DOI: http://dx.doi.org/10.18502/cjn.v22i2.???

Current Journal of Neurology

Original Paper

Curr J Neurol 2023; 22(2): 39-45

Epidemiological parameters of multiple sclerosis in Chaharmahal and Bakhtiari Province, Iran

Received: 11 Dec. 2022
Accepted: 06 Feb. 2023

Mohammad Amin Omrani[1], Asghar Bayati[2], Mohammad Ali Sahraian[1], Sharareh Eskandarieh[1]

[1] Multiple Sclerosis Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran
[2] Department of Neurology, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran

Keywords
Multiple Sclerosis; Epidemiology; Iran

Abstract

Background: Multiple sclerosis (MS) is a neurological disease with a high burden and disability. There are reports of various medications' side effects on patients with MS. The aim of the study is to determine the characteristics and medicine usage distribution among patients with MS in Chaharmahal and Bakhtiari Province in Iran.

Methods: This registry-based cross-sectional study was performed among MS cases in Chaharmahal and Bakhtiari Province. The epidemiological data were collected from the nationwide MS registry of Iran (NMSRI) from 2019 to 2022. The information collected included age, sex, family history, type of MS, age at MS onset and diagnosis, MS symptoms, physical condition, and history of medication use. All tests were performed at a significance level of 0.05 using SPSS software.

Results: A total of 416 patients included in this study. Among them, 325 individuals (78%) were women with mean ± standard deviation (SD) of age of 37.35 ± 8.51 years. No significant difference was observed between men and women in terms of age, type of MS disease, family history of MS, and physical condition ($P > 0.05$). The results showed that the Expanded Disability Status Scale (EDSS) score in female patients (1.41) was different from the EDSS score in male patients (1.77) ($P < 0.05$). Most of the patients often used interferon beta (IFN-β).

Conclusion: The results provided new insight into the epidemiology and medicine patterns of patients with MS in Chaharmahal and Bakhtiari Province. The epidemiological situation of MS in this province is similar to other parts of Iran. Planning according to national programs is suggested for the management and control of MS.

Introduction

Multiple sclerosis (MS) is known as the most common neurodegenerative disease, which leads to inflammation, demyelination of neurons, and damage to the central nervous system (CNS).[1,2]

How to cite this article: Omrani MA, Bayati A, Sahraian MA, Eskandarieh S. Epidemiological parameters of multiple sclerosis in Chaharmahal and Bakhtiari Province, Iran. Curr J Neurol 2023; 22(2): 39-45.

Corresponding Author: Sharareh Eskandarieh
Email: sh_eskandarieh@yahoo.com

Epidemiological studies have shown that women are approximately 2-3 times more likely to develop MS than men.[3] The incidence of MS among women, especially young women, is about 3 times higher than that of men worldwide.[4,5] Additionally, most affected patients are between 20 and 50 years old.[1] The occurrence is common mainly in the age group of 20 to 40 years and is rare in the age group of fewer than 10 years and more than 60 years. According to conservative estimates, today there are 411000 patients with MS in the United States (US) and more than 2.8 million people are living with this disease worldwide.[6] There is epidemiological evidence of the recent surge in MS in Asia, especially in Iran during 2 last decades.[7]

These patients should receive health services. Despite the efforts of government and non-governmental organizations to provide health services to patients with MS, there is evidence that these services cannot meet all the needs of patients with MS.[8] There is a wide variation in the prevalence of MS in different geographical areas.[9] In fact, this disease has affected at least 2.8 million people around the world, and the results of epidemiological research indicate that the prevalence and incidence of MS are increasing in many countries, including Iran.[1,7]

In the past, Iran was thought to be a low-risk area for MS. Currently, epidemiological studies in different provinces of Iran, including Tehran and Isfahan, and other parts of Iran, have revealed that Iran is an area with a moderate or high risk of MS disease.[10] According to the published atlas of MS disease in Iran, it appears that the high-risk belt of MS disease in Iran extends from the northwest to the southeast.[11]

In addition, considering that the socio-economic status (SES) in Iran is different from other countries, the provinces of Iran with a higher SES level show a higher prevalence rate of MS disease.[12] Of course, considering the improvement of public health in Iran might lead to a reduction in the risk of exposure to foreign antigens, which could increase the risk of developing autoimmune diseases such as MS.[13]

Although there are several studies consistent with the role of epidemiological factors of MS occurrence in some provinces,[14-16] no study has till date been conducted on the epidemiological factors of MS disease in Chaharmahal and Bakhtiari Province (located in the southwest of Iran). Our research aims to investigate the epidemiological factors affecting the incidence of MS at determining the frequency distribution of demographic (age and gender), diagnostic, progressive, and treatment factors among patients with MS in Chaharmahal and Bakhtiari Province.

Materials and Methods

Study design and sampling method: This research is a cross-sectional registry-based study of a descriptive type and a survey of patients with MS living in Chaharmahal and Bakhtiari Province. This study was conducted by examining the files of patients with MS in Chaharmahal and Bakhtiari Province who were registered in the dynamic nationwide MS registry system of Iran (NMSRI) (WWW.NMSRI.IR) from 2019 to 2022.

Inclusion criteria: The files of patients who were diagnosed with MS by neurologists based on McDonald's criteria were studied.[17] All cases and their information in NMSRI were gathered with the received reports from neurological departments, hospitals, clinics, and MS society. The registration of information was done by a neurologist.

Data collection tools, measurement, and categorization of data: The required information was collected through filling up a standard questionnaire, including four sections: demographic information, disease/family history information, diagnostic information, and disease progress information and prescribed medicine. Through the registered national code and checking its similarity with the patients' names and surnames, we identified the patients who were registered twice or more in different centers and duplicate cases were removed.

Ethical consideration: Extraction of information was done without name and identification code. The information was only limited to the team and the time of the project. All rights of participants and researchers were respected and the Helsinki rules related to research on human samples were observed.[18]

All analysis tests were performed by using SPSS software (version 25, IBM Corporation, Armonk, NY, USA) at a significance level of 0.05.

To describe the data, mean and standard deviation (SD) or number (percentage) were used. Data analysis was performed using likelihood ratio chi-square, a two-sample test of proportions, and independent t-test.

Variables

Demographic characteristics of patients with MS

A) Age of patients with MS: Qualitative and quantitative variables were presented as number

(percentage) and mean ± SD of all patients that were ordered into men and women. The age/time of onset of the principal symptoms and age of diagnosis of patients with MS were considered. The Mann-Whitney U test was used to compare the age of patients with MS between the two groups.

B) Family history of disease in patients with MS: Family history in patients with MS was compared between two groups of men and women using the chi-square test. The correlation between the gender and the family history was determined through the odds ratio (OR) calculation.[19]

C) Type of MS disease: Patients were classified into 5 groups based on the type of disease, including relapsing-remitting MS (RRMS), secondary-progressive MS (SPMS), primary-progressive MS (PPMS), progressive-relapsing MS (PRMS), and clinically isolated syndrome (CIS). Men and women with MS were compared using the chi-square test regarding the type of disease they had.

D) Expanded Disability Status Scale (EDSS) score: The Soup Calculator database was considered to calculate the EDSS score and SD between male and female patients based on clinical examinations by neurologists. Furthermore, the Mann-Whitney U test was used to compare the EDSS score between two groups. Based on the age of diagnosis, patients were categorized into 4 groups: less than 20 years, 21-30 years, 31-40 years, and more than 40 years. The average EDSS score was determined in each age group separately.

E) History of medicine usage: The number of each consumption drug was counted, and based on the available information about continuing or stopping the drug, the number of people who stopped taking the drug for any reason was calculated, and then the ratio of the patients who stopped taking the medication compared to persons who took the medication determined the percentage of people who stopped taking the medication. Duration of medicine usage to stopping it was determined based on onset and end of drug use.[20]

Ethics approval and consent to participate: This study was conducted under the consideration of the Ethics Committee of Tehran University of Medical Sciences. The official registration code for this study is: IR.TUMS.SINAHOSPITAL.REC.1400.083.
Informed written consent was obtained from all participants, following an understandable individual explanation of steps.

Results

Demographic features

Age/onset of first symptoms and age of diagnosis of patients with MS: This study examined 416 patients with MS from Chaharmahal and Bakhtiari Province, including 325 (78%) women and 91 (22%) men [female to male ratio (F:M) = 3.57:1].

The average age of the subjects examined was 37.15 ± 8.75 years. The mean age of onset of the first MS symptoms was 30.32 ± 8.17 years for the studied subjects, 30.54 ± 8.52 years for men, and 30.08 years for women. The mean age of MS diagnosis by a physician was 30.71 ± 8.15 years for studied participants, 30.71 ± 8.04 years for women, and 54.54 years for men.

Family history of patients with MS: In the studied MS population, 16.5% of men and 20.7% of women had a positive family history without statistically significant difference (chi square statistic = 0.908, P = 0.635). The results of the correlation analysis showed that the gender of the affected person did not show a remarkable correlation with the family history. Approximately, 51.2% of examined patients, who had a positive family history, demonstrated the disease in their first-degree relatives, including parents (16.7%) sisters/brothers (73.8%), and siblings (9.5%).

Type of the MS disease: The most common type of MS disease in both women and men among the examined patients was RRMS (about 60%). As it was shown in table 1, other types including PPMS and PRMS were about 1.2% and 0.48%, respectively.

Table 1. The correlation between gender and type of multiple sclerosis (MS) disease

Gender	Type of MS disease [n (%)]					
	RRMS	SPMS	PPMS	PRMS	CIS	Unidentified
Men	58 (63.74)	6 (6.59)	1 (1.10)	0 (0)	11 (12.09)	15 (16.48)
Women	219 (67.38)	19 (5.85)	4 (1.23)	2 (0.62)	34 (10.46)	47 (14.46)
Total	277 (66.59)	25 (6.01)	5 (1.20)	2 (0.48)	45 (10.82)	62 (14.90)

MS: Multiple sclerosis; RRMS: Relapsing-remitting multiple sclerosis; SPMS: Secondary-progressive multiple sclerosis; PPMS: Primary-progressive multiple sclerosis; PRMS: Progressive-relapsing multiple sclerosis; CIS: Clinically isolated syndrome

No statistically notable correlation was found between gender and type of the MS disease (CIS, P = 0.57), (SPMS, P = 0.50), (RRMS, P = 0.43).

Physical condition of patients with MS: The physical status of patients with MS was assessed and more than 70% of patients of both sexes were able to move freely. Each of the physical condition states in patients with MS was compared between the two groups of men and women using the chi-square test and no statistically significant difference was observed between the two groups (P > 0.05).

EDSS score: The mean EDSS score in the patients studied was 1.49 ± 1.51 (1.77 ± 1.74 in men and 1.41 ± 1.43 in women). The EDSS score in patients with MS was compared between the two examined groups using one-way analysis of variance (ANOVA) test and a statistically significant difference was found between affected men and women groups by using post-hoc analysis (P = 0.03).

Based on natural course of MS, we found a correlation between the age of MS diagnosis and the mean EDSS, that is, as the age of MS diagnosis increases, the mean EDSS score (Table 2).

Table 2. Mean Expanded Disability Status Scale (EDSS) in age groups of multiple sclerosis (MS) diagnosis

The age of MS diagnosis (year)	EDSS score (mean ± SD)	P
≤ 20	1.28 ± 1.39	0.38
21-30	1.47 ± 1.49	0.49
31-40	1.49 ± 1.54	0.47
> 40	1.65 ± 1.40	0.22

MS: Multiple sclerosis; EDSS: Expanded Disability Status Scale; SD: Standard deviation

History of medicine usage: In this study, all medications taken were evaluated among the studied patients and the number of people who started/discontinued medication and the duration of drug use were analyzed. Research into interferon-beta 1a (IFN-β-1a) (Rebif) use in patients with MS revealed 10% usage of this medicine and the average duration of drug use in patients who discontinued the drug for various reasons was 67 months. The amount of IFN-β-1b (Betaferon) drug use in patients with MS showed that 15% of patients accepted this drug during their illness, and almost 78% (49 people) of them stopped taking the drug due to side effects (31 cases), inability to control (11 cases), medical opinion (4 cases), non-compliance with treatment (2 cases), and pregnancy (1 case).

The study of the use of fingolimod (Marela) in patients with MS revealed that 33 people, i.e., 8% of the patients, took this drug, of whom one person because of side effects and one person because of inability to control stopped taking the drug. The average duration of drug use was 16 months. Research into the use of glatiramer acetate (Copamer) in patients with MS found that 93 people, or 22% of the patients, took this medicine during their illness and 26% of the participants stopped using this medicine. On the other hand, the study on the use of teriflunomide in patients found that 4.1% of patients took this drug, while 17.6% of people stopped using it for various reasons. The frequency of use of dimethyl fumarate (Tecfidera) in the patients with MS studied was 12.5% with an average duration of 5 months. In addition, the study of the use of the drug rituximab in patients found that 21.6% took it and 2.2% stopped the drug. Finally, taking IFN-β-1a (Avonex) in patients with MS showed 54.6% of usage and 55.5% of its withdrawal in studied patients (Figure 1).

Discussion

The present study was conducted to determine recent epidemiology and clinical characteristics of MS in Chaharmahal and Bakhtiari Province in Iran.

Although Iran used to be a region with low MS prevalence, in recent decades, the number of patients has increased and the prevalence of this disease showed a remarkable rise in many provinces of Iran.[7,21] Considering the high prevalence of MS disease in Isfahan Province, which is located in the center of Iran and borders with Chaharmahal and Bakhtiari Province, the present study was conducted on patients with MS in Chaharmahal and Bakhtiari Province to raise awareness for the patients with MS and its correlation with demographic characteristics of this disease. In this regard, affected patients ranged in age from 7 to 68 years, and most patients, both men and women, were observed in the age range of 38 to 39 years. In a previous study conducted in western Iran, most patients were reported in the age range of 35 to 39 years.[22] In the studies conducted in Poland and Iceland, the majority of patients were observed in the age range of 35-44 and 40-44 years, respectively.[23,24] The mean ± SD of age of this study subjects (37.15 ± 8.75) is comparable with MS cases in Kermanshah Province, Iran (38.66 ± 9.90),[22] but higher than that of patients with MS in Tehran Province (32.11 ± 8.93).[25]

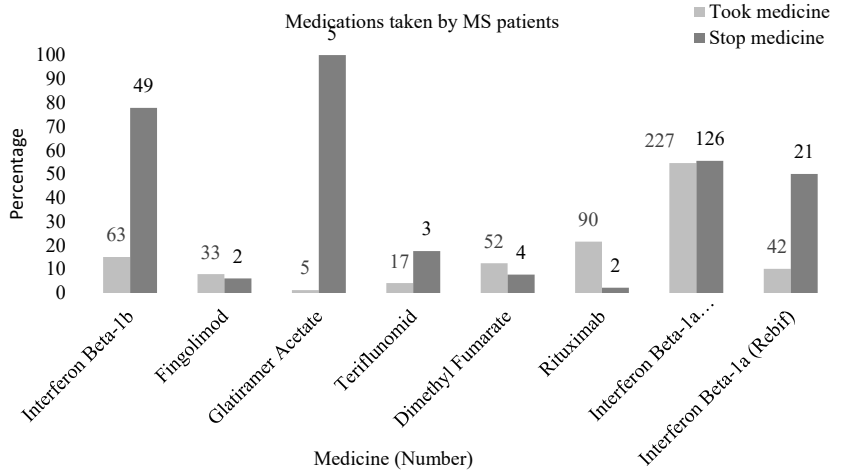

Figure 1. Medications taken by patients with multiple sclerosis (MS) in this study
[1- Interferon beta-1b (Betaferon), 2- Fingolimod (Marela), 3- Glatiramer acetate (Copamer), 4- Teriflunomide, 5- Dimethyl fumarate (Tecfidera), 6- Rituximab, 7- Interferon-beta 1a (Avonex), 8- Interferon-beta 1a (Rebif)]

It seems that the prevalent age of MS in Iranian patients is changing towards younger ages.

According to the 2001 US National Health Center report, the F:M ratio is 2:1.6. According to the latest epidemiological study of MS in Iran, F:M ratio was 3.01:1.[11]

A cohort study conducted in Canada showed that the F:M ratio for this disease increased from 1.19:1 to 1.32:1 over at least 50 years.[26] This is consistent with what has been found in previous studies in Iran, a ratio of 1.12:1 and 1.51:1 in 1999 and an increase of 1.25:1 and 1.26:1 in 2003.[27] This implies that an increase in this ratio could be associated with several environmental factors, including changes in women's lifestyle, which play important roles in changing this sex ratio.

This analysis found evidence for the correlation of MS with family history; 19.71% of patients had a positive family history of MS in both men and women (16.5% of men and 20.7% of women). In a previous study conducted in the Iranian population, consistent results have been reported regarding family history of MS from highest to lowest prevalence as Fars (21.1%), Tehran (20.5%), Isfahan (20.3%), Mazandaran (18.0%), and Kermanshah (12.5%) provinces.[19]

According to complex nature of MS and the role of genetic influence to MS risk, consanguineous marriage should be considered among patients with MS with positive family history in Iran, due to high rates of parental consanguinity.[19]

The mean age of onset of the first symptoms of MS disease in our findings was consistent with what has been found in previous studies. The former corresponds in the Kurdish population.[22] In contrast, the age of symptom onset in other studies varies widely, ranging from 25 to 40 years, which is close to reproductive age.[28] In Saudi Arabia, about 2.2% of patients under the age of 18 had onset of clinical symptoms.[29] We found that the age of diagnosis of the first clinical symptoms in almost 41% of the patients was under 18 years. The results demonstrated a relative increase in the incidence of MS at a young age.

The most common form of MS disease in both sexes is the RRMS type with a frequency of more than 60%, that is, this result ties well with the previous study conducted in Khuzestan, Iran. It was found that almost 32% of patients with SPMS had a very severely disabled physical condition (bedridden and wheelchair-bound).[30]

Interestingly, it should be mentioned that the frequency of the CIS subset was approximately 11% which was similar to the frequency reported in Saudi Arabia[29] and Qatar.[31]

The EDSS score is used to describe disease progression in people with MS. Low EDSS scores indicate nervous system dysfunction, which can be assessed by neurological examination methods, while high EDSS scores indicate disability in affected patients.[32] In the present study, the mean ± SD of the EDSS score for men with MS was lower than the EDSS score in other studies such as Kurdish patients in Iran[22] and MS population of Khuzestan.[27] The results of a 2013 systematic study also showed the value of 3.6 ± 2.3 and

2.7 ± 2.1 for the mean ± SD of EDSS score in men and women, respectively.[9] Of course, in line with previous studies, the mean EDSS score was higher in men than in women.

Another promising demographic characteristic of patients with MS was medicine usage. An investigation conducted in 2015 demonstrated that approximately, 80% of patients with RRMS in Australia, Sweden, and Switzerland, 70% of patients in Belgium and France, 65% of patients in Greece, and 69% of MS individuals received drug therapy.[33] In the current study, which took place in 2022 in Chaharmahal and Bakhtiari Province of Iran, only 10 patients (2.4%) out of 416 patients were not taking any medication at the time of the study, and almost more than 97% of the patients received drug treatment for their illness.

The drugs most frequently used by patients with MS are IFN-β-1a, which is similar to prescription trends of disease-modifying treatments in another provinces of Iran.[20]

In a 2020 study of Polish patients with MS, IFN-β and dimethyl fumarate were reported as the most popularly used drugs in patients with MS.[34] In the present study, among 21.6% of the patients who used rituximab, only 2.2% of them stopped taking the drug due to side effects. This drug is a kind of antibody against CD20 that was approved for people with hematological and autoimmune diseases, but has not yet been approved for MS.[35] Extensive results carried out showed its safety and effectiveness on 822 patients in 2016.[36,37]

IFN-β-1a, the drug that has been mostly used, may reduce the degree of disability, number, and volume of magnetic resonance imaging (MRI) lesions in patients with MS.[38] In the current study, IFN-β-1a was the most commonly used drug among patients with MS studied, although almost half of the patients stopped taking the drug during the study due to side effects or other reasons, consistent with the results of previous studies. A 2013 study also showed that 30% to 50% of patients with MS using this drug failed to respond. An important factor in non-response is the presence of neutralizing antibodies (NAbs) to IFN-β.[39-41] Studies have shown that IFN-β-1a is associated with the lowest prevalence of NAbs, while the highest prevalence of NAbs has been reported for IFN-β-1b.[42] Although only 15% of patients used IFN-β-1b in the present study, 78% of them stopped using the drug after an average of 51 months.

Conclusion

The prevalent age of MS in Iranian patients in Chaharmahal and Bakhtiari Province is changing towards younger age groups. In addition, the F:M ratio has increased to 3.5:1, meaning that changing social lifestyles in recent years can have a significant impact on changing this sex ratio. Analysis of the drug use pattern of affected patients in Chaharmahal and Bakhtiari Province showed that more than 97% of the patients took drugs to reduce the clinical symptoms of the disease, which may be due to the increase in drugs proposed in recent years for the MS treatment. Future research should more carefully consider the potential impact of environmental factors affecting F:M ratios, drug effectiveness, and drug use patterns in neighboring Chaharmahal and Bakhtiari Province.

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

Tehran University of Medical Sciences supported this study.

References

1. Dehghani R, Yunesian M, Sahraian MA, Gilasi HR, Kazemi M, V. The Evaluation of multiple sclerosis dispersal in iran and its association with urbanization, life style and industry. Iran J Public Health 2015; 44(6): 830-8.
2. Ramsaransing GS, De Keyser J. Benign course in multiple sclerosis: A review. Acta Neurol Scand 2006; 113(6): 359-69.
3. Greer JM, McCombe PA. Role of gender in multiple sclerosis: clinical effects and potential molecular mechanisms. J Neuroimmunol 2011; 234(1-2): 7-18.
4. Correale J, Marrodan M, Ysrraelit MC. Mechanisms of neurodegeneration and axonal dysfunction in progressive multiple sclerosis. Biomedicines 2019; 7(1): 14.
5. Ellwardt E, Zipp F. Molecular mechanisms linking neuroinflammation and neurodegeneration in MS. Exp Neurol 2014; 262 Pt A: 8-17.
6. Walton C, King R, Rechtman L, Kaye W, Leray E, Marrie RA, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. Mult Scler 2020; 26(14): 1816-21.
7. Eskandarieh S, Sahraian M. Epidemiological evidence of the recent surge in MS in Asia and Australia: A systematic review. J Kermanshah Univ Med Sci 2021; 25(2): e111028.
8. Sahraian MA, Naser Moghadasi A, Eskandarieh S. Economic sanctions against Iran as an important factor in threatening the health of patients with multiple sclerosis. Curr J Neurol 2021; 20(1): 15-22.
9. Etemadifar M, Sajjadi S, Nasr Z, Firoozeei TS, Abtahi SH, Akbari M, et al. Epidemiology of multiple sclerosis in Iran: A systematic review. Eur Neurol 2013; 70(5-6): 356-63.
10. Etemadifar M, Mehrabi B, Kiani-Peykani R, Abtahi SH, Nekouie-Isfahani K, Ramagopalan SV, et al. Soil heavy metals are associated with the distribution of multiple sclerosis in Isfahan, Iran. Acta Neurol Scand 2016; 134(4): 292-9.

11. Azami M, YektaKooshali MH, Shohani M, Khorshidi A, Mahmudi L. Epidemiology of multiple sclerosis in Iran: A systematic review and meta-analysis. PLoS One 2019; 14(4): e0214738.
12. Pakdel M, Karin HA, Bidkhori M, Hadei M, Kazemi M, V, Sarmadi M, et al. Do socioeconomic factors affect the prevalence of multiple sclerosis in Iran? Acta Neurol Scand 2019; 140(5): 328-35.
13. Elhami SR, Mohammad K, Sahraian MA, Eftekhar H. A 20-year incidence trend (1989-2008) and point prevalence (March 20, 2009) of multiple sclerosis in Tehran, Iran: A population-based study. Neuroepidemiology 2011; 36(3): 141-7.
14. Cheraghmakani H, Baghbanian SM, Habibi Saravi R, Azar A, Ghasemihamedani F. Age and sex-adjusted incidence and yearly prevalence of multiple sclerosis (MS) in Mazandaran province, Iran: An 11-years study. PLoS One 2020; 15(7): e0235562.
15. Rezaeimanesh N, Moghadasi AN, Sahraian MA, Eskandarieh S. Dietary risk factors of primary progressive multiple sclerosis: A population-based case-control study. Mult Scler Relat Disord 2021; 56: 103233.
16. Maroufi H, Mortazavi SH, Sahraian MA, Eskandarieh S. Environmental risk factors of multiple sclerosis in the Middle East and North Africa region: A systematic review. Curr J Neurol 2021; 20(3): 166-84.
17. Shahin S, Eskandarieh S, Moghadasi AN, Razazian N, Baghbanian SM, Ashtari F, et al. Multiple sclerosis national registry system in Iran: Validity and reliability of a minimum data set. Mult Scler Relat Disord 2019; 33: 158-61.
18. Ezabadi SG, Sahraian MA, Maroufi H, Shahrbaf MA, Eskandarieh S. Global assessment of characteristics of multiple sclerosis registries; A systematic review. Mult Scler Relat Disord 2022; 63: 103928.
19. Salehi Z, Almasi-Hashiani A, Sahraian MA, Ashtari F, Baghbanian SM, Razazian N, et al. Epidemiology of familial multiple sclerosis in Iran: A national registry-based study. BMC Neurol 2022; 22(1): 76.
20. Ghadiri F, Sahraian MA, Baghbanian SM, Ashtari F, Razazian N, Majdinasab N, et al. Prescription trends of disease-modifying treatments for multiple sclerosis in Iran over the past 30 years. Mult Scler Relat Disord 2022; 61: 103777.
21. Mirmosayyeb O, Shaygannejad V, Bagherieh S, Hosseinabadi AM, Ghajarzadeh M. Prevalence of multiple sclerosis (MS) in Iran: A systematic review and meta-analysis. Neurol Sci 2022; 43(1): 233-41.
22. Razazian N, Eskandarieh S, Siabani S, Afshari D, Sahraian MA, Khezri O, et al. Prevalence of multiple sclerosis and its clinical and demographic characteristics in Kurdish populations in western Iran (2020). Mult Scler Relat Disord 2022; 57: 103441.
23. Kapica-Topczewska K, Brola W, Fudala M, Tarasiuk J, Chorazy M, Snarska K, et al. Prevalence of multiple sclerosis in Poland. Mult Scler Relat Disord 2018; 21: 51-5.
24. Eliasdottir O, Kjartansson O, Olafsson E. Prevalence of multiple sclerosis in Iceland. Neuroepidemiology 2018; 51(1-2): 50-6.
25. Nasiri M, Maroufi H, Sahraian MA, Eskandarieh S. Prevalence of multiple sclerosis and its risks in Tehran, Iran, in 2019. Neurol Sci 2021; 42(6): 2575-6.
26. Orton SM, Herrera BM, Yee IM, Valdar W, Ramagopalan SV, Sadovnick AD, et al. Sex ratio of multiple sclerosis in Canada: A longitudinal study. Lancet Neurol 2006; 5(11): 932-6.
27. Sharafaddinzadeh N, Moghtaderi A, Majdinasab N, Dahmardeh M, Kashipazha D, Shalbafan B. The influence of ethnicity on the characteristics of multiple sclerosis: A local population study between Persians and Arabs. Clin Neurol Neurosurg 2013; 115(8): 1271-5.
28. Eskandarieh S, Heydarpour P, Minagar A, Pourmand S, Sahraian MA. Multiple sclerosis epidemiology in East Asia, South East Asia and South Asia: A systematic review. Neuroepidemiology 2016; 46(3): 209-21.
29. Al-Abdullah MS, Siddiqui AF. Demographic and disease characteristics of multiple sclerosis in the Southwest Region of Saudi Arabia. Neurosciences (Riyadh) 2018; 23(4): 320-5.
30. Radmehr M, Meghdadi S, Bahmanzadeh M, Sabbagh S. Prevalence, demographics and clinical characteristics of multiple sclerosis in North of Khuzestan Province, Iran. Jentashapir J Health Res 2015; 6(5): e23831.
31. Deleu D, Mir D, Al Tabouki A, Mesraoua R, Mesraoua B, Akhtar N, et al. Prevalence, demographics and clinical characteristics of multiple sclerosis in Qatar. Mult Scler 2013; 19(6): 816-9.
32. Ineichen BV, Schneider MP, Hlavica M, Hagenbuch N, Linnebank M, Kessler TM. High EDSS can predict risk for upper urinary tract damage in patients with multiple sclerosis. Mult Scler 2018; 24(4): 529-34.
33. Berger T, Adamczyk-Sowa M, Csepany T, Fazekas F, Hojs FT, Horakova D, et al. Management of multiple sclerosis patients in central European countries: Current needs and potential solutions. Ther Adv Neurol Disord 2018; 11: 1756286418759189.
34. Kapica-Topczewska K, Collin F, Tarasiuk J, Chorazy M, Czarnowska A, Kwasniewski M, et al. Clinical and epidemiological characteristics of multiple sclerosis patients receiving disease-modifying treatment in Poland. Neurol Neurochir Pol 2020; 54(2): 161-8.
35. Brancati S, Gozzo L, Longo L, Vitale DC, Drago F. Rituximab in multiple sclerosis: Are we ready for regulatory approval? Front Immunol 2021; 12: 661882.
36. Airas L, Nylund M, Mannonen I, Matilainen M, Sucksdorff M, Rissanen E. Rituximab in the treatment of multiple sclerosis in the Hospital District of Southwest Finland. Mult Scler Relat Disord 2020; 40: 101980.
37. Alldredge B, Jordan A, Imitola J, Racke MK. Safety and efficacy of Rituximab: Experience of a single multiple sclerosis center. Clin Neuropharmacol 2018; 41(2): 56-9.
38. Cohan SL, Hendin BA, Reder AT, Smoot K, Avila R, Mendoza JP, et al. Interferons and multiple sclerosis: Lessons from 25 years of clinical and real-world experience with intramuscular interferon beta-1a (Avonex). CNS Drugs 2021; 35(7): 743-67.
39. Bertolotto A, Gilli F. Interferon-beta responders and non-responders. A biological approach. Neurol Sci 2008; 29(Suppl 2): S216-S217.
40. Fattahi M, Eskandari N, Sotoodehnejadnematalahi F, Shaygannejad V, Kazemi M. Comparison of the expression of miR-326 between interferon beta responders and non-responders in relapsing-remitting multiple sclerosis. Cell J 2020; 22(1): 92-5.
41. Filipi M, Jack S. Interferons in the treatment of multiple sclerosis: A clinical efficacy, safety, and tolerability update. Int J MS Care 2020; 22(4): 165-72.
42. Bertolotto A, Malucchi S, Sala A, Orefice G, Carrieri PB, Capobianco M, et al. Differential effects of three interferon betas on neutralising antibodies in patients with multiple sclerosis: A follow up study in an independent laboratory. J Neurol Neurosurg Psychiatry 2002; 73(2): 148-53.