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EPIDEMIOLOGY OF MULTIPLE SCLEROSIS IN THE BJELOVAR-BILOGORA COUNTY

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SUMMARY – Multiple sclerosis (MS) is a chronic neurologic disease of unknown etiology, which shows a peculiar pattern of prevalence in the world, varying among different countries and regions of a particular country. The aim of the study was to assess the prevalence and incidence of MS in the Bjelovar-Bilogora County in the last two decades (1982-2001), including the period of war in Croatia. Retrospective analysis of a database containing medical history of 71 patients using Poser's criteria revealed the prevalence and incidence of MS to have significantly increased during the study period, in the years preceding the war in particular. At the beginning of the study period (1982), the prevalence of MS was 13.38/100,000, ranking the County an area of moderate risk, whereas at the end of the study period (2001) the prevalence of MS was 47.36/100,000, characterizing the County as an area of high risk of MS. In the first and last 5-year period, the incidence was 0.53 and 2.40, respectively, showing a female predominance (F:M: 2.40:1). According to Poser's criteria, the relapsing remitting type of disease was present in 54%, secondary progressive in 21% and primary progressive in 17% of patients, whereas 8% of patients remained unclassified. Optic neuritis was found in 14.96% of study patients. The mean age at disease onset was 32.5 years. The study showed the County to have become an area of high risk of MS in the last decade of the twentieth century.

Key words: *Mulitple sclerosis – epidemiology; Multiple sclerosis – etiology; Croatia*

Introduction

Multiple sclerosis (MS) shows a peculiar pattern of prevalence worldwide, with areas of high, moderate and low exposure[1,2]. Considering that the etiology of the disease has not yet been clarified, a number of factors have been implicated as the potential triggers for the disease development, from geographical, demographic, socioeconomic to genetic characteristics. New concepts offer new treatment options associated with considerable cost.

The aim of the study was to determine the prevalence of MS in the Bjelovar-Bilogora County, continuing previous studies, with special reference to the war and postwar period; to provide a critical review of diagnostic criteria during the study period, current state-of-the-art, and diagnostic possibilities[3,4]; and to analyze the rate of particular types of the disease as well as the number of potential candidates for novel treatment options.

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Patients and Methods

The investigation was designed as a retrospective study, to analyze medical history of all MS patients treated over the past 20 years according to the age at disease onset, sex, diagnostic criteria, type of disease, and presence of optic neuritis; and to assess the prevalence and incidence of MS in the County.

The study covered the area of the Bjelovar-Bilogora County, located in central Croatia, in the Lonja-Ilova valley with the Bilogora mountain. The County has five local districts: Bjelovar, Čazma, Garešnica, Grubišno Polje and Daruvar, covering an area of 2,647 km^2. According to the 1981, 1991 and 2001 census, the County had a population of 149,458; 144,042; and 133,034, respectively.

In 1982, an inpatient registry was established at Department of Neurology, Bjelovar General Hospital, containing files of all individuals presenting for neurologic or psychiatric examination, or hospitalized at the Department. In the mid-1990s, a registry of MS patients treated at Bjelovar General Hospital was established. Upon the establishment of the Multiple Sclerosis Society of the Bjelovar-Bilogora County in 2000, a list of MS patients was made, now containing 42 members. Based on these three registries, a group of 73 MS patients were selected for this study. Data from the registries were previously entered in the specially designed questionnaire. In case of incomplete data, patients were contacted to provide the missing data whenever possible. The 1982-2001 period was chosen for data availability, possibility of comparison between prewar and postwar period, and appropriate timing for MS type assessment in newly detected patients.

Table 1. Total number of multiple sclerosis patients 1982-2001 according to 5-year periods

Year(s)	1981	1982-1986	1987-1991	1992-1996	1997-2001
Total number of patients	20	20	32	48	64
male	4	3	9	15	19
female	15	17	23	33	45
Newly detected patients		4	14	17	16
male		2	6	5	4
female	1	2	8	12	12
Died		4	2	1	
male		3			
female		1	2	1	

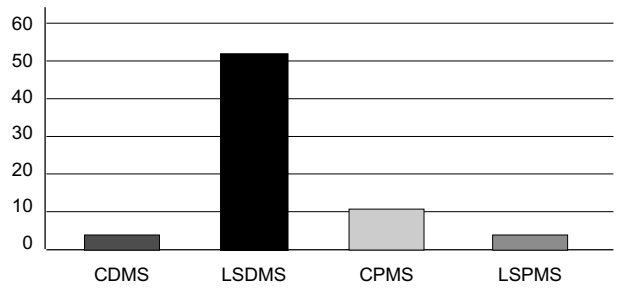
Case histories of all patients treated for the diagnosis of MS were examined and excluded those that did not meet Poser's criteria or where MS was ruled out by subsequent diagnostic work-up. As in the 1970s and 1980s the disease was generally diagnosed at university departments of neurology in Zagreb and other large centers, and patients were also treated at those institutions, the incidence, i.e. the rate of newly affected patients was assessed by analysis of their case histories. Based on this analysis, the age at disease onset, type of disease, classification according to Poser's criteria, and the incidence and prevalence of MS were retrogradely estimated.

Results

Data on 73 patients registered and treated for the diagnosis of MS during the 1981-2001 period were analyzed. Two patients were excluded from further analysis because subsequent use of neuroradiologic imaging techniques revealed basilar impression and post-traumatic encephalopathy in one patient each, after they had been treated for MS for some twenty years. Analysis of case histories according to Poser's classification of the disease[3] showed 52 (73%) patients to belong to the group of laboratory supported definitive MS, four (6%) patients to the group of clinically definitive MS, 11 (15%) to the group of clinically probable MS, and four (6%) patients to the group of laboratory supported probable MS (Table 1, Fig. 1).

At the beginning of the study period, i.e. towards the end of 1981, twenty patients treated for MS were recorded. In the next 20 years, MS developed in 51 patients, seven of them died. The number of hospitalizations for MS increased in parallel with the rising number of patients (Fig. 2).

Twenty MS patients were registered at the end of 1981; total number of MS patients remained unchanged over the first 5 years because the number of newly detected patients was identical to the number of deaths. However, 14 newly detected MS patients were registered in the next 5-year period; two of these patients



CDMS, clinically definitive multiple sclerosis; LSDMS, laboratory supported definitive multiple sclerosis; CPMS, clinically probable multiple sclerosis; LSPMS, laboratory supported probable multiple sclerosis

Fig. 1. Classification of multiple sclerosis

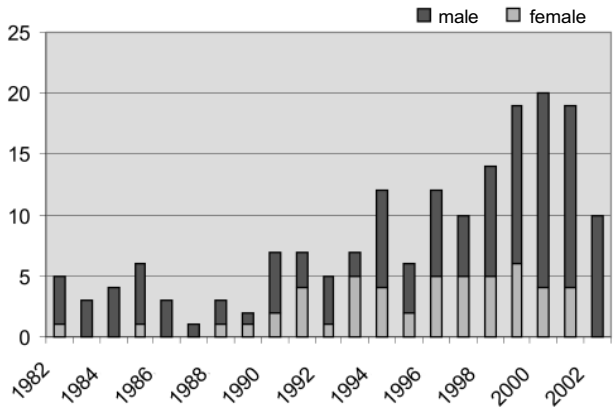


Fig. 2. Number of hospitalizations for multiple sclerosis 1982-2001

died, so the number of MS patients rose to 32. In the next 5-year period there were 17 newly detected MS patients; one of them died, so there were 48 MS patients in 1996, a year denoting the end of the war. In 2001, there were 64 MS patients because another 16 patients had been registered over the preceding 5-year period. Accordingly, the prevalence of the disease was 13.38 *per* 100,000 in 1981, and remained unchanged in 1986. In 1991, i.e. at the beginning of the war, the prevalence of MS increased to 22.21, in 1996 to 33.32, and in 2001 to 47.36 *per* 100,000 inhabitants (Table 2).

The incidence of MS also showed a rising tendency, from 0.53 in 1982-1986 to 1.94 in 1987-1991, 2.36 in 1992-1996, and 2.40 in 1997-2001 period (Table 3).

The mean age at the disease onset was 32.3 in men and 32.7 women. According to sex distribution of MS patients, there were 50 women and 21 men, yielding a 2.40:1 female predominance (Fig. 3). Optic neuritis was present in 22 of 68 (14.96%) MS patients.

Assessment of MS type was not always easy, pointing to the need of better patient documentation keeping. According to Poser's criteria, the relapsing remitting type of MS was present in 38 (54%), secondary progressive type in 15 (21%), and primary progressive type in 12 (17%) of 71 study patients. The type of disease could not be determined in six (8%) patients due to incomplete data (Fig. 4).

Table 2. Prevalence of multiple sclerosis according to years

Year	1981	1986	1991	1996	2001
Prevalence	13.38	13.38	22.21	3 3.32	47.36

Discussion and Conclusion

Analysis of the results obtained in the study primarily pointed to a significant increase in the number of MS patients and transition from a moderate risk area in 1981 (13.38/100,000) to a high risk area in 1996 (33.32/100,000). The growing prevalence was previously indicated by a study conducted by Šarko *et al.* in 1996 (22.85/100,000)[5], the rising tendency being now confirmed to continue in the next few years. The pronounced increase in the prevalence of MS after 1986 to continue during the war (1991-1996) and postwar periods should be noted. Such a pattern is rather disturbing, the more so as MS is a disease affecting young people, and should be considered in combination with the pronounced general and generation female depopulation accompanied by unfavorable changes in the population age structure (a decrease of young and steep increase of elderly population), potentiated by war suffering and negative migration score[6]. On the other hand, the study period was generally characterized by intensive brain research, development of novel diagnostic tools, generation of new specialists in neurology, and large-scale dissemination of information on health and disease through mass media, along with patient self-organization.

Table 3. Incidence of multiple sclerosis 1982-2001 according to 5-year periods

Period	1982-1986	1987-1991	1992-1996	1997-2001
Incidence	0.53	1.94	2.36	2.40

The attempt at determining the incidence of MS turned to be a rather unrewarding job. The incidence of the disease depends on the disease manifestation and the system readiness to perceive it. Some patients had

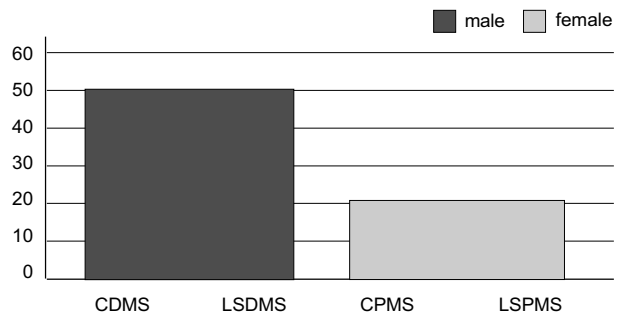


Fig. 3. Sex distribution of multiple sclerosis patients

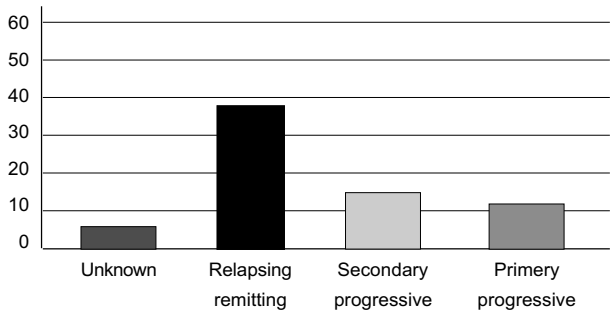


Fig. 4. Patient distribution according to types of multiple sclerosis

been suffering from symptoms and exhibited a clinical picture fully consistent with MS for years before the diagnosis was established (one female patient had been treated for recurrent optic neuritis and neurasthenia for 18 years, when the cerebrospinal fluid analysis, magnetic resonance imaging and evoked potential recordings confirmed MS). If these patients were categorized as new cases according to the time of diagnosis, they would have been related to the war as a possible provoking factor; however, it was only the need of better diagnosis. Also, some patients came from other parts of the former state, who had for some ten years been diagnosed with MS, some arrived with a several-year history of symptoms, yet without definitive diagnosis. Therefore we decided to perform retrograde analysis of case histories, substantiated by personal contact with patients with incomplete data or those previously treated at other institutions. This analysis yielded the incidence of MS of 0.53 in the 1982-1986 period, to steeply rise to 1.94 in the next 5-year period (1987-1991), reaching 2.36 in the 1992-1996 period, and remaining almost unchanged (2.40) in the last 5-year period (1996-2001).

The female to male ratio showed marked female predominance (2.40:1). According to type of disease, the relapsing remitting type of MS was present in 54%, secondary progressive in 21%, and primary progressive in 16% of study patients, whereas in 9% of patients the type of disease could not be determined due to incomplete data. Considering these data in the light of current concepts on MS treatment, a half of these patients would be potential candidates for therapy with interferon-beta.

The rate of hospitalization for MS increased in the postwar period, reflecting the higher number of patients, development of novel diagnostic methods, changed attitude to treatment options, better patient information and organization, and stimulation to use all therapeutic options available[5,7,8].

In conclusion, the incidence and prevalence of MS have been on an increase since the mid-1980s, being most pronounced in the prewar period, and rather even during the war and postwar periods. Towards the end of the war, the Bjelovar-Bilogora County turned to an area with a high risk of MS. Interestingly, however, the rise of MS incidence was greatest in the prewar period, at the time of profound social changes.

It appears that the present study does not allow any definite conclusion on such a complex phenomenon. However, improved diagnosis and health care have certainly contributed to the earlier and more reliable diagnosis of the disease. In addition, attitudes on MS have been modified, both in physicians and patients, and new therapeutic options have certainly motivated many a patient to leave passive waiting behind and to turn to active demand for most appropriate therapy. This has resulted in an increased number of hospitalization, higher cost of treatment, and a rising number of MS patients able to work.

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Sažetak

EPIDEMIOLOGIJA MULTIPLE SKLEROZE U BJELOVARSKO-BILOGORSKOJ ŽUPANIJI

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Multipla skleroza (MS) je kronična neurološka bolest nepoznate etiologije koja pokazuje neobičan model rasprostranjenosti u svijetu s različitom učestalošću u pojedinim zemljama, kao i u različitim regijama iste zemlje. Cilj istraživanja bio je utvrditi učestalost i incidenciju MS u Bjelovarsko-bilogorskoj županiji u posljednjih dvadeset godina (1982.-2001.) uključujući razdoblje rata. Retrospektivnom analizom obrađena je na temelju Poserovih kriterija baza podataka koja sadrži povijesti bolesti 71 bolesnika. Zabilježen je značajan porast učestalosti i incidencije MS tijekom ispitivanog razdoblja, osobito u godinama koje su prethodile ratu. Učestalost MS na početku promatranog razdoblja (1982. g.) iznosila je 13,38/100.000 te je županija bila područje srednje izloženosti; na kraju razdoblja (2001. g.) učestalost je bila 47,36/100.000 i županija je postala zona visokog rizika za MS. Prosječna incidencija u prvom petogodišnjem razdoblju iznosila je 0,53, a u zadnjem 2,40. Spolna predilekcija bila je u korist žena (2,40 :1). Prema Poserovim kriterijima 54% bolesnika imalo je relaps-remitirajući oblik bolesti, 21% sekundarno progresivni, 17% primarno progresivni, dok se 8% bolesnika nije moglo klasificirati. Optički neuritis je bio prisutan u 14,96% oboljelih. Srednja dob kod pojave bolesti bila je 32,5 godina. Istraživanje pokazuje da je naša županija postala zona visokog rizika za MS u zadnjih deset godina prošloga stoljeća.

Ključne riječi: *Multipla skleroza – epidemiologija; Multipla skleroza – etiologija; Hrvatska*