Original Article

Late-onset Multiple Sclerosis in Isfahan, Iran

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Abstract

Background: Multiple sclerosis (MS) typically affects young adults; however, the first symptoms can occur after age 50 and is classified as late-onset MS (LOMS).

Methods: In this retrospective study, we extracted the records of 3522 MS patients (2716 females and 806 males) registered in the Isfahan MS Society (IMSS) from 2003 to 2010. Next, we searched for LOMS cases. We aimed to compare these cases with 1698 non-LOMS subjects also extracted from the IMSS database.

Results: We found 48 LOMS patients (28 females and 20 males), which gave a crude frequency of 1.36%. The frequency by sex of LOMS in males (2.4%) was significantly greater than in females (1.0%, $P = 0.002$). The mean age at onset was 55.1 ± 4.3 years. The female to male ratio of 1.4:1 in these patients was significantly lower than in non-LOMS subjects (3.37:1, $P = 0.003$). The leading pattern of MS was relapsing-remitting (RR) in 62.5%, followed by primary progressive (PP) in 27.1%, and secondary progressive (SP) in 10.4%. Predominant presenting symptoms and signs were motor disturbances (35.4%), followed by brainstem (25%), optic neuritis (22.9%), and sensory related deficits (18.7%). The mean progression index (PI) in LOMS patients (0.88 ± 0.48) was significantly higher than in non-LOMS cases, 0.37 ± 0.17 ($P < 0.0001$).

Discussion: In comparing LOMS patients with the non-LOMS cohort, there was a higher frequency of the PP pattern and a higher PI in the LOMS group. In comparing other high-risk populations with the Isfahan cohort, LOMS formed a lower percentage of the total Isfahan MS population.

Keywords: Late onset multiple sclerosis, Epidemiology, Isfahan, Iran.

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Introduction

Multiple sclerosis (MS) usually occurs in young adults, aged 20 to 40. However, 1.1% to 12% of MS patients experience their first symptoms after the age of 50, and this group is defined as late-onset MS (LOMS).[1–11] There is a scarcity of epidemiologic LOMS data, and thus no consensus regarding mode of presentation, disease course, or rate of progression to disability, especially when compared with the younger adult onset MS (non-LOMS) group who develop the disease before the age of 50.[5,7,12,13]

In spite of the increasing prevalence of MS in the Middle East, and specifically in Iran,[14–16] LOMS epidemiological studies have rarely been performed in this part of the world.[14] As far as we are aware, to date, there have been no population-based studies that exclusively describe the characteristics of LOMS patients in Iran.

The aim of our study is to highlight the clinical and demographic features of LOMS in a relatively large Persian cohort that reside in Isfahan, Iran and to compare these characteristics with those of the non-LOMS population. In addition, this study provides more MS epidemiological data from a heretofore under-studied geographical area.

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Materials and Methods

In 2003, a registry of MS patients was created by the Isfahan MS Society (IMSS). The IMSS is the only MS patient referral center that caters to the Isfahan Province; nearly all MS patients living in this geographical area are now being registered. Since 2005, every patient with a diagnosis of clinically definite MS must be registered by the IMSS in order to obtain support for insurance, laboratory investigations, treatment, and rehabilitation. Due to these incentives, almost all diagnosed MS patients in the Isfahan Province have been included in this registry.[14] All diagnosed (McDonald's criteria) LOMS patients registered by the IMSS from April, 2003 to July, 2010 were studied. These cases were extracted from the corresponding total Isfahan MS (TIMS) cohort of 3522 subjects, which was concisely described in our recent demographic report.[16,17]

LOMS patients were defined by the occurrence of first MS symptoms after the age 50. Data gathered from their clinical records included: age at onset, gender, onset and follow-up symptoms and signs, disease course, last visit expanded disability status scale (EDSS), initial MRI pattern, associated co-morbid diseases, and MS family history that extended to and included third degree relatives. All our LOMS patients had an EDSS between 1.0–8.0 and were divided into three sub-groups: mild (1.0–3.5), moderate (4.0–6.0), and severe (6.5–8.0).[18] The progression index (PI) for each patient was calculated by dividing the final study visit EDSS by the disease duration in years.

Table 1. Frequency of onset and follow-up symptoms and signs in the LOMS cohort.

Symptoms/signs	At onset % (*n*)	During maximum six years of follow-up % (*n*)
Motor	35.4 (17/48)	37.5 (18/48)
Sensory	18.7 (9/48)	29.1 (14/48)
Optic neuritis	22.9 (11/48)	16.6 (8/48)
Brainstem	25 (12/48)	27.0 (13/48)
Cerebellar	16.6 (8/48)	20.8 (10/48)
Sphincteric	2.0 (1/48)	6.2 (3/48)
Cognitive	6.2 (3/48)	8.3 (4/48)

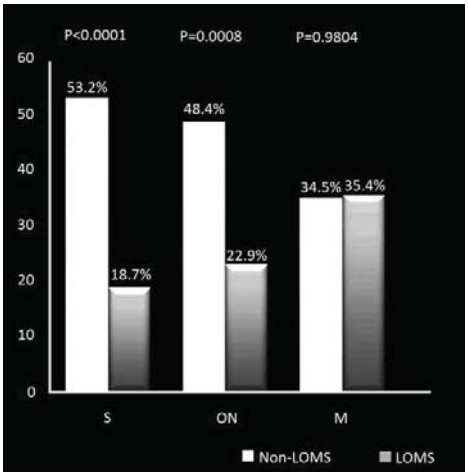

Figure 1. Comparison of LOMS and non-LOMS cohorts according to onset of symptoms and signs (S = sensory, ON = optic neuritis, M = motor).

In 2007, we described in detail the characteristics of the TIMS cohort that included 1718 subjects extracted from the IMSS database from April 2003 to July 2006.[14] In order to compare the clinical and demographic characteristics of the present LOMS patients with non-LOMS cases, we decided to compare the results of the current study with those patients of the 1718 TIMS cohort without LOMS (n = 1698), since the method of case collection and ascertainment in that population was the same.[14] Of note, the mean ± SD follow-up period of these 1698 non-LOMS patients was 6.9 ± 5.3 years.

This study is reviewed and approved by the Institutional Ethics Committee of Isfahan University of Medical Sciences. The data was assumed to be parametric. The sample *t*-test was applied to the quantitative data and the Chi-square test was used for categorical data. All tests were two-tailed. A *P*-value of ≤ 0.05 was considered the significance threshold. Data were analyzed by SPSS software, version 19.0. Results have been reported as mean ± SD.

Results

Of the 3522 TIMS patients, 2716 were women and 806 were men.[16] From this total cohort, 48 (1.36%) were classified as LOMS (28 females and 20 males). The female to male ratio was 1.4:1, which was significantly lower ($P = 0.003$) when compared with the non-LOMS group's gender ratio of 3.4:1. The frequency by sex of males (20/806, 2.4%) was significantly greater than that of females (28/2716, 1.0%, $P = 0.002$).

For the LOMS cohort, the mean disease duration was 5.1±4.7 years (range: 0.5–12 years) and the mean age at onset was 55.1±4.3 years (range: 50 to 68 years). There was no significant gender difference with regards to age at onset, males being 55.5±3.8 years of age and females, 54.7±3.6 ($P = 0.46$). The disease course in 30 (62.5%) patients of the LOMS cohort was relapsing-remitting (RR), 5 patients (10.4%) were secondary progressive (SP), and the remaining 13 cases (27.1%) were primary progressive (PP). The frequency of PP in our LOMS cohort (27.1%) was significantly greater than the non-LOMS group (5.4%, $P < 0.0001$). The mean age at onset of MS for the LOMS patients with PP was 53.1±2.7, RR was 55.1 ± 4.9, and SP was 53.2 ± 2.3 years of age. The most prevalent disease course in both sexes was RR, which comprised 60.7% of female cases and 65.0% of males. RR patients had a mean relapse rate (total number of relapses/year) of 1.42 ± 0.5.

Table 1 shows the frequency of initial and follow-up symptoms and signs in the LOMS cohort. Figure 1 illustrates the comparison between 48 LOMS and 1698 non-LOMS patients regarding onset of symptoms and signs. Among LOMS patients, 9 (17.8%) had multiple symptoms and signs at onset while the remaining 39 patients (81.2%) had only a single symptom.

The mean EDSS at the last visit was 2.4 ± 1.4. At this visit, the following degrees of disability were observed: 41 patients (85.4%) were mildly disabled, 6 (12.5%) had moderate disabilities, and only 1 (2.1%) was severely disabled. The mean PI in LOMS patients (0.88 ± 0.48) was significantly higher than in the non-LOMS group, which was 0.37 ± 0.17 ($P < 0.0001$).

MRI scans performed at diagnostic presentation were available for all LOMS patients. MRI plaque locations were supratentorial in 45 (93.7%), infratentorial in 17 (35.4%), and spinal in 14 (29.1%) patients.

Among the LOMS group, six cases (12.5 %) had a positive MS family history in either their first, second or third degree relatives. This finding was in line with the characteristics of non-LOMS patients (12.1%), which was not statistically different ($P = 0.86$). All LOMS patients were married, but only 67.2% of non-LOMS patients were or had been married; such a difference was statistically significant ($P<0.0001$). Associated co-morbid disorders included cardiovascular disease, myasthenia gravis, hypothyroidism, breast cancer, and diabetes mellitus, each disease occurring in an individual.

Discussion

Compared to other study cohorts our calculated rate of LOMS is relatively very low[3–11] and this may be attributable to genetic and/or environmental differences, different criteria for defining/diagnosing LOMS, or perhaps our under-recognition of LOMS. MS after age 50 may be underestimated because of the difficulty of differentiating MS from other neurological diseases which occur in this age range.[3,5,7,12] On the other hand, overestimation can easily occur since the disease can start surreptitiously before the age of 50 in some patients with minor, overlooked, or forgotten symptoms.

The female to male ratio in LOMS patients has been generally reported to be the same as in younger patients,[5] but our findings demonstrated a significantly lower ratio of women to men in the Isfahan LOMS group compared to the non-LOMS cohort as well as some previous studies, although women were still predominant.[5,9,12,13]

Our LOMS patients tended to be in marital relationships more often than those of the non-LOMS cohort. This was probably reflective of their disease occurring later in life and enabling marriage before disability interfered with such a relationship.

Most studies have found that the frequency of the PP pattern of MS is greater among LOMS patients in comparison with younger adult MS patients, which tends to lead to more rapid disability in this older group.[2,5,7,8,11,12] Our results have also shown a higher PP frequency in the LOMS group (27.1% LOMS vs. 5.4% non-LOMS). The mean PI of our LOMS patients compared with the non-LOMS cohort was significantly higher as has been reported in other studies.[5,7–10,12] This may indicate more rapid disease progression in LOMS.

The majority of our LOMS patients had a monosymptomatic onset; our findings were consistent with a previous report in which 71.9% had a monosymptomatic onset.[5]

Our results are also in line with other investigations reporting that the most common initial presentation in LOMS is a motor symptom or sign.[5,7,8,11,12] Motor symptoms and signs have been reported to occur more frequently in LOMS than in younger adult MS patients.[4,5,7–9,12] However, in our study (Figure 1), the frequency of motor symptoms and signs at LOMS presentation was approximately similar to that of the non-LOMS population. As found in other studies,[5,12] the frequency of optic neuritis and sensory signs and symptoms as initial manifestations in our LOMS patients was less than that of our non-LOMS cohort.

In conclusion, in Isfahan Province, Iran, we observed a lower percentage of LOMS, which was in contrast to other high risk areas for MS. In addition, LOMS was more frequent in male than female MS patients. The LOMS group had a predominantly monosymptomatic onset, most commonly being of a motor type. Our LOMS patients, in contrast to the non-LOMS cohort, had a more rapid disease progression, higher frequency of PPMS, and a lower frequency of sensory symptoms and optic neuritis at presentation.

Disclosure Statement

The authors have no proprietary interest in the materials presented herein.

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