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Review Article

Multiple Sclerosis in Iran

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Abstract

Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system (CNS). This highly disabling disorder is characterized by a variable clinical course. MS is a heterogeneous disease with a complex pathology and significant social and economic impact. MS is associated with dysfunction of parts of the nervous system which results in a range of signs and symptoms, including physical, mental, and sometimes psychiatric problems. There is no definite treatment for MS. Iran has been thought to be located in the low risk zone of MS prevalence. However, recent studies and investigations in some cities such as Isfahan, a central province of Iran, have suggested a medium-to-high risk level of MS prevalence. Pathophysiological processes in MS contribute to the disease course and clinical manifestations. Therefore, biomarkers that are indicators of these events would provide significant potential for diagnosis, prediction of disease course, and optimization of therapeutic responses. This review provides information on the prevalence of MS and some risk factors among Iranian people.

Keywords: Demyelination Multiple sclerosis, Epidemiology of Multiple sclerosis in Iran, Immune modulation, Inflammation, miRNA and multiple sclerosis, Regeneration

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Introduction

Multiple sclerosis (MS) is an immune-mediated demyelinating disease with high disabling disorders and significant social and economic impact. It is the most important cause of non-injury-related disability in young adult with unknown causes and distresses that have influence on twice as many women as men and affect individuals in their productive years. Current information confirm the view of MS as a multifactorial disease caused by a series of interactions between the environment and one's genetic susceptibility. For instance, smokers run an increased chance of MS. Beyond smoking, massive epidemiological studies have illustrated the relation between vitamin D deficiency and MS and showed the protective effects of vitamin D as the risk of developing MS. Moreover, the increase within the prevalence of vitamin D deficiency is also another cause for the rise in the prevalence rate of MS in Iran.[1-6] Furthermore, viral infections, accumulation of copper and iron, reduction in zinc, magnesium, selenium, vitamins B2, B6, D, E, and essential fatty acid, and improved hygiene are the factors that lead to MS.[7-10] After physical injury and trauma, MS is the second most common cause of neurological disabilities in young adults. Diversity of genes and changes in environment lifestyle and their interaction might be attributed to the prevalence of MS on an irregular basis.[1,2,11-14] The genetic flair of MS has been related to variations of the class II major histocompatibility complex (MHC) and non-MHC variants that are involved in T-cell activation/regulation. In addition, different population studies highlight the proportion of HLA locus in susceptibility to MS among different genes as similar as other autoimmune disorder. HLA-A*03 and HLA-B*07 were the primary alleles whose associations were illustrated with MS.[2,3,15,16] Two million three hundred thousand people suffer from MS worldwide, reported by the World Health Organization (WHO) in 2013. Studies in Arab countries have also demonstrated that MS prevalence was between 4 and 8 per 100 000. The epidemiology of MS has been shifted in current decades in Iran and other Middle East regions to contain the majority of western Asia and Egypt but excluding the Caucasia.[12,17-20] Iran is located in the eastern Mediterranean region. Neurologists in Iran believe that the number of patients with MS in Iran has been increasing in recent years.[21-23] There is a wide variation within the prevalence of MS in different geographical regions and also between genders as MS usually affects young women in Iran.[24-27] The prevalence of MS is between 2 and 160 per 100 000 in several populations and over 2 million people

suffer from this malady worldwide. Recent studies have shown that the prevalence of MS in Iran has increased considerably, especially during the last decade. Similarly, studies in Arab countries have represented that MS prevalence have been increased. There is a wide variation within the prevalence of MS in Iran from 5.3 to 74.28 per 100 000 in several provinces.[15,28,29] Future research ought to focus on revealing the epidemiological features of MS within the neglected provinces with different ethnicities. Such an endeavor along with further research towards improvement of information on previously studied areas can enable a field to be opened up to recognize the patterns of MS in varied genetic backgrounds and environments of Iran.

Prevalence of Multiple Sclerosis in Iran

Table 1 reveals the prevalence demonstration as n per 100 000 for different provinces of Iran that may be ranked from the highest to lowest as follows in 2014: Isfahan (n = 93.06), Charmahal and Bakhtiari (n = 92.7), Fars (n = 77.3), Tehran (n = 74.3), Qom (n = 50.4), Gilan (n = 35.9), Zanjan (n = 33.27), and Golestan (n = 18.0).[16,25]

One of the most important reasons of MS prevalence may be the age of the population in Iran.[30] Iran has a very young population, with the majority of the population in Iran being within the age range of 15-30 years. The fact that the disease is more prevalent in young adults indicates that age may be an important agent for the prevalence rise.[1,31] According to the study by Etemadifar et al and Saadatnia et al Isfahan is the highest risk level of MS prevalence among other provinces.[31,32] In addition, Hashemilar et al reported that the prevalence of MS in the north west of Iran was at the medium frequency range.[33] In other epidemiology studies in Tehran, Sahraian and colleagues, showed that single patients, compared to divorced or widowed patients, appeared to be at a higher risk level of MS.[34] Moreover with reference to research of Rezaali et al a remarkable percentage of the patients hold a family history of other immune deficiency disorders.[35]

Risk Factor and Vitamin D in MS

Iranian statistical center based on the national census issues revealed that whole population of the city in 2006 was 7 803 883, which 3 817 464 were females and 3 986 419 were males.[32] In summary, the most important risk factors that linked to a higher risk of MS include smoking, low level of vitamin D, people aged from 15 to 60, Epstein-Barr virus, autoimmune diseases, etc.[36] Asadollahi et al demonstrated that smoking increases the risk of MS and there is a direct relationship between them.[37] Vitamin D3 is an environmental factor that along with molecular mechanisms within the genetic risk, contributes to MS promotion.[38-40] People who live far from the equator are the most susceptible to MS. Vitamin D has an immunomodulatory factor in suppressing MS and fewer exposure to sunlight leads to vitamin D production deficiency.[41-43] People who are exposed to sunlight significantly reduce the incidence of MS.[44]

Table 1. Prevalence of MS in Different Cities of Iran Ranked From the Highest to Lowest[8]

Cities in Iran	Prevalence of MS (n) Per 1000000 Population
Isfahan	93.6
Charmahal and Bakhtiari	92.7
Fars	77.3
Tehran	74.3
Qom	50.4
Gilan	35.9
Zanjan	33.7
Golestan	18

Prevalence of Multiple Sclerosis in Persian Gulf Countries

The studies in Bahrain, Qatar, United Arab Emirates, and Oman have reported a moderate to-high rampancy with an increase in incidences in recent years.[17-28] For the first, Inshasi and Thakre illustrated that the prevalence of MS in Dubai is surprisingly high and Dubai should be considered as one of the regions with the medium to high risks of MS.[45]

miRNAs in Multiple Sclerosis

miRNA are small non-coding RNAs which have a length range of 19-24 nucleotides and regulate gene expression at the post transcriptional levels by binding to 3´UTR of the target gene.[46] They mediate an important process such as metabolism, differentiation, proliferation, development, and intrinsic and acquired immunity.[47,48] Many studies have been carried out to collect miRNAs signature in MS, for instance, relapsing-remitting multiple sclerosis (RRMS), including about 85% of patients, primary progressive multiple sclerosis (PPMS), and secondary progressive multiple sclerosis (SPMS).[49] Since 2011, experiments on the miRNA profiles have been transmitted to investigate changes within the expression of miRNAs in response to MS specific therapies in order to achieve a better understanding of the molecular mechanisms of drugs and those biomarkers to monitor the treatment. In plasma of patients with MS, the expression of 6 miRNAs was increased (miR-22, miR-422a, miR-572, miR-614, miR-648, and miR-1826) and 1 miRNA (miR-1979) was regulated down compared to control.[50] Also, down regulation of miR-145 in plasma of patients was reported.[51]

Conclusion

MS is a CNS disease that is characterized by multiple

regions of demyelization and affecting many people, especially young women. The patients most frequently develop the first symptoms between the third and fifth decade of life. Though the exact cause of the growing incidences of MS is unknown, both genetic and environmental factors are likely. The prevalence of MS in the various cities in Iran is shown in Table 1. In Iran, the lowest (n = 18) and the highest (n = 93.6) population of MS were reported for Golestan and Isfahan, respectively. To summarize, the current study suggests that Iran has a moderate-to-high MS prevalence rate, with a recent sharp increase in it.

Ethical Approval

Not applicable.

Conflict of Interest Disclosures

None.

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