

CLINICAL AND EPIDEMIOLOGICAL STUDY OF MULTIPLE SCLEROSIS IN SVOGE AND TROYAN

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Abstract

Multiple sclerosis is a chronic inflammatory, autoimmune, demyelinating and neurodegenerative disease of the central nervous system. It is characterized by various symptoms depending on the area affected – brain, spinal cord or optic nerves. Multiple sclerosis typically presents at age 20–40 years and affects women more often than men. It is the most frequent nontraumatic disease causing neurologic deficit among young people. According to the 3rd edition of Atlas of MS, published by The Multiple Sclerosis International Federation in 2020, there are 2.8 million people living with the disease around the world. The last study on the epidemiology of multiple sclerosis in Bulgaria was published in 1999. It estimated prevalence of 44.5/100 000 and incidence 1.03/100 000.

We present an epidemiological study conducted between January 2016 and December 2020 in two small areas in Bulgaria with homogenous and stable population – Svoge and Troyan. The estimated prevalence of multiple sclerosis in Troyan was 116.5/100 000 with incidence of 28.2/100 000. The prevalence and incidence of multiple sclerosis in Svoge were 117.7/100 000 and 24.5/100 000, respectively. The reason for the higher prevalence and incidence rates in our study may be explained by the better diagnosis of the disease according to well defined diagnostic criteria, the longer survival of the affected individuals and the availability of various disease modifying therapies.

Key words: epidemiology, multiple sclerosis, prevalence, incidence

Introduction. Multiple sclerosis is an autoimmune, chronic inflammatory, demyelinating and neurodegenerative disease of the central nervous system. It is

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characterized by various symptoms, depending on the area affected by the pathological process – brain, spinal cord or optic nerves [1]. The disease typically affects young people between 20 and 40 years of age and is more common in women than men. Multiple sclerosis is the most frequent non-traumatic cause of neurologic deficit among young, working people which determines the great social significance of this illness [2]. The clinical course of the disease is divided into four definite phenotypes – clinically isolated syndrome (CIS), relapsing-remitting multiple sclerosis (RRMS), secondary-progressive (SPMS) and primary progressive (PPMS) [3]. Multiple sclerosis is diagnosed through well-defined diagnostic criteria (McDonald's criteria) which demonstrate dissemination of the process in space and time [4].

Multiple sclerosis is characterized by an uneven geographical distribution as the frequency of the disease increases with distance from the equator both north and south, thus forming a geographical gradient. In recent years, a number of studies have been published that demonstrate a general trend of increasing prevalence and incidence worldwide [5]. There are also studies that show a decrease in the established geographical gradient [6, 7]. According to the Atlas of MS published by the International Federation of Multiple Sclerosis in 2020, there are 2.8 million patients with multiple sclerosis in the world with prevalence of 36/100 000 [8].

The first detailed epidemiological study of multiple sclerosis in Bulgaria was conducted between 1970 and 1979 and found prevalence of 21.3/100 000 [9]. The last clinical epidemiological study covers the period 1995–1998 and found prevalence of 44.5/100 000 and incidence 1.03/100 000, establishing a trend of progressive increase in the frequency of the disease in the country in line with the global trend [10]. These results show that there are about 3 600 affected people and each year 60 new get sick. We do not have new data on the spread of multiple sclerosis in our country but if we accept doubling of the epidemiological indices, there are about 7000 people with multiple sclerosis and about 160 new people getting sick each year [11].

Materials and methods. A population based epidemiological study was conducted between January 2016 and December 2020 in two small districts with stable and homogenous population – Svoge and Troyan. On the prevalence day – December 31, 2020 there were 20 395 people living in Svoge (10 222 women and 10 173 men) and 28 319 in Troyan (14 660 women and 13 659 men) according to data of the National Statistical Institute. Statistical methods were used to estimate prevalence and incidence rates with 95% uncertainty interval and patients were divided into subgroups regarding age, sex, symptoms at onset, age at onset, clinical course of disease, mean duration of disease and EDSS (Expanded Disability Status Scale).

Results. On the prevalence day – December 31, 2020 there were 33 people with multiple sclerosis living in Troyan – 24 women (72.7%) and 9 men (27.3%). All of the patients were diagnosed in a university hospital and the diagnosis was

confirmed using MRT (Magnetic Resonance Tomography) imaging. Prevalence of multiple sclerosis was estimated to be 116.5/100 000 (95% uncertainty interval (UI) – 81 to 164/100 000), 163.7/100 000 (105–244/100 000 for women and 65.9/100 000 (30–125/100 000) for men. The ratio between women and men was 2.7:1 in favour of women. The new cases of the disease in the period between 2016 and 2020 were eight, of which six women and two men, revealing an incidence rate of 28.2/100 000 (12–55/100 000), 40.9/100 000 (15–89/100 000) for women and 14.6/100 000 (2–53/100 000) for men.

The mean age of patients in our study was 45.9 ± 12.3 years. The mean age at onset of disease was 33.3 ± 10.9 years with most of the people in the age group 19–29 years. Mean duration of disease was 12.5 (range 1 to 40) years.

In ten of the patients (30.3%) the onset of disease was with coordination disturbances, nine patients (27.3%) had visual disorders, four patients (12.1%) – sensory disturbances, and four patients had movement disorders. One patient had pelvic-reservoir disorders and another one had cognitive/mental disorders. The disease had polysymptomatic onset in two patients (6.1%).

Twenty-three patients (69.7%) were treated with disease-modifying therapy during the period of the study and ten patients (30.3%) had never undergone disease-modifying therapy.

Table 1 shows the distribution among patients (men and women) living in Troyan municipality according to age at onset.

T a b l e 1

Distribution of patients in Troyan by age at onset

Age at onset	Men		Women		Men + Women	
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%
0–18	0	0	2	6.1	2	6.1
19–29	6	18.2	6	18.2	12	36.4
30–39	2	6.1	7	21.2	9	27.3
40–49	0	0	6	18.2	6	18.2
50–59	1	3.0	3	9.0	4	12
Total	9	27.3	24	72.7	33	100

Figure 1 shows the distribution of patients, living in Troyan according to course of disease. Clinically isolated syndrome was diagnosed in one patient (3%), 20 patients (60.6%) had relapsing-remitting MS, ten patients (30.3%) had secondary-progressive MS and three patients (6.1%) had primary-progressive MS.

On the prevalence day December 31, 2020 there were 24 patients suffering from multiple sclerosis living in the other district – Svoge; seven were men (29.1%) and 17 (70.9%) were women. Prevalence of multiple sclerosis was 117.7/100 000 (76 to 175/100 000), 166.3/100 000 (97–266/100 000) for women and 68.8/100 000 (28–142/100 000) for men. The ratio between women and men was calculated to

Clinical course of disease

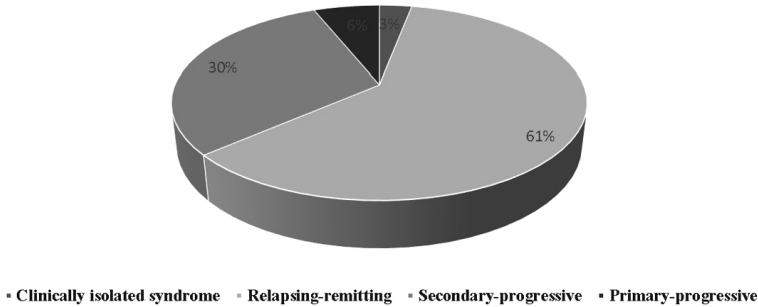


Fig. 1

be 2.4:1 in favour of women. The new cases of the disease in the period between January 2016 and December 2020 were five, of which only one was a man and the other four patients were women. We estimated incidence rate of 24.5/100 000 (8–57/100 000). For women the incidence rate was 39.1/100 000 (11–99/100 000) and for men it was 9.8/100 000 (2–55/100 000).

The mean age of all the patients with multiple sclerosis in Svoge was 46.5 ± 13.7 years. The mean age at the onset of the disease was 32.2 ± 10.9 years with most of the people being again in the age group 19–29 years. Mean duration of disease was 14.3 (range 1 to 35) years.

The onset of the disease was with sensory disturbances in 11 patients (45.8%). In six patients (25%) the beginning of the disease was with visual disturbances, four patients (16.7%) had coordination disturbances at onset and only one patient (4.2%) had movement disorders. None of the patients had pelvic-reservoir or cognitive/mental disorders at onset. Two patients (8.3%) had polysymptomatic onset of the disease.

Seventeen patients (70.8%) were treated with disease-modifying therapy during the period of the study and seven patients (29.2%) had never undergone disease-modifying therapy.

Table 2 shows the distribution among patients (men and women) living in Svoge municipality according to age at onset.

Figure 2 shows the distribution of patients, living in Svoge according to course of disease – clinically isolated syndrome (4.2%), relapsing-remitting MS (54.2%), secondary-progressive MS (37.5%), and primary-progressive MS (4.2%).

Discussion. The first epidemiological studies of multiple sclerosis in Bulgaria date back to the 60s of the 20th century. They covered the period between 1952 and 1959. The prevalence of MS in the studied areas was low and varied between 3.2/100 000 and 11/100 000. On behalf of these investigations it was estimated that prevalence of multiple sclerosis in Bulgaria was 4.94/100 000 for men and 4.61/100 000 for women [12]. After that, two more studies were de-

T a b l e 2

Distribution of patients in Svoге by age at onset

Age at onset	Men		Women		Men + Women	
	N	%	N	%	N	%
0–18	0	0	3	12.5	3	12.5
19–29	3	12.5	6	25	9	37.5
30–39	2	8.3	4	16.7	6	25
40–49	2	8.3	3	12.5	5	20.8
50–59	0	0	1	4.2	1	4.2
Total	7	29.1	17	70.9	24	100

Clinical course of disease

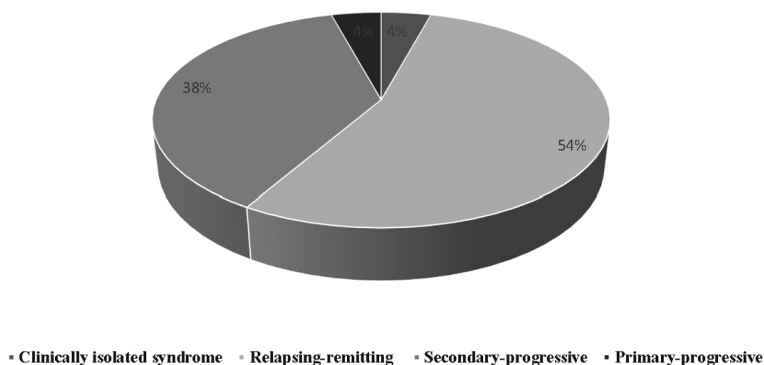


Fig. 2

voted to establishing frequency of multiple sclerosis in the country. The first one was conducted between 1959 and 1969 and covered the area of Varna, estimating prevalence of 15.9/100 000 [13]. The second was in the period 1967–1976 in North-Eastern Bulgaria and reported prevalence of 17/100 000 [14].

The first detailed study of the epidemiology of multiple sclerosis in Bulgaria was conducted by KALAFATOVA [9] in the period 1970–1979. It covered two regions in Northern Bulgaria – Mihaylovgrad and Veliko Tarnovo, two regions in Southern Bulgaria – Sliven and Burgas, as well as the capital of the country Sofia. It reported prevalence of 21.3/100 000. There were not statistically significant differences in the frequency of the disease between the northern and southern regions. The prevalence of multiple sclerosis in Sofia in 1992 was 30.2/100 000, significantly higher than the total prevalence in the country. For a period of 20 years no significant change in the value of the indicator had been established. It was 29.8/100 000 in the period 1970–1979 and 30/100 000 in 1983 [15].

In the period 1993–1995 MILANOV et al. [16] investigated the epidemiology of multiple sclerosis in two small districts – Svoге and Troyan. The prevalence of

multiple sclerosis in Svoge was 39.3/100 000, mean age of patients – 43 years and mean age at onset was 29.3 years. In Troyan the prevalence was 39.1/100 000, mean age of patients – 43.7 years and mean age at onset was 30.6 years.

The second detailed and last published study of the epidemiology of multiple sclerosis in the country was conducted by TOPALOV [10] in the period 1995–1998. The study covered the following cities – Samokov, Pavlikeni, Veliko Tarnovo, Stamboliyski, Svoge, and two regions in the capital – Iskar and Mladost. It estimated prevalence of 44.5/100 000 and incidence 1.03/100 000.

All of these studies demonstrate well defined trend of progressive increase in the frequency of multiple sclerosis in Bulgaria during the last decades. In our study we found much higher values of the investigated indices. In Svoge we estimated prevalence of 117.7/100 000 and incidence of 24.5/100 000. For Troyan the values are 116.5/100 000 and 28.2/100 000, respectively. It may be due to the availability of well-defined diagnostic criteria (McDonald's criteria) and better diagnostic tools and imaging techniques (including MRT), as well as the longer survival of the affected individuals because of the various disease-modifying therapies available. Last but not least our study was conducted in areas with decreasing population because of various demographic, social and economic reasons. A study covering more districts in different regions of the country is needed so that we get more detailed picture of the epidemiology of multiple sclerosis in Bulgaria.

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