

Characteristics of a Series of Multiple Sclerosis (MS) Patients Observed at the National MS Beta-Interferon Committee in Jordan Over a One-Year Period (August 2009-August 2010)

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Abstract

Objective: To study the characteristics of multiple sclerosis (MS) in a series of Jordanian patients observed at the Beta-Interferon Committee and compare them with those from other Arab/Middle Eastern or Western countries.

Methods: Data from 101 patients with MS attending the Jordanian National MS Beta-Interferon Committee over a one-year period, from August 1, 2009 to August 1, 2010, were collected.

Results: Mean age at MS onset was 27.1 years, with 70 females and 31 males (F/M ratio=2.26:1) with a peak incidence in the 3rd decade. Ten patients, all female, had early onset (below 18 years of age). The mean disease duration was 3.3 years, with almost 1/2 of the patients having a short duration below one year. The most common clinical manifestation was limb weakness with pyramidal signs related to myelopathy followed by optic neuritis and brainstem symptoms. The most common MS pattern was relapsing-remitting (RR) in 66 patients with a relatively high number of clinically isolated syndromes (CIS) in 28 patients. There were 34 new cases in 2009 and 23 new cases over the study year (August 2009-August 2010), showing a trend toward an increase in incidence compared to previous years. All 101 patients were born and/or live in the center/North of Jordan and none in the South, with 69 patients in the capital Amman. Beta-Interferon was used in 81 patients.

Conclusions: The general characteristics of MS in Jordan were similar to most Arab countries and Western reports. There is a possible north/south gradient of MS in Jordan and a trend toward an increase in incidence in recent years.

Keywords: Multiple sclerosis, Beta-Interferon, Jordan

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Introduction

Multiple sclerosis (MS) is a disease of the

central nervous system of unknown etiology.¹

It is the second most common cause of neurological disability arising in early to

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middle adulthood, after trauma, in Western countries.² MS has an unequal distribution worldwide,^{3,4} and it affects approximately one million young adults, mostly women, worldwide.⁵ It is known to show variable prevalence rates, demographic and clinical manifestations depending on geography and ethnic background.¹ It is generally believed that MS prevalence is low in Middle Eastern countries.⁶ Many studies about MS came from Arab countries.⁷ Therefore, this study was done with the aim of delineating the characteristics of MS in Jordan, including incidence, geographic distribution, age of onset/ gender ratio, clinical presentation, and MRI features, MS pattern and use of Beta-interferon. Results will be compared with those from other Arab/Middle Eastern and Western countries.

Methods

Beta-interferon is fully covered by the medical insurance of the Jordanian Ministry of Health(MOH) for all classes of Jordanians. Due to its high cost, the MOH decided to establish a National MS Beta-interferon Committee in 2002 (which will be referred to as the 'committee'), including 4 neurologists from the public sector, with the aim of applying international criteria for the use of Beta-interferon. Up to this date, 450 patients referred from the private and public sectors(except military-insured patients) are receiving Beta-interferon through this 'committee', which is still functional. The patients were referred either from 3 major MOH hospitals(one in the capital Amman, one in Irbid in the North of the country, and one in Karak in the South), one major university hospital in Amman, or from neurologists in the private sector.

Following the signature on a consent form, information was collected from a predesigned data sheet including the patient's age/gender, place of birth, actual area of residence in Jordan, date of the onset of symptoms, number/type/date of relapses, disease duration, MS pattern/course, Expanded Disability Status Scale (EDSS)⁸ at presentation, the number of lesions on the MRI brain/spinal cord, and the eligibility for Beta-interferon. Consecutive Jordanian MS patients fulfilling the McDonald's criteria⁹ for clinically definite MS as well as MS patients with a clinically isolated syndrome(CIS), attending the 'committee' over a one-year-period (from August 1, 2009 to August 1, 2010) were included. The diagnosis of a CIS was based on a well-defined demyelinating neurological event suggestive of MS and confirmed by neurological examination in addition to a brain MRI showing at least 4 lesions characteristic of MS, with a minimum diameter of 3 mm (one of which was ovoid or periventricular).¹⁰ The clinical course classification included relapsing-remitting (RR), secondary progressive (SP) and primary progressive (PP) MS according to the criteria of Lublin and Reingold.¹¹ The acute relapse was defined according to Poser's criteria as an acute onset of new symptoms or signs or worsening of previous symptoms for more than 24 hours, preceded by stability for at least 6 weeks in the absence of metabolic cause such as fever.¹² The patients were evaluated at one stage of their illness (either early after onset or after a few years). The diagnosis was based on McDonald's criteria.⁹ Inclusion criteria for the use of Beta-interferon were for patients above the age of 12 years, who were clinically stable (namely, either not in relapse or having had a relapse before at least 3 months), and they were enrolled if they had at least 2 relapses in

the preceding 2 years and were ambulatory with an EDSS of 0 to 5.⁸ We also included CIS patients who had 4 or more MRI lesions. We excluded patients with SP MS, PP MS, pregnancy, severe depression, or psychiatric disease and patients who received previous immunosuppressive agents in the year preceding the enrollment.

A simple statistical analysis was used by calculating percentages of all findings and then by tabulating them.

Results

We included 101 patients, 70 females and 31 males; F/M ratio=2.26:1. The age and gender distribution at MS onset is shown in table 1.

The mean age of onset was 27.1 yrs (range 13-48 yrs); the mean age in males was 31.2 yrs and in females 25.7 yrs. Ten patients (all females) had an early MS onset below 18 yrs of age. The mean age of onset in RR patients was 28.4 yrs and PP patients 33.6 yrs. The mean disease duration (from the onset to the clinical assessment) was 3.3 yrs (range 1 month-26 yrs). Fifty out of 101 patients (49.5%) had a duration of less than one year, 27 (26.7%) less than 5 yrs, 10 (9.9%) between 5 and 9 yrs, 9 (8.9%) between 10 and 14 yrs, and 5 (5%) 15 yrs or longer. Thus, half the patients had a short duration of illness and a low proportion had a long duration (5% more than 15 yrs).

Table (1): Age and gender distribution

| <i>Age of onset(yrs)</i> | <i>Gender</i> | | <i>Total</i> |
|--------------------------|---------------|---------------|--------------|
| | <i>Male</i> | <i>Female</i> | |
| <i>11 – 20</i> | - | 23 | 23 |
| <i>21 – 30</i> | 18 | 28 | 46 |
| <i>31 – 40</i> | 8 | 17 | 25 |
| <i>41 – 50</i> | 5 | 2 | 7 |
| <i>Total</i> | 31 | 70 | 101 |

The most common clinical manifestations are shown in table 2. The mean number of relapses was 1.8 with a 0.6 relapse/year. We noticed a relatively high number of cases of CIS (28 patients) and among them 14 were monofocal, i.e., MS affecting only one organ system at onset, and 14 multifocal affecting more than one organ system. Among the 14 patients with monofocal CIS, 6 had motor symptoms, 3 sensory, 4 optic neuritis, and one with diplopia. The mean EDSS score at presentation was 2.6 (range 0-5.5), with the majority (81 patients) having an EDSS between 0 and 3.

Table 3 shows the number of newly diagnosed MS patients according to the year of clinical onset, and it demonstrates a trend toward an increase in the number of cases in the last decade (2000-2009): only one patient for the period 1980-1989, 11 patients for 1990-1999, and 89 patients for the period 2000 to mid-2010 (the last new MS case in our cohort was recruited in May 2010). There were 34 new MS cases diagnosed in 2009 and 23 cases during the study year (August 1, 2009 to August 1, 2010), thus showing a trend toward an increase of new MS cases compared to the previous years in the same decade. The 34 new

cases diagnosed in 2009 were homogeneously distributed over the year with, however, 2

small peaks in June and October (7 and 6 patients, respectively).

Table (2): Clinical manifestations and MS pattern

| Manifestation | number(%)* |
|-------------------------------------|-------------------|
| <i>Myelopathy</i> | |
| <i>Motor</i> | 72 (71.3%) |
| <i>Sensory</i> | 61 (60.4%) |
| <i>Optic neuritis</i> | 43 (42.6%) |
| <i>Brainstem</i> | 41 (40.7%) |
| <i>Diplopia (III,VI)</i> | 30 (29.8%) |
| <i>Others#</i> | 11 (10.9%) |
| <i>Cerebellar syndrome</i> | 30 (29.8%) |
| <i>Seizures</i> | 2(2%) |
| MS PATTERN | |
| <i>Relapsing remitting</i> | 66 (65.3%) |
| <i>Clinically isolated syndrome</i> | 28 (27.8%) |
| <i>Secondary progressive</i> | 4 (3.9%) |
| <i>Primary progressive</i> | 3 (3%) |

*number of occasions, some patients having more than one symptom.

dysarthria, facial palsy, V neuralgia, vertigo, inter-nuclear ophthalmoplegia.

Table (3): Number of newly diagnosed MS cases according to year of onset

| Year of onset | Number of cases |
|--------------------------------|------------------------|
| 1984 | 1 |
| 1993 | 1 |
| 1994 | 1 |
| 1995 | 2 |
| 1996 | 1 |
| 1997 | 4 |
| 1998 | 2 |
| 2000 | 2 |
| 2002 | 3 |
| 2003 | 2 |
| 2004 | 2 |
| 2005 | 4 |
| 2006 | 6 |
| 2007 | 13 |
| 2008 | 11 |
| 2009 | 34 |
| 2010(I st 5 months) | 12 |
| TOTAL | |

The map shows the geographical distribution of Jordanian MS patients born and/or living in Jordan. Seventy-one out of 101 patients were born in Jordan and 30 abroad, among them 18 in the Gulf states (majority in Kuwait=10 patients).

In total, Beta-interferon was used in 81 patients. Among 66 patients with RR MS, Beta-interferon was used in 62 (Beta-interferon 1 b in 30 and Beta-interferon 1 a in 32), not

being used in the remaining 4 because they had a recent relapse prior to the visit to the MS committee with an EDSS score above 5.

Among 28 patients with CIS MS, Beta-interferon was used in 19. It was not used in the remaining 9 because they had less than 4 MRI brain/spinal cord lesions. None of the patients with SP MS or PP MS received Beta-interferon.



Geographical distribution of MS patients born and / or residing in Jordan: Amman (n=69); Zarqa (n=12); Irbid (n=12); Jerash(n=2); Madaba(n=2); Salt (n=3); Mafraq (n=1); n=number of patients.

Discussion

Several points emerge from this study of 101 Jordanian MS patients seen over a one-year-period at the National MS Beta-Interferon

committee.

The mean age of onset in our patients was 27.1 yrs with a peak incidence in the 3rd decade, similar to studies from other Arab countries,¹³⁻

²² but lower than in others where the highest prevalence was in the age range 30-39 yrs.^{23,24} In accordance with reports from Lebanon and Iraq,^{22,23} the mean age of onset was higher in our male patients (31.2 yrs) compared to females (25.1 yrs), and almost 2/3 of our patients had onset between the ages of 21 and 40 yrs. Our patients with PP MS developed the symptom onset at a later age than those with RR MS (mean age 33.6 yrs vs.28.4 yrs), in agreement with others.²² Ten of our patients (10%) had early onset MS, i.e., before the age of 18 yrs, whereas in another Jordanian study,¹³ 44 out of 227 patients (19.4%) had early onset MS. According to Western reports,²⁵⁻²⁷ only about 3-5% of patients of all MS cases occur before the age of 15 yrs.

In our study, females were more affected than males, at a ratio of 2.26:1, which is similar to all other Arab studies^{13-23,28-31} where female-to-male ratios ranged from 1.1:1 to 3:1, and also agrees with other Western and Middle Eastern studies.³²⁻³⁴ All our 10 patients with early onset MS (under 18 yrs) were female indicating a possible role for puberty hormonal changes in MS onset. This disagrees with another Jordanian study¹³ where the female to male ratio in patients with early onset MS (under 19 yrs) was 5:1 which was, however, higher than the ratio in late onset MS. According to Bohlega,³⁵ female MS patients predominate in the ratio of 1.5:1 and a majority have the disease onset between the ages of 20-39 yrs, with more females presenting before the age of 20 yrs. In accordance with others,³⁶ a monofocal presentation was noted in 60% of early onset MS.

Limb weakness with pyramidal signs was the most common presentation in our MS patients (71.2%), followed by sensory and visual

symptoms (60.4% and 42.5%, respectively). This is in full agreement with reports from other Arab countries where the percentages range from 22 to 84% for motor weakness, 5 to 50% for sensory features, and 19 to 62% for visual problems,^{13-21,23,28,29,37-39} and also with another study from Iran.⁴⁰ Yet other Arab studies noted a predominance of visual impairment followed by motor and then sensory symptoms, i.e., the optico-spinal form of MS,^{14,41,42} one study from Lebanon showed a predominance of brainstem-cerebellar symptoms²² and another one from Iran a predominance of sensory impairment.⁴³ Reports from India, Iran, the Middle East and Iraq show optico-spinal MS to be rarer in these countries than in Eastern Asia⁴⁴ and Japan.⁴⁵

A RR course, which agrees with all other studies in Arabic populations, was noted in 66 out of 101 of our patients (65.3%). However, we had fewer cases of SP MS and PP MS (3.9% and 3%) compared with other reports.^{13,16,17,19,20,22, 29,30,35,38,39} These were not referred to the 'committee' because they were not candidates for Beta-interferon. Thus, this study is not representative of the MS population in Jordan as a whole. Almost 1/3 of our patients (28 patients) had a clinically isolated syndrome, much higher than the 6.9% found in a Lebanese study.²² This is mostly due to the referral bias to the 'committee'.

The mean EDSS score at presentation in our patients was 2.6, comparable with another Jordanian study.¹⁹ The mean duration from the disease onset to the assessment by the 'committee' was 3.3 yrs, with half of our patients (50 out of 101) having a short duration of illness of less than 1 year and only 5% a long duration (more than 15 yrs), much shorter than in another study from Iraq (mean 7.25 yrs,

range 1-28 yrs).²³ This due to a better recognition of the disease because of the presence of better diagnostic facilities, especially MRI, but might also be explained by the referral bias to the 'committee'.

Regarding geographical distribution, as shown in the map, 69 out of 101 patients were born and/or live in the capital Amman and the remaining 32 in the North/North-East of the country. None of the patients were born or live in the South of the country. This might be explained by the fact that Amman, being the capital, is the most populated city in Jordan where patients have a better socio-economic status and thus, an easier access to a neurologist compared to other parts of the country. However, this might also indicate a possible north-south gradient related to environmental factors whereby the weather in Jordan is moderate in the North compared to the South, and sun exposure and temperatures are higher in the South. The first clinical study of MS done in Iraq in 1958 also showed that most of its reported 13 cases, seen between 1944 and 1954, came from north/mid-Iraq rather than the South, MS cases accounting for 0.2% of their neurological hospital admissions.⁴⁶ Another study from Kuwait on 89 MS cases found a focus of high incidence and another possible north-south gradient in Palestine, a country neighboring to Jordan.³⁹

Our study showed a trend toward an increase in the number of newly diagnosed MS cases in the last decade (89 cases) compared to the previous one (11 cases) and also an increase in the number of new cases in 2009 (34 cases) compared with the previous years within the same decade (see table 3). This might be explained by the fact that a large proportion of MS cases diagnosed before 2000 have already

progressed to the secondary progressive stage, and thus they were not referred to the 'committee', which was established in 2002, because they were considered by their primary physician as not eligible for Beta-Interferon. An overall prevalence rate of 32/100000 was reported in Jordan in 1993,¹⁶ whereas in 1977, it was reported as 7/100000.⁴⁷ This apparent increase might be due to improving access to neurological care, increased awareness of MS among the public and health professionals, change in the diagnostic criteria with better diagnostic facilities (role of MRI), and in the actual study, a referral bias. Nevertheless, it may indicate a real increase in the incidence of MS in Jordan. Prevalence in neighboring Arab countries has a similar tendency to increase with time. In Baghdad, Iraq, a prevalence of 4/100000 was estimated in 1969,²¹ while another recent study from Iraq showed that the number of MS cases according to year of clinical onset increased steadily in the 2 decades between 1980-1999:56 cases for the period 1980-1989 compared with 197 cases for the period 1990-1999, and thus indicating an increasing frequency of the disease.²⁹ Another study from Kuwait reported that the total incidence rate of MS increased from 1.05/100000 population in 1993 to 2.62/100000 in 2000 and the prevalence rate from 6.68/100000 in 1993 to 14.77/100000 in 2000.³⁸ In Saudi Arabia, the prevalence rates increased from 8/100000 in 1977²⁰ to 25/100000 in 1998.¹⁷ These reports of increased prevalence are partially attributed to a genuine increase in the incidence of the disease. Over the past 20 years, there have also been multiple reports of increased frequency of MS worldwide.^{48,49} In addition, a genuine increase in the incidence of MS has been reported in several areas of the United States and Canada.⁵⁰ Other reports noted rising trends

of MS incidence in regions of low prevalence.^{18,51} However, MS is still rare in Black African Arab countries: only 30 cases of MS were newly diagnosed and prospectively followed in 2 major referral centers in Khartoum, Sudan over a 10-year-period (January 1998-December 2008).⁵²

In conclusion, this study shows that the general characteristics of MS in this series of Jordanian patients were similar to most other Arab countries and Western reports. However, this cohort does not represent all the Jordanian MS population because it was skewed toward young patients with fairly recent disease and it was skewed heavily in favor of RRMS patients, the majority of SPMS and PPMS being excluded. There is a possible north-south gradient of MS in Jordan and a trend toward an increase in the incidence in recent years. This indicates the importance of establishing MS registries in Jordan and the Arab world in order to appropriately meet the health needs of the population.

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خصائص مرض التصلب اللويحي في مجموعة من المرضى الأردنيين الذين تمت مراقبتهم في لجنة دواء بيتا انتيرفيرون لمدة سنة واحدة (آب 2009 – آب 2010)

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الملخص

الهدف: دراسة خصائص مرض التصلب اللويحي في مجموعة من المرضى الأردنيين التي تمت مراقبتهم في لجنة دواء بيتا انتيرفيرون وتمّ مقارنتهم مع مرضى من دول عربية أو شرق أوسطية أخرى أو دول غربية.

الطريقة: تم أخذ معلومات من 101 مريض مصاب بمرض التصلب اللويحي في أثناء مراجعتهم للجنة الوطنية لعلاج بيتا انتيرفيرون لمرضى التصلب اللويحي خلال سنة واحدة، من الأول من شهر آب 2009 إلى الأول من شهر آب 2010.

النتائج: لقد كان متوسط أعمار المرضى عند بداية المرض 27.1 سنة، مع وجود 70 أنثى و31 ذكراً (نسبة الإناث إلى الذكور=2.26) وكان أعلى معدل للإصابة في العقد الثالث من العمر. بدأ المرض مبكراً عند 10 مرضى، كلهم إناث، قبل عمر 18 سنة. كان متوسط طول فترة المرض 3.3 سنة وعند نصف المرضى كان طول فترة المرض قصيراً (أقل من عام). الأعراض السريرية الأكثر شيوعاً كانت إصابة النخاع الشوكي تتبعها التهاب العصب البصري ثم إصابة جذع الدماغ. كان نمط المرض الأكثر شيوعاً هو متعدد الهجمات في 66 مريضاً مع وجود عدد نسبي كبير من المرضى المصابين بمحمة واحدة (28 مريض). كانت هنالك 34 حالة مرضية جديدة في عام 2009 و23 حالة جديدة خلال السنة التي تمت فيها الدراسة (آب 2009 إلى آب 2010)، وهذا يبين وجود زيادة في عدد الحالات مقارنة بالسنوات السابقة. كل الـ 101 مريض ولدوا أو عاشوا في وسط أو شمال الأردن ولم يوجد أي مريض من جنوب الأردن. 69 مريضاً ولدوا في العاصمة عمان حيث توجد نسبة كبيرة من السكان من أصل فلسطيني. تم استعمال علاج بيتا انتيرفيرون لـ 81 مريضاً.

الاستنتاجات: خصائص مرض التصلب اللويحي في الأردن كانت مشابهة للتقارير الصادرة من معظم الدول العربية والدول الغربية. هنالك احتمالية لوجود زيادة واضحة في عدد الحالات في شمال الأردن مقارنة بالجنوب. كذلك يبدو أن المرض أكثر شيوعاً بين السكان الأردنيين من أصل فلسطيني. أخيراً يبدو أن هنالك زيادة في عدد الحالات خلال السنوات الأخيرة.

الكلمات الدالة: التصلب اللويحي، دواء بيتا انتيرفيرون، خصائص مرض التصلب.