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Multiple sclerosis in East Azerbaijan, North West Iran

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Abstract

Background and Objective: Multiple sclerosis (MS) is variable in its prevalence and manifestations in different regions of the world. Iran is one of the most populous countries in Middle East, it is important to have a better understanding of the epidemiology and clinical pattern of MS in different parts of Iran. Although Iran is said to be located in the low-risk area, recent studies have shown that the prevalence of MS in Iran may be much higher than what was previously thought. This study determines the current prevalence and clinical features of MS in East Azerbaijan province, North West Iran. *Methods:* All patients for this study were MS cases listed in the Committee for Diagnosis and Treatment of MS (CDTMS) registry. The study patients were all residents of East Azerbaijan Province who were diagnosed with MS by neurologists. *Results*: Out of one thousand cases, 269 were males (26.9%) and 731 females (73.1%).The female/male ratio was 2.7. The crude prevalence of MS in East Azerbaijan was 27.7/100,000 population. The mean age (SD) of patients was 33.4 (8.9) years. The relapse-remitting form of disease was seen in 67.7% of patients; primary-progressive disease in 2.8%; and secondary progressive disease in 11.2%.
Conclusion: Our study suggests that MS prevalence in North West Iran lies in the medium frequency range.

INTRODUCTION

Multiple sclerosis (MS) is a common demyelinating autoimmune-mediated disorder of the central nervous system.[1,2] MS has considerable social impact and economic consequences despite its relatively low prevalence. It is the major cause of non-traumatic and permanent disability in young adults.[3,4] Despite the wealth of epidemiological data from the many studies over the last 70 years, studies to redefine the pattern of MS in a geographic region can be a difficult task.[5] Previous studies have shown that MS is distributed throughout the world with three zones of high, medium, and low frequency. High-frequency areas have prevalence rates of 30 and above per 100,000 populations. These regions are bounded by areas of medium frequency with prevalence rates of 5–29, and mostly 15–25 per 100,000. The low frequency area has a prevalence rate of fewer than 5 per 100,000 populations.[6] MS in Asia, and many parts of the non-Western world lies in the low frequency area; their clinical manifestations are also different from that described in standard text books.[7]

Previous studies from the Middle East have indicated the importance of genetic-historical factor in affecting the distribution of MS. MS prevalence among the Arabs was reported to be between 4 and 8 in 100,000.[5] However; some recent studies in Arabic countries have suggested that the MS prevalence may be on the rise, and MS frequency in parts of the regions may be in the medium range.

As Iran is one of the most populous countries in the Middle East, a study of the epidemiology and clinical pattern of MS from various parts of Iran is important. Although Iran has also been said to have low frequency of MS, researchers have demonstrated that exceptions do exist. For example Saadatnia and colleagues reported that the MS prevalence in Isfahan was approximately 43.8/100,000.[8] Another study in Mazandaran (a province in North Iran) in 2007 also reported a relatively high MS prevalence of 20.1/100,000, with a 95% confidence interval (CI) of 18.7-22.1.[9] In this study, our objective was to determine the current prevalence of MS in the East Azerbaijan province of Iran.

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METHODS

East Azerbaijan province is located in North West Iran. The province covers an area of approximately 47,830 km^2 with most of the area situated over 1,000 meters above sea level. It has common borders with the Republics of Azerbaijan, Armenia and Nakhchivan. East Azerbaijan has a cool and dry climate, being in the main a mountainous region. Temperatures run up to 8.9 °C and 20 °C in summer, and dropping to -10 to -15 °C in winter.[10] The province has a population of approximately 3.6 millions (male 1.84 million and female 1.76 million), according to the national census in 2006.[11] The study patients were from the registry of the Committee for Diagnosis and Treatment of MS (CDTMS). CDTMS was developed by the Ministry of Health (MOH) of Iran. It is the only referral centre for MS patients in all the provinces throughout the country. It was established to supervise and control the distribution and use of governmental resources for the treatment of MS with interferons. Three academic Neurologists who are elected by the Departments of Neurology in the Schools of Medicine take part in the CDTMS. East Azerbaizan. Registration of MS patients was started in 2005. All the study patients were residents of East Azerbaijan Province. They were all diagnosed with MS by their neurologists. The patients were also personally examined by one of the neurologists of CDTMS to confirm the diagnosis. The details of the study patient were extracted from the records. Patients were diagnosed and classified according to McDonald criteria by the International panel for MS diagnosis.[8,12] The population data of East Azerbaijan used for calculating the prevalence rate was based on the 2006 census, from the Iranian Central Bureau of Statistics.

Data analysis

The analysis of data was performed with SPSS software (16th edition). MS prevalence rates per 100,000 persons were calculated by gender and age groups. All tests for statistical significance were two-tailed, with the level of significance at $\alpha<0.05$.

RESULTS

In August 2009, there were 1,000 cases of MS in CDTMS who were East Azerbaizan residents. Two hundred sixty nine were males (26.9%) and 731 females (73.1%). Of the 1,000 patients 964 (96.4%) were Azeri, 25 (2.5%) were Farsi speaking and 1% were of other ethnic groups (Kurd, Lor, Baluch, and others).The female/male ratio was 2.7. The crude prevalence of MS in East Azerbaijan was estimated to be 27.7/100,000 population. Age-sex specific prevalence is shown in Table 1.

The mean age (SD) of patients was 33.4 (8.9) years. The youngest patient was a 12 year-old girl and the oldest was a 61-year-old woman. Patients with disease onset at 16 years or younger were considered as early-onset.[13] In this study women had statistically higher percentage of early-onset MS when compared to men (6.4% vs. 3%). As for the form of illness, relapse-remitting (RRMS) disease was seen in 67.7% of patients, secondary progressive (SPMS) disease in 11.2%, relapsing progressive (RPMS) disease in 3.8%, and primary progressive (PPMS) disease in 2.8% (Table 2). The mean age (SD) at onset of illness was 32.5 (8.3) years in RRMS, 37.3 (7.3) years in RPMS and 38.52 (8.40) years in SPMS, and 39.3 (9.0) years in PPMS. The differences between ages at onset of patients with the four forms of illness

Table 1: Age- specific prevalence of MS in East Azerbaijan, 2009

Age	Male			Female			Total		
	n	population	Prevalence*	N	population	Prevalence*	n	population	prevalence*
0-14	0	427,036	–	1	404,456	0.2	1	831,492	0.1
15-24	35	455,583	7.7	138	426,464	32.4	173	881,847	19.5
25-34	104	335,163	31.0	279	329,191	84.8	383	664,354	57.6
35-44	86	238,695	36.0	227	230,468	98.5	313	469,143	66.7
45-54	37	167,238	22.1	72	166,801	43.2	109	234,039	46.6
>55	5	215,626	2.3	8	206,955	3.8	13	422,581	3.1

***prevalence per 100,000 population**

Table 2: Comparison of the clinical patterns and disability according by sex

	Male N (%)	Female N (%)	P value
Age : mean (SD) in years	34.7 (9.31)	32.9 (8.8)	0.093
Age at onset: mean (SD) in years	28.9 (8.3)	27.9 (8.2)	0.736
Early onset of MS (≤16 years)	8 (3.0)	47 (6.4)	0.034**
Family history of MS			
No	239 (89.8)	679 (93.9)	0.028**
YES	27 (10.2)	44 (6.1)	
EDSS: mean (SD)	3.7 (2.1)	3.3 (2.2)	0.452
*Diagnostic delay : months (SD)	21.8 (32.8)	21.4 (33.8)	0.757
Clinical forms of MS:			
Relapsing- remitting	159 (64.6)	471 (68.8)	0.122
Primary progressive	10 (4.1)	16 (2.3)	0.178
Secondary progressive	29 (11.8)	75 (10.9)	0.811
Relapsing- progressive	17 (6.9)	18 (2.6)	0.003**
Clinically isolated syndrome	31 (12.6)	105 (15.3)	0.245

* Time between onset of symptoms and diagnosis of MS
**P values derived by chi^2

were not statistically significant. Table 2 compares some of the characteristics according to gender. Significantly more men with MS (10.2%) had family history of MS as compared to women (6.1%).

DISCUSSION

Previously, Iran was regarded as a low-risk area for MS.[14] In this study the prevalence of MS in East Azerbaijan, North West Iran was determined to be 27.7/100,000. This study shows that the prevalence of MS in East Azerbaijan falls into the medium frequency range.[6] Reports of prevalence studies of MS in other parts of Iran also show similar finding. Abedini and colleges estimated that the MS prevalence in north of Iran was 20.1/100,000.[9] Etemadifar[14] and Sadatnia[8] reported higher prevalence of MS in Isfahan, central region of Iran, as 35.5 and 43.8/100,000 respectively. We believe that in our study, only negligible numbers of patients were missed by CDTMS. This was because the cost of MS treatments was too expensive for the average individuals without access to governmental resources, and CDTMS provided for the treatment for all patients diagnosed with MS. Table 3 lists the prevalence of MS in various parts of Iran and other countries in the Middle Eastern region. As shown, there is a considerable variation in the prevalence reported. Factors contributing to this variability probably include different methods of study, evolving diagnostic criteria, and referral bias. Genetic factor, geographical differences, environmental risk factors probably also affect the prevalence rate.[5,15,16] Recent advances in magnetic resonance imaging (MRI) and an easier access to MRI in Iran is probably another important factor in the increase in diagnosis of MS, and thus its prevalence estimation.[8]

In this study approximately two thirds of our patients were females. This female preponderance is higher than other Arabic countries in the Middle East such as Kuwait[17], Iraq[18], Saudi Arabia and Jordan.[19] In Lebanon, Yamout and colleagues found a high female/ male ratio of approximately 3.[20] The female/male ratio in previous studies in other parts of Iran varied from 1.2 to 3.6.[8,9,12,21-23]

A number of previous studies have reported that 0.4–5.6% of MS patients have their onset of symptoms before the age of 16.[24,25] In our study, there were 24 cases (5.6%) of early-onset of MS. The female/male ratio in the early-onset patients was 5.8. This ratio was higher than the study in Isfahan.[8] Ashtari and her colleagues also reported a high female/ male ratio in early-onset MS of 4.47.[26] As for previous studies from the Arabic countries, the data on early-onset MS is

Table 3: The prevalence of multiple sclerosis (per 100,000) in Iran and some of Middle East countries

Study	Study population	Year	Diagnosis citeria	Total Prevalence in 100,000
Yousefipour[23]	Iranian (Fars)	1990	-	5.3
WHO[28]	Iranian	1991	-	4
Sadatnia[8]	Iranian (Isfahan)	2003-2006	Mc Donald	43.8
Etemadifar[14]	Iranian (Isfahan)	2004	Mc Donald	35.5
Abedini[9]	Iranian (North of Iran)	2007	Mc Donald	20.1
Milo[16]	Iranian	2010	-	44
Tharakan[15]	Omani	1990-2000	Poser	4
Hamdi[15,18]	Iraqi	1967-1969	Schumacher	3.4
Yaqub[15]	Saudi	1983-1986	Poser	8
Al-Din[15]	Jordanians	1993	Poser	20
Al-Din[15]	Palestinians	1992-1993	Poser	42
Al-Din[15]	Palestinians	1981-1983	Poser	7.3
Al-Din[15]	Kuwaitis	1981-1983	Poser	4.44
Alshubaili[15]	Kuwaitis	2000	Poser	31.15

difficult to interpret. This is mainly because there were varied definitions of early-onset MS in the different studies. For example, in a study from Oman where patients under 19 years old were defined as early-onset MS, the female to male ratio was 5:1.[15]

Consistent with prior studies conducted in Tehran and Isfahan[8,14,21], the most prevalent clinical form of MS in our study was RRMS (67.7%). The RRMS affected 60–90% of patients in the Arabic populations.[15,17-20] PRMS featured in 2.8% of our patients. The proportion of PRMS in East Azerbaijan appears to be lower than that reported from the other parts of Iran, as well as the rest of Middle East.[8,14,17-19,22]

Figure 1. Location of East Azerbaijan within Iran

In our cohort of MS patients, there was a family history of MS in 71 patients (7.2%). Of these, 63.8% had first-degree affected relatives. The proportion of patients with positive family history in the other regions of Iran was higher (approximately 12%).[8,14] A positive family history of MS in studies from elsewhere varied from 0 to 9.3%.[15,18-20] There is a very strong evidence that familial aggregation is determined by multiple genes. This is based on the data from twins, adoptees, half-sibling and the offspring of conjugal pairs.[27]

As shown in Table 3, according to WHO in 1991, the prevalence of MS in Iran was estimated to be approximately 4/100,000 population. Yousefipour and his colleges in 1990 also reported the prevalence of MS in Iran to be about 5/100,000. However, in two recent studies in Isfahan[8,14], the prevalence of MS in Central Iran was estimated

to be much higher, at 35.5 and 43.8 in 100,000 population. Abedini[9] in 2007 also reported a relatively high prevalence of MS in North Iran, at about 20.1/100,000, similar to our estimation of 27.7/100,000 populations in East Azerbaijan. It thus appears that there is an increase in prevalence of MS in Iran in the recent years. However, it remains uncertain whether this apparent increase is real, or a reflection of increased diagnosis of the disease, due to easier access to neuroimaging facilities, and increasing number of neurologists in the Iranian health system. Future repeat studies on the same population using the same diagnostic criteria may help to resolve this question.

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