis A continued to have an endemic existence up to the 1990s in parts of Banja Luka, Sarajevo and Tuzla regions.

In developing countries with low socio-economic status most children become infected with hepatitis A virus early in their childhood – up to 95%.(17)

The exact transmission route for the gastrointestinal infectious diseases in the region of the Herzegovina-Neretva Canton remains obscure, however, the role of contaminated water has been confirmed.

The estimates show 25% of hospital beds to be taken up by patients suffering from infectious diseases related to inadequate water intake.(18)

Worldwide, foodborne and waterborne diseases result in the death of 2.2 million people annually.(19)

Conclusion

The incidence and the prevalence of gastrointestinal infectious diseases in the community of the Herzegovina-Neretva Canton is substantial, also with significant share in the total number of reported illnesses, thus representing an important public health issue. Acute enterocolitis had the highest prevalence of reported gastrointestinal infectious diseases, with 66,9%. The disease type and frequency data is of vital importance for the prevention planning measures.

One of the key measures in reducing the risk of the infection is effective hygiene and sanitation, primarily including proper water-supplies and sufficient control over the production, preparation and distribution of food.

Also, it is essential that the improvement of diagnostics should be adressed, establishing etiology of the disease, thus providing the basis for the introduction of necessary measures.

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Sensivity and specificity of microalbuminuria in early detection of chronic kidney disease in diabetic and hypertensive outpatients in canton Sarajevo

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Abstract

Introduction: The recognition of kidney damage and impaired kidney function, which is often asymptomatic, is a key of improving health outcomes in the community. Aim of this study was to determinate the presence of early kidney damage in subjects with high risk, and to evaluate the sensitivity and specificity of biomarkers for early detection of chronic kidney disease.

Methods: The study was conducted in the primary care ambulance for a period of one year and included 200 patients with type 2 diabetes mellitus and/or hypertension. Renal function was monitored by using estimated glomerular filtration rate and measurement of microalbuminuria and proteinuria. K/DOQI classification of CKD was used for defining the stages of chronic kidney disease.

Results: Early stages (first and second) of chronic kidney disease were detected in 47.2% hypertensive patients, 54.0% diabetic patients and 59.6% patients with hypertension and diabetes mellitus type 2 associated. Microalbuminuria is most often found in the group of patients with associated hypertension and type 2 diabetes mellitus (22.4%, $p<0.05$). In hypertensive patients microalbuminuria was significantly more frequent in patients who had hypertension for more than 10 years ($p<0.05$). Microalbuminuria was the best predictor of early renal disease (specificity 95.0%, sensitivity 74.0%).

Conclusion: Our results indicate a high prevalence of early stages of chronic kidney disease in high risk groups of patients. Microalbuminuria represents a link between hypertension, diabetes mellitus and chronic kidney disease and very sensitive biomarker in detection of early chronic kidney disease in those patients.

Key words: hypertension, diabetes mellitus, chronic kidney disease, microalbuminuria, early detection of CKD.

Introduction

Chronic kidney disease (CKD) is a significant global health problem (1,2). In last years the most common causes of chronic kidney disease were type 2 diabetes and hypertension (3,4,5). The incidence and prevalence of hypertension and type 2 diabetes is increasing worldwide, contributing to a further increase of patients with chronic kidney disease. Hypertension is both, an important cause and consequence of chronic kidney disease. The prevalence of hypertension is higher among patients with CKD, progressively increasing with the severity of CKD (6). The main cause of tissue damage in diabetes is hyperglycemia, particularly vulnerable are glomerular capillary endothelial cells and mesangial cells of glomeruli (7). Appearance of albumin in the urine indicates dysfunction and damage of the glomerular filtration barrier, and further progression of this process leads to macroalbuminuria, continuous increase of blood pressure, reduction of glomerular filtration rate and finally to development of end-stage renal disease (8). It is assumed that arterial hypertension is at least partly a result of an increase of extracellular fluid volume, which contributes to reabsorption of sodium, hyperglycemia and in the end to renal insufficiency development. Insulin has a hypertensive role in patients with insulin resistance (9). Most patients with early stages of chronic kidney disease are asymptomatic and this condition remains unrecognized in high percentage of cases. More than 50% of renal function must be lost

before the serum creatinine concentration is above the upper limit of normal (10). Published studies are suggesting that proteinuria or microalbuminuria are representing one of the most important and earliest signs of kidney damage (11,12,13). In the study of Plantinga et al (14). prevalence of chronic kidney disease, defined on the basis of elevated albuminuria and reduced renal function, was 39.6% in patients with newly diagnosed and in 41.7% those with undiagnosed diabetes mellitus. The aim of this study was to determine the level of microalbuminuria and estimated glomerular filtration rate (eGFR) in patients with hypertension and/or type 2 diabetes mellitus and to determine the potential significance of this biomarker in early detection of chronic kidney disease in primary health care in Bosnia and Herzegovina.

Subjects and methods

This cross-sectional observational study was conducted over a period of one year in the primary care ambulance at Institute for Occupational Medicine of Canton Sarajevo. A total of 247 patients known to have diabetes mellitus and/or arterial hypertension were included in the study, but finaly the study population consisted of 200 adult patients of both genders, aged between 18 and 60 years. Twenty two patients were excluded because they did not want to collect urine for laboratory analysis (personal reasons), fifteen patients had already a history of renal disease and ten patients had fever or urinary tract infection. Excluding criteria were acute kidney injury, previously present chronic renal insufficiency, renal disease of other etiology, patients with conditions that may affect the value of microalbuminuria and proteinuria (acute febrile condition, heart failure, diet with high protein intake and urinary tract infection). Subjects were randomly selected in compliance with all ethical principles of medical research. The study was conducted with the approval of Ethics Committee of Medical faculty University of Sarajevo. All patients gave their informative consent for their participation in the study. Measurement of blood pressure and body mass index has been done to each patient on a routine medical examination, as well as a determination of the hypertension duration and duration of diabetes mellitus type 2 after

examining the medical records. Staging of hypertension has been done by using the classification of the World Health Organization. Angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs) and other medications that can influence the values of monitored laboratory parameters were excluded seven days before taking blood sample and urine in all patients.

Laboratory measurements

Concentration of the serum creatinine was measured with spectrophotometry using the kinetic Jaffe reaction (continuous method with alkaline picrate) on Dimension RxL Max system, Siemens. The level of microalbuminura in 24-hour urine was measured by using nephelometric method at the Institute of Clinical Chemistry and Biochemistry of the University Clinical Center in Sarajevo. Microalbuminuria was defined as an excretion >30 mg of albumin in 24 hours. Protein excretion more than 200 mg per urine daily represented clearly proteinuria. Estimated GFR (eGFR) was based on the Modification of Diet in Renal Disease model (15), while the National Kidney Foundation's classification (K/DOQI CKD Quidelines) was used for staging of eGFR (16).

Statistical analysis

The difference between the mean values of more than two investigated groups was determined with using ANOVA method, while the difference between variables of two groups was tested by paired t-test. The correlation coefficient was determined by Spearman analysis. Categorical variables were evaluated with Chi-square test. The importance of laboratory parameters in early detection of renal disease was evaluated with using sensitivity and specificity test. P values less than 0.05 were considered statistically significant.

Results

From total number of the 200 patients included in the study 75 (37.5%) were female. There was no significant difference in average age of female and male patients (54.81 ± 6.1 vs. 52.46 ± 8.2 years). Most of the subjects were older than 50 years (79.5%). In the follow-up period more than half of patients (54.0%) were hypertensive, while in

33.5% hypertension associated with diabetes type 2 was confirmed. Most patients had hypertension for less than 10 years (73.1%), with an average disease duration of 5.9 ± 2.8 years. Diabetes mellitus type 2 was present less than 10 years in 81.5% of monitored diabetic patients (mean 4.8 ± 3.0 years). The average values of albuminuria in relation to the basic disease and in smokers compared to nonsmokers were not significant, neither in patients depending on the duration of diabetes mellitus. Average values of albuminuria were significantly higher in man than in woman, in patients with BMI 25-30 than in those with lower BMI and in those who had hypertension for more than ten years (<0.01). The average values of proteinuria were significantly different only in relation to the type of basic disease in subjects included in the study (<0.01) (Table 1).

Average values of albuminuria are increasing with decreasing of renal function in all monitored groups of subjects. The average values of albuminuria, in the second (26.4 ± 21.4 mg/L) and in the third stage (279.5 ± 55.9 mg/L) of chronic kidney disease, in type 2 DM group of patients were significantly higher than the values of albuminuria in hypertensive patients with the same stage of CKD (14.9 ± 12.1 mg/L in the second and 28.0 ± 16.1 mg/L in the third stage), p <0.05. Significantly higher levels of albuminuria were found in all stages of chronic kidney disease in patients who had hypertension associated with type 2 diabetes mellitus compared to those who had only hypertension (p<0.05). A significant difference in values of albuminuria were found between patients with hypertension associated with type 2 diabetes mellitus and

patients with type 2 diabetes mellitus only in the third stage of chronic kidney disease (330.5 ± 57.4 vs. 279.5 ± 55.9 mg/L, p <0.01) (Table 2).

Table 1. The average values of albuminuria and proteinuria in relation to the basic disease and monitored parameters

Parameters	Proteinuria (g/d)		Albuminuria (mg/L)	
	X±SD	p	X±SD	p
Total 200	0.21±0.4	-	30.14±76.9	-
HTN	0.15±0.1		14.28±12.2	
DM 2	0.43±1.1	<0.01	40.88±76.0	<0.05
HTN/DM 2	0.22±0.3		51.57±120.7	
Man	0.20±0.2	>0.05	62.50±90.3	<0.01
Woman	0.22±0.7		37.50±46.6	
Age 18-35	0.15±0.1		24.34±38.5	
Age 36-49	0.18±0.2	<0.01	16.85±14.4	<0.05
Age over 50	0.22±0.5		33.05±85.3	
BMI 20-24	0.24±0.8		12.54±7.5	
BMI 25-30	0.19±0.2	>0.05	35.44±92.6	<0.01
BMI over 30	0.21±0.2		34.53±75.1	
HTN up to 10	0.17±0.2	>0.05	26.46±82.2	<0.01
HTN over 10	0.20±0.2		34.45±61.7	
DM up to 10	0.21±0.3	<0.01	46.88±114.5	>0.05
DM over 10	0.57±1.3		57.09±90.3	
Smokers	0.19±0.3	>0.05	35.69±106.5	>0.05
Nonsmokers	0.21±0.5		27.53±58.3	

Notes: Data are presented as average values and standard deviation, X±SD. HTN- Hypertensio arterialis; DM- Diabetes mellitus; BMI- Body Mass Index, MIN- lowest value of body mass index, MAX-highest value of body mass index.

Significantly positive correlation between albuminuria and proteinuria (p<0.001) and the duration

Table 2. Average values of albuminuria in relation to the stages of chronic kidney disease and comparing with the basic disease

The stage of CKD	MIKROALBUMINURIA (mg/L)		
	HTN group	DM type 2 group	HTN/DM type 2 group
	X±SD	X±SD	X±SD
Without CKD	10.5±2.3	10.0±0.1	10.3±0.8
Stage I	15.2±11.5	20.6±14.4	33.0±26.3**
Stage II	14.9±12.1	26.4±21.4*	39.9±23.8**
Stage III	28.0±16.1	279.5±55.9*	330.5±57.4**†
StageIV	-	10.0	231.0

Notes: Data are presented as mean and standard deviation. CKD-chronic kidney disease; HTN-hypertension; DM-diabetes mellitus; *difference between albuminuria values in HTN and DM type 2 groups, p<0.05; **difference between albuminuria values in HTN and HTN/DM type 2 groups, p<0.05; †difference between albuminuria values in HTN/DM tip 2 and DM type 2 groups of patients, p<0.01.

of hypertension (p=0.017) was confirmed. A statistically significant negative correlation was found between albuminuria and the presence of microhematuria (p<0.001), and albuminuria and estimated glomerular filtration rate (p=0.006) (Table 3).

Table 3. Relationship between albuminuria and monitored markers of renal function according to the type of basic disease

Paremeters	Albuminuria	
	r	*p* Value
Proteinuria (mg/d)	0.483	0.000
eGFR (mL/min/1,73m²)	-0.215	0.006
Microhematuria	-0.505	0.000
Duration of HTN	0.180	0.017
Duration of DM tip 2	0.075	>0.05
Stage of HTN	0.147	>0.05
Male gender	0.008	>0.05
Age	0.038	>0.05

Notes: eGFR-estimated glomerular filtration rate; HTA-hypertension; DM-diabetes mellitus.
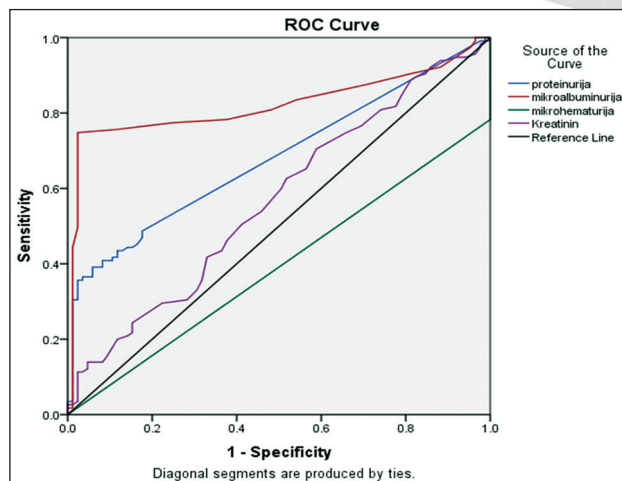

Figure 1. ROC curve of sensitivity and specificity of monitored renal biomarkers in detection of early stages of chronic kidney disease
Notes: The area under the ROC curve (AUC) for microalbuminuria is 0.822 (0.032 with a standard error, confidence interval 95% CI 0.760 to 0.884) vs. AUC for proteinuria of 0.681 (0.037 with a standard error, confidence interval 95% CI 0.609 to 0.754) vs. AUC for serum creatinine of 0.567 (0.041 with a standard error, confidence interval 95% CI 0.487 to 0.647) vs. AUC for microscopic hematuria of 0.391 (0.039 with a standard error, confidence interval 95% CI 0.314 to 0.468), p<0.001.

Examining the sensitivity and specificity of renal markers we found that microalbuminuria has a specificity of 95% and sensitivity of 74% in early stages of chronic kidney disease detection.

Proteinuria has specificity of 93% and sensitivity of 35%, serum creatinine specificity of 98% and sensitivity of 28%, while specificity of microhematuria is 100% and sensitivity 21% in detecting the initial stages of chronic kidney disease. Results are presented with using the ROC curve (Receiver Operator Characteristic). According to the results, microalbuminuria is the most sensitive marker for early stages of chronic kidney disease (AUC 0,822, CI 95% from 0760-0884, p<0.001) (Figure 1).

Discussion

Data from large studies conducted in the United States, Europe and Australia have shown that microalbuminuria presence is 11-17% in patients with hypertension (17,18). Some authors report incidence of microalbuminuria in patients with essential hypertension, from 4.7-54.7%, depending on age and ethical origin of the subjects (19,20). Microalbuminuria is an independent predictor of cardiovascular mortality and cardiovascular diseases such as cardiac, cerebrovascular, and peripheral arterial disease in patients with diabetes or hypertension in the general population. A study conducted in United Kingdom (UK), Kidney Evaluation and Awareness Program in Sheffield (KEAPS), reported that prevalence of microalbuminuria in general population was 7.1% and 1.3% in those without known risk factors for CKD (21). Results of our study indicate that microalbuminuria is the most sensitive biomarker in detection of early stages of chronic kidney disease (stage I and II), followed by proteinuria and serum creatinine (74.0% vs. 28.0% vs. 21.0%). Average values of microalbuminuria were significantly higher in patients suffering from hypertension and type 2 diabetes mellitus associated. The increase of average values of microalbuminuria with decline of renal function was registered in all investigated groups of subjects (p<0.05). Microalbuminuria was significantly higher in those patients who had hypertension longer compared to those in whom hypertension lasted shorter (p<0.05). Some authors reported statistically significant positive correlation between duration of diabetes and the prevalence of microalbuminuria (22,23). However, we did not found a relationship between microalbuminu-

ria and duration of diabetes, which can be explained by the relatively small number of subjects in the study. Significantly higher values of microalbuminuria were found in the group of patients suffering from hypertension and type 2 diabetes mellitus associated in first three stages of chronic kidney disease compared to those who suffer only from hypertension or only from diabetes mellitus type 2. NHANES III study (23) identified the presence of microalbuminuria in 28.8% diabetic patients and in 16.0% hypertensive patients, while Scheven et al. (24) microalbuminuria found in 21.7% patients with hypertension, diabetes mellitus or cardiovascular events. In our reasrch microalbuminuria was present in 9.3% hypertensive patients and in 20.0% diabetics. Most patients who had microalbuminuria suffered from hypertension and diabetes mellitus associated (22.4%, p<0.05). Obese people had microalbuminuria more often (in 19.3% of cases) than patients with lower BMI (p<0.05). Scheven et al. (24) also reported increased values of albuminuria in patients with higher BMI and present hypertension and diabetes mellitus. Data from Hallan et al. (25) suggest that a combination of microalbuminuria and glomerular filtration are providing much better information on the risk for developing of chronic kidney disease compared to glomerular filtration alone. On the basis of collaborative meta-analysis of 13 CKD studies, Astor et al. (26) confirmed that estimated glomerular filtration rate (eGFR) and albuminuria are independent risk factors for mortality and end-stage renal disease (ESRD) in individuals with chronic kidney disease (CKD). So, recently KDIGO (the Kidney Disease: Improving Global Outcomes) guidelines (27) recommended that chronic kidney disease should be defined by structural and functional abnormalities of the kidney that persist for longer than three months, classified based on the cause and severity categories of glomerular filtration rate, as well as prognostic classification according to the criteria of severity of glomerular filtration rate and proteinuria criterion. Our results clearly indicate that the use of glomerular filtration rate and microalbuminuria together improve much better early chronic kidney disease identification in high-risk patients, such as diabetics and hypertensives. Patients with type 2 diabetes mellitus should be tested for albuminu-

ria first time when diabetic disease is diagnosed, and after that, once yearly. Worldwide, the number of hypertensive patients is 3-4 times higher than the number of diabetics, however, the number of hypertensive patients who develop the terminal stage of chronic renal disease is two times greater than the number of diabetics who develop kidney failure, which makes the cost of screening significantly higher (28). In conclusion, microalbuminuria represents a link between type 2 diabetes, hypertension and early chronic kidney disease and a very sensitive biomarker for early kidney disease. In general practice in Bosnia and Herzegovina, it is necessary to introduce screening tests on albuminuria in patients at risk for chronic kidney disease, with close cooperation between physicians from primary health care and nephrologists. Early diagnosis, prevention and treatment of chronic kidney disease depends on identification of highly sensitive biomarkers for early stages of chronic kidney disease. The lack of of this study is the relatively small number of respondents. Needed are much larger and more comprehensive studies in this region with the aim of prevention and early detection of this large public health problem.

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Instructions for the authors

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Abstract

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

Key words: Camera ready paper, Journal.

Introduction

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Instructions for the authors

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

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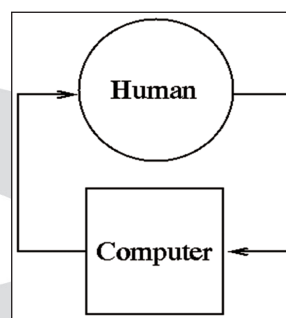

Figure 1. Text here

Conclusion

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

Acknowledgements (If any)

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

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