

# Prevalence of multiple sclerosis and environmental factors in Kerman province, Iran

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## Abstract

**Objective:** In this study we investigated the epidemiology of MS and some related environmental factors in Kerman province, southeastern Iran. **Methods:** The MS diagnosis was based on the revised Mc-Donald criteria. The patients were those registered at the Iran MS society, Kerman branch; those in the MS registration centers of Kerman and Rafsanjan University of Medical Sciences, and the Department of Neurology at Shafa Medical Center were studied. **Results:** The prevalence of MS was 31.5 per 100,000 population in Kerman province, and 57.3 per 100,000 population in Kerman city. The male to female ratio was 1:3. Average age at onset was 28.35 years, and 3.9% of cases were early onset at  $\leq 16$  years of age. A linear relationship was observed between prevalence and average environmental temperature as prevalence tended to be lower in areas where the annual average temperature was higher. However, in the town of Shahrbabak which has cold weather, prevalence was low, which might be related to the presence of copper in this area. Average disability was  $4.5 \pm 1.9$  ( $4.83 \pm 1.9$  in men and  $4.26 \pm 1.8$  in women,  $p=0.0035$ ) on the Kurtzke Disability Status Scale. The mean duration of illness was  $8.2 \pm 1$  year. Almost all patients in this study used beta-interferon for a period of at least 4 years.

**Conclusion:** The prevalence of MS in Kerman province was 31.5 per 100,000 people. A linear relationship between an increase in prevalence and low average temperature was observed. Copper may have a preventive effect.

## INTRODUCTION

Multiple sclerosis (MS) is a complex neurological condition with associated loss of myelin and axons.<sup>1</sup> This disease is the most common human demyelinating illness<sup>2,3</sup> and afflicts twice as many women as men.<sup>4</sup> The average age at onset of illness is 30 years<sup>3</sup>, and almost 1,000,000 people in the world between the ages of 17–65 have been afflicted.<sup>5</sup> The onset of MS typically is in young adults, and thus it is associated with long term physical effects. The socio-economic impact may be greater than that of Alzheimer's and myocardial infarction due to its extended duration of illness.<sup>6</sup> The highest prevalence of MS is in Europe and North America. However, evidence shows an increase of this disease in arid regions and developing countries.<sup>7</sup> The MS prevalence rate in Tehran-Iran is estimated to be 51.9 per 100,000 population; and in Isfahan-Iran, 43.8 per 100,000 population.<sup>8,9</sup>

It is believed that MS is a complex disease caused by the interaction of genetics and the environmental factors.<sup>10</sup> There are many environmental factors that are thought to affect

MS. They are: viral infections<sup>11</sup>, smoking<sup>12</sup>, improved hygiene<sup>13</sup>, ultraviolet radiation<sup>14</sup> such as living in high latitudes areas where ultraviolet radiation is low<sup>15</sup>, vitamin D metabolism<sup>16</sup>, accumulation of copper, lead, and iron; reduction in zinc, magnesium, selenium, vitamins B2, B6, D, E, and essential fatty acids.<sup>17,18</sup> In this study, we investigated how temperature is associated with MS, focusing on the vast province of Kerman which is composed of different cities of varying climates.

## METHOD

All MS patients, whose diagnosis was based on the revised Mc-Donald criteria, which were registered at the Iranian MS society, Kerman branch, as well as those in the MS registration centers of Kerman and Rafsanjan Medical Sciences Universities, and the Department of Neurology at Shafa Medical Center, were recruited. Telephone contacts were made with the patients and their families to ascertain the patients' conditions and particularly if any changes might have occurred after their last follow-up. If necessary, they were invited

for a repeat examination. Patients were asked where they lived before the first MS attack, and a detailed examination of their clinical records at the time of the first attack was conducted. Their average daily exposure to sunlight was evaluated. The duration of sun exposure was the period in which the patients were in open space during daytime (without any obstacles blocking the sun light), as stated by the patients or their relatives. Iranian women were mostly covered by clothing except for their faces and hands. Most patients were in close contact with the MS society, which facilitated obtaining of information. The level of disability of patients was assessed based on the Kurtzke Disability Status Scale (EDSS).

Kerman province is a vast region with an area of 714,181 square kilometers located in southeastern Iran (latitude 30° north).<sup>19</sup> The climate varies in different parts of Kerman province. For this study, average temperatures in the main cities were taken. In the northern, northwestern, and central areas, the weather is dry with mild temperatures. In the south and southeastern parts, the climate is humid with higher temperatures. In Kerman city and the suburbs, the climate is dry with semi-mild temperatures. Cities of Kerman, Baft, and Shahrabak, were colder with an average temperature < 16°C. The cities of Sirjan, Rafsanjan, and Zarand, were mild with an

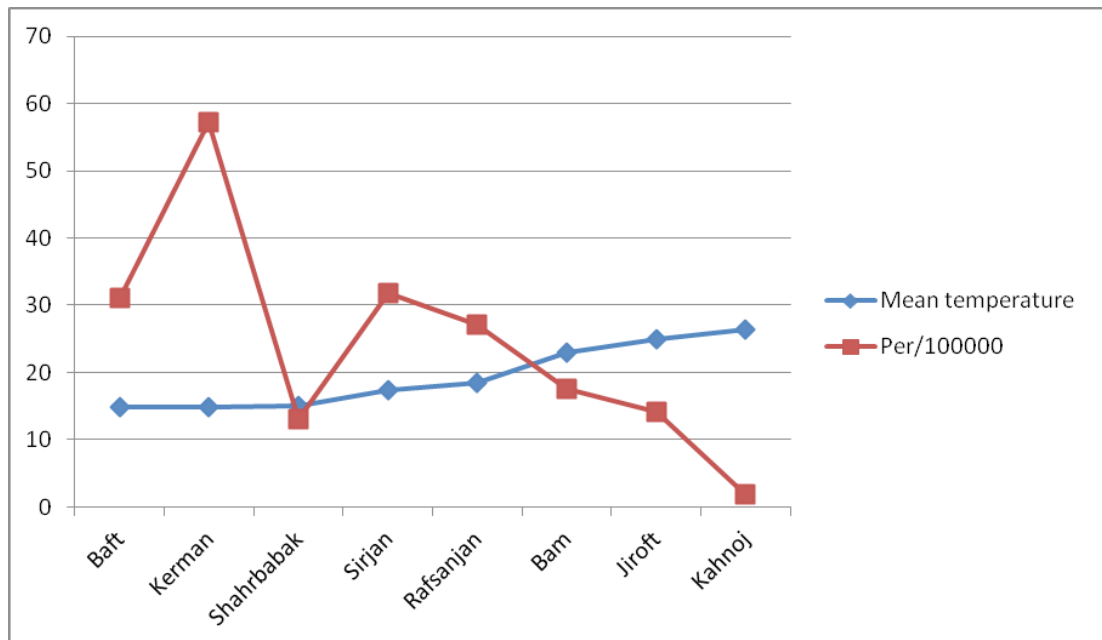
average temperature range of 16–20°C, and cities of Kahnuj, Bam, and Jiroft, were warm with an average temperature of >20°C. The city of Bardsir, with low population, close proximity to Kerman and similarity of climate was considered part of the city of Kerman.<sup>20</sup> Kerman’s population in 2011 was estimated to be 3 million.<sup>21</sup> We determined the prevalence of MS in the study area for the first six months of 2011. Patients were divided into relapsing-remitting MS (RRMS), primary-progressive MS (PPMS), secondary-progressive MS (SPMS), and Devic’s syndrome.<sup>22</sup> The results were analyzed using descriptive analysis and t-tests in some instances.

**RESULTS**

The total number of registered patients in the province was 932. The distribution with mean temperature in different cities is shown in Table 1. MS prevalence in Kerman province was 31.5 per 100,000 people. The male to female ratio of the MS patients was 1:3. The prevalence of MS in the various cities and their average temperature is shown in Figure 1.

The average age at onset of illness was 28.4 years (29 ± 8.7 for men and 28 ± 8.3 for women, P<0.05). The proportion of cases with onset of illness ≤16 years old was 3.9%. The average EDSS

Figure 1. Relation of mean temperature and prevalence of MS



Mean temperature: Celsius temperature scale.  
Per/100000: prevalence of MS

of the 762 patients (from 932 patients) examined was  $4.5 \pm 1.9$  ( $4.8 \pm 1.9$  for men and  $4.4 \pm 1.8$  for women,  $p=0.0035$ ). The mean duration of illness was  $8.2 \pm 1$  year ( $8.4 \pm 1.2$  for men and  $8.7 \pm 0.5$  for women,  $P=0.30$ ).

Almost all patients had used beta-interferon for a minimum of four years (except for patients who were diagnosed as having MS for less than 4 years).

The clinical classification of the 762 patients were: RRMS (70%), SPMS (28%), PPMS (1%), and Devic's syndrome (0.9%). Clinically isolated syndrome (CIS) cases were included in the RRMS group.

Average daily exposure to sunlight for each person (in 556 cases) was  $80 \pm 30$  min ( $112 \pm 60$  for men and  $75 \pm 30$  for women,  $P<0.001$ ).

## DISCUSSION

Geographical variation of MS prevalence depends on genetics and environmental factors. In addition, its full and precise determination depends on patient access to medical care, number of neurologists available, application of new diagnostic methods, level of community awareness of MS, commitment to research, and interest of researchers. Kerman province has easy access to medical care, and almost all regions are served by a number of neurologists (with the exception of Kahnuj), making beta-interferon and immunosuppressive drugs easily available to patients free of charge. We believe we have successfully identified almost all MS cases in

Kerman province. Based upon our evaluation, prevalence of MS in the province was 31.5 per 100,000 population. Prevalence in the city of Kerman was 57.3 per 100,000 people, some of whom may have migrated from other regions. The prevalence in cities with cold climates was higher than those with milder climate, and the prevalence in cities with mild climate was higher than cities with warm climates (Table 1). The city of Shahrabak, with a population of 113,938 was the exception. In spite of cold weather, the prevalence of MS was low. This could be due to the preventive effect of copper or other factors. There are several copper mines and factories located in and around this city. In unpublished study by the corresponding author of this paper, it was found that people working in close proximity to a copper smelting factory had higher serum levels of copper. Some previous studies have found that serum levels of copper in MS patients are low.<sup>23</sup> In the rest of the region, a linear relationship between frequency of MS illness and average temperature was observed in Figure 1.

The ratio of men to women among our patients was 1:3, which could be due to men being exposed more to sunlight and ultraviolet radiation which have a protective effect. It could also be due to infections, immune responses, or other unknown factors.<sup>24-26</sup> In a study by Alonso *et al.* in Iran, the frequency of MS decreased with increasing exposure to sunlight, similar to other reports.<sup>4</sup> In Canada, the ratio of men to women in MS is 1:3.2.<sup>27</sup> In USA, the ratio is 1:3, and overall the

**Table 1: Relation of prevalence of MS with mean temperature.**

City	Mean temperature in degree centigrade	Population	No. of MS patients	MS/100000
Kerman	14.9	0852192	489	57.3
Baft	14.8	0161138	50	31
Shahrabak	15.1	0113939	15	13.1
Rafsanjan	18.5	0327998	89	27.1
Sirjan	17.3	0273145	87	31.8
Zarand	17.5	0205739	56	27.2
Bam	23	0313702	55	17.5
Jiroft	25	0336201	48	14.2
Kahnoj	26.4	0363291	7	1.9
Kerman province	15.5	2947346	932	31.75

prevalence of MS in women is 2 to 3 times that in men.<sup>4</sup>

The average disability (EDSS) of our patients was  $4.5 \pm 1.8$ , with more men than women becoming disabled ( $4.8 \pm 1.9$  for men, and  $4.3 \pm 1.8$  for women,  $P=0.003$ ). The average duration of illness was  $8.2 \pm 1$  year ( $8.4 \pm 1.2$  for men and  $8.7 \pm 0.5$  for women,  $P=0.30$ ). Since there was no significant statistical difference between men and women with regards to duration of illness, it appears that men suffered more disability, and the rate of progression of MS in men was faster than in women. One study suggests a 38% faster progression in males, and that younger age of illness onset foretells a slower rate of progression.<sup>28</sup> This is in agreement with our finding that women tend to be afflicted earlier than men. In the region under study, more men than women smoked and there is evidence that smoking could intensify MS.<sup>29,30</sup> Based on some reports, the average time to reach EDSS 3.5 (mild disability) is between 0.3-26 years.<sup>31</sup> The advancement of disability with longer duration of illness is well recognized, and depends on individual patient, the gap between attacks, the type of MS, symptoms and signs of the first attack.<sup>22</sup> Immunomodulatory or immunosuppressive drugs can reduce the number of attacks but their effect on long term disability remains controversial.<sup>32-34</sup>

The frequency of different types of MS in this study was 70% RRMS, 28% SPMS, 1% PPMS, and 0.9% Devic's syndrome. PPMS cases were low in this study, which may be partly due to underdiagnosis.

In this study, the age at onset of MS was  $28.4 \pm 8.5$  years old, ( $29.7 \pm 8.7$  for men and  $28.1 \pm 8.3$  women,  $P<0.05$ ). Women tended to be afflicted earlier than men, with the age of onset in 3.9% of female patients being  $\leq 16$  years old. The age of onset of MS is known to vary greatly, and may be due to environmental factors. The peak age of onset was around 30. In most studies, age of onset in women was earlier than in men (31.2 for men and 29.3 for women), with 0.7% of cases occurring in infants, 2.7% in adolescence, and 2.8% in those  $\geq 50$ . Other studies have reported early onset as occurring in 3-5% of cases.<sup>35-37</sup>

In conclusion, we found the prevalence of MS in the province of Kerman to be 31.5 per 100,000 population. A linear relationship was observed between prevalence of MS and average temperature with more cases occurring in colder climates. Copper may have a preventive effect with regards to MS since disease prevalence was low, despite cold temperatures, in the city

of Shahrabak where there are several copper mines and factories located in close proximity.

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