Epidemiology of Multiple Sclerosis in Western Herzegovina and Herzegovina – Neretva Canton, Bosnia and Herzegovina

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A B S T R A C T

The aim of this study was to investigate the selected indicators of multiple sclerosis (MS) in Herzegovina (Western Herzegovina Canton and Herzegovina-Neretva Canton). By using all available health and medical sources in the studied area and using McDonald's criteria, a total of 96 patients were identified in the period from 1996 to 2006. Results of the study show that the crude prevalence of MS was 30.99/100,000 (95% confidence interval [CIĆ 24.8–37.2), the highest one in the municipality of Posušje (49.6/100,000) and the lowest one in the municipalities of Neum and Ravno (no recorded cases); the female/male ratio was 1.5; the mean age of the patients on the prevalence day was 41.4±10.2 years and the mean age at the disease onset was 30.7±6.4 years; the most often clinical course of the disease was relapsing-remitting (58%), secondary progressive course was present in 28% patients, primary progressive in 9% and progressive relapsing in 1% of patients; the most frequent initial signs of the disease were motor (33%) and sensory ones (24%). According to the results of the study, the south-western part of Bosnia and Herzegovina is an area on the crossing from moderate risk to high risk zone for MS. The distribution of MS is heterogeneous. MS was more prevalent in the municipalities with colder climate and more winter precipitation and it is not present in the coastal region with warmer climate and almost without winter precipitation.

Key words: multiple sclerosis; prevalence; incidence; Herzegovina; Bosnia and Herzegovina

Introduction

The distribution of multiple sclerosis in the world is different and it represents the key for establishing of the causes of this disease[1,2]. The changes in the frequency in a certain area can also contribute to the same goal. The objective of this study is to present the descriptive epidemiological characteristics of multiple sclerosis in Herzegovina.

Material and Methods

Study area

The studied area, Western Herzegovina Canton and Herzegovina-Neretva Canton are in the south-western region of Bosnia and Herzegovina (BiH), between 42 53 and 43 39 degrees northern latitude and 17 19 and 17 58 degrees eastern longitude. The area of 5763 km, is divided into the areas of high karst (up to 1000 m above sea level), of moderate continental climate with abundant precipitation and Mediterranean zone. The flora is subtropical; the fauna has Mediterranean and karst animal species[3]. A cattle breeding is dominant in mountain region; while tobacco, grape and vegetable growing is dominant in coastal region. Considerable layers of bauxite provide opportunity for the development of aluminum industry[4]. The growth of population is unfavorable due to the low birth-rate and emigration. The population is of Illyrian origin, with the presence of old Italics in the settlements along the main roads. This region, known as Herzegovinian Sandžak under the Turks (1463–1878) was renamed Herzegovina in Austro-Hungarian Empire (1878–1918) and this name was used in the states of Yugoslav peoples. Since 1992 the studied region has been a part of the independent state of BiH[5]. The primary health care is organized in all municipalities. Specialist neurological services are provided at the University Hos-

pital, at the Regional Medical Center and at the General Hospital in Konjic.

On the 31st December 2006 the studied region had 309,712 inhabitants (in the data of the Federal Bureau for Statistics there are no data about the number of females and males when assessing the number of population in 2006).

Patients

The list of potential MS patients was composed by the analysis of the archives of the Department of Neurology of the University Clinical Hospital and the Department of Neurology and Psychiatry of the Regional Medical Center in Mostar, the Department of Neurology and the Neurological outpatients service of the Hospital in Konjic as well as the medical record of the neurological outpatients services in Jablanica, Čapljina, Čitluk, Ljubuški, Široki Brijeg, Grude, Posušje, Prozor-Rama, Neum and Stolac. MR brain imaging and cervical spine analysis was performed on all patients, and cerebrospinal fluid test was performed on 76 (79%) patents, whereas evoked potentials (visual and the potentials of brain stem) were tested on 26 (27%) patients. All the patients met the criteria by McDonalds (2005)[6]. The date of the disease onset, defined as the time of the first neurological symptoms attributable to MS have been acquired from the patient or from the medical records[7]. The patients were categorized into four groups according to the type of the disease: relapsing-remitting (RRMS), secondary progressive (SPMS), primary progressive (PPMS) and progressive-relapsing (PRMS)[8]. The study included the patients who lived in the studied region on the prevalence day 31st December 2006.

Statistical analysis

Statistical analysis was performed using the software package 7.0 and the computer program for the epidemiological analysis PEPI version 4.0. For data processing the descriptive epidemiological indicators were used – prevalence and incidence. The »crude« indicators were calculated. The prevalence in the studied region was assessed by means of a ratio calculated from the number of the patients in the studied region in the given time *per* 100,000 inhabitants. The given time was determined by the prevalence day. The incidence is presented with the number of new patients in the studied region in a given time period (for every year in the investigated period, for 5 and 10 years) on 100,000 inhabitants. The statistical differences were tested by χ^2-test. The results were interpreted on the level of significance $p < 0.05$. Confidence interval, CI, expressed for non-standardized indicators was acquired by the exact method for rare events. The differences among the groups were tested by t-test.

Results

On the prevalence day 31st December 2006, according to the assessment of the number of the inhabitants,

309,712 people lived in the Western Herzegovina Canton and Herzegovina-Neretva Canton. By the analysis of the available medical records 104 potential MS patients were identified. Eight of potential patients were not included in the study (Table 1).

TABLE 1
PATIENTS EXCLUDED FROM THE STUDY – THE REASONS FOR EXCLUSION, WHC AND HNC, 1997–2006

Reasons for exclusion	Number of patients
Incorrect diagnosis of MS	4
Moved from the studied area	0
Possible MS (did not meet the criteria)	1
Died	3
Total	8

A total of 96 MS patients, out of which 63 (65.5%) females and 33 (34.3%) males, met McDonald's criteria and were included in the study. Out of the total number of patients 81 (84.4%) were domicile population and 15 (15.6%) immigrated in the last 15 years. In four patients previously established diagnosis of MS was rejected. Two patients had cerebrovascular disease, one had dissociated movement and sensation disorder and one had acute encephalomyelitis. Female/male (F/M) ratio is 1.5. Crude annual prevalence *per* 100,000 inhabitants on 31st December 2006 was 30.99 (95% CI: 24.8–37.2). 93 patients (96.9%) were aged between 15 and 64 and 3 (3.1%) were 65 years old. There were no patients younger than 15 years of age. Prevalence in the age group 15–64 was 45.05 (95% CI: 35.9–54.2), and at the age of 65 it was 5.93 (95% CI: 0–12.6). The distribution of multiple sclerosis in Herzegovina is not homogenous (Table 2).

Prevalence was the highest in the municipalities of Posušje, 49.6/100,000 inhabitants (95% CI: 15.2–83.9) and Čapljina 42.3/100,000 inhabitants (95% CI: 16.1–68.5). In the municipalities of Neum and Ravno on the prevalence day there were no patients. The average annual in-
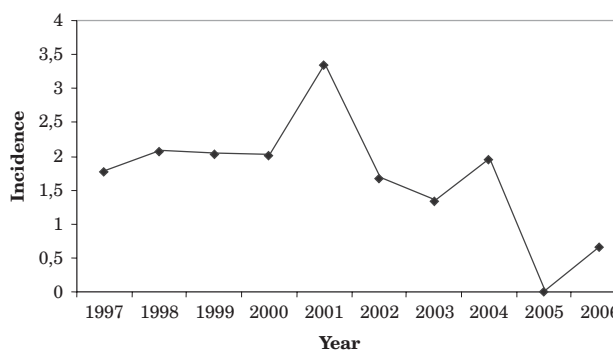

Fig. 1. The annual incidence of multiple sclerosis in WHC and HNC, 1997–2006 WHC – Western Herzegovina canton, HNC – Herzegovina-Neretva canton.

TABLE 2
PREVALENCE OF MULTIPLE SCLEROSIS IN WHC AND HNC IN MUNICIPALITIES (31/12/2006)

Place of living	Number of inhabitants	Number of patients	Prevalence per 100,000 inhabitants	95% CI
WHC AND HNC	309712	96	30.99	24.8–37.2
Čapljina	23650	10	42.3	16.1–68.5
Čitluk	15935	4	25.1	0.5–49.7
Jablanica	11892	3	25.2	0.0–53.8
Konjic	29111	8	27.5	8.4–46.5
Mostar	111282	39	35.05	24.0–46.0
Neum	4695	0	0	0
Prozor	16368	6	36.7	7.3–66.0
Ravno	1346	0	0	0
Stolac	13351	4	29.96	0.6–59.3
Grude	15673	1	6.4	0.0–18.9
Ljubuški	24102	6	24.9	5.0–44.8
Posušje	16144	8	49.6	1 5.2–83.9
Široki Brijeg	26163	7	26.8	6.9–46.6

WHC – Western Herzegovina canton, HNC – Herzegovina-Neretva canton, CI – confidence interval

cidence of MS for the period from the 1st January 1997 to the 31st December 2006 was 1.7/100,000 inhabitants (95%CI: 1.2–2.1).

The incidence rate for the period 1997–2001 was 2.2 (95%CI: 1.5–3.0) and for the period 2002–2006 it was 1.1 (95%CI: 0.6–1.6). The highest incidence rate was in 2001 (3.35/100,000) and the lowest one in 2005 when there were no new cases of MS. The mean age of the patients on the prevalence day was 41.4±10.2 (min–max 20–68), for males 40.7±11.2 (min–max 20–61), for females 41.8± 10.2 (min–max 22–68). The mean age of the patients at the onset of the disease was 30.7±6.4 (min–max 17–47), for males 29.9±6.5 (min–max 17–40) and for females 31.1±6.4 (min–max 18–47). The average duration of the
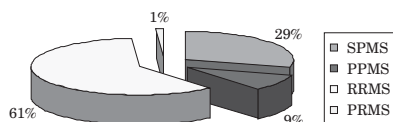

Fig. 2. The distribution of clinical types of multiple sclerosis, WHC and HNC, 1997–2006. WHC – Western Herzegovina canton, HNC – Herzegovina-Neretva canton, SPMS – secondary progressive multiple sclerosis, PPMS – primary progressive multiple sclerosis, RRMS – relapse-remitting multiple sclerosis, PRMS – progressive-remitting multiple sclerosis.
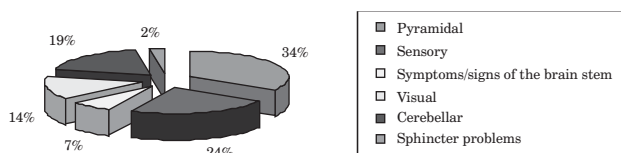

Fig. 3. The distribution of the initial symptoms/signs of multiple sclerosis, WHC and HNC, 1997–2006. WHC – Western Herzegovina canton, HNC – Herzegovina-Neretva canton.

disease from the onset to the prevalence day was 10.7± 7.5 years, for men 10.8±7.6, and for women 10.7±7.5.

The categorization of the clinical types of MS is as follows: relapse-remitting (RRMS) 58 patients (60.4%), secondary progressive (SPMS) 29 patients (28.2%), primary progressive (PPMS) 9 patients (9.4%) and progressive--relapsing (PRMS) 1 (1.0%) patient (Figure 2). Primary progressive type is more present in females (7 patients) compared to males (2 patients). There was not any statistically significant difference between genders in the frequency of RRMS and SPMS (p=0.82).

The most often initial symptoms in our sample were motor symptoms 33.3%. Sensory symptoms were the initial ones in 23.8% patients, symptoms of the brain stem were in 3% of the patients, visual symptoms in 14.3% of the patients, cerebellar in 19% and sphincter problems in 2.4% of patients.

Discussion

The first attempt to determine the distribution of MS in Bosnia and Herzegovina was made by Zec in 1956[9]. By the analysis of 202 hospitalized MS patients he concluded that »0.5–1 out of 2.800,000 inhabitants in the Sarajevo region had the disease of MS«. Sulejmanović et al., by the analysis of the data from the period 1982–1987, reported that the incidence of MS in the municipality of Tuzla was 2.3 *per* 100,000 inhabitants/year and in the broader Tuzla region 1.3 *per* 100,000 inhabitants/ year. The prevalence of MS in Tuzla microregion (Northeast Bosnia) on the 31st March 1981 was 7.8 *per* 100,000 inhabitants[10]. Đelilović-Vranić J. et al. have recently confirmed the higher frequency of MS in Sarajevo in the post-war period (1996–2000): 107 patients (64.2% fe-

males; 35.8% males) compared to the pre-war and war period (1986–1995): 72 patients (35.6% females, 64.4% males)[11]. This is an example of the inversion of the percentage of the incidence of MS between genders, which suggests that women are more sensitive to MS when exposed to severe environmental conditions (wartime). Based on the information obtained from the Association of the MS patients in Republic Srpska the prevalence of MS was assessed to 16.6 per 100,000 inhabitants (S. Grgić, MD, oral communication, February 2007).

The crude prevalence of MS of 30.99 per 100,000 inhabitants and the average annual incidence of 1.7 per 100,000 inhabitants/year places the studied region, south-western part of BiH, on the border between zones of moderate and high risk of MS. The prevalence rate is somewhat higher than the one established for the same region in 2003, 26.9 per 100,000 inhabitants[12]. The bordering regions of Republic of Croatia are characterized by very similar indicators: Dubrovnik-Neretva County 23.8 per 100,000 inhabitants, 2.2 per 100,000 inhabitants/year; Šibenik-Knin County 30.2 per 100,000 inhabitants; Zadar County 31.2 per 100,000 inhabitants, 2.8 per 100,000 inhabitants/year[13]. Continental municipalities (Posušje), with cold climate and more winter precipitation, have higher prevalence than the coastal municipalities with warmer climate and high number of sunny days (Neum, Ravno) in which on the prevalence day no patient was identified. Marked variations of the distribution of MS within the small geographical regions of the state have already been observed in south-eastern Europe[14]. Heterogeneous distribution of MS in Herzegovina is the consequence of the recent war (April 1992–November 1995). The area, especially the municipalities of Mostar, Čapljina and Stolac were the scenes of turbulent migration: emigration of around 40,000 inhabitants; immigration of approximately 6,000 inhabitants. The post-war period, compared to the pre-war one, is characterized in the domicile population with the 5-fold increase of MS incidence. The introduction of magnetic resonance (MR) in the diagnostics of MS cannot be the only factor responsible for such an increase of the incidence rate, since neuroimaging techniques have been used by the neurologists since 1990s.

The female/male (F/M) ratio based on the prevalence, higher prevalence in females and the mean age at the onset of the disease are consistent with the results of the similar studies in the world[15]. The average age and the average duration of MS on the prevalence day are shorter than in similar studies in Europe. The lower counts of these indicators show the unfavorable quality of life, especially during the last decade in the studied region in which the MS patients very rarely live beyond 60 years of age. Some clinical characteristics of the examined sample of MS patients deserve a comment. Optical neuritis is less frequently observed as the initial symptom of MS than in other classic studies[16]. Contrary to the observation by Cottrella et al., primary progressive type of MS in our MS patients is more present in females[17]. The research proves that Western Herzegovina is a region on the border between zones of moderate and high risk of MS.

Acknowledgements

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EPIDEMIOLOGIJA MULTIPLE SKLEROZE U ZAPADNO-HERCEGOVAČKOJ I HERCEGOVAČKO-NERETVANSKOJ ŽUPANIJI, BOSNA I HERCEGOVINA

S A Ž E T A K

Cilj ove studije je utvrditi deskriptivne epidemiološke pokazatelje multiple skleroze (MS) u Hercegovini (Zapadno--hercegovačka županija i Hercegovačko-neretvanska županija). Analizom svih raspoloživih zdravstvenih i medicinskih izvora u istraženome području, u razdoblju od 1996. do 2006. godine, na dan prevalencije, 31.12. 2006. godine primjenom I.W. McDonaldovih kriterija, izdvojeno je 96 bolesnika koji boluju od MS. Rezultati studije su sljedeći: sirova prevalencija MS iznosila je 30,99/100,000 (95% confidence interval (CI): 24,8–37,2), najviša u općini Posušje (49,6/100,000), najniža u općinama Neum i Ravno, (incidencija 0); godišnja incidencija MS bila je 1,7/100000 (95%CI: 1,2–2–1); spolni indeks (F/M) je bio 1,5; prosječna životna dob bolesnika na dan prevalencije bila je 41,4±10,2 godina; a na početku bolesti 30,7±6,4 godina; najčešći klinički tijek bolesti je bio relaps-remitirajući (58%), sekundarno progresivni je bio zastupljen sa 28%, primarno progresivni sa 9% i progresivno relapsirajući sa 1%; najčešći početni znaci bolesti bili su motorni (33%) i senzorni (24%). Na temelju rezultata studije zaključujemo da je jugozapadni dio Bosne i Hercegovine (BiH) područje na prijelazu umjerenog ka visokom riziku za MS. Distribucija MS je inhomogena. MS je više prisutna u općinama sa hladnijom klimom i više zimskih padavina a nije prisutna u priobalnom području sa toplom klimom i gotovo bez zimskih padavina.