Prevalence of Multiple Sclerosis in the Middle Black Sea Region of Turkey and Demographic Characteristics of Patients

Neslihan AKDEMİR[1], Murat TERZİ[1], Nilden ARSLAN[2], Musa ONAR[1]

[1]Department of Neurology, Ondokuz Mayıs University School of Medicine, Samsun, Turkey
[2]Department of Public Health, Ondokuz Mayıs University School of Medicine, Samsun, Turkey

ABSTRACT

Introduction: Multiple sclerosis (MS), a demyelinating disease of the central nervous system, is increasing in prevalence worldwide. Other than small-scale studies, there is a scarcity of data on the prevalence of MS in Turkey. The present study aimed to elucidate the prevalence of MS in the Middle Black Sea Region and the demographic characteristics of patients.

Methods: Patients living in the Middle Black Sea Region and who were diagnosed with MS were included. The study was designed based hospital of Turkey.

Results: A total of 1,787 patients were interviewed, and a diagnosis of MS was confirmed in 1,584. The prevalence of MS was found to be 43.2/100,000 in the Middle Black Sea Region; this was calculated based on the total population and number of patients in the provinces and districts in this region. The mean age at the disease onset was 29.39±7.6 years. Among the patients, 1,299 (81.9%) had relapsing-remitting MS, 74 had secondary progressive MS, 77 had relapsing-progressive MS, 47 had primary progressive MS, and 87 had clinically isolated syndrome.

Conclusion: The Middle Black Sea Region was found to have a high risk for the prevalence of MS. This study is the most comprehensive epidemiologic study having the largest geographical distribution on the prevalence of MS in Turkey.

Keywords: Middle Black Sea Region, multiple sclerosis, prevalence, epidemiology

INTRODUCTION

Multiple sclerosis (MS) is defined as a chronic, inflammatory, and demyelinating disease of the central nervous system. MS is more frequently diagnosed in women and in individuals aged between 20 and 40 years (1). Its prevalence is 30–80/100,000 in the population in high-risk areas including Canada, North America, and North Europe (2,3).

The number of studies on the prevalence of MS in Turkey is insufficient; however, studies conducted in Maltepe district of İstanbul (4) and in Erbaa, a rural area in the coastal Black Sea region of Turkey (5), have reported the a moderate-to-high prevalence of MS. Alp et al. (6) have demonstrated that the prevalence of MS in the North Caucasus Region of Turkey is higher than expected (68.97/100,000).

The prevalence of MS, which is known to be affected by genetic and environmental factors, varies in different regions. It is considered that this variation is caused by different seasonal characteristics, geographic locations, and ethnic profiles of the population (1,3). Turkey is located between Asia and Europe and constitutes a link between these two continents. Along with the high rate of migration from both inland regions and foreign countries, this migration may affect the prevalence of MS in Turkey. The present study investigated the prevalence of MS in the Middle Black Sea Region of Turkey as well as the demographic characteristics of patients.

METHODS

Patients who were diagnosed with MS and who were living in the Middle Black Sea Region were included. The study was conducted between August 2010 and May 2011. All patients were informed about the study, and their consent was obtained. Approval of the Ethical Committee of Ondokuz Mayıs University was obtained for the study.

Patient admission records between January 2001 and February 2011 were obtained from secondary and tertiary hospitals in Samsun, Sinop, Ordu, Amasya, Tokat, and Çorum provinces and in the districts of these provinces in the Middle Black Sea Region. Neurology specialists working in these centers were informed about the study. In district hospitals without neurology specialists, chief physicians were informed. Information was obtained from data processing services after receiving permission from the chief physicians. All hospitals accepted to participate in the study and shared patient information on admission.

All clinical and radiological characteristics of patients were evaluated in the MS unit at Ondokuz Mayıs University. Patients who did not meet the clinical and radiological criteria for MS or who met the radiological criteria for MS but did not have any clinical history of MS

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attacks were excluded. Those whose clinical and magnetic resonance imaging (MRI) findings are compatible with MS were enrolled. The 2001 McDonald criteria were used as the diagnostic criteria.

Brain MRI was performed based on the Barkhof criteria. The presence of juxtacortical, periventricular, and infratentorial lesions on MRI and the total number of lesions and contrasting lesions were determined. Patients with normal brain MRI findings were excluded. Those with a history of lesions radiologically similar to demyelinating lesions were assessed in detail for diseases with similar radiological characteristics such as hypertension, vasculitis, diabetes, and migraine.

Patients who had a single attack with clinical and demographic characteristics compliant with the MS criteria and imaging features supporting the presence of MS were evaluated as having clinically isolated syndrome in the present study. The disability status of each patient was assessed according to the Expanded Disability Status Scale (EDSS). Patients were grouped as those able to walk without an aid (EDSS score of <4), those requiring a walking aid (EDSS score of 4-6), those requiring a wheelchair (EDSS score of 6-8), and those confined to bed (EDSS score of >8).

Statistical Analysis

The total population, male/female distribution, and age distribution for each province and district were based on data from the last census (in 2010). These data were received from the Turkish Statistical Institute. Prevalence is defined as the number of people with a certain disease or diseases included in the scope of a study in a certain period of time and in a certain population. The following formula was used in our study for calculating the prevalence: Prevalence (P)=(Number of people with MS between August 2010 and May 2011/Number of people in the population at risk of having MS between August 2010 and May 2011)×10^5. The prevalence of MS in each province was calculated by combining the prevalence for the districts within that province, and the prevalence in the Middle Black Sea Region was calculated by combining the prevalence in all provinces within that region.

Data were analyzed using Statistical Package for the Social Sciences (SPSS Inc.; Chicago, IL, USA) version 15.0. Data were expressed as mean±standard deviation and in numbers and percentages. The Mann–Whitney U test and chi-square test were used for intergroup comparisons, and the Zafson software package was used for double p-value comparisons. Statistical significance was set at p<0.05.

RESULTS

Based on the data obtained from hospitals, 1,787 patients were determined to be living in the Middle Black Sea Region and were diagnosed with MS. The clinical and radiological diagnoses of MS of 1,584 patients were confirmed, whereas the diagnoses of MS in 203 were withdrawn. The highest number of patients was observed in Samsun province and its districts (Table 1). The prevalence of MS in Samsun province was 46.5/100,000. It was 43.2/100,000 in the Middle Black Sea Region, which was calculated based on the total population and total number of patients in the provinces and districts (Table 1).

The mean±standard deviation age of the patients was 38.2±10.9 years; 1,121 (70.8%) patients were females, while 463 (29.2%) were males. The mean age at disease onset was 29.3±7.6 years, with a mean age at disease onset of 29.33±7.5 years in females and 29.53±7.9 years in males (Table 2). There was no significant difference between males and females in terms of age at disease onset (p=0.34).

A history of MS in other family members of patients was present in 177 (11.2%) patients. MS occurred in the sisters of 25 (14.1%) patients, moth-

ers of 22 (12.4%) patients, brothers of 19 (10.7%) patients, daughters of 10 (5.7%) patients, fathers of 8 (4.5%) patients, and other relatives of 93 (52.5%) patients.

Regarding the clinical type of MS, 1,299 (81.9%) patients had relapsing-remitting MS (RRMS), 74 had secondary progressive MS (SPMS), 77 had relapsing-progressive MS, 47 had primary progressive MS (PPMS), and 87 had clinically isolated syndrome (Table 2). All clinical types were more prevalent in females.

Among the patients, 1,339 (84.5%) were able to walk without an aid, 187 (11.8%) required a walking aid, 43 (2.7%) required a wheelchair, and 15 (0.9%) were confined to bed. Clinical symptoms associated with the affected neurological systems at onset included motor symptoms in 546 (34.5%) patients, sensorial symptoms in 505 (31.9%), optic neuritis in 409 (25.8%), vertigo in 378 (23.9%), brain stem findings in 186 (11.7%), ataxia and tremor in 168 (10.6%), other symptoms (headache, hearing loss, or tinnitus) in 94 (5.9%), and sphincter defects in 32 (2%).

DISCUSSION

The prevalence of MS increases yearly worldwide. Although there are insufficient studies on the prevalence of MS in Turkey, it is considered that the population in Turkeyis at a moderate risk of MS. In the present study, the prevalence of MS was 43.2/100,000 in the Middle Black Sea Region of Turkey. The prevalence of MS was high in all provinces and throughout the Middle Black Sea Region according to the classification of Kurtzke (2). It was higher in city centers than in districts. The rate of migration from rural

Table 1. Prevalence of multiple sclerosis in the Middle Black Sea region

City	Total population	Patients (n)	Prevalence of multiple sclerosis
Sinop	202,740	123	60.6/100,000
Ordu	719,183	276	38.4/100,000
Samsun	1,252,693	583	46.5/100,000
Tokat	617,802	270	43.7/100,000
Çorum	535,405	208	38.8/100,000
Amasya	334,786	124	37/100,000
Middle Black Sea Region	3,662,609	1,584	43.2/100,000

Table 2. Clinical and demographic characteristics of MS patients

	MS patients (n=1584)
Mean age	38.2±10.9
Female/Male	70.8%/29.2%
Mean age at onset	29.3±7.6
Family history of MS	11.2%
Clinical type of MS	RRMS (n=1299)
	SPMS (n=74)
	RPMS (n=77)
	PPMS (n=47)
	CIS (n=87)

MS: multiple sclerosis; RRMS: relapsing-remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis; RPMS: relapsing-progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis; CIS: clinically isolated syndrome

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areas to cities in Turkey has increased, particularly after 1985, leading to a larger urban population, especially in city centers, and a smaller rural population. As the number of MRI centers in secondary and tertiary hospitals located in city centers is higher and they are better equipped, the number of patients diagnosed with MS is higher in city centers.

Northern Europe is a high-risk area for MS, while Asia is a low-risk area (7,8,9). Turkey is a passage point between Europe and Asia. The prevalence of MS, 2–150/100,000 worldwide, varies between different geographical areas (7). The number of studies on the prevalence of MS in Turkey is limited. In a door-to-door study conducted in Maltepe district of Istanbul, the prevalence of MS was 101.4/100,000 (4). In a door-to-door study conducted in Erbaa district of Tokat province, which is located in the Middle Black Sea Region, the prevalence of MS was 53.2/100,000 (5). Alp et al. (6) have found the prevalence of MS to be 68.97/100000 in Kars, which is in the north-eastern region of Turkey. All these values indicate that Turkey is in the high-risk group according to the classification of Kurtzke (2).

Recent epidemiological studies have shown an increased prevalence of MS worldwide. Iran, which was a low-risk area for MS, is now one of the high-risk areas; the incidence of MS increased from 0.68/100,000 in 1989 to 2.93/100,000 in 2008 and then to 50.57/100,000 in 2009 (9). In Japan, the prevalence of MS increased from 8.6/100,000 to 13.1/100,000 (8). In Europe, the prevalence increased in countries already classified as high-risk areas. The prevalence of MS was 110/100,000 in Great Britain, 200.5/100,000 in Northern Ireland, 27/100,000 in Bosnia–Herzegovina, 62/100,000 in Hungary, 165.8/100,000 in Italy (Sicily and Sardinia), 120/100,000 in France, 120.4/100,000 in Norway, 125/100,000 in northern Switzerland, 105/100,000 in Finland, and 154.5/100,000 in Denmark (7,10,11,12,13).

In countries surrounding Turkey, the prevalence was 44.4/100,000 in Bulgaria, 119.6/100,000 in Western Greece, 35–70/100,000 in Russia (based on different studies), and 68.8/100,000 in Georgia (13,14,15,16,17). While the prevalence of MS was 3.4/100,000 in Iraq in 1969, 300 new MS patients from different races were identified in Baghdad in a study conducted in 2005 (18). This indicates that the prevalence of MS is gradually increasing in countries surrounding Turkey. The prevalences obtained in the present study were similar to those in the neighboring countries, and this supports the classification that Turkey is a high-risk area in terms of MS.

The Prevalenceof MS increases with increasing distance from the equator in both hemispheres (19). MS is more frequently encountered in cold and rainy countries such as in northern countries. It is most frequently encountered between the latitudes of 40 and 60° (20). Turkey lies between the northern latitudes of 36–42°. In regional terms, Turkey is between the latitudes where MS is most frequently observed.
In general, the frequency of MS is higher in females worldwide (21). In the present study, the prevalenceof MS was twice as high in females than in males. This may be due to various reasons. Today, women benefit from healthcare services more, and this increases the rate of diagnosis. Some of the possible reasons behind this high rate of MS in women include the fact that women have more vitamin D deficiencies, which is a risk factor for MS; the increased number of women using hormone replacement treatment; the increased use of oral contraceptives; the increased rate of smoking among females; increased obesity; and related changes in diet (22,23,24,25,26).

Multiple sclerosis is an autoimmune disease caused by genetic and environmental factors that may be accompanied by other autoimmune diseases (26,27). Among our patients, 177 (11.2%) had a history of MS in other members of the family. The incidence of MS in the families of MS patients is 5%-26% (28). In a study conducted in Iran, the frequency of MS was 9.5% in the immediate family and 4.1% in first-degree relatives (29). Furthermore, first-, second-, and third-degree relatives of MS patients were at higher risk for developing MS than the general population. This risk is considered to be associated with the degree of relatedness (30). In the present study, familial MS was observed most often in second- and third-degree relatives. Among first-degree relatives, the frequency of familial MS was the highest in sisters, followed by mothers, brothers, daughters, and fathers. Although a higher frequency of familial MS in sisters and mothers is explained by the higher frequency of MS in women, some studies have reported a high rate of maternal inheritance of MS (31). A higher inheritance rate of familial MS in sisters than in mothers might be related to environmental factors. This can be explained by the fact that sisters and brothers are exposed to the same environmental factors during their childhood. The high frequency of familial MS in brothers in the present study might also support this opinion.

Among patients included in the present study, 1,299 (81.9%) had RRMS and 47 (3%) had PPMS. Data regarding the clinical progress of MS obtained from different cross-sectional studies in the literature are similar, with approximately 85% of MS cases exhibiting a relapsing-remitting pattern, with the remaining 15% exhibiting a progressive pattern (1). In a prevalence study conducted in Maltepe district of Istanbul, among 33 patients, 19 (57.5%) had RRMS, 11 (33.3%) had SPMS, and 3 (9.2%) had PPMS (4). Similar to other studies, most patients in the present study had RRMS, while PPMS was the least commonly observed clinical form.

While the most prevalent clinical symptom at onset in our patient group was motor symptoms (34.5%), this was followed by sensorial symptoms (31.9%), optic neuritis (25.8%), and vertigo (23.9%). Sphincter defects (2%) were the least observed symptoms at onset. In a study conducted in MS patients in Turkey, symptoms at onset were reported to be sensorial symptoms (43.4%), motor symptoms (40.4%), brainstem and cerebellar symptoms (29.7%), optic neuritis (20.4%), and sphincter defects (7.3%) (32). These values were similar to the distribution of symptoms at onset in the present study. In other studies conducted in other Western countries in the literature, motor and sensory symptoms were ranked first, which was in agreement with the results of our study.

Studies and data on the prevalence and clinical and demographic characteristics of MS are increasing daily worldwide. The present study is the most comprehensive epidemiologic study with the largest geographical distribution that provided information on the prevalence of MS in Turkey. The present study demonstrated that the Middle Black Sea Region was found to be the region with a high risk for the prevalence of MS. This shows that the prevalence of MS has increased in Turkey. There is need to conduct epidemiologic studies on the prevalence of MS in Turkey that include larger areas and to investigate the clinical, radiological, and demographic characteristics of more patients.

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