

## Prevalence of Multiple Sclerosis (MS) in Zanjan Province of Iran

### Abstract

**Background:** The prevalence of multiple sclerosis (MS) varies in different geographical regions and has dramatically increased in Iran. Revealing the high prevalence rate draws the attention of policymakers and helps them allocate necessary resources. The aim of this study is to determine the prevalence of MS in Zanjan province of Iran. **Methods:** We included all registered residents of Zanjan province with MS on the prevalence day (July 31, 2019). All cases met the McDonald criteria. All registered cases in Zanjan MS society were identified as index cases. Data regarding patient's national code, gender, age, age at the first symptom onset, city of residence, marital status, education level, occupation, ethnicity, family history of MS and the time span between symptom's onset and disease diagnosis were recorded. **Results:** We identified 758 patients, 551 of whom (72.7%) were female. The mean age at the first symptom onset was 28.9 ±8.7 years old. The crude prevalence was 71.6 per 100,000 population (95% CI 66.6–76.9). The disease was most prevalent in Zanjan city (100.5 per 100,000). The gender-specific prevalence per 100,000 population was 105.4 for women (95% CI: 96.8–114.6) and 38.7 for men (95% CI: 33.6–44.1), with female to male ratio of 2.6. The standardized mortality ratio (SMR) was calculated as expected/observed for both men and women as 2.3 (207/88.2) (551/234.1). **Conclusions:** Our data confirm that the MS prevalence rate is high in Zanjan province of Iran.

**Keywords:** *Epidemiology, Iran, multiple sclerosis, prevalence*

### Background

In recent years, studies have shown that the prevalence of multiple sclerosis (MS) has increased in different geographical regions.<sup>[1,2]</sup> The prevalence is increasing by growing distance from the equator.<sup>[3]</sup> Higher prevalence rates have been reported in northern regions of Western Europe, and North America while lower rates have been reported in Asia, the Middle East, and Africa.<sup>[1,4-9]</sup>

Iran is considered as a high-risk country for MS, although it is located in a low-risk geographical area.<sup>[10]</sup> The distribution of MS is complex and prevalence differs between the areas of similar latitudes as well as within a country.<sup>[11]</sup> Previous studies estimated point prevalence of MS between 7.4 and 89 per 100000 in different provinces of Iran (using data of Ministry of Health)<sup>[12]</sup> while all prevalent cases of all provinces were not included.

There is no specific study focusing on the prevalence of MS in the Zanjan province of Iran, although knowing the prevalence of

the disease in each province is essential and will help policymakers. So, we designed this study is to determine the prevalence of MS in the Zanjan province of Iran.

### Methods

Zanjan is one of the 31 provinces of Iran which is located in the north-west of the country with a latitude of 36.7° and longitude of 48.5° eastern and an area of 36,400 km<sup>2</sup>. It has eight cities including Zanjan (the capital city of the province), Abhar, Khorramdarreh, Ijrud, Khodabandeh, Tarom, Mahneshan, and Soltanieh.<sup>[13]</sup> The total population of the province is 1,057,461 (534,849 male and 522,604 female) based on the census in 2017.<sup>[14]</sup> It has cold snowy weather and the temperature could be -27° in winter and 32° in summer.

In 2010, the MS Society of Zanjan province was established which is the referral center for the registry of MS cases in the province. All cases were registered by providing a letter from the neurologists based on definite MS diagnosis according to McDonald criteria.<sup>[15]</sup> All candidates for

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registration were interviewed by an expert to complete a comprehensive questionnaire while the medical records were reviewed to obtain necessary information. Each year, registered cases were contacted and their state of health was updated.

### Case Identification

For the current study, the reference population was all inhabitants of Zanjan province on the prevalence day, July 31, 2019 (total population of the province: 1,057,461).

All registered cases in Zanjan MS society were identified as index cases ( $n = 960$ ) and duplicate ones according to national numbers, patient's name, and gender were deleted ( $n = 202$ ).

Finally, 758 cases were enrolled for analysis.

Data regarding patient's national code, gender, age, age at the first symptom onset, city of residence, marital status, education level, occupation, ethnicity, family history of MS, and duration between symptom's onset and disease diagnosis were recorded.

All included cases ( $n = 758$ ) were evaluated again and their documents were reviewed.

To calculate the standardized mortality ratio (SMR), the number of expected cases was obtained based on the result of the systematic review, which provided the pooled prevalence of MS in the Iranian population. The pooled prevalence rate was 16.5 per 100,000 for men and 44.8 for women.<sup>[16]</sup> So, the expected number of MS cases calculated as 88.2 for men and 234.1 for women in Zanjan province.

### Statistical analysis

All statistical analyses were performed using STATA (Version 13.0; Stata Corp LP, College Station, TX, USA). Data are presented as mean  $\pm$  SD for continuous or frequencies for categorical variables. MS prevalence rates per 100,000 persons were calculated. The prevalence rate also was adjusted for age and sex. 95% confidence intervals (95% CIs) were calculated.

### Results

A total of 758 confirmed cases were identified, 551 (72.7%) were female and 207 (27.3%) were male.

Most of them were married (67.5%) and unemployed (76.7%). The ethnicity of 92% was Turk [Table 1].

Ninety-six (12.6%) had a family history of MS and the mean duration of the disease was  $10.1 \pm 6.7$  years.

The mean age at the first symptom onset was  $28.9 \pm 8.7$  years, and in most cases (55.9%) the diagnosis was made during 2 months after symptom onset. The most frequent initial symptom was the weakness of the limbs followed by paresthesia [Table 2].

### Prevalence

The crude prevalence was 71.6 per 100,000 population (95% CI 66.6–76.9), MS was mostly prevalent in Zanjan city (100.5 per 100,000), followed by Khoramdarreh (64.7 per 100,000) and Ijrud (57.3 per 100,000) cities [Table 3].

**Table 1: Demographic characteristics of included cases**

Variables	Frequency (%)
Education (year)	
≤18	522 (68.8%)
>18	236 (31.2%)
Marital status	
Single	194 (25.6%)
Married	512 (67.5%)
Divorce/widow	52 (6.9%)
Occupation	
Unemployed	582 (76.7%)
Employed	176 (23.2%)
Ethnicity	
Fars	43 (5.6%)
Turk	699 (92.2%)
Kord	12 (1.5%)
Gilak	3 (0.3%)
Bakhtiari	1 (0.1%)

**Table 2: Disease-related variables**

Variables	(Mean $\pm$ SD)/ frequency (%)
Mean age at the first symptom onset (years)	28.9 $\pm$ 8.7
Mean duration of the disease (years)	10.1 $\pm$ 6.7
Duration between the onset of symptoms and diagnosis	
<2 months	424 (55.9%)
2-6 months	98 (12.9%)
6 months to 2 years	123 (16.2%)
>2 years	113 (14.9%)
First symptoms	
Paresthesia	308 (40.6%)
Weakness of the limbs	311 (41%)
Blurred vision	302 (39.8%)
Diplopia	183 (24.1%)
Vertigo	243 (32.1%)
Family history of multiple sclerosis (MS)	96 (12.6%)

**Table 3: Prevalence of MS in eight cities of Zanjan province**

Name of the city	Number of cases	Population in 2017	Prevalence /100,000	95% CI
Zanjan	524	521,302	100.5	92.1-109.5
Abhar	77	151,528	50.8	40.1-63.5
Khoramdarreh	44	67,951	64.7	47-86.9
Mahnesan	11	39,425	27.9	13.9-49.9
Soltanieh	8	29,480	27.1	11.7-53.4
Ijrud	21	36,641	57.3	35.4-87.6
Tarom	13	46,641	27.8	14.8-47.6
Khodabandeh	60	164,493	36.4	27.8-46.9

### Gender

The gender-specific prevalence per 100,000 population was 105.4 for women (95% CI: 96.8–114.6) and 38.7 for men (95% CI: 33.6–44.1) with female to male ratio of 2.6.

### Age

The mean age of all included cases was  $39.2 \pm 9.4$  years on prevalence day which was higher in men ( $40 \pm 9.3$  vs  $38.7 \pm 9.2$  years,  $P = 0.08$ ). The mean age at the first symptom onset was  $28.9 \pm 8.7$  years, while there was no significant difference between two groups ( $28.5 \pm 8.6$  in men and  $29.8 \pm 8.9$  in women,  $P = 0.08$ ).

The prevalence was higher in the 35–44 age group followed by the 45–54 age group [Table 4]. The standardized morbidity ratio (SMR) was calculated as expected/observed for both men and women as 2.3 (207/88.2) (551/234.1).

### Discussion

The crude prevalence of MS in the Zanjan province of Iran was estimated as 71.6 per 100,000 population (95% CI 66.6–76.9), which was higher in women than in men (105.4 for women and 38.7 for men). Among all the cities in this province, MS was most prevalent in Zanjan city which is the capital. We also found that the MS prevalence rate was highest in the 35–44-year-old age group, then in the 45–54-year-old age group and decreased with age.

In a previous systematic review conducted in Iran, the pooled prevalence of MS was estimated as 29.3 per 100,000 population. In the same study, the prevalence of MS in Zanjan was reported as 19 per 100,000, which was underestimated,<sup>[12,16]</sup> as the data were based only on the registered patients in Iran’s Ministry of Health and Medical Education (MOHME), and it seems that all those registered in Zanjan MS society were not included. According to their data, the province in which MS was most prevalent was Isfahan, followed by Tehran (both located in the central part of Iran), and it was least prevalent in Sistan and Baluchestan (located in the southeast of Iran).

In a previous study, estimating MS prevalence in Tehran (capital of Iran) in 2014, the point prevalence was 101.39 per 100,000 population (134.03/100,000 for females and 42.45/100,000 for males),<sup>[17]</sup> which was higher than that in Zanjan province.

In another study conducted in Torbat Heydarieh (located in the Northeast of Iran), the prevalence of MS was reported as 30.48 in 100,000 population in 2016.<sup>[18]</sup> In their study, the mean age of patients on the prevalence day was  $35 \pm 8.5$  and F/M ratio was 2.8:1. In the current study, the mean age of patients on the prevalence day was 39.2 and F/M ratio was 2.6.

Izadi *et al.* assessed the prevalence of MS in the Fars province of Iran. They reported the point prevalence as 72.1/100,000 persons in 2013 (116.5/100,000 in females and 28.3/100,000 in males).<sup>[19]</sup>

Previously, the latitude of the region was considered as an important factor for MS prevalence and regions closer to the equator (such as Iran) were suggested to have lower prevalence. While this pattern has changed as the prevalence and incidence of MS have increased significantly by increasing the year of studies.<sup>[6]</sup>

Zanjan, located in the north-west of Iran, has a latitude of  $36.7^\circ$ , which is higher than the latitude of other provinces such as Isfahan, Fars, and Tehran.

The point prevalence of MS is high in Scandinavian countries which have high latitudes. The point prevalence of MS in Finland, Sweden, Denmark, and Norway was reported as 105, 188.9, 173, and 203, respectively.<sup>[4-6,20]</sup>

One of the most important risk factors of MS is vitamin D deficiency, which plays as immune system modulator. A previous study in Iran shows vitamin D deficiency in 39% of MS patients, 38% of their siblings, and 42% of healthy controls.<sup>[21]</sup> In a study conducted on an adult population in Iran for 12 years, the prevalence of vitamin D deficiency decreased from 30.5 to 24, although insufficiency rates did not change.<sup>[22]</sup> These findings show that vitamin D deficiency and insufficiency is common in Iran, which predisposes individuals to MS.

**Table 4: Age and sex-specific prevalence on prevalence day (July 31, 2019)**

Age groups	Men			Women			Both sexes		
	Population	Number of cases	Rate (per 100,000)	Population	Number of cases	Rate (per 100,000)	Population	Number of cases	Rate (per 100,000)
0-14	129,813	----	-----	123,111	---	-----	252,924	----	-----
15-24	79,451	7	8.8	77,390	15	19.3	156,841	22	14.0
25-34	112,618	52	46.1	108,492	174	160.3	221,110	226	102.2
35-44	87,172	85	97.5	83,601	224	267.9	170,773	309	180.9
45-54	55,362	47	84.8	54,400	104	191.1	109,762	151	137.5
55-64	36,707	16	43.5	38,730	28	72.2	75,437	44	58.3
65-74	17,851	-----	---	22,098	6	27.1	39,941	6	15.0
≥75	15,875	-----	---	14,790	-----	-----	30,665	-----	-----
Total	534,849	207		522,612	551		1,057,461	758	

Genetics (ethnicity) is another predisposing factor in MS. Although the human leukocyte antigen locus is a powerful predictor of MS, it could not explain all genetic etiology of MS.<sup>[23]</sup> Vitamin D receptor gene polymorphism has been reported in different studies in MS cases, which has been also present in the Iranian population.<sup>[24]</sup>

It should be also mentioned that this study had some limitations; First, we did not have the first expanded disability status scale (EDSS) of included cases. Second, during the follow-up, the EDSS values were not registered for cases.

## Conclusions

Our data confirm that MS prevalence is high in the Zanjan province of Iran.

## Abbreviations

MS: Multiple Sclerosis.

## Declarations

## Ethics approval and consent to participate

Not applicable.

## Consent to publish

Not applicable.

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## Conflicts of interest

There are no conflicts of interest.

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