Frequency distribution of the first clinical symptoms in the Iranian population with multiple sclerosis

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Abstract
Background: Initial symptoms of multiple sclerosis (MS) may be varied and nonspecific. We tried to find the frequency distribution of the first clinical symptoms in Iranian patients with MS.

Methods: In a case series study, 1130 patients with definite diagnosis of MS who had been referred to three referral university hospitals of Tehran, Iran, were enrolled. The patients’ medical records were reviewed for neurological history to find the first symptom at presentation.

Results: 884 (78.2%) patients were female and 246 (21.8%) were male. The mean ± SD age of patients was 31.4 ± 9.1 years. The most common initial symptoms were motor in 492 (43.5%), ocular in 366 (32.4%), cerebellar in 91 (8.1%), sensory in 76 (6.7%), cranial nerve involvement in 51 (4.5%), and fatigue in 23 (2%) patients. There was no difference between female and male patients in first clinical symptoms (P > 0.05).

Conclusion: The motor symptoms were the most common finding at presentation in the Iranian population with MS. Complementary studies with larger sample sizes are needed to increase the external validity.

Introduction
Multiple sclerosis (MS) is primarily an inflammatory demyelinating disease of the central nervous system with varied clinical presentations and heterogeneous histopathological features. MS results in a plethora of neurological manifestations and is a leading cause of nontraumatic disability among young adults. The pathogenesis of MS is unknown, and its pathophysiology is complex and involves genetic susceptibility, environmental factors, and development of a pathologic immune-mediated response leading to focal myelin destruction, axonal loss, and focal inflammatory infiltrates.

MS incidence rates vary significantly depending on geographic location and ethnic origin. Recent studies indicate a relatively high prevalence of MS in the Iranian population. The reason for this increasing prevalence remains elusive.

Sensory and/or motor dysfunction, increased tendon reflexes, ataxia, blurred vision, brain stem symptoms (dizziness, double vision, impaired speech), and urinary disorders are the main neurological symptoms and signs of MS. This study tried to survey the frequency of first clinical symptoms in MS patients.

Materials and Methods
This case series study was done from 2008 to 2010 in Loghman Hakim, Imam Hossein, and Shohada referral University Hospitals in Tehran, Iran. Patients suffering from definite MS based on McDonald criteria were enrolled in this study. Patients with the following disorders were excluded: stroke, B12 deficiency, HIV, Lyme, HTLV1, collagen vascular diseases, sarcoidosis, leukodystrophy, Spino-
cerebellar diseases, Arnold-Chiari malformation, brain tumors, and abscesses.

Informed written consents had been collected from the patients before the study began. The background history, and the patients' clinical signs and neurological examinations were recorded. The first clinical neurological symptoms such as blurred vision, sensory, motor, pyramidal, cerebellar, sphincter control abnormalities, seizures, allodynia, involvement of other cranial nerve, affective disorders, or fatigue were recorded.

Results
Of the 1130 patients who participated in this study, 884 (78.2%) were female and 246 (21.8%) were male. The mean ± SD age of patients was 31.4 ± 9.1 (10-58 years). 129 (11.4%) patients were below 20 years of age, 790 (69.9%) were 20-40 years old, and 211 (18.7%) were above 40.

Table 1 shows the frequency and ratio of first clinical symptoms according to patients' gender. There was no difference between female and male patients in first clinical symptoms (P > 0.05).

Discussion
According to our series motor symptoms such as paraplegia, paraparesis, monoparesis, quadriplegia, quadriparesis, and hemiparesis were the most common neurological symptoms in MS patients. Ocular symptoms like blurred vision and diplopia were common in this group. Cerebellar signs (ataxia and spastic ataxia), sensory symptoms, involvement of other cranial nerves, and fatigue were less common. Seizures, affective disorders, tremor, allodynia and sleep paralysis were rarely seen as the first symptoms of MS. Observed movement disorders in patients were dystonia, postural tremor, and hemifacial spasm.

MS is a highly polymorphic disease characterized by diverse neurological signs and symptoms. The susceptibility of various populations to and the clinical patterns of the disease are thought to be different. In 2008, Ashtari et al. surveyed 227 MS patients to identify the characteristics of early-onset Multiple Sclerosis (EOMS) in comparison to the adult-onset form (AOMS) in Isfahan, IRAN. The most common presenting symptom was optic neuritis in the EOMS group and paresthesia in AOMS. Optic neuritis was also common in AOMS, but brainstem/cerebellar signs were more common in EOMS than AOMS. Seizure occurred more frequently in EOMS than in the AOMS group. In our previous study on 200 patients suffering from MS in Iran, we showed that female to male ratio was five and the pyramidal signs were the most common symptom.

Two patients have been reported to have choreiform dyskinesia, and ataxia as the initial clinical manifestation. In both cases MRI findings showed MS plaques in the midbrain and in the lower surface of the right red nucleus. In another study conducted by Gout et al., in France, they showed that visual and sensory symptoms were the most common clinical manifestations. This study indicated that about one third of MS patients had demonstrated previous inflammation before onset of first clinical and laboratory findings.

In another study that was conducted by Berger et al., unilateral dystonia has been reported as the first manifestation of MS.

In a systemic review on the Arab population from 1975 to 2007, available data for the Kuwaiti, Jordanian, Libyan, Saudi, Iraqi, Palestinian, and Omani populations were studied. The clinical pattern of MS was generally similar to that in western countries. However, one study from Oman found a high rate of optic-spinal disease (affecting one third of patients) and a low rate of oligoclonal bands (OGBs) (only one third of patients); this pattern resembles that of MS described in Asian countries.

| Gender | First symptoms | Seizure | Abnormal movement | Sleep paralysis |
|--------|----------------|---------|-------------------|----------------|
|        |     |        |       |                |                |
| Female | 884 | 3 | 65 | 44 | 6 | 18 | 6 | 58 | 374 | 300 | 6 | 3 | 1 |
|        | 100% | 0.3% | 7.4% | 5% | 0.7% | 2% | 0.7% | 6.6% | 42.3% | 33.9% | 0.7% | 0.3% | 0.1% |
| Male   | 246 | 1 | 26 | 7 | 0 | 5 | 2 | 18 | 118 | 66 | 2 | 1 | 0 |
|        | 100% | 0.4% | 10.6% | 2.8% | 2% | 0.8% | 7.3% | 48% | 26.8% | 0.8% | 0.4% |
| Total  | 1130 | 4 | 91 | 51 | 6 | 23 | 8 | 76 | 492 | 366 | 8 | 4 | 1 |
|        | 100% | 0.4% | 8.1% | 4.5% | 0.5% | 2% | 0.7% | 6.7% | 43.5% | 32.4% | 0.7% | 0.4% | 0.1% |
Conclusion
There are some variability in the first clinical manifestations of and findings on MS patients comparing to previous reports. More epidemiological studies are necessary to evaluate the first clinical symptoms of MS.

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