

Evidence of increased prevalence of Multiple Sclerosis: A Population-Based Study of Tehran Registry, 1999–2018

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Research article

Keywords: Multiple Sclerosis, Prevalence, Epidemiology, Tehran, Iran

Posted Date: January 20th, 2020

DOI: <https://doi.org/10.21203/rs.2.21220/v1>

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Abstract

Background: The epidemiological characteristics of Multiple Sclerosis (MS) in various studies have been investigated and studies suggested that there is a different geographic disparity worldwide. The present study conducted to investigate the longitudinal prevalence of MS in Tehran, Iran.

Methods: The population-based study was conducted in Tehran, the capital of Iran from 1999 to 2018 based on the annual report data through the Iranian MS Society (IMSS) registry system. The age-standardized and crude prevalence proportions were estimated by applicant of population data, established from the Statistical Centre of Iran.

Results: Totally 21,580 MS cases were registered and included in the analysis. Out of them, 24.99% (5,393 cases) was male and 75.01% (16,187 cases) was female. The mean age of MS onset was 28.8 years (S.D: 8.7). The age standardized prevalence proportion (ASP) of MS ranged from 73.7 (95%CI: 72.1-75.2) in 2006 to 137.6 (95% CI: 135.7-139.5) per 100,000 in 2018. The MS ASP- was estimated 54.1 (95%CI: 53.6-54.6) among males and 174.5 (95%CI: 173.6-175.4) per 100,000 among females. The age standardized female to male ratio of MS in study period was 3.03.

Conclusion: Our finding suggested that the prevalence of MS in Tehran province is relatively high and the disease occurrence is more common in the under-40 age group than in the older ones. As in the rest of the world, the prevalence of the MS was higher in women, and the female to male sex ratio was 3.03 in our study.

Background

Multiple sclerosis (MS) is considered as a chronic autoimmune neurological disease [1] which is known as the most prevalent inflammatory neuroimmunological disorder among young adults [2, 3]. MS usually occurs in young people and occurs more often before the age of 40 and in women [4, 5]. Due to the onset of a disease at an early age, the burden of MS and its direct and indirect costs are significant [6].

In 2016, there were 2,221,188 MS cases in the world, representing an increase of over 10% compared with 1990. The highest prevalence of MS was in North America, Western Europe and Australia, while the lowest rates were reported in Sub-Saharan Africa, Central Africa and Oceania [7].

The incidence and prevalence of MS in various studies have been investigated and diverse results have been reported [3, 4, 8–11]. Also, there are considerable geographical variations in incidence of MS in Iran [12]. Based on the Eskandarieh et al study, the prevalence of MS increased from 45 per 100,000 in 2011 to 54.5 per 100,000 in 2013 in Iran [13] and in another study they reported that the prevalence proportion in Tehran, 2014, was 101.39 per 100,000 [14]. Also, in a study conducted in Isfahan in 2014, the prevalence rate was 85.8 per 100,000 [15]. In addition, familial MS cases have increased in Tehran in recent years [8, 16]. Based on the division of the world's regions by Kurtzke [17], Tehran is considered a high frequency areas (prevalence $\geq 30/100,000$) for the MS.

According to Hosseinzadeh et al [12], Tehran is considered as one of the high-frequency provinces for MS. Since the frequency of MS in our region is high, therefore, the present study aimed to investigate the longitudinal prevalence of MS in Tehran, Iran.

Methods

This population-based study was conducted in Tehran province of Iran based on the annual report data through the Iranian MS Society (IMSS) registry system from 1st April 1999 to 31st December 2018. The registration program and its validity and reliability were described in the previous study [18]. The prevalence estimate values for MS were calculated by applicant of population data, obtained from the Statistical Centre of Iran.

The age-standardized prevalence proportion (ASP) were calculated based on years of disease onset.

The Iranian MS Society, established in 1999, is the one registry center in Tehran that comprehensively registers baseline characteristics including gender, birth date (age), age at disease onset, date of diagnosis, familial history of MS, as well as social and clinical data of MS patients. Disease diagnosis was confirmed using the latest McDonald criteria by neurologists [19].

IMSS provide extensive facilities for members and all patients were encouraged by neurologists to refer to the IMSS for registration and receiving tracking code for receiving treatment. The IMSS membership card must activate by patients to keep their presence active every 5-year. To design the population based cross-sectional study, the scholar tried to cover the most important epidemiological variables, which were related at the individual level to MS recurrence including gender, birth date (age), age at disease onset, and date of diagnosis.

A trained interviewer was explained the goals of the MS registry in IMSS and inform consent was taken from all patients before disclosing study processes.

Statistical Methods

Categorical and continuous data were presented as number (percent) and mean (Standard Deviation, (S.D.)) as well as 95% Confidence Interval (CI). To calculate familial MS prevalence, direct standardization was used to adjust the age effect by using world standard population [20].

Age standardized prevalence proportion (ASP) was calculated per 100,000 by "dstdize" command in Stata software. Excel software were used to clean the data and to depicting the graphs. The Poisson regression model was used to estimate significance of change over time for total prevalence, sex-specific prevalence and sex ratio. All analyses were performed using Stata software version 14 (Stata Corp, College Station, TX).

To calculate prevalence proportion, the interested population was extracted from statistical center of Iran in years in which census was done (2006, 2011 and 2016); otherwise, exponential formula was used to estimate the population as below:

$$P_T = P_0 (1 + r)^t$$

Where, P_T is the population to be estimated (population at time T), P_0 stands for population at time zero, r is growth rate (it was considered as 1.44 for 2007-10 and 1.72 for 2012-15 and 2017 and 2018) and t is elapsed time in years from time zero.

Results

Age at disease onset and its trends

In our population-based MS registry, totally 21,580 cases of MS were registered and included in the analysis. Out of them, 24.99% (5,393 cases) was male and 75.01% (16,187 cases) was female. The mean age of MS onset was 28.8 years (S.D: 8.7, ranged from 3–77 years). The mean age of males (29.5S.D: 8.9) was significantly ($p < 0.001$) higher than female (28.6S.D: 8.6). The means age of MS onset in males and females in 2018 were 30.9 (S.D: 8.3) and 31.8 (S.D: 8.9), respectively. 13.4% of MS cases were familial MS. Demographic characteristics of MS cases were presented in Table 1.

Table 1
Demographic characteristics of MS cases in
Tehran, Iran

Variables		N (%)
Sex	Male	5393 (24.99)
	Female	16187 (75.01)
Age	≤ 18	2023 (9.7)
	19–24	5098 (24.7)
	25–29	4807 (23.3)
	30–34	3704 (18.0)
	35–39	2395 (11.6)
	40–44	1518 (7.4)
≥ 45	1091 (5.3)	
Familial MS	Yes	2815 (13.4)
	No	18145 (86.6)

Age standardized prevalence proportion of MS

In Table 2, the crude and ASP of MS were reported by gender and year. The ASP of MS ranged from 73.7 (95%CI: 72.1–75.2) per 100,000 in 2006 to 137.6 (95% CI: 135.7-139.5) per 100,000 in 2018. The MS ASP was estimated 54.1 (95%CI: 53.6–54.6) per 100,000 among males and 174.5 (95%CI: 173.6-175.4) per 100,000 among females. The results of Poisson regression model suggested that there is a significant change over time for total prevalence ($p = 0.001$), prevalence among males ($p = 0.001$) and prevalence among females ($P = 0.001$).

Table 2
The crude and age standardized prevalence proportion of MS in Tehran, Iran during 2006–2018

Year	Female				Male				Total			
	Population	Count	Prevalence	ASP.. (95%CI)	Population	Count	Prevalence	ASP.. (95%CI)	Population	Count	Prevalence	ASP.. (95%CI)
2006	5513872	6848	124.2	115.4 (112.6-118.2)	5831418	2146	36.8	33.9 (32.4-25.3)	11345290	8994	79.3	73.7 (72.1-75.2)
2007	5593267	7633	136.5	126.7 (123.8-129.6)	5915395	2397	40.5	37.2 (35.7-38.7)	11508662	10030	87.2	80.9 (79.3-82.5)
2008	5673810	8447	148.9	137.9 (134.9-141.0)	6000577	2665	44.4	40.9 (39.3-42.5)	11674387	11112	95.2	88.3 (86.6-90.0)
2009	5755513	9232	160.4	148.3 (145.2-151.4)	6086985	2930	48.1	44.3 (42.7-45.9)	11842498	12162	102.7	95.1 (93.4-96.8)
2010	5838393	10160	174.0	160.6 (157.4-163.8)	6174637	3198	51.8	47.7 (46.0-49.3)	12013030	13358	111.2	102.8 (101.0-104.6)
2011	6045398	11187	185.1	170.2 (167.0-173.4)	6137993	3513	57.2	52.4 (50.6-54.2)	12183391	14700	120.7	111.2 (109.3-113.0)
2012	6149379	12028	195.6	179.4 (176.1-182.7)	6243566	3780	60.6	55.3 (53.5-57.1)	12392945	15808	127.6	117.2 (115.4-119.1)
2013	6255149	12867	205.7	188.2 (184.9-191.5)	6350955	4083	64.3	58.7 (56.8-60.5)	12606104	16950	134.5	123.3 (121.4-125.2)
2014	6362737	13583	213.5	194.9 (191.5-198.2)	6460192	4357	67.5	61.4 (59.6-63.3)	12822929	17940	139.9	128.0 (126.1-129.9)
2015	6472176	14211	219.6	200.0 (196.7-203.4)	6571307	4591	69.9	63.6 (61.7-65.4)	13043483	18802	144.2	131.6 (129.7-133.6)
2016	6593965	14875	225.6	205.0 (201.7-208.4)	6673672	4828	72.3	65.7 (63.8-67.6)	13267637	19703	148.5	135.3 (133.4-137.3)
2017	6693000	15304	228.7	207.6 (204.2-210.9)	6768000	5037	74.4	67.5 (65.6-69.4)	13461000	20341	151.1	137.5 (135.6-139.5)
2018	6784000	15505	228.6	207.3 (204.0-210.7)	6853000	5131	74.9	67.9 (66.0-69.8)	13636000	20636	151.3	137.6 (135.7-139.5)
Total	-	-	190.5	174.5 (173.6-175.4)	-	-	59.3	54.1 (53.6-54.6)	-	-	-	-

*Crude Prevalence Proportion (Per 100,000) ---Age Standardized Prevalence Proportion (Per 100,000)

The results showed that the MS prevalence among females were remarkably higher than males in all years. However, we provided sex-specific prevalence data (count, population, prevalence) over study period in Table 2.

Sex ratio trends

The MS sex ratios over the 13-year study period were displayed in Fig. 1 and it decreased from 3.7 (in 2010) to 2.06 (in 2017) and its trend was decreasing and also there is no notable difference among crude and age-standardized sex ratio. The results of Poisson regression model revealed that there is a significant change over time for sex ratio ($p = 0.001$),

Discussion

The current study examined the trend of MS prevalence in Capital of Iran, Tehran, from 2006 till 2018. The results of this study suggested that the prevalence of MS in Tehran is growing, and unadjusted prevalence proportion has increased from 79.3 cases in 2006 to 151.7 cases (per 100,000) in 2018 and also age-standardized prevalence proportion has increased from 73.7 cases in 2006 to 137.6 cases (per 100,000) in 2018.

Therefore, According to the global divisions [17], Tehran is considered as a region with high prevalence (prevalence $\geq 30/100,000$) and the prevalence of MS in Tehran is the highest in Asia and among Middle Eastern countries [13]. In addition, the results revealed that the time trend of age standardized MS female to male sex ratio in recent years has been declining and it has fallen to 2.14 in 2018.

According to Wallin MT et al study [3] in United States in 2010, the prevalence of MS in the population over 18 years, cumulated over 10 years was 309.2 per 100,000 and the highest prevalence was in the 55- to 64-year age group. Compared to our study findings which most cases were observed in the age group below 40 years, it has a higher prevalence and different age distribution. When coupled with prior estimates of MS prevalence in Iran, it seems that there has been a relatively increase during the last decades. In Eskandarieh et al study [4] in Tehran, the MS prevalence was 101.39 per 100000 in 2014 and age-adjusted prevalence proportion were 134 and 42.5 for females and males respectively. In another review study, MS prevalence for Iran in 2013 was 85.8 per 100,000 [13].

According to Hosseinzadeh et al [12], Tehran is considered as one of the high-frequency provinces for MS. It sounds that the high MS frequency in Tehran may be related to the level of urbanization, their social and economic status and air pollution.

On the other hand, better access to health services can play an important role, which in turn leads to better diagnosis and cases registration.

Tehran is known as one of the most polluted cities in the world [21]. Although some studies have not reported a significant association between air pollution markers ($PM_{2.5}$, NO_2 , and O_3) and MS [22], several studies had shown some evidences that air pollution can have a significant relationship with the incidence and recurrence of MS [23–25].

The possible association between air pollution and MS incidence and recurrence has been justified through several mechanisms, most likely being that air pollution leads to vitamin D deficiency, excessive free radical production, inflammatory factors expression, induction of chronic inflammation, mitochondrial dysfunction, and increased oxidative stress, which can be linked to MS incidence and recurrence [24, 25].

One issue that has been shown in most studies is that women are more susceptible to MS than men [26, 27]. In a relatively large study on Canadian patients with MS, sex ratio was estimated 3.2, which is so similar to our result [26]. Also, it has been reported as 3.06 in Eskandarieh et al study [8]. In a study conducted in Turkey [28], the prevalence of MS in Karabük and Akçakoca were 95.9 and 46.1 per 100,000 and the prevalence of MS in the Middle East and north Africa was 51.52 cases per 100,000 [29]. The estimated prevalence proportion in our study revealed that MS is more prevalent in Tehran in compared to the Middle East countries.

It should be noted that the trend of sex ratio in our study was somewhat declining (from 3.20 in 2006 to 2.14 in 2018). However, some studies have reported an increase in this trend [30, 31], However, no significant trend was observed in a study in Sweden [32].

In terms of age groups, in our study, nearly 60% of cases were diagnosed before age 30 years. Other similar studies have also shown a higher incidence of disease at an early age [4, 5]. The disease onset in the early age leads to an increase in the number of years lived with disability (YLDs) and eventually to a Disability-adjusted life years (DALYs) [33–35].

There are some limitations and strengths to our study. Because the province of Tehran is both large in population and geographical area, and MS registration is elective, the MS registration may be incomplete and some cases may not be registered. Therefore, the obtained prevalence proportion maybe is underestimated. On the other hand, it should be highlighted that IMSS registration facilitates access to health care and services for patients. This is a strong inducement that likely facilitates registration and retention and thus, it is considered as study strengthens.

Conclusion

Our finding suggested that the prevalence proportion of MS in Tehran province is relatively high and disease occurrence is more common in the under-40 age group than in the older ones. The results suggested that the prevalence of the MS was higher in women, and the trend of female to male sex ratio in study period has been declining.

Abbreviations

MS
Multiple Sclerosis,
IMSS
Iranian MS Society
CI
Confidence Interval
S.D
Standard Deviation
ASP
Age Standardized Prevalence

Declarations

Ethics approval and consent to participate: The study was approved ethically by institutional review board of Tehran University of Medical Sciences. An informed consent was obtained from each participant. In the study, the privacy of the participants was maintained.

Consent for publication: Not Applicable.

Availability of data and materials: The datasets used and analysed during the study available from the corresponding author on reasonable request.

Competing interests: The authors declare no competing interests.

Funding: This study was funded by Tehran University of Medical Sciences (TUMS). The founder had no role in the design of the study and collection, analysis, and interpretation of data and in the manuscript preparation.

Authors' contributions: MAS conceived and designed the study, and data collection was done by SE. Data analysis and interpretation was done by AAH and SE. The manuscript was drafted by AAH and SE and critically revised by MAS. All authors read and approved the final version of manuscript.

Acknowledgments: We would like to thank for research grant of Tehran University of medical sciences, code 40376-188-01-98.

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Figures

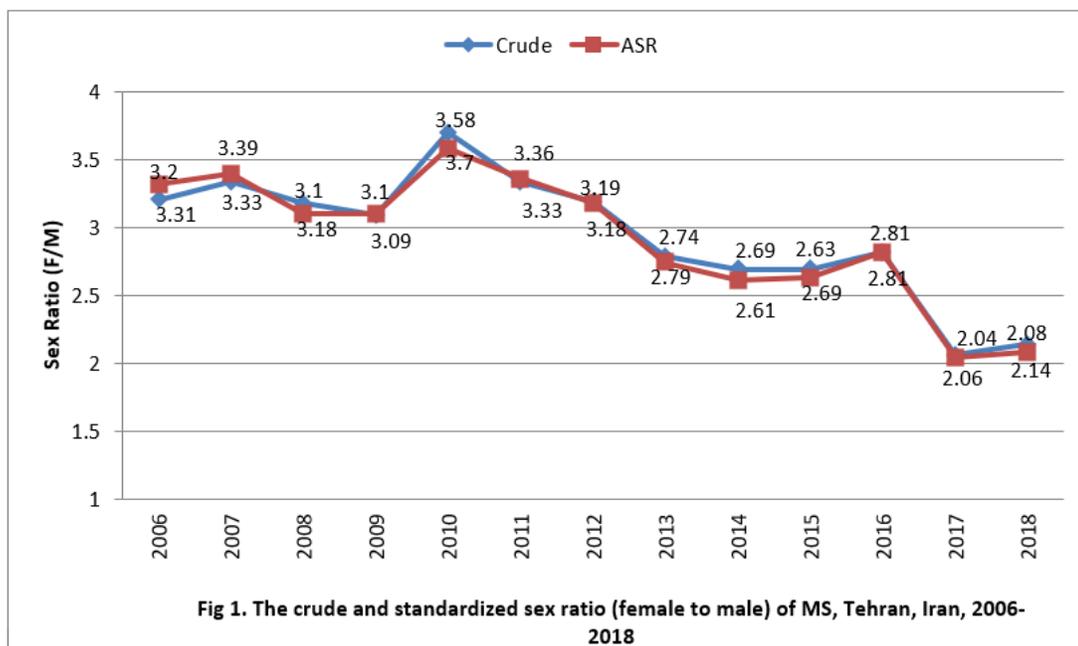


Figure 1

