

# Epidemiology and genetic aspects of multiple sclerosis in India

Rohit Bhatia, Prerna Bali, Rima M Chaudhari

Department of Neurology, Cardiothoracic and Neurosciences Centre, All India Institute of Medical Sciences, New Delhi, India

## Abstract

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system with a complex pathophysiology. Considered a rare disease in India in the past, studies over time suggest an increase in subjects with MS in India, although the observations are limited by the lack of formally conducted epidemiological studies and the absence of a nationwide registry. The current World Health Organization (WHO) Multiple Sclerosis International Federation (MSIF) "Atlas of MS" 2013 estimates a prevalence rate of 5-20 per 100,000, which also seems an underestimate. Although there have been reports of phenotypic differences between MS in Indians and the Western counterparts, recent studies report a reasonable similarity in disease types and characteristics. A few studies on the genetics of MS have been reported, including human leukocyte antigen (HLA) associations and non-major histopathology complex (MHC) disease loci. The current review discusses the pivotal studies of the past, newer observations on MS from India, and the need for a national registry.

## Key Words

Epidemiology, genetic, multiple sclerosis (MS)

## For correspondence:

Dr. Rohit Bhatia, Department of Neurology, Room No 603, 6<sup>th</sup> Floor, Cardiothoracic and Neurosciences Centre, All India Institute of Medical Sciences, New Delhi - 110 029, India.

E-mail: rohitbhatia71@yahoo.com

*Ann Indian Acad Neurol 2015;18 (Supplement 1):S6-S10*

## Introduction

Multiple sclerosis (MS) is an inflammatory, demyelinating disease of the central nervous system with a complex pathophysiology and interplay of environmental and genetic factors in disease etiopathogenesis.<sup>[1,2]</sup> The disease adds to the disability and productive burden of any country by afflicting the young and dynamic population. Epidemiological studies provide an almost global map of the distribution of a disease. The incidence and prevalence of MS is variable across the globe and include low-, middle-, and high-prevalence zones.<sup>[2]</sup> MS was thought to be rare in India in the past, until the pivotal initial studies by Singh *et al.*<sup>[3]</sup> and Bharucha *et al.*<sup>[4]</sup> were published. The last decade has seen an increase in the number of MS cases being reported in both adult and pediatric populations, and this is likely related to the following: Emergence and easy availability of magnetic resonance imaging (MRI); increase

in the number of neurologists; and improved diagnostic criteria, techniques, and awareness about the illness. This has, ultimately, led to more cases being reported from across the whole country.<sup>[5]</sup> This article aims to provide an overview of studies on MS in the country [Table 1]; how this disease has evolved over time; the prevalence, genetic aspects, phenotypic presentation, and other factors related to MS.

## Incidence and Prevalence

In the 1980s, the prevalence of MS in India was estimated to be nearly 1/100,000. Evidence collected from hospitals

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

**How to cite this article:** Bhatia R, Bali P, Chowdhary R. Epidemiology and genetic aspects of multiple sclerosis in India. *Ann Indian Acad Neurol* 2015;18:6-10.  
**Received:** 14-07-15, **Revised:** 29-07-15 **Accepted:** 05-08-15

### Access this article online

#### Quick Response Code:



#### Website:

www.annalsofian.org

#### DOI:

10.4103/0972-2327.164814

**Table 1: Important studies on MS conducted from India**

Author	Study title	Patients/controls	Observations
Singhal <i>et al.</i> 1985 <sup>[6]</sup>	Multiple sclerosis – Indian experience	105 CDMS (60 female and 45 male) and 14 with NMO	Estimated the prevalence of MS to be approximately 1.33/100,000
Chopra <i>et al.</i> 1980 <sup>[7]</sup>	Multiple Sclerosis in North - West India	54 MS patients (includes 2 pathogenically proven cases of MS, 5 NMO patients)	MS constituted 1.58% of total admission of neurology during 1968-77, and there was more common occurrence of visual impairment at onset, predominant involvement of optic nerves and spinal cord, and higher incidence of NMO
Syal <i>et al.</i> 1999 <sup>[8]</sup>	Clinical profile of multiple sclerosis in North-West India	100 MS patients (includes prospective analysis of 35 patients and retrospective analysis of 65 patients)	MS was found to constitute 2.54% of neurology admissions between Jan 93 and Dec 97. The age of onset was 28.49± years, the female-to-male ratio of 1.32: 1, and 23.6% of visual impairment was reported
Jain <i>et al.</i> 1985 <sup>[10]</sup>	Multiple sclerosis: Indian experience in the last thirty years	354 MS patients	MS may be more common in northern (4.15 cases) as compared to southern India (3.2 cases). Optic neuritis was seen as the initial presentation in 22.2-58% of the cases
Bharucha <i>et al.</i> 1988 <sup>[11]</sup>	Prevalence of multiple sclerosis in the Parsis of Bombay	Door-to-door survey done to screen a community of 14,010 people (Parsis living in colonies in Bombay, India) for possible neurologic diseases, and defined diagnostic criteria used to evaluate people who tested positive on the screening survey	There were three clinically definite cases of MS. (Prevalence of 21/100,000)
Wadia <i>et al.</i> 1990 <sup>[12]</sup>	Multiple sclerosis is prevalent in the Zoroastrians (Parsis) of India	16 clinically definite cases of MS were counted, 14 in Bombay and 2 in Poona, from total Zoroastrian populations of 50,053 and 3,399, respectively	Prevalence ratio was 26 per 100,000 for Bombay and 58 per 100,000 for Poona. The age-adjusted prevalence ratio for Bombay was 24 per 100,000, with 95% confidence limits of 13.1-40.3
Gangopadhyay <i>et al.</i> 1999 <sup>[13]</sup>	Profile of multiple sclerosis in Bengal	45 patients of MS diagnosed on the basis of Poser's criteria from West Bengal were studied. Records of 31 patients were retrospectively studied and 14 cases were prospectively analyzed	The male-to-female ratio was 1:1.5; mean age of onset 31.83 years in male and 29.11 years in females. The incidence of MS was 0.32% of all hospital admissions and 0.62/100,000 of neurology clinic patients. Visual impairment was the commonest presentation (33.33%); 71% of patients had visual impairment sometime during the illness
Mathew <i>et al.</i> 1971 <sup>[15]</sup>	Incidence and pattern of demyelinating disease in India	69 MS patients	A higher male-to-female ratio from western region of India and the mean age of onset was 27-29 years Higher visual involvement of 42% compared to European and American data available
Singhal <i>et al.</i> 2015 <sup>[16]</sup>	Multiple sclerosis in India: An institutional study	101 patients (61 females) from June 2011 to December 2012	Mean age of the patients at 33.3±9.2 years. Sites involved in first relapse were spinal cord in 43.7% patients, followed by brainstem 25.3% and optic nerve in 24.1% patients
Bhatia <i>et al.</i> 1996 <sup>[19]</sup>	Multiple sclerosis in India: A.I.I.M.S. experience	55 MS patients	The commonest initial neurologic symptom was motor weakness (30%) followed by visual impairment (26%). Optic neuritis was seen in 26% of the patients, making it the most common initial neurological symptom in MS
Sarma <i>et al.</i> 2005 <sup>[20]</sup>	Multiple sclerosis in South India	68 MS patients	A frequency of 44% of visual impairment in MS patients was found
Singhal <i>et al.</i> 1975 <sup>[18]</sup>	Profile of multiple sclerosis in the Bombay region. On the basis of critical clinical appraisal	30 probable MS patients (in addition, 9 patients with NMO and 6 with a mixed neurological picture of MS and NMO were described)	A relatively high proportion of patients (nearly half of the MS patients with optic nerve involvement and two-third of the MS-NMO group) had bilateral optic nerve involvement. MS was more frequent in patients with better socioeconomic status, in the Parsi community and in patients with a fair complexion, whereas NMO was more frequent in patients with poor socioeconomic status
Khadilkar <i>et al.</i> 2005 <sup>[24]</sup>	A Case control study of environmental risk factors in Indians with Multiple Sclerosis	63 MS patients and 63 age- and sex-matched controls	There were 10 smokers (7 males and 3 females) among the MS patients, as compared to 4 among controls. There was a significantly higher family history of MS (32%) and other autoimmune diseases among the patients, compared to controls (14%)
Pandit <i>et al.</i> 2013 <sup>[25]</sup>	Association of vitamin D and multiple sclerosis in India	110 MS patients and 108 matched controls	Patients had significantly lower 25(OH)D levels than matched controls and patients in relapse had significantly lower vitamin D levels compared to those in remission. Vitamin D deficiency was seen in a higher proportion of cases than among controls
Elian <i>et al.</i> 1990 <sup>[26]</sup>	Multiple sclerosis among United Kingdom-born children of immigrants from the Indian subcontinent, Africa and the West Indies	76 ethnic Indian, Pakistani, or Bangladeshi immigrants	UK-born children of Asian, West Indian, and African immigrants have a high prevalence of MS

**Table 1: (Continued)**

Author	Study title	Patients/controls	Observations
Dean <i>et al.</i> 1997 <sup>[27]</sup>	Age at immigration to England of Asian and Caribbean immigrants and the risk of developing multiple sclerosis.	76 ethnic Indian, Pakistani or Bangladeshi immigrants had definite or probable MS by the calculated population at risk in a 1992 survey where January 1990 was designated as the prevalence day	The Indian and Pakistani immigrants to England who come as children, below the age of 15, have a significantly higher risk of developing MS
Wadia <i>et al.</i> 1980 <sup>[28]</sup>	Association of HLA-B12 with multiple sclerosis in India	27 MS patients	HLA-B12 antigen was present in excess in comparison with normal controls. In fact, in the subgroup of "clinically definite" patients, the B12 antigen excess was remarkable. These preliminary findings seem to point to a different immunogenetic profile of Indian MS patients in comparison with Western and Japanese series
Wadia <i>et al.</i> 1981 <sup>[29]</sup>	HLA antigens in multiple sclerosis amongst Indians	27 MS patients	HLA-A3 and HLA-B7 haplotypes among Indians were found to be lower than Caucasians. It was also observed that the Parsi community had a higher incidence of MS and the high association of HLA-B12 was reported among these patients
Kankonkar <i>et al.</i> 2003 <sup>[30]</sup>	Evidence for novel DRB1*15 allele association among clinically definite multiple sclerosis patients from Mumbai, India	23 MS patients and 146 matched controls	HLA-DRB1 allele associations among non-Parsi MS patients and comparison with controls
Pandit <i>et al.</i> 2011 <sup>[31]</sup>	Evaluation of the established non-MHC multiple sclerosis loci in an Indian population	197 Indian patients and 197 unrelated controls	Non-MHC disease susceptibility loci in Asian population, and that the disease identifying genes in the Indian population were similar to those in the West

NMO = Neuromyelitis optica; CDMS = Clinically definite multiple sclerosis; HLA = Human leukocyte antigen; MHC = Major histocompatibility complex

throughout India suggests that the number of MS patients diagnosed annually has nearly doubled. There are no large-scale studies from India on the incidence and prevalence of MS. In an earlier study by Singhal *et al.* the prevalence of MS was estimated to be approximately 1.33/100,000.<sup>[6]</sup> Another hospital-based study from northwestern India observed that MS constituted 1.58% of the total neurology admissions from 1968 to 1977.<sup>[7]</sup> These data were compared with more recent data collected from the same institute in the period 1993-1997,<sup>[8]</sup> and an increase was found, to 2.54% of neurology admissions. The current World Health Organization (WHO) Multiple Sclerosis International Federation (MSIF) "Atlas of MS" 2013 quotes prevalence rates of 5-20 per 100,000, which is much higher than the studies reported previously.<sup>[9]</sup> This also seems an underestimate due to the lack of well-conducted epidemiological studies. Previously conducted studies had estimated that MS may be more common in northern as compared to southern India, where 3.2 cases were seen yearly, compared to 4.15 cases in the north.<sup>[10]</sup> Two community-based prevalence studies by Barucha *et al.*<sup>[11]</sup> and Wadia *et al.*<sup>[12]</sup> used Schumacher's criteria among the Parsi population in the late 80s and revealed a prevalence of 21-58/100,000. Using Poser's criteria, Gangopadhya *et al.*<sup>[13,14]</sup> reported an incidence of 0.32% of all hospital admissions and 0.62/100,000 of neurology clinic patients with the mean age at onset of 31.83 years in males and 29.11 years in females. Initial studies from Vellore and northern India reported a higher male-to-female ratio as against studies from the western part of India.<sup>[15]</sup> The mean age of onset in all the studies was 27-29 years.<sup>[6,8,15]</sup> The mean age in the recent study from the All India Institute of Medical Science (AIIMS) registry by Singhal and Bhatia *et al.* quoted a slightly higher age range of 33 ± 9 years.<sup>[16]</sup> There was also a female preponderance, with a male-to-female ratio of 0.65. Syal *et al.*<sup>[8]</sup> reported the age of onset to be 28.49 ± 9.54 years and the female-to-male ratio of 1.32:1.

## Phenotypic Variability

Initial reports about MS in India from all the studies in the 70s mainly emphasized the opticospinal variant in the country. Singhal *et al.* reported that 71% of the patients seen in western India had this phenotype.<sup>[6]</sup> The Vellore group also reported a higher visual involvement of 42% as compared to the then available European and American data.<sup>[15]</sup> However, a study analyzing the symptoms at onset in patients admitted to a national hospital in southern India showed a dramatic reduction in spinal cord dysfunction by almost 50%.<sup>[17]</sup> A multicentric study by Jain and Maheshwari reported that among nine centers and 354 cases, optic neuritis was seen as the initial presentation in about 22.2-58% of the cases in five centers.<sup>[10]</sup> Singhal and Wadia also found that a relatively high proportion of patients had bilateral optic nerve involvement in the west/western.<sup>[18]</sup> Studies done in the MRI era from New Delhi, India, reported that the involvement of the brainstem and other systems was as frequent in our MS population and that it was not only the opticospinal disease that was common in this part of the continent.<sup>[8,17,19]</sup> Various studies reporting visual impairment have been published from India, with Syal's study showing a frequency of 23.6% from the northwestern region and another study showing 44% from the south.<sup>[8,20]</sup> Bhatia *et al.* found optic neuritis in 26% of the patients, making it the second most common initial neurological symptom in MS patients.<sup>[19]</sup> From the eastern region, Gangopadhya *et al.* reported a frequency of 33.3%.<sup>[13]</sup> The recent literature from the AIIMS registry showed that brainstem involvement was as frequent as visual impairment and that relapsing/remitting multiple sclerosis (RRMS) was the most frequent disease type.<sup>[16]</sup> The improved diagnostic aid with enhanced MRI techniques and the application of the sensitive revised McDonald's criteria<sup>[21]</sup> in these studies is the likely explanation for the observed phenotypic change.

## Environmental Factors

It is believed that exposure to some environmental factors in genetically susceptible individuals may lead to the development of MS. Therefore, studying the predisposing factors in a population may provide important insights into the causation of the disease.<sup>[22,23]</sup> In India, no specific studies on the environmental factors have been reported so far. Khadilkar *et al.*<sup>[24]</sup> reported that there was a significant history of mumps among patients with MS compared with controls. Although history of measles and chicken pox was higher in patients with MS than controls, it was statistically not significant. From their data set of 63 MS patients they reported that there were 10 smokers in the MS group, compared to 4 among the controls. They also reported that there was a significant higher family history of MS and other autoimmune disease among the patients as compared to controls.

Higher prevalence of MS is seen in patients with higher socioeconomic status and better sanitary conditions. In a study, 30 patients with probable MS from Mumbai, India were followed up for a period of 15 years. MS was more frequent in patients with better socioeconomic status in the Parsi community.<sup>[18]</sup> Epidemiological and experimental data support the role of vitamin D as a potentially important environmental risk factor for MS. A study by Pandit *et al.* measured serum 25-hydroxyvitamin D, i.e., 25(OH)D levels and reported that patients with MS had significantly lower 25(OH)D levels than matched controls, and patients in relapse had a significantly lower vitamin D level compared to those in remission. Vitamin D deficiency was seen in a higher proportion of cases than among controls. Higher quartiles of vitamin D showed an inverse relationship with MS.<sup>[25]</sup> Previous studies have shown that United Kingdom (UK)- and North America-born children of Asians have higher prevalence of MS, indicating that MS is more common as distance from the equator increases, and that a certain ethnicity may confer some degree of protection against the increased risk of MS.<sup>[27,28]</sup>

## Genetic Susceptibility

The likelihood of an individual developing MS is strongly influenced by her or his ethnic background and family history of disease, suggesting that genetic susceptibility is a key determinant of risk. Various human leukocyte antigens (HLAs) that have been noted to be more common in MS are being studied worldwide, but the role of HLA genes in the Indian population has not been adequately reported. Only a few studies from India have identified an immunological and genetic basis for MS.

Wadia *et al.* observed that there is a significant relative risk of MS among Indians with the HLA-B12 haplotype. This antigen was detected in 80% of cases, compared with 15% of controls.<sup>[14]</sup> These preliminary findings seem to point to a different immunogenetic profile of Indian MS patients in comparison with Western and Japanese series.<sup>[28]</sup> Another study by the same group showed that the lower incidence of MS in India may have genetic implications. HLA-A3 and HLA-B7 haplotypes were found to be lower among Indians than among Caucasians. It was also observed that the Parsi community had a higher incidence of MS, and the high association of HLA-B12 was reported among these patients.<sup>[29]</sup>

Kankonkar *et al.*<sup>[30]</sup> analyzed the HLA-DRB1 allele associations among non-Parsi MS patients and compared them with controls. HLA serologic as well as DRB1 typing was followed. The study revealed a significant increase of HLA-A11, and further molecular subtyping of HLA-DRB1\*15 among the patients revealed two novel alleles, DRB1\*1506 and DRB1\*1508, along with the commonly reported DRB1\*1501 for the first time in MS patients, which had been hitherto unidentified from other parts of India and the world. The association of MS with the HLA class II loci DR and DQ were studied in the Asian Indian population in the UK. The putative haplotype, DRB1\*1501.DQA1\*0102.DQB1\*0602, was found to be nominally associated with MS. The data suggested that other genetic and/or environmental factors may be more important in predisposing to MS in Asian Indians living in the UK.

Pandit *et al.*<sup>[31]</sup> found the role of non-major histopathology complex (MHC) disease susceptibility loci in the Asian population and that the disease-identifying genes in the Indian population were similar to those in the West. They tested for 15 loci outside the MHC in 197 Indian patients and 197 controls. It was found that the single nucleotide polymorphism (SNP) in IL7R (interleukin-7 receptor) showed a strong protective effect and was similar to the one reported from the West.<sup>[31]</sup>

## Conclusion

MS exists in India, although its prevalence is lower than among European and American populations. The phenotypic presentation of MS in India seems quite similar to the West, and it has also been observed that some of the genes in Indian patients are similar to those seen in the Western patient population. Large epidemiological studies are needed to study MS incidence and prevalence in India. Collaborations among the neurologists and MS registries across the country are not only critical for knowing the epidemiological status of the disease in the country but would also pave the way for research in genetics, drug development, and in exploring the pathogenesis of this complex disease. New methods such as a genome-wide association study (GWAS), a tool for investigating the genetic architecture of polygenic disease in humans,<sup>[32]</sup> is being used for the identification of genetic factors of disease susceptibility, clinical phenotypes, and treatment response in MS. The ability of a GWAS to explore the variation between patients and controls has presented a common path for the identification of genetic susceptibility for complex diseases such as MS. The results may open new avenues for the clinical implications of MS-associated genetic variants reported from a large GWAS.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Srivastava MVP, Bhatia R. In: Clinical Practice of Multiple Sclerosis. Srivastava MVP, Bhatia R (Eds). Kontentwrx Communications. 2014, New Delhi, India.

2. Singhal B, Ganeshan M. Multiple Sclerosis: The disease and its burden. In: Clinical Practice of Multiple Sclerosis. Srivastava MVP, Bhatia R (Eds). Kontentworx Communications. New Delhi, India. 2014;1-12.
3. Singh B, Isaiah P, Chandy J. Multiple sclerosis (studies on sixteen cases). *Neurology* 1954;1:49-59.
4. Bharucha EP, Umarji RM. Disseminated sclerosis in India. *Int J Neurol* 1961;2:182-8.
5. Gupta S, Tewari A, Nair V. Multiple Sclerosis: Indian Perspective. [apiindia.org.563-69](http://www.apiindia.org/medicine_update_2013/chap120.pdf). Available at: [http://www.apiindia.org/medicine\\_update\\_2013/chap120.pdf](http://www.apiindia.org/medicine_update_2013/chap120.pdf).
6. Singhal BS. Multiple sclerosis — Indian experience. *Ann Acad Med Singapore* 1985;14:32-6.
7. Chopra JS, Radhakrishnan K, Sawhney BB, Pal SR, Banerjee AK. Multiple sclerosis in North-West India. *Acta Neurol Scand* 1980;62:312-21.
8. Syal P, Prabhakar S, Thussu A, Sehgal S, Khandelwal N. Clinical profile of multiple sclerosis in north-west India. *Neurol India* 1999;47:12-7.
9. Multiple Sclerosis international Federation , Atlas of MS 2013. [www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf](http://www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf). [Last accessed on 2015 Jul 4].
10. Jain S, Maheshwari MC. Multiple sclerosis: Indian experience in the last thirty years. *Neuroepidemiology* 1985;4:96-107.
11. Bharucha NE, Bharucha EP, Wadia NH, Singhal BS, Bharucha AE, Bhise AV, *et al.* Prevalence of multiple sclerosis in the Parsis of Bombay. *Neurology* 1988;38:727-9.
12. Wadia NH, Bhatia K. Multiple sclerosis is prevalent in the Zoroastrians (Parsis) of India. *Ann Neurol* 1990; 28:177-9.
13. Gangopadhyay G, Das SK, Sarda P, Saha SP, Gangopadhyay PK, Roy TN, *et al.* Clinical profile of multiple sclerosis in Bengal. *Neurol India* 1999;47:18-21.
14. Wasay M, Khatri IA, Khealani B, Sheerani M. MS in Asian countries. *Int MS J* 2006;13:58-65.
15. Mathew NT, Mathai KV, Abraham J, Taro GM. Incidence and pattern of demyelinating disease in India. *J Neurol Sci* 1971;13:27-38.
16. Singhal A, Bhatia R, Srivastava MV, Prasad K, Singh MB. Multiple sclerosis in India: An institutional study. *Mult Scler Relat Disord* 2015;4:250-7.
17. Bansil S, Singhal BS, Ahuja GK, Ladiwala U, Behari M, Friede R, *et al.* Comparison between multiple sclerosis in India and the United States: A case-control study. *Neurology* 1996;46:385-7.
18. Singhal BS, Wadia NH. Profile of multiple sclerosis in the Bombay region. On the basis of critical clinical appraisal. *J Neurol Sci* 1975;26:259-70.
19. Bhatia M, Behari M, Ahuja GK. Multiple sclerosis in India: A.I.I.M.S. experience. *J Assoc Physicians India* 1996;44:765-7.
20. Sarma GR, Nagaraj DK. Multiple sclerosis in South India. *Ann Indian Acad Neurol* 2005;8:71-4.
21. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, *et al.* Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol* 2011;69:292-302.
22. Ebers GC, Sadovnik AD, Risch NJ. A genetic basis for familial aggregation in multiple sclerosis. Canadian Collaborative Study Group. *Nature* 1995;377:150-1.
23. Ebers GC. Genetics and multiple sclerosis: An overview. *Ann Neurol* 1994;36(Suppl):S12-4.
24. Khadilkar S, Sahni A, Agarwal S. A Case control study of environmental risk factors in Indians with Multiple Sclerosis. *Neurology Asia* 2005;10:47-52.
25. Pandit L, Ramagopalan SV, Malli C, D'Cunha A, Kunder R, Shetty R. Association of vitamin D and multiple sclerosis in India. *Mult Scler* 2013;19:1592-6.
26. Elian M, Nightingale S, Dean G. Multiple sclerosis among United Kingdom-born children of immigrants from the Indian subcontinent, Africa and the West Indies. *J Neurol Neurosurg Psychiatry* 1990;53:906-11.
27. Dean G, Elian M. Age at immigration to England of Asian and Caribbean immigrants and the risk of developing multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1997;63:565-8.
28. Wadia NH, Trikannad VS, Krishnaswamy PR. Association of HLA-B12 with multiple sclerosis in India. *Tissue Antigens* 1980;15:90-3.
29. Wadia NH, Trikannad VS, Krishnaswamy PR. HLA antigens in multiple sclerosis amongst Indians. *J Neurol Neurosurg Psychiatry* 1981;44:849-51.
30. Kankonkar S, Jeyanti G, Singhal BS, Shankarkumar U. Evidence for novel DRB1\*15 allele association among clinically definite multiple sclerosis patients from Mumbai, India. *Hum Immunol* 2003;64:478-82.
31. Pandit L, Ban M, Sawcer S, Singhal B, Nair S, Radhakrishnan K, *et al.* Evaluation of the established non-MHC multiple sclerosis loci in an Indian population. *Mult Scler* 2011;17:139-43.
32. Favorova OO, Bashinskaia VV, Kulakova OG, Favorov AV, Boiko AN. Genome-wide association study as a method for genetic architecture analysis in polygenic diseases (by the example of multiple sclerosis). *Mol Biol (Mosk)* 2014;48:573-86.