DEMOGRAPHIC, CLINICAL AND PARACLINICAL CHARACTERISTICS OF A SAMPLE OF EGYPTIAN MULTIPLE SCLEROSIS (MS) PATIENTS ATTENDING MS CLINIC IN AL-AZHAR UNIVERSITY HOSPITALS

By

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ABSTRACT

Background: Multiple sclerosis is an autoimmune inflammatory demyelinating disorder, affecting people in the most productive period in their lives with more predilection to affect females more than males, many demographic studies of multiple sclerosis had been done in many western countries, in the middle east particularly in Arabic countries multiple sclerosis now being heavily studied in all aspects ofthe disorder after the incidence of multiple sclerosis has been increased.

Objective: The aim of this work was to study the clinical and paraclinical characteristics of patients with multiple sclerosis (MS) attending Al-azhar university hospitals, (Al-Hussein and Bab-El-Sherya) along the time of the study (from April 2017 to April 2019) aiming for better management and rehabilitation of Multiple sclerosis patients to improve their quality of life.

Patients and Methods: This was a cross sectional descriptive study carried on 400 definite multiple sclerosis patients who were recruited from Al-Azhar university hospitals diagnosed according to revised McDonald's criteria 2017.

Results: The current study included 400 MS patients, 113 were males and 287 were females, the main age of disease onset was 28.42±8.48, the motor manifestations was the most common presenting manifestation, followed by optic neuritis then the sensory manifestations, the relapsing remitting phenotype was the commonest phenotype, the family history of MS was positive in 2% in the current study, we observed a statistically significant difference between MS patients as regard MS phenotype and the sex of the patient, age and the total EDSS, first clinical symptoms and the total EDSS, time to 2nd clinical event and the total EDSS and the lesions in the spinal cord and the total EDSS.

Conclusion: The first clinical presentation of MS affects the patient EDSS, patients with visual and sensory presentation had commonly lower EDSS, compared to patients with motor presentation had commonly higher EDSS.

Keywords: Egyptian, Demographic, Clinical data, Multiple Sclerosis.

INTRODUCTION

Multiple sclerosis (MS) is the most-common autoimmune inflammatory demyelinating disorder of the central nervous system, with highly variable clinical presentations. Common symptoms and signs of MS include sensory symptoms in the limbs or face, unilateral (mainly) visual symptoms, sub-acute motor deficits, double vision, ataxia and gait disturbances, vertigo, bladder symptoms, and pain *(Miller et al., 2012).*

The main phenotypes of MS are relapsing and progressive disease.

About 85–90 % of patients starting by relapsing-remitting (RRMS) course, with clinically isolated syndrome (CIS) presenting as the first demyelinating manifestation in the form of optic neuritis, motor symptoms, brainstem, and spinal-Cord symptoms *(Miller et al., 2012).*

Small percentage (5–10%) of patients has primary progressive multiple sclerosis (PPMS) with progression from the start, mainly spinal-cord syndrome *(Rice et al., 2013).*

After the RRMS onset, by about 10–20 years some patients enter the secondary progressive phase of the disease where there is gradual worsening of disability *(Lublin, 2013).*

The epidemiology of MS has been studied extensively mainly for Western countries due to high prevalence of MS in Caucasians *(Evans et al., 2013).* Many reports indicate increasing disease prevalence in parts of the world with previously low prevalence *(Alroughani, et al., 2014).*

The aim of this work was to study the clinical and paraclinical characteristics of patients with multiple sclerosis attending Al-Azhar university hospitals, (Al-Hussein and Bab-El-Sherya) along the time of the study (24 months from April 2017 to April 2019) aiming for better management and rehabilitation of our patients to improve their quality of life.

PATIENTS AND METHODS

This study was a cross sectional descriptive carried on definite multiple sclerosis patients who were recruited from Al-Azhar university hospitals (Al-Huessin and Bab-El-Sherya) over 24 months from April 2017 to April 2019.

Inclusion criteria: All definite multiple sclerosis patients diagnosed as MS according to revised McDonald criteria 2017 (Thompson et al., 2017), both males and females were included.

Exclusion criteria:

1. Patients with other medical or metabolic conditions that can mimic MS clinically or radiologically.

2. Presence of other neurological conditions simulating MS clinically or radiologically.

All patients were subjected to

I. Clinical assessment of MS patients.

II. Radiological investigations: MRI brain (MS protocol) with contrast done for all patients and MRI cervical and dorsal with contrast done for 362 patients.

III. Neurophysiological investigations: Visual evoked potentials.

IV. Laboratory investigations: CSF oligoclonal band done only for 127

patients who are newly diagnosed or their diagnosis need to be confirmed by CSF examination.

Ethical Considerations: Data collection for this registry received written approval of the medical ethics committee of the Ethics Board of Al-Azhar University, school of medicine, and further investigations applied to our study group were medically consented by the patient himself.

Statistical Analysis:

Data were collected, revised coded and entered to the statistical package for social sciences (SPSS), version 20. Qualitative data were presented as number and percentages, while quantitative data were presented as mean, standard deviations and ranges. The comparisons between two groups with qualitative data were done using Chi-square test. The comparison between two groups regarding quantitative data with parametric distribution was done using Independent t-test. So, P-value was considered significant when P was < 0.05.

RESULTS

The present study included 400 definite multiple sclerosis patient recruited from Al-Azhar University Hospitals (Al-Hussein and Bab-El-Sherya) from April 2017 to April 2019 **(Table 1)**, They were 113 males and 287 females, Mean age of the disease onset was 28.42 ± 8.48, the most common presenting manifestation was motor weakness, the most common phenotype was relapsing remitting course, and the family history was positive for multiple sclerosis in only 2 % of the study group.

About 2/3 of patients were female and 1/3 were male.

The mean age of the patients were 32.59 ± 9.41 years old, while the main age at disease onset was 28.42 ± 8.48 years old.

Most of the patients (84.3%) started their disease between 18 to 40 years old.
First clinical manifestations were motor weakness, optic nerve affection, sensory, brain stem and cognitive affection respectively.

The most common MS phenotype was relapsing remitting multiple sclerosis (RRMS) followed by clinically isolated syndrome (CIS), then secondary progressive multiple sclerosis (SPMS) lastly primary progressive multiple sclerosis (PPMS).

Family history of MS was positive in only 2.0 % of the study group.

HUSSEIN MOHAMED HUSSEIN *et al.,*

Table (1): Main Characteristics of the patients

Parameter	Value
Sex (Female: Male)	287 : 113
AGE (years ± SD)	32.59 ± 9.41
AGE at Onset (years ± SD)	28.42 ± 8.48
Below 18 years N (%)	29 (7.3%)
18-40 years N (%)	337 (84.3%)
Above 40 years N (%)	34 (8.5%)
RRMS N (%)	321 (80.3%)
SPMS N (%)	19 (4.8%)
CIS N (%)	57 (14.3%)
PPMS N (%)	3 (0.8%)
First Clinical Manifestations N (%)	
Motor Weakness	201 (50.3%)
Sensory Manifestation	46 (11.5%)
Optic Neuritis	90 (22.5%)
INO	28 (7.0%)
Ataxia	30 (7.5%)
Cognitive Affection	2 (0.5%)
Oculomotor Affection	3 (0.75%)
Family History of MS N (%)	
Negative	392 (98.0%)
Positive	8 (2.0%)
RRMS: Relapsing Remitting Multiple Sclerosis, SPMS: Secondary Progressive Multiple Sclerosis, CIS: Clinically Isolated Syndrome, PPMS: Primary Progressive Multiple Sclerosis, INO: Internuclear ophthalmoplegia.	

Table (2): Correlation between different patient disease characteristic and clinical disability measured by EDSS

EDSS / Patient Characteristic	EDSS (0 - 3) (N) = 290		EDSS >3 (N)=110		p-value
Age in Years Mean ± SD	31.28 ± 9.00		36.02 ± 9.64		0.0001
First Presenting Symptom					
Optic Neuritis	77 (26.5 %)		13 (11.8 %)		
Sensory	40 (13.8%)		6 (5.5%)		
Motor Weakness	121 (41.7%)		80 (72.7%)		
INO	26 (9.0%)		2 (1.8%)		0.0001
Ataxia	22 (7.6%)		8 (7.3%)		
Cognitive Affection	1 (0.3%)		1 (.9%)		
Oculomotor Affection	3 (1%)		0 (0.0%)		
Clinical Phenotype					
RRMS	233	80.3%	88	80.0 %	
SPMS	1	.3%	18	16.4 %	0.0001
CIS	56	19.3%	1	.9%	
PPMS	0	0.0%	3	2.7%	
DMT Given					
No Treatment	48	16.6%	9	8.2%	
INFB1a	215	74.4%	46	41.8 %	
INFB1b	16	5.5%	9	8.2%	0.0001
Finglomod	10	3.5%	32	29.1 %	
Azathioprine	0	0.0%	6	5.5%	

EDSS: Expanded Disability Status Scale, RRMS: Relapsing Remitting Multiple Sclerosis, SPMS: Secondary Progressive Multiple Sclerosis, CIS: Clinically Isolated Syndrome, PPMS: Primary Progressive Multiple Sclerosis, INO: Internuclear ophthalmoplegia, DMT: Disease Modifying Treatment.

There was an inverse relationship between patient's age and the degree of disability being lower in young and higher in older age groups **(Table 2)**.

In correlating the first clinical manifestations with the degree of disability measured by EDSS score there were highly significant relationship as patients started by motor and cognitive affection had high EDSS score than those started by sensory or optic nerve affection. There was inverse relationship between the time to 2nd clinical event and the EDSS score.

Patients with spinal cord affection and atrophy has high EDSS score compared to those without cord affection.

Highly significant relationship was observed when MS phenotype was

correlated with the degree of disability measured be the EDSS score as relapsing courses was associated with lower EDSS score while progressive courses was associated with high EDSS score.

DISCUSSION

Multiple sclerosis is one of the autoimmune inflammatory diseases so like most autoimmune diseases the incidence always common in female than in males and this may be explained by the effects of sex hormones in the causation of these disorders.

The current results are in agreement with results of the study done in Abu Dhabi included 105 multiple sclerosis patients showed that male: female ratio was 1: 2.75.

Overall, peak age of MS onset is only slightly higher in men (25 years) and then in women (24 years), with some suggestion that age at presentation is increasing over time *(Schiess et al., 2014).*

The current study showed the same results as the mean age of onset in men was 29.13 ± 8.99 and in female was28.13 ± 8.27.As regard mean age of patients in the current study, it was 32.59 ± 9.41years old and the mean age of onset of disease was 28.42 ± 8.48 years old with peak age of onset between 18-40 years old (84.3%) of all patients. The present result was in agreement with result of the Egyptian study in Cairo University that showed that mean age of onset of disease in female was 27.7±7.99 years old, while in males was 29.02 2.63 *(Hashim et al., 2010).*

As regard clinical presentation, in the current study the most frequent presenting

As regard the type of disease modifying treatment (DMT) and the EDSS score there was highlysignificant relationship as patientsreceiving interferons has low EDSS score in comparison to those receiving cytotoxic drugs who has high EDSS score.

symptoms were motor (50.3 %), visual (22.5%), sensory (11.5%), and brainstem lesions (15.25 %). This may be explained by the fact that patients may not seek medical consultation in minor symptoms as sensory, mild cognitive or mild sphinctric affection as opposed by motor weakness the patient asked for medical consultation more rapidly.

This was in agreement with result of the Egyptian study in Cairo University showed that the highest clinical presentation was motor presentation followed by sensory, visual, brainstem and cerebellar lesions, and the least was sphincteric manifestations *(Hashim et al., 2010).*

In the current study, we found that 80.3% of patients had RRMS, 4.8 % had SPMS, 0.8 % had PPMS as the inflammatory component was much higher in the early disease stages than in the late stages where the degenerative changes take the upper hand as more and more axons being lost. These results were near to the results of the Egyptian study in Cairo University showed that the ratio between different courses as RRMS was 73.45%, SPMS was 9.55 and PPMS was 17%, *(Hashim et al., 2010).*

Also, our results that RRMS were 80.3 % these were in agreement with result of studies showed that percentage of RRMS in Dubai (77%), Kuwait (78%) and Qatar (83%) Yet higher result in Jordan was

90% and lower result in KSA was 60% and Iraq was 66%, The PPMS type in the current study was smaller than the previous studies *(Dirk et al., 2013)* which may be due to relatively small number in our study. As regard western countries, a study carried in Colombia showed that 65 % of patients were RRMS *(Ojeda et al., 2009).*

A positive family history of MS was present in 2 % of patients in the current study. These results were near to the results in Lebanon that showed positive family history for MS in 5% of patients, This variation in different countries may be related to the nature of marriage where the marriage in between close relatives is associated with high risk of developing diseases with genetic backgrounds like multiple sclerosis *(Alroughani, et al., 2014).*

Older age at onset is associated with a more rapid disability progression likely due to prevalence of the primary progressive disease course, age dependent degenerative processes, and dysfunction of repair mechanisms in older subjects. The present study showed that first clinical presentation affect future disability of patients such as patients presented by visual and sensory presentation had lower EDSS yet in patients presented by motor, brain stem, focal spinal and combined presentation had higher EDSS with significant relationship, also mean EDSS differ significantly according to their first clinical presentation. The current study revealed highly significant inverse relationship between the time to second clinical event and the total EDSS as the more time to 2nd clinical manifestations reflect less inflammatory changes and slow disease progression. Spinal cord affection and atrophy of the cord demonstrated via spinal MRI examination is an important indicator of disease progression and more disability accumulation as measure by EDSS. Also, the correlation between MS phenotypes and EDSS showed a highly significant relation as relapsing MS is associated with lower EDSS where inflammatory changes is more than axon loss while progressive MS associated with axon loss and low chance for repair is associated with high EDSS score. In the current study the percentage of patients receiving Interferon was 71.5 % compared to 14.3 % did not receive any disease modifying drug and 3.5 % on cytotoxic drug. We have high percent of patients did not receive any disease modifying drug due to financial causes and lack of efficient health insurance system for all patients and some patients presented in progressive stage of disease and the EDSS score is low in patient receiving disease modifying treatments (DMT) than in patient who receive no DMT which reflect the importance of early diagnosis and treatment of the patients.

CONCLUSION

The present study showed that, the first clinical presentation of MS affect the patient EDSS, patients with visual and sensory presentation had commonly lower EDSS, compared to patients with motor presentation had commonly higher EDSS.

CONFLICTS OF INTEREST

There are no conflicts of interest.

HUSSEIN MOHAMED HUSSEIN *et al.,*

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الخصائص الديموجرافية والإكلينيكية والإكلينيكية المساعدة لدي عينة من مرضي التصلب المتناثر المصريين المترددين على عيادات التصلب المتناثربمستشفيات جامعة الأزهر

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خلفيـــة البحـــث: إن التصـلب المتعـدد هـو مـرض التهـاب مناعـي يـؤثر علـى غشـاء الميلانــين المغلــف لأعصــاب الجهــاز العصـبي المركـزي (المـخ والحبـل الشـوكي).وهو عــادة يصـيب الشـخاص فـي أكثـر المراحـل العمريـة إنتاجيـة وتكثـر نسبته لـدي الإنــاث عنــه لـدي الـذكور شـأنه فـي ذلـك شـأن معظـم الأمـراض المناعيـة التـي تكــون أكثـر فـي الإناث.وهنــاك دراســات ديموغرافيـة عديـدة أجريـت علـي مرضي التصلب المتعدد في المجتمعات الغربية.

أمــا المجتمعــات الشــرقية خاصــة البلـدان العربيــة فتحظـي بدراســات متزايـدة لمرضـي التصــلب المتعـدد فـي جميـع نواحيــه مــع تزايـد نسـبة انتشـار المـرض فـي الأونة الأخيرة.

الهـدف مـن البحـث: معرفــة الخصــائص الديموجرافيــة والإكلينيكيــة والإكلينيكيـة المسـاعدة لـدي عينـة مــن مرضـي التصـلب المتنـاثر المصـريين المتـرددين علـى عيـادات التصـلب المتناثربمستشــفيات جامعــة الأزهر(مستشـفى الحسـين ومستشـفى بـاب الشـعرية الجامعيـة) فـي الفتـرة مـن إبريـل 2017 إلـي مـن إبريـل 2019 للوقـوف علي خصائص المرض للارتقاء العلاجي والتأهيلي للمرضي المصابين.

المرضـي وطـرق البحـث: وهي دراسـة وصـفية أجريـت علـي أربعمائـة مـريض (113 مـن الـذكور و287 مـن الإنـاث) تـم تشخيصــهم باسـتيفاء معـايير ماكدونالـد لعـام 2017.

نتـائج البحـث: واسـتنتج منهـا ان نسـبة الإنـاث تقـارب ضـعف نسـبة الـذكور كمـا أن متوسـط عمـر بدايـة المـرض 8.48±28.42 وأن أكثـر الأعـراض ظهـورا فـي بدايـة المـرض الاضـطرابات الحركيـة يليهـا تـأثر العصـب البصـري ثـم الاضـطرابات الحسـية.وأنماط المـرض متعـددة وأكثرهـا شـيوعا هـو النـوع الانتكاسـية المرتـد.كما لـوحظ أن هنـاك إرتباطـا بحـدوث المـرض بنسـبة 2% لـدي الأقـارب الـدين لـديهم تـاريخ عـائلي لوجـود المرض.أيضـا هنـاك علاقـة تـربط بـين جـنس المريضـوعمره وأول الاعـراض ظهـورا ونمـط المـرض والانتظـام فـي العـلاج فـي التـأثيرعلي نسـبة الإعاقة الناتجة عن المرض.

الاسـتنتاج: يوصـي بـإجراء الدراسـة علـي عـدد أكبـرمن المرضـي وفـي مراكزمتعـددة للوقوف علي رؤية أوضح لخصائص المرضي وطرق علاجهم المناسبة.