Clinical and radiological study of Iraqi multiple sclerosis patients with childhood onset

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ABSTRACT

الأهداف: دراسة الخصائص السريرية والإشعاعية لمرض التصلب العصبي المتعدد وذلك عند بداية المرض في الفئة العمرية التي تقل عن 18 عاماً.

الطريقة: أُجريت هذه الدراسة الاسترجاعية في عيادة التصلب العصبي المتعدد، مستشفى المدينة الطبية في بغداد، العراق، حيث قمنا بعمل مسح لبيانات المرضى الطبية خلال الفترة من مارس 2008م إلى مارس 2009م. شملت الدراسة 77 مريضاً مصاباً بالتصلب العصبي المتعدد والذين تقل أعمارهم عن 18 عاماً. وبعد ذلك تم تحليل بيانات المرضى السريرية والإشعاعية من أجل الدراسة.

النتائج: لقد كانت نسبة المرضى الإناث إلى الذكور 1.6:1، وكان متوسط العمر عند بداية المرض 14.95 عاماً. أشارت الدراسة إلى أن 7 مرضى (9.1%) قد كانوا أطفالاً (أي تقل أعمارهم عن 10 سنوات)، فيما كان 70 مريضاً (90.9%) من المراهقين (أي تتراوح أعمارهم ما بين 10–18 عاماً) وذلك عند بداية ظهور أعراض المرض. وكان 70 مريضاً (90.9%) مصاباً بالتصلب المتعدد الانتكاسي المتقطع في بداية الأمر، وقد تطور هذا النوع إلى التصلب المتعدد الثانوي المتقدم لدى 9 من هؤلاء المرضى (11.7%)، وحدث هذا التطور بعد مرور فترة كان معدلها 9.87±4.135 عاماً. بالمقابل فقد أُصيب 7 مرضى بالتصلب العصبي الأولي المتقدم في بداية الأمر. ولقد كان أكثر الأعراض شيوعاً بين المرضى هو التهاب الأعصاب البصرية (35.8%)، وأُصيب 59 مريضاً (76.6%) بأعراض أحادية البؤر، و18 مريضاً (23.4%) بأعراض متعددة البؤر، وأُصيب 51 مريضاً (63%) بالآفات المحيطة بالبطين والتي ظهرت في أشعة الرنين المغناطيسي. لقد أظهرت نتائج الدراسة بأن نسبة ظهور الآفات فوق الخيمة كانت أعلى من نسبة الآفات تحت الخيمة، كما أن نسبة إصابة الأطفال بالآفات العقدية القاعدية كانت عالية مقارنةً بالمراهقين (p=0.002). وكانت نسبة إصابة الذكور بالآفات تحت الخيمة أعلى من الإناث (p=0.033).

خاتمة: أثبتت نتائج أشعة الرنين المغناطيسي في هذه الدراسة بأن نسبة إصابة الذكور بالآفات تحت الخيمة كانت أعلى من الإناث، كما وكانت نسبة إصابة الأطفال بالآفات العقدية القاعدية أعلى من المراهقين.

Objectives: To study the clinical and radiological characteristics of multiple sclerosis (MS) with onset below 18 years.

Method: This retrospective study was carried out at the MS Clinic in the Medical City Hospital in Baghdad, Iraq between March 2008 and March 2009. The records of the center were surveyed, and 77 patients with the onset of MS below 18 years were identified. Their clinical and radiological data were then analyzed.

Results: The female:male ratio was 1.6:1, and the mean age at onset was 14.95 years. Seven (9.1%) patients where children (age below 10 years), and 70 (90.9%) patients where adolescents (age 10-18 years) at onset. Seventy patients (90.9%) had an initial course of relapsing remitting MS, 9 (11.7% of the total) of them progressed to secondary progressive MS after a mean duration of 9.87±4.135 years. Seven patients had primary progressive MS as the initial course. The most common presenting symptom was optic neuritis (35.8%). Fifty-nine (76.6%) patients had monofocal presentation, and 18 (23.4%) had polyfocal presentation. Fifty-one (63%) patients had periventricular MRI lesions. The percentage of supratentorial lesions was higher than infratentorial lesions, children had a higher incidence of basal ganglionic lesions than adolescents (p=0.002), and males had a higher incidence of infratentorial lesion than females (p=0.033).

Conclusions: Male patients have a higher incidence of infratentorial MRI lesions than female patients. Children had a higher incidence of MRI lesions in the basal ganglia than adolescents.

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Multiple sclerosis (MS) is a chronic demyelinating focal disorder of the optic nerve, spinal cord, and brain, which remits and recurs to a varying extent. The diagnosis of MS is based on dissemination of the attacks over time (remission and relapses) and dissemination in space. The advent of MRI and its capacity to identify clinically hidden lesions has obviated the exclusive dependence on clinical criteria for the diagnosis.[1] Multiple sclerosis in children and adolescents is increasingly recognized worldwide. The disorder presents almost exclusively as a relapsing-remitting disease in children. The MRI has contributed substantially to the increasing recognition of, and certainty in the diagnosis of MS in children.[2] The MRI has a pivotal role in confirming the presence of CNS inflammatory demyelinating lesions, and in the exclusion of other CNS disorders.[3,4] Multiple sclerosis in children comprises demyelinating lesions with a greater degree of edema, and bears more widespread white matter involvement during acute relapses than demyelinating lesions found in adults.[3,4] McDonalds' diagnostic criteria are the corner stone for diagnosis of MS in adults.[5] These criteria have a sensitivity of only 52-54% in children at the time of the first MS attack,[5,6] and a sensitivity of 67% at the time of the second MS event. Low sensitivity (37%) was particularly notable when the MRI criteria were applied to MS children less than 10 years old.[5] The objective of this study is to assess the clinical and radiological characteristic of MS with onset below 18 years in Iraqi patients.

Methods. This retrospective study was conducted in the MS clinic archive system in the Medical City Hospital in Baghdad, Iraq. Data collection was carried out between March 2008 and March 2009. To be included, patients must first be diagnosed to have MS according to the revised McDonald's diagnostic criteria[7] for MS, and onset of disease must be before the eighteenth birthday. The exclusion criteria included evidence for the diagnosis of another disease that explained the clinical picture, or age more than 18 years at onset. As this comprised retrospective data collection from the data system of the MS clinic, we did not require ethical approval or patient consent.

For each patient, the following information was gathered: age, gender, date of onset, date of diagnosis, date of second attack, presenting symptom, course of disease (relapsing remitting [RRMS] or primary progressive [PPMS]), secondary progression and the date, extended disability status scale (EDSS) and the date, and type and location of MRI lesions. Initial MRI was performed with 1.5T, MRI data using a standardized procedure (sagittal, axial, and coronal and T1, T2, fluid attenuated inversion recovery FLAIR sequences and gadolinium enhancement) were collected from patients file records. The age limit was based on the WHO definition of "children" (under the age of 10) and "adolescents" (aged 10-18 years).[8] Relapse and progressive phases of MS were defined according to the established criteria.[7] Neurologic disability was assessed according to the EDSS score, a 7 functional system score that includes motor, sensory, cerebellar, brain stem, visual, mental, and sphincter.[1]

The Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 15 was used for data input and analysis. Mann Whitney test was used to test the significance of difference between 2 means, Z test to test the significance of difference between 2 proportions, chi square test to test the significant association between discrete variables, and Pearson correlation to test the relation between 2 continuous variables. A p-value <0.05 was considered the cutoff point to determine significant findings.

Results. Of the 1125 patients records surveyed for the research, 77 with the diagnosis of MS and onset of disease before their eighteenth birthday, (a prevalence of 6.8%) were eligible for the study. Forty-eight of the patients where females (62.3%), and 29 patients where males (37.7%), with a female:male ratio 1.6:1 (**Table 1**). Mean age at onset was 14.95 years, (minimum 5, maximum 18, SD 3.2 years). Seven patients where children (age below 10 years) (9.1%), and 70 patients where adolescents (age 10-18 years) (90.9%) at onset (**Table 1**). No significant difference was found regarding distribution of gender in each age group, and no significant difference was found when age at onset was compared between males and females. Seventy patients had an initial course of RRMS (90.9%), 9 of them progressed to SPMS (11.7% of the total) after a mean duration of 9.87±4.135 years. Seven patients had PPMS as the initial course. The most common presenting symptom was optic neuritis (35.8%) followed by brain stem lesion. Fifty-nine (76.6%) patients had a

Table 1 - Distribution of 77 Iraqi multiple sclerosis patients under the age of 18 according to their age at onset and gender.

Gender	Age, n (%)				
	Under 10 years		From 10-18 years		*P*-value
Male	2	(28.6)	27	(38.6)	
Female	5	(71.4)	43	(61.7)	0.704
Total	7	**(100)**	**70**	**(100)**	

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monofocal presentation, and 18 (23.4%) had a polyfocal presentation.

The distribution of patients according to gender and MRI findings are shown in **Table 2**. This table shows the comparison of different radiological sites between males and females, and shows a significant difference with more males having infratentorial lesions compared with females. The study showed no other significant differences between males and females regarding other MRI findings. When MRI findings in children and adolescents were compared, 29% of children had basal ganglionic lesions compared with 2.9% of adolescents (p=0.002) (**Table 3**). No other significant difference was found between the 2 age groups regarding other MRI findings. The distribution of patients according to their mode of presentation and MRI findings is shown in **Table 4**, and the results showed no significant difference between monofocal and polyfocal mode of onset. We did not record any case of Schilder's disease or another variant of demyelinating disease in our study group.

Table 2 - Distribution of 77 Iraqi multiple sclerosis patients under the age of 18 according to their gender and some MRI findings.

Findings	Male	Female	N	(%)	*P*-value
Periventricular	21	30	51	(66.0)	0.608
Brainstem	11	8	19	(24.6)	0.062
Spinal cord	5	5	10	(13.0)	0.598
Cerebellar	5	4	9	(11.5)	0.369
Centrum semiovale	4	11	15	(19.5)	0.467
Corpus callosum	4	2	6	(7.0)	0.258
Basal ganglia	1	3	4	(5.0)	0.979
Juxtacortical	1	4	5	(6.5)	0.711
Thalamic	0	2	2	(2.5)	0.686
Supratentorial (ST)	25	39	64	(83.0)	0.829
Infratentorial (IT)	14	15	29	(38.0)	0.033
Both (ST&IT)	11	11	22	(28.5)	0.260

Table 3 - Distribution of 77 Iraqi multiple sclerosis patients under the age of 18 according to their age and MRI findings.

Findings	Under 10 years (N=7)		From 10-18 years (N=70)		*P*-value
Periventricular	3	(43)	48	(69)	0.880
Brainstem	2	(29)	17	(24)	0.664
Centrum semiovale	1	(14)	14	(20)	0.635
Cerebellar	0	(0)	9	(13)	0.687
Spinal cord	2	(29)	8	(11)	0.131
Corpus callosum	0	(0)	6	(9)	0.944
Juxtacortical	0	(0)	5	(7)	0.946
Basal ganglia	2	(29)	2	(3)	0.002
Thalamic	1	(14)	1	(1)	0.117
Supratentorial (ST)	5	(71)	59	(84)	0.323
Infratentorial (IT)	3	(43)	26	(37)	0.228
Both (ST&IT)	3	(43)	19	(27)	0.092

Table 4 - Distribution of 77 Iraqi multiple sclerosis patients under the age of 18 according to their mode of presentation and MRI findings.

Findings	Monofocal (N=57)		Polyfocal (N=17)		*P*-value
Supratentorial	51	(89.5)	13	(76.5)	0.330
Infratentorial	20	(35.1)	9	(52.9)	0.300
Both	16	(28.6)	6	(35.3)	0.820

Discussion. The present study showed that 6.8% of the 1125 patients attending the MS clinic had the onset of MS before the age of 18 years. This figure is much less than El-Salem & Khader's study[9] who reported that 19.4% of patients had early onset MS, and this may reflect under diagnosis of childhood MS in Iraq. The reported mean age at onset in the present study is also higher than that of Weng et al,[10] clarifying the environmental, ethnic, and genetic differences between Iraqi and Taiwanese patients. An initial course of RRMS was reported in 90.9% of the present study patients, which is approximate to the 86% reported by Weng et al,[10] and the 88% of patients reported by El-Salem & Khader.[9] Nine patients (11.7% of the total) progressed to SPMS after a mean duration of 9.87±4.135 years. This duration to a secondary progressive course is shorter than reported in El-Salem & Khader's study.[9] This shorter duration to the secondary progressive phase may be due to non-availability of disease modifying drugs in Iraq for all the patients. The present study showed a high percentage of monofocal presentation. This is in agreement with El-Salem & Khader's study[9] and contrasting with Weng et al's study,[10] who found a higher percentage of poly symptomatic presentation. This contrast is part of racial, genetic, and environmental differences between the Far East Asian and Middle East district.

The present study showed that optic neuritis is the most common presenting feature; this is in agreement with El-Salem & Khader's study,[9] and Weng et al's[10] study. We did not find the optico-spinal form of MS, Schilder's disease, or another variant of demyelinating disease in our patients.

Regarding the MRI findings, the incidence of periventricular white matter lesion was similar to Weng et al's study[10] and Waubant et al's study.[11] While the incidence of juxtacortical, thalamic, and basal ganglionic lesions were much less in our study. The difference can be explained as a different pattern of disease or different MRI techniques. The high incidence of supratentorial white matter lesions is similar to what is expected in adult patients. The present study showed a high incidence of infratentorial lesions in comparison with adult patients. These adult/childhood differences in lesion prevalence and location could reflect immunological differences between children and adults, or differences in the state of myelination in the pons relative to supratentorial white

matter, as myelination proceeds along in a caudorostral gradient.[12] This result is consistent with Waubant et al.[11] One significant difference could be found between children and adolescents regarding MRI findings, and that is the higher incidence of basal ganglionic lesion in children compared with adolescents (p=0.002), which is in agreement with results of Weng et al's study.[10] Ill-defined lesions that include the deep grey nuclei in MS are more commonly seen in young children.[4] Another significant difference in the MRI findings was the finding that males had a higher incidence of infratentorial lesion than females (p=0.033). This higher male rate is related to the fact that the pons myelinates faster in males than female individuals.[13]

In conclusion, MS in Iraqi children has an incidence similar to that in other countries. The most common presentation is optic neuritis. Male patients have a higher incidence of infratentorial MRI lesions than female patients, and children have a higher incidence of MRI lesions in the basal ganglia than adolescents.

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