Multiple sclerosis in Jordan and Iraq

Clinical and social overview

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ABSTRACT

الأهداف: وضع أسس تشخيصية لمرض التصلب المتعدد (MS) في الجهاز العصبي من خلال العلامات السريرية. كما حاولنا إثبات بعض الفروقات السريرية عند المرضى الأردنيين والعراقيين.

الطريقة: أجريت هذه الدراسة السريرية من قبل طبيبين في مجال المخ والأعصاب بمستشفى البشير العام في عمان – المملكة الأردنية الهاشمية، ومستشفى رزكاري التعليمي في أربيل – العراق، في الفترة مابين يناير 2004م وحتى يوليو 2007م. تناولت هذه الدراسة المتغيرات في العلامات السريرية ونتائج فحص الرنين المغناطيسي لـ(52) مريضاً، منهم (35 مريض أردني) و (17 مريض عراقي). صممت هذه الدراسة بإجراء فحص سريري كامل لمرض التصلب المتعدد (MS). تم التحقق من العلامات و الأعراض ونسبة تواجدها في المرضى، ومن ثم مقارنة النتائج مع الدراسات والمعلومات الأخرى المتوفرة حول هذا المرض.

النتائج: في هذه الدراسة تم تحديد النسبة المئوية لأعراض مرض التصلب المتعدد (MS) ونتائج الاشعة لـ52 مريضاً مصاباً بالمرض. كان ضعف أحد الأطراف السفلية وخاصه في الساق أكثر عارضاً مرضياً تم ذكره من قِبل المرضى بنسبة (90.4%)، كما كان ازدياد الانعكاسات العصبية في الأطراف هي من اكثر العلامات التي تمت مشاهدتها عند هؤلاء المرضى (75%). كان معظم المرضى من أصحاب الشهادات العلمية والمستوى المعيشي المتوسط إلى جيد. استُخدمت نتائج أشعة الرنين المغناطيسي والتي أُخذت من عدة اتجاهات، منها موقع الاصابة في الدماغ والحبل الشوكي، وأوضحت هذه الاشاعة وجود صفائح متصلبة لدى أغلب المرضى.

خاتمة: لم يكن هناك اختلافات كثيرة بين النسب المختلفة للعلامات السريرية للمرضى في هذه الدراسة والنسب الموجودة حسب دراسات أخرى للمرض في مناطق مختلفة من العالم، باستثناء الرأرأة في العينين، حيث كانت نسبتها اقل عند المرضى الأردنيين و العراقيين.

Objectives: To verify clinical features of multiple sclerosis (MS) patients throughout the course of their illness and to study the socioeconomic status of MS patients in Jordan and Iraq.

Methods. Fifty-two patients were examined by 2 neurologists looking for the clinical and radiological features of MS at Al-Bashir Teaching Hospital, Amman, Jordan (35 patients), and Rezgary Teaching Hospital-Erbil, Kurdistan, Iraq (17 patients) from January 2004 to July 2007. The study design was based on full clinical examination of MS patients, investigate the signs, and symptoms, tabulating them, and show the percentage of their presence in all patients, and then comparing the results with other findings through systematic review of the available data from other reviews.

Results: The percentage of different symptoms, signs, and radiological features of the 52 MS patients were recorded. Weakness in one limb, mostly the leg (90.4%) was the most common symptom described by our patients, while hyperreflexia was the most prominent sign in MS patients (75%). Higher level of school performance, and moderate to good socioeconomic status were the common status between MS patients. The MRI results were interpreted according to the anatomical sites, and according to different MRI sequences, and the MRI showed MS plaques in almost all patients.

Conclusion: This study showed comparable findings with other studies, except nystagmus, which was less observed in Jordanian and Iraqi patients.

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Multiple sclerosis (MS) is a chronic wide spread demyelination of the brain and spinal cord, with subsequent formation of sclerotic patches. Multiple sclerosis is the second most common cause of neurological disability arising in early to middle adulthood, after trauma in western countries.[1] For centuries, the diagnosis of MS was based on its traditional dissemination in space and time, supported by the characteristic signs and symptoms, while valuable diagnostic data, namely, immunoglobulin G oligoclonal bands identified in the CSF, and evoked potentials studies, were added to the diagnostic process.[2]

Motor manifestations in MS include weakness, spasticity, and ataxia, and accompanied hyperreflexia, abnormal cutaneous reflexes (for example, Babinski sign), and rarely weakness accompanied by atrophy, due to lesion involving the anterior horn cells or anterior root zone, while somatosensory symptoms may include loss of sensation in any anatomic region, combination of loss of pain, temperature, light touch, vibratory sense, or position sense, positive sensory phenomena is also common causing, paresthesia, hyperpathia, allodynia, and dysesthesias.[3] Visual manifestation, mostly due to decreased visual acuity due to optic neuritis, or oculomotor dysfunction is very common in MS[4] almost any pattern of visual loss has been reported in MS.[3] Lesions involving the brainstem structures, and cranial nerves nuclei may produce loss of test, facial weakness, and loss of hearing, tinnitus, or vertigo. Central hyperacusis with phonophobia has been recently mentioned by Weber et al.[5] Cognitive dysfunction is not evaluated in this study, however, it is common in up to 75% of MS cases after 10 years according to Amato et al.[6] Autonomic manifestation of bladder, bowel and sexual dysfunctions are late common manifestations of MS, and their prevalence depends mostly on the degree of disability, and especially pyramidal features. Impaired ambulation is an important source of disability, and decreased quality of life in MS patients, gait dysfunction caused by leg weakness, spasticity, and imbalance due to cerebellar or vestibular dysfunction, proprioceptive loss, or visual disturbances. Benedetti et al,[7] found that subclinical abnormalities of gait are present even in mildly affected patients. The prevalence of MS in Arab countries has been studied, and generally considered to be low as compared to that in Northern Europe, North America, and Australia,[8] a new study in Jordan showed that the prevalence of MS is 39 per 100,000 in the capital (Amman), and approximately 38 per 100,000 in Erbid to the North of Amman.[9] Two epidemiological studies have been carried out comparing the prevalence of MS in the 2 major ethnic groups living in Jordan (the Palestinian and the original Jordanian), the prevalence was higher among the Palestinians.[8,10]

The objective of this study was to delineate the common clinical features of MS patients, and to find out any differences between MS patients in Jordan and Iraq (Middle East zones), and other findings from different geographical areas, and to show also the distribution of MS between different socioeconomic classes, and differences in educational backgrounds between Jordanian and Iraqi patients.

Methods. This study was designed to investigate the various clinical features of MS in a group of Jordanian (35) and Iraqi (17) patients throughout the course of their illness, and to compare the results with the previous studies held in Jordan or other parts of the world. The study size was collected through randomized patient selection, from the outpatient's neurology clinic, and inpatient's in the neurology wards. Two consultant neurologists carefully examined the clinical and radiological features of 52 MS patients at Al-Bashir Teaching Hospital, Amman, Jordan and Rezgary Teaching Hospital, Erbil, Kurdistan, Iraq from January 2004 to July 2007. All patients agreed to take part in this study, each patient had been assigned a number, and their names remained confidential throughout the study, and data were collected from each patient through single interview, and examination. All eligible MS patients agreed to participate in this study, and they are cases of definite MS according to McDonald's criteria.[11] The 52 MS patients were either in patients or out patients attending frequently for follow up, or during attacks. Each patient was asked regarding MS symptoms according to the system of questions designed according to clinical features collected from textbooks and literatures. An inquiry regarding the socioeconomic status of the patients, and their level of school performance was also obtained. All patients had blood count, blood film, sedimentation rate, collagen disease screen, electrolytes level, renal function test, serum cholesterol, and liver function tests. All these investigations are either within normal limits, or their results were insignificant. Cerebrospinal fluid examination for oligoclonal band, or immunoglobulin G (Ig G) level was obtained from some patients to complete their clinical criteria for definite MS diagnosis, however, the results were not included in this study. Magnetic resonance films were available at the time of examination with all patients, and for those who had old readings, MRI was carried out again to investigate for progression of the disease.

Simple statistical analysis was used to obtain the results of the study by counting the percentage of each finding after collecting these symptoms, and signs, and tabulating them, then a detailed search was carried out to investigate similar findings in other literature that

Table 1 - Age at onset and presentation of MS patients.

Age groups	Age at onset n (%)	Age at presentation n (%)
10-19	7 (13.4)	1 (1.9)
20-29	22 (42.4)	20 (38.5)
30-39	18 (34.6)	22 (42.3)
40-49	5 (9.6)	7 (13.4)
>50	0 (0)	2 (3.8)
Total	**52**	**52**

MS - multiple sclerosis

Table 2 - Level of education and socioeconomic status of patients.

Degree of education	n (%)	Socioeconomic status	n (%)
Primary school	5 (9.6)	Low	12 (23.1)
Secondary school	21 (40.4)	Moderate	32 (61.5)
College or bachelor's degree	26 (50)	High	8 (15.4)
Total	**52**		**52**

discusses clinical features of MS. Microsoft Excel 2003 was the software used in this study.

Results. Fifty-two patients living in Jordan and Iraq form the bases of this study, 39 (75%) were females, and 13 (25%) were males. The disease is more common at onset in the second and third decade of life. The disease onset declines sharply in other age groups (**Table 1**). The mean age at onset is 28.6 years with a range from 16-49 years. Five patients had a family history of MS in the first and second degree relatives (9.6%). **Table 2** shows the school performance and the socioeconomic status in MS patients, and most of the patients were well educated, being either college graduates (50%), and some of them had postgraduate degrees in different sciences, or having at least secondary school degree (40.4%). This reflects that MS patients are young active patients representing important recruits in any community. Most MS patients are of moderate socioeconomic status. **Table 3** shows the various clinical features of MS in Jordanian and Iraqi patients. Weakness in one limb, mostly the leg, is the most common neurological symptom described by our patients, while sensory loss at some occasion in a hand or a leg, heat sensitivity, easy fatigability, and decreased performance at work are the second most common

Table 3 - Symptoms and signs in multiple sclerosis patients.

Symptoms	n	(%)	Signs	n	(%)
Weakness in one limb	47	(90.4)	Hyperreflexia	39	(75.0)
Sensory loss	44	(84.6)	Pallor of the optic disc (optic atrophy)	36	(69.2)
Heat sensitivity	44	(84.6)	Absent superficial abdominal reflex	36	(69.2)
Fatigue	44	(84.6)	Disturbance of gait	35	(67.3)
Unsteadiness of gait	41	(78.8)	Weakness of the limbs	33	(63.5)
Heat sensitivity	41	(78.8)	Extensor plantar response	33	(63.5)
Pain	41	(78.8)	Increase motor tone (spasticity)	29	(55.8)
Bladder	33	(63.5)	Loss of vibration sense	25	(48.1)
Optic neuritis	32	(61.5)	Cerebellar signs	12	(23.1)
Diplopia	31	(59.6)	Loss of position sense	12	(23.1)
Paresthesias	30	(57.7)	Decreased pain and temperature sense	12	(23.1)
Vertigo	30	(57.7)	Nystagmus	8	(15.4)
Myokymia	26	(50)	Gaze disturbances	5	(9.6)
Lhermitte's symptom	22	(42.3)	Loss of tendon reflex	5	(9.6)
Bowel disturbances	15	(28.9)	Extraocular muscle weakness	2	(3.8)
Facial palsy	10	(19.2)			
Impotence	9	(69.3)			
Trigeminal neuralgia	5	(9.6)			
Seizures	2	(3.8)			

symptoms in MS patients. Clinical signs of MS were examined carefully in our patients. Hyperreflexia was the most prominent sign in MS patients, most of the time it is unilateral or indicating unilateral pyramidal tract lesion. Optic nerve pallor and atrophy, and absent superficial abdominal reflex are the second most common signs in MS patients reflecting old optic neuritis or slowly evolving disease process involving the optic nerve. Extensor planter reflex either unilateral or bilateral present in the patients indicates unilateral or bilateral pyramidal signs (**Table 3**). The disease course is variable between MS patients, the most common variety of MS is the relapsing remitting form (**Table 4**). The second common type is the secondary progressive form as shown in **Table 4**. Radiological manifestation of MS is the mainstay of the diagnosis although it is never pathognomonic for the disease, nearly all MS patients show periventricular or white matter hyperintense lesions in T2 weighted images. Lesions of MS when associated with axonal degeneration will appear as black holes in T1 weighted images. The appearances of hyperintense lesions around the corpus callosum that radiate upward in the hemispheres white matter are called Dawson's fingers, which appear in 80.8% of the patients MRI (**Table 5**). Magnetic resonance imaging with gadolinium enhancement was not studied in this series of patients, as most patients are stable cases of MS and do not present with new attacks at the time of assessment. **Table 6** shows sites of MS lesions observed in the 52 patients, the lesions most commonly seen in the white matter of the cerebral hemispheres, mostly in the periventricular region, while lesions in the brainstem white matter were observed in some patients. Spinal cord involvements were noticed in 23.1% of all patients in whom spinal cord lesions were suspected clinically, and subsequently a spinal cord MRI was performed (**Table 6**).

Table 4 - Disease course in multiple sclerosis (MS) patients.

Disease course	n	(%)
Relapsing-remitting MS	44	(84.6)
Secondary progressive MS	5	(9.6)
Primary progressive MS	3	(5.8)
Progressive relapsing MS	0	0

Table 5 - Magnetic resonance imaging findings in MS patients.

MRI image	n	(%)
T2 weighted images	52	(100)
FLAIR	52	(100)
Dawson's fingers	42	(80.8)
T1 weighted images with black holes	16	(30.8)

MS - multiple sclerosis, FLAIR - fluid attenuated inversion recovery, T1 - time for 63% longitudinal relaxation

Table 6 - Sites of MS lesions in the MRI of patients.

Sites of MS lesions in T2 MRI sequences	n	(%)
Cerebrum	51	(98.1)
Brainstem	18	(34.6)
Cerebellum	12	(23.1)
Spinal cord	12	(23.1)

MS - multiple sclerosis, T2 - time for 63% of transverse relaxation, MRI - magnetic resonance imaging

Discussion. In this study the peak age of onset was in the second and third decade of life (20-40 years), some patients mentioned earlier age of onset especially female patients, and others mentioned later age of onset and they were mainly of male gender. No patient in this study presented at middle age (50-60 years). Many studies proved that first-, second-, and third-degree relatives of patients with MS are at increasing risk of the disease from 3-23%.[12-14] Other studies showed siblings of affected individuals have a lifetime risk of approximately 5%.[15-17] In our series, 5 patients had family history of MS affecting the first and second degree relatives, which showed that familial incidence of MS in Jordan and Iraq does not differ greatly from other studies in other parts of the world.

A number of surveys in the United Kingdom, and the United States of America had mentioned that the disease is more frequent in the higher socioeconomic groups than the lower ones, and no relationship has been established to the poverty or social deprivations that are part of low socioeconomic status.[12,18] Most of the patients in this study are from the middle and high socioeconomic class, so as for the education level, most of the patient showed high standard of education, and a good number of them had graduated from college and high standard institutes (**Table 2**). When the diagnosis of MS becomes virtually certain, a number of clinical syndromes are observed to occur with regularity.[12] Approximately one half of the patients will manifest a clinical picture of mixed or generalized type with signs pointing to the involvement of the optic nerves, brainstem, cerebellum, the pyramidal system, and the spinal cord. Another 30-40% will exhibit varying degrees of spastic ataxia, and deep sensory changes in the extremities, for example, essentially a spinal form

of the disease. In either case, an asymmetrical spastic paraparesis is probably the most common manifestation of progressive MS. Thus, the mixed and the spinal forms together comprised at least 80% of all cases.[5] From the results in this study, signs and symptoms of pyramidal system involvement in the form of hyperreflexia, absent abdominal reflexes, pyramidal weakness, and sensory disturbances, with optic nerve involvement present in the majority of patients, and that would suggest that the mixed variety, and the spinal form of MS are also the most common types in Jordanian and Iraqi patient (**Table 3**). History of optic neuritis was reported from patients, while temporal pallor or optic atrophy was found in some patients after funduscopic examination. Visual or oculomotor involvement mentioned occurred in up to 100% throughout the course of illness according to Poser et al,[19] while Rosenberg et al,[20] mentioned that 53% will develop visual loss, or impairment in 5 years period of the illness. In a recent survey, the overall risk of the development of MS in optic neuritis patients after 10 years was 38%,[21] while Rizzo and Lessell,[22] mentioned that 74% of women and 35% of men will develop MS by the 15th year after the onset of visual loss. Diplopia had been mentioned by 59.6%, gaze disturbance in the form of weakness of horizontal gaze or interrupted pursuit, hypermetric or hypometric saccade was noticed in 9.6% of patients, and only 3.8% of patient exhibit extraocular muscle weakness at the time of examination. This may reflect lesser brainstem involvement in Jordanian and Iraqi patients or earlier disappearance of brainstem signs in MS.[11]

In this study, nystagmus was not a prominent clinical feature at the time of examination, it has been observed in only 15.4% of patients, and this is due to the fact that patients cannot describe nystagmus as a symptom, although they describe oscillopsia sometimes, and it is a fact that neurologist do not explain this clinical features to their patients, so those patients cannot recall such a feature retrospectively. In addition, most of those patients had no clear medical records that show their clinical features throughout the course of their illness. Rosenberg,[20] described various kinds of nystagmus in half of MS patients throughout the course of their illness, big part of it is due to ataxic nystagmus of internuclear ophthalmoplegia. In this study, at the time of examination only 2 patients exhibit features of internuclear ophthalmoplegia. Kurne and Karabudak[23] mentioned a much higher incidence of nystagmus (85%) in their study series. Sensory disturbances are commonly due to spinal involvement.[24] In a recent survey, sensory symptoms were reported as a first symptom by 43% of patients including visual symptoms.[25] Rosenberg[20] mentioned sensory disorders to be present in 38% at diagnosis, and in 82% within 5 years of the illness in his series of MS patients. He mentioned also that the vibration, and position senses are usually dissociated, proprioception is more often being abnormal. Moulin et al[26] mentioned that on examination, vibratory loss in the lower extremities is the most common abnormality, which was compatible to the findings in this study.

In this study, 84.6% of patients mentioned that hot weather and increase in body temperature would cause sensory or motor symptoms. Pain was described by 78.8% of the patients, which was either in the form of annoying sensory manifestation like allodynia, or burning pain in some sensory nerve distribution, and sometimes radicular pain, painful leg spasms, band like dysesthesia, or pain accompanying optic neuritis (periorbital). Moulin et al,[26] and Stenager et al[27] mentioned that up to 65% of MS patients had reported acute or chronic pain during the course of their disease. These sensory signs and symptoms mostly reflect spinal cord involvement, especially the posterior column in the cervical region.[24-27] Trigeminal neuralgia was mentioned by 9.6% of patients, mostly unilateral and representing one of the consistently annoying complaints, Rushton[28] mentioned a lower percentage, (1-2%) in his patients series. Lhermitte's symptom was recalled by 42.3% of patients in this study. This symptom signifies posterior column involvement in the cervical cord, and one of the patients exhibited in addition to the symptom, a clear myoclonic jerk involving all the body on passive movement of the neck, while one third of the MS patients reported Lhermitte's symptom according to Kanchandani.[29] Timothy and John[13] and Freal et al,[30] mentioned that fatigue is rated as the most disabling symptom in approximately 40% of MS patients. Fatigue causes no objective abnormality on neurological examination, however, the patient usually describes chronic lack of energy.[3] Chronic fatigue was mentioned by 84.6% of the patients in this series (**Table 3**). The same findings has been described by Miller and Coyle,[3] Kurne and Karabudak,[23] and Moulin et al.[26] Leocani et al,[31] proved that there is EEG evidence of cortical dysfunction with repetitive performance of a simple motor task, while Filippi et al[32] described abnormal patterns of activation on functional MRI studies in patients with fatigue.

Weakness or paresis of one or 2 limbs, and less commonly as semihemiplegic weakness (without cranial nerves weakness), which is mostly due to spinal cord involvement was a frequently mentioned symptom (90.1%), while true pyramidal weakness was observed in (63.5%) of the patients (**Table 3**). Poser et al[19] mentioned nearly the same finding in 88% of patients throughout the course of the illness, however, according to Rosenberg[20] 78% of patients will develop weakness and or spasticity in a 5-year-period. Gait disturbances

in the form of ataxic or spastic gait were observed in 67.3% of patients, approximately the same had been described in others series.[8,23] Bladder disturbances in the form of urgency and incontinence were a prominent feature in this study. Bladder symptoms were mentioned by 63.5% in this study (**Table 3**), the same percentage had been reported by Poser et al,[19] while Donaghy and Compston[24] reported that up to 80% of MS patients exhibit bladder disturbances, especially coupled with spinal cord involvement, bowel disturbances were observed to a lesser extent than the bladder symptoms, mostly in the form of constipation. Impotence in males was also a prominent feature in this study (69.3%), approximately the same was mentioned by Kurne and Karabudak[23], and Kurdi et al.[8]

Approximately 1-5% of patients with MS, at some time during the course of their illness, will have a seizure or recurrent seizures which are mostly of partial secondary generalized type, and sometimes generalized. The seizure disorder was presumably due to lesions approaching the cerebral cortex or subjacent white matter according to McDonald et al,[11]Rosenberg,[20] and Thompson et al.[33] Approximately the same percentage has been found in this study (**Table 3**). Disease course in MS is variable, the relapsing remitting form (RRMS) being the most common variety observed in this series, and this form responds partially to the present conventional prophylactic treatment such as interferon beta, the same had been described by Miller et al,[3] approximately 50% of patients with the RRMS converted at a time to the secondary progressive (SPMS) form of the disease. The SPMS is characterized by gradual progression of disability with or without superimposed relapses, it was the presenting variety of 9.6% of patients in this study. In contrast, patients with primary progressive MS (PPMS), experience gradual progression of disability from onset without superimposed relapses, and representing the clinical pattern of 5.8% of patients in this study, others mentioned higher percentage up to 10%.[1,12] Patients with progressive relapsing MS (PRMS) experience gradual progression of disability from disease onset later accompanied by one or more relapses, this clinical pattern affects approximately 5% of patients,[1] and was not found in patients in this study (**Table 4**).

The New York Multiple Sclerosis Consortium performed a survey of 3019 patients, and found that 55% had RRMS, 31% SPMS, 9% PPMS, and 5% RPMS. The difference observed in the findings of this study is due to the fact that, most patients in this series are frequent attendants at our hospital due to interferon B treatment, and since interferon B in Jordan and Iraq is given only for RRMS patients, this might reflect the bias in this study.

It is now widely accepted that MRI is the most helpful radiological examination in MS.[11] White matter lesion was observed in 98% of MS patients according to Donaghy,[24] and in almost all MS patients in both T2 and fluid attenuated inversion recovery sequences in this study, the same findings has been described also by Goodkin et al[34] and Bot et al.[35] Lesions in the brainstem white matter were observed in 34.6% of the patients, and that may be due in part to that symptoms, and signs of brainstem MS remit as a rule, and to a surprisingly complete resolution in many cases.[11] Spinal cord lesions in the MRI were found in 12 of 17 patients who had MRI for their spinal cord which represents 23.1% of the patients (**Table 6**), and the reason was that, not all patients had spinal cord imaging as most patients are ordered to have spinal cord MRI only after clinical suspicion of spinal cord involvement due to the coast effect, and long waiting lists of patients, however, most spinal cord lesions exhibit clinical findings and that is in accordance with others findings.[11,36]

In conclusion, clinical manifestation of MS in Jordanian and Iraqi patients resembles those presented in others' descriptions of the disease, and only minor differences had been found in some clinical features, namely, nystagmus, which was less common as a chronic presentation than that described by other studies, and this might reflect lesser brainstem involvement in Jordanian and Iraqi patients, or overall brainstem signs in MS are not as long lasting as spinal cord and hemispheres involvement. It has been found also that MS patients are mostly of higher and moderate socioeconomic class, and most of them are of high education standard.

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