Characteristics of familial multiple sclerosis in Isfahan, Iran: A cross-sectional study

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Abstract

*Background & Objectives:*Multiple sclerosis (MS) is one of the most common demyelinating diseases of the central nervous system. The disease occurs with higher frequency among families. This study aimed to investigate the frequency and type of familial MS among patients with definite MS registered in the Isfahan Society for MS. *Methods:* A cross sectional study was performed on 3911 MS patients in Isfahan. All patients had a diagnosis of definite MS. Demographic characteristics, medical history, signs and symptoms at onset, course of disease, having a relative with MS, degree and type of relationship were recorded. *Results:* Familial MS was found in 11% of patients, with 57. 7% having a first degree relative with MS. Mean age of patients with familial MS was 36.9±10.4 years, with higher rates among women (female to male ratio 2.6). Highest rate for familial MS was observed in sister-sister relations, and brother-sister relation. Lowest rate was observed in father-son relation.
Conclusions: Familial MS is more common among sisters while father-son relationship has the lowest association. Female to male ratio is 2.6 in familial MS which shows higher rates of males relative to general population.

INTRODUCTION

Multiple sclerosis (MS) is a demyelinating disease of the nervous system. It has been attributed to a variety of factors including genetic factors, autoimmunity and environmental factors.[1] The natural course of the disease varies, from benign to disabling disease with rapid progression.[2] The disease is more common among women and in special geographic locations.[2] Isfahan is considered a low prevalence region in international classification.[1]However, a recent study showed a prevalence of 35/100,000 that indicates a moderate to high prevalence with a sharp increase.[3]

MS has been reported to occur in clusters, in epidemics and in familial form.[1,4] According to some studies, 10-15% of MS patients have an affected relative.[5-7] This risk is higher in siblings than parents or children. The disease is seen in 26% and 2.4% of mono- and dizygotic twins, respectively.[8]Higher rates of MS in families may be explained by both environmental and genetic theories, as relatives might share similar genetic and environmental conditions.[9]

The frequency and characteristics of familial MS has not been studied in Iran extensively. This study aims to investigate the frequency of MS among relatives of MS patients and to determine degree and type of relationship in MS patients in Isfahan.

METHODS

A cross-sectional study was performed on MS patients registered in the Isfahan Societyfor MS in 2011. All patients with a definite diagnosis of MSwere included. Immigrants were excluded. The diagnosis was based on McDonald criteria for MS 2005.Demographic characteristics, medical history, age at onset of MS, EDSS, signs and symptoms at onset, course of disease, having a relative with MS, degree and type of relationship were recorded. Those reporting MS in their first, second or third degree relatives were selected. The relatives were invited for an interview.

Data were analysed using SPSS software. Frequencies were reported as number and percent.

RESULTS

From 3911 patients with MS 430 had a positive family history. Mean age of patients with familial

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MS was 36.9±10.4 years, ranging from 14 to 70 years. Mean age at onset was 29.7±9.6 which is similar among men and women.

In 430 patients with familial MS, 57.7%, 10.5% and 25.6% had only one first, second or third degree relative with MS, respectively. Also, 3.3% had at least one first and third degree relative with MS, 2.6% had second and third degree relative and 0.47% had a first, second and third degree relative with MS. Among patients with familial MS, 27.7% were male and 72.3% were female, with a ratio of 2.61.

From 264 cases with first degree familial MS, 48.5% and 15.9% had a sister and brother with MS, respectively. Mother, father, daughter and sister were the only relative affected in 10.6%, 3.4%, 8% and 0.8%, respectively. The highest relationship was for sister-sister relation, so that 42.4% were sisters, and 24.2% were brother-sister. The lowest relation was among father-son and mother son, and the highest rate was in sister-sister, father-daughter and mother-daughter as shown in Table 1.

The most frequent presenting symptoms was paresthesia of the limbs which was found in 40.7%, and after that vision loss, diplopia, disequilibrium, fatigue and vertigo were seen in 27.7%, 11.6%, 10.5%, 5.1% and 4.2% respectively. EDSS scored did not differ among men and women significantly (not shown in tables).

Relapsing–remitting Ms was the most frequent subtype among first degree relatives with familial MS. Secondary relapsing and primary progressive were in the later stages.

DISCUSSION

This study showed that rate of familial MS is higher among sisters and brothers while father-son relationship had the lowest relationship. Male to female ratio was 2.6 in familial MS which shower higher rates of males relative to general population.

In Saudi Arabia familial MS has been reported in 21% of MS patients.[10] This can be due to the higher rate of parental consanguinity among Arab MS patients which was reported at 37.6%. A large 10-year cohort in Denmark showed that first degree relatives of MS patients have a seven fold increase in risk of MS and a lifetime risk of 2.5%.[11] Another cohort study found a prevalence of 19.8% for familial MS.[2] We found a prevalence of 10.9% which is similar to most studies. Another study in Khouzestan province, Iran found that 11.3% of MS patients had positive family history.[12]

Our patients with familial MS had a mean age of 36.9±10.4 years old. Mean age at onset was 29.7±9.6 with a higher rate among 20-29 and 30-39 age group that included 73% of patients with familial MS. However, mean age of disease occurrence has been reported to be 25 years in Isfahan[13] and 27.24 in Tehran.[14] The mean age in MS patients is 30-39 years in other studies.[2,5] Familial MS has been found in younger ages than non-familial MS in other studies. A study in Spain found that familial MS presents about 8 years sooner than non-familial MS (22 vs 30 years old).[5] Another study on a large population-based sample of PPMS patients found that familial MS starts sooner, with a median age of 37.6 vs 42.7 years.[15]

Familial MS was more common among first and third degree relatives with MS. In other studies frequency of MS in first and second degree relatives of MS patients has been estimated 22.8%.[1-4] A meta-analysis found that relative risk for MS is 9.2, 3.4 and 2.9 in first, second and third degree relatives of MS patients, respectively.[16] In the study performed in Khouzestan province, all patients with positive family history had a first degree relative, with 56.3% and 43.7% having one and two first degree relative with MS, respectively.[12] Higher rate for first and second degree relatives is compatible with theories that support the genetic background of this disease.[8,16]

In our study, familial MS was more common among siblings, with sister-sister relationship having the highest rate. The lowest relation was among father-son and mother son. Mantomoli showed that the risk of MS among siblings is 4.7% which is 31 times higher than general population.[17] Ebers showed that the probability of having MS is 3.5% among siblings.[18] Higher rates among sisters can be attributed to higher prevalence of disease among females. This may be also due to similar genes, similar environment or both.[2] However, a cohort study in Denmark showed relatively similar relative risk for familial MS in parents, offspring and non-twin siblings.[11]

Although MS is higher in women in the general population, among patients with familial MS, men had a significantly higher ratio than women, with a ratio of 2.61. The study in Khouzestan province, Iran also found that positive family history of MS was significantly higher among men.[12] Also, the national cohort performed in Denmark, found that the relative risk of familial MS was lower in females and relatives of male MS patients had higher relative risk compared with female patients.[11]

Table 1: Characteristics of patients with familial multiple sclerosis

	Number	Percent
Sex		
Male	119	27.7
Female	311	72.3
Age group (yr)		
10-19	59	13.8
20-29	196	46/4
30-39	131	30.5
40-49	38	8.9
50-59	12	32.8
60-69	2	0.5
70-99	1	0.2
Degree of relationship		
First degree	248	57.7
Second degree	45	10.5
Third degree	110	25.6
First+third	14	3.3
Second+third	11	2.6
First+second+third	2	0.5
Type of relationship		
Sister-sister	128	
Brother-brother	42	
Sister-brother	27	
Mother	28	
Daughter	21	
Son	2	
Father	9	
Presenting symptom		
Paresthesia	175	40.7
Vision loss	119	27.7
Weakness	22	5.1
Diplopia	50	11.6
Ataxia	45	10.5
Vertigo	18	4.2
incontinence	1	0.2
EDSS		
1-2	3216	
2.5-3.5	317	
4-5	43	
6-7	28	
8-10	7	
Subtype		
RRMS	184	69.7
SPMS	37	14.0
PPMS	19	7.2

EDSS: Extended Disability Status Scale, RRMS: Relapsing Remitting Multiple Sclerosis, SPMS: Secondary Progressive Multiple Sclerosis, PPMS: Primary Progressive Multiple Sclerosis

The most frequent symptoms at onset were limb paresthesia and visual abnormalities which is relatively similar to the general population of MS patients.[3] However, visual symptoms that had been reported higher in Etemadifar study.[3]

We used interview method to investigate familial MS prevalence in the studied population. However, some MS patients might not disclose their disease to their relatives and others as the disease might be associated with social stigma, potentially affecting their marriage and employment opportunities. Therefore, the prevalence of familial MS might have been underestimated.

The main findings of our study show that familial MS is more common among siblings especially sisters in Isfahan. Also men have a higher ratio relative to women in familial MS. Further studies are needed to clarify the underlying genetic or environmental factors that explain this association.

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