Zagazig University Medical Journal
www.zumj.journals.ekb.eg

https://doi.org/10.21608/zumj.2022.117321.2458 Volume 29, Issue 4, Jully 2023

Manuscript ID ZUMJ-2201-2458 (R4)
DOI 10.21608/zumj.2022.117321.2458

ORIGINAL ARTICLE

Multiple Sclerosis in Sharkia Governorate through Patients Attending Zagazig University Multiple Sclerosis Unit

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Submit Date 2022-01-25 13:23:54
Revise Date 2022-04-19 22:09:36
Accept Date 2022-03-02

ABSTRACT

Background: Epidemiology of MS in Sharkia is not properly recognized. Clinical evaluation including demographic, laboratory and radiological features of MS patients will help to achieve better understanding of the distribution of disease for a good management that offers better quality of life. This clinical study aims at detection and evaluation of multiple sclerosis patients in Sharkia Governorate in Egypt.

Methods: This was a retrospective, observational study undertaken in the period between January 2021 and July 2021 in the multiple sclerosis unit (MSU), outpatient clinics of the neurology department, Zagazig University Hospitals. Medical records of all patients were reviewed and data were identified and extracted. Any patient not from or living outside Sharkia Governorate had excluded.

Results: The total number of patients recorded in MSU was 258 patients. Female to male ratio was 2.03:1. The mean age (± SD) of onset of the disease was 27 (± 4.3). Family history of MS was reported in 1.94% of patients. RRMS was the most common MS type in our study (77.1%). The overall are suffering from motor symptoms (22.48%), followed by the visual (20.5%) then sensory symptoms (17%). The mean (± SD) EDSS score of our patients was 2.17 (±1.87).

Conclusion: This is the first MS register from Sharkia Governorate. The frequency of MS in Sharkia Governorate is 3.376 / 100,000 population. The most common type is RRMS, and the motor symptoms are the most frequent presenting symptoms. Our results are comparable to the results of other literature.

Keywords; Multiple Sclerosis, Evaluation, Sharkia Governorate, Egypt.

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory auto-immune disease of the central nervous system (CNS) [1]. MS is a leading cause of neurological disability in young adults. The social impact of the disability caused by MS is profound. It results in loss of employment and leads to dependency on care providers and social isolation [2]. The definite etiology of MS is unknown, but it is believed to be triggered by various environmental factors (unhealthy lifestyle with unhealthy dietary habits, vitamin D deficiency, childhood obesity, cigarette smoking and viral infections) in genetically susceptible individuals [3,4]. MS attacks women more than men; the prevalence ratio reaches 3.2:1, respectively [5]. The global median prevalence of MS was about 33/100,000 in 2013 [6]. In Egypt, the prevalence of MS was ranged from 1.41% to 14.1% with maximum distribution of cases in Cairo [7]. The reported prevalence ranged from 0.4% at Assuit, while it was 1.78% at Cairo [8]. In Al-Qusair City, the prevalence of MS was 1.37% [9]. However, a higher prevalence of MS (25/100.000) in Egypt was

reported in other different centers [10]. As the mimicries and society of patients who live in Cairo is by far differs than that in Sharkia Governorate, so we made this research to study the MS disease on patients of our governorate to detect the environmental and genetic affection then comparing our results with other Egyptian studies. This clinical study aims at detect and evaluate characteristics of multiple sclerosis patients in Sharkia Governorate in Egypt.

METHODS

This was an observational, retrospective study that included 258 MS patients attending the multiple sclerosis unit (MSU), outpatient clinics of the neurology department, Zagazig University Hospitals. Randomly collection of all data records in the period between January 2021 and July 2021. Approval was obtained from Zagazig Institutional Review Board (IRB). Exclusion criteria: Any patient not from or living outside Sharkia Governorate. All patients were subjected to full history taking including age, sex, past history of other medical conditions, all patients had been subjected to general and neurological examination with thorough review of reports of previous or recent investigations and ophthalmological evaluation. Full laboratory investigations in the form of complete blood count (CBC), liver function tests, kidney function tests, C-reactive protein, random blood sugar, cerebro-spinal fluid (CSF) immunoglobulins and Oligoclonal bands. Magnetic Resonance Imaging (MRI) brain and spinal cord was done for all patients. We followed the criteria of Filippi et al., (2012) for multiple sclerosis that are based on the presence of focal lesions in the white matter of the CNS, which are considered typical for this disorder in terms of distribution, morphology, evolution, and signal abnormalities on conventional MRI sequences (e.g., T2-weighted and T2-weighted fluid attenuated inversion recovery [FLAIR] scans, and pre-contrast and post-contrast T1-weighted scans), whereas T1-weighted images demonstrate cerebral atrophy and "black holes". These black holes represent areas of axonal death [11]. cerebro-spinal fluid (CSF) examination to confirm the diagnosis was done for all patients. Typical CSF findings in MS include a slightly elevated leukocyte count (5–50 cells per μl), elevated IgG synthesis and oligoclonal bands (OCBs), although normal CSF findings are present in up to 10% of patients with MS [12].

Statistical analysis: All data were collected, tabulated and statistically analyzed using SPSS 26.0 for windows (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as the mean ± SD & median (range), and qualitative data were expressed as absolute frequencies (number) & relative frequencies (percentage). Independent samples Student's t-test was used to compare between two groups of normally distributed variables while Mann Whitney U test was used for non- normally distributed variables. Percent of categorical variables were compared using Chi-square test. All tests were two sided. p-value < 0.05 was considered statistically significant (S), p-value ≥ 0.05 was considered statistically insignificant (NS).

RESULTS

The total number of MS patients was 258 with the mean age of onset was 27 ± 6.9 and mean BMI was 27.77±7.88. Most of the patients were females (174 patients, 67.4%). The family history was recorded in (1.94%) of cases. Smoking was recorded in 5.8% of the patients (table 1).

The majority of MS patients were Relapsing-Remitting MS (77.1%), followed by secondary progressive MS (17.1%). Clinically isolated syndrome (CIS) type and Primary progressive MS represented 3.5% and 2.3% respectively (table 2). Medical history of hypertension was recorded in 17.8% and 28.3% had arthritis. About 30.6% of patients gave a positive history of headache. Skin rash was reported in 10.8 % of patients (table 3).

Motor symptoms were present in 22.48% of patients, followed by visual symptoms (20.5%) as the first presentation. Sensory manifestations represented about 17.1% of patients while cerebellar symptoms were reported in 5.4% of patients. There was a statistically significant difference between male and female patients regarding smoking, age, BMI, age of onset and duration of the disease with male patients being smokers with older age, lower BMI, later onset and longer duration (table 5).

Table(1): Demographic characteristics of the patients:

Variables	Total (n=258)
	(%) N
Sex Male Female	 (%32.5) 84 (%67.5) 174
Family history Positive Negative	 (%1.94) 5 (%98.06) 253
Smoking	(%5.81) 15
Age at onset (Mean ± SD)	6.9 ± 27.0
BMI **(Mean ± SD)**	7.88±27.77

BMI = Body mass index.

Table(2):Number of patients with different clinical disease types:

Variables	Total
	(%) N
Clinically isolated syndrome (CIS)	**(3.5) 9**
Relapsing-remitting MS (RRMS)	**(77.1) 199**
Secondary progressive MS (SPMS)	**(17.1) 44**
Primary progressive MS (PPMS)	**(2.3) 6**

Table(3): Types of co-morbidity among studded patients:

Variables		Males (n=84)	Females (n=174)
	(%)N	(%) N	(%) N
Chronic heart diseases	**(2.3) 6**	**(4.8) 4**	**(1.14) 2**
Chronic lung diseases	**(7.4) 19**	**(9.5) 8**	**(6.3) 11**
Hypertension	**(17.8) 46**	**(36.9) 31**	**(8.6) 15**
Diabetes mellitus	**(5.4) 14**	**(9.5) 8**	**(3.44) 6**
Arthritis & joint pain	**(28.3) 73**	**(38.1) 32**	**(23.5)41**
Thyroid diseases	**(2.3) 6**	**(0.0) 0**	**(3.44) 6**
Gastro-intestinal diseases	**(21.7) 56**	**(29.7) 25**	**(17.8) 31**
Recurrent oral & genital ulcers	**(1.16) 3**	**(0.0) 0**	**(1.7) 3**
Raynaud's phenomenon	**(0.4) 1**	**(0.0) 0**	**(0.6) 1**
Collagen vascular diseases	**(0.4) 1**	**(1.2) 1**	**(0.0) 0**
Skin rash	**(10.8) 28**	**(19.04) 16**	**(6.9) 12**
Photosensitivity	**(0.0) 0**	**(0.0) 0**	**(0.0) 0**
Renal impairment	**(0.8) 2**	**(1.2) 1**	**(1.14) 1**
Liver impairment	**(8.9) 23**	**(10.7) 9**	**(8.04) 14**
Deep venous thrombosis	**(0.8) 2**	**(0.0) 0**	**(1.14) 2**
Headache	**(30.6) 79**	**(39.3) 33**	**(26.4) 46**
Recurrent abdominal pain	**(0.8) 2**	**(1.2) 1**	**(0.6) 1**

There was no statistically significant difference between male and female patients regarding biomarkers results but there was significant difference regarding IgG index in CSF (table 6). There was a statistically significant difference between MS types regarding the presenting symptoms with sensory and visual symptoms associated with RRMS type, while brain stem symptoms were associated with all types. Uncommon symptoms were all reported in RRMS type.

There was a statistically significant difference between MS types regarding EDSS with higher values reported in SPMS and PPMS types (table 7). There was a statistically significant difference between MS types regarding all MRI findings ($p<0.05$) with the most significant brain activity in the RRMS type (table 8).

Table (4): Clinical characteristics at onset of the disease:

Variables	Total n=(258)	
	N	%
Brain stem	38	14.73
Cerebellar	14	5.4
Combined	15	5.8
Motor	58	22.48
Sensory	44	17.1
Focal spinal	36	13.9
visual	53	20.5

Table(5):Differences between males and females regarding to type of the disease and clinical findings:

Variables		Total N=258	males N=84	Females N=174	X2	P value
		(%) N	(%) N	(%) N		
Types of MS. (%)N	RRMS	(77.13) 199	(31.16) 62	(68.84) 137	0.31	0.937
	SPMS	(17.05) 44	(29.55) 13	(70.45) 31		
	PPMS	(2.33) 6	(33.33) 2	(66.66) 4		
	CIS	(3.49) 9	(22.22) 2	(77.78) 7		
Family history	Positive	(1.94) 5	(1.16) 3	(0.77) 2	2.7	0.842>
Smoking	Smoker	(5.8) 15	(4.65) 12	(1.16) 3	15.8	*0.001>
		Mean ± SD **(Range)**			T	P value
Age (years), Mean±SD		4.3±33.2	4.3±34.6	4.3±31.8	4.9	*0.001>
BMI (kg/m2), Mean±SD		7.88±27.77	6.88±26.24	7.29±29.30	3.2	*0.0015
Onset (years), Mean±SD		6.9 ±27.0 (40-19)	7.2± 25.1 (32-19)	8.2 ±19.2 (35-20)	5.6	*0.001>
Duration (years), Mean±SD		3.5±3.7 (15-1)	2.9±4.3 (6-1)	3.8±3.1 (18-1)	2.55	*0.011
Total relapse number, Mean±SD		1.63±3.23 (7-1)	1.84±3.45 (8-1)	1.53±3.12 (6.5-1)	1.51	0.13
EDSS, Mean±SD		1.87±2.17 (7-0)	1.96±2.34 (7-0)	1.87±2.1 (6-0)	0.95	0.342
ARR, Mean±SD		0.89±1.08 (5-0.24)	0.82±1.2	0.93±0.99	1.76	0.078

Table (6): Males and females differences as regard laboratory findings.

Variables	Total N=258	males N=84	Females N=174		
	Mean (Rang)			test	P value
Total :cholesterol(mg/dl) Mean±SD	35.6±194	36.3±194.1	34.8±194.8	0.149	0.881
	(328.4-149)	(330-148)	(329.3-149)		
:TGL (mg/dl) Mean±SD	51.8±141.9	52.0±140.3	51.3±141.8	0.219	0.826
	(253 – 120)	(254 – 120)	(252 – 120)		
:LDL (mg/dl) Mean±SD	36±115.6	37.0±115.3	37.1±115.8	0.101	0.919
	(184-38)	(186-38)	(186-38)		
:HDL (mg/dl) Mean±SD	7±40.8	7.0±40.7	7.2±40.9	0.199	0.842
	(56.9-31)	(56.9-31)	(56.9-31)		
:ESR first hour Mean±SD	24.6±27.7	21.9±27.3	25.3±28.2	0.268	0.788
	(55-3)	(55-3)	(55-3)		
:ESR 2 hours Mean±SD	24.6±55.7	25.6±53.21	24.8±55.9	0.783	0.434
	(98-8)	(99-7)	(97-8)		
CRP	17.15±19.52	16.4±19.4	17.3±19.61	0.088	0.929

Variables		Total N=258	males N=84	Females N=174		
		(46.64-0.24)	(46.5-0.23)	(46.71-0.25)		
CSF	IgG in CSF	2.8±5.16	2.88±5.24	2.6±5.03	0.551	0.582
examination		(9.13-0.63)	(8.9-0.61)	(0.33-0.82)		
N=88) (	IgG index	0.32±0.81	0.3±0.8	0.33±0.82	2.81	*0.005
	in CSF	(1.18-0.3)	(1.18-0.3)	(1.19-0.31)		
	Oligoclonal	(%) N	(%) N	(%) N	x2	
	al bands	(94.3) 83	(14.8) 13	(79.5) 70	15.9	*0.001>

t test : independent t test
X^2 : Chi square test
N : number
CSF : cerebrospinal fluid
CRP: C- Reactive protein
LDL:Low Density Lipoprotein
ESR:Erythrocyte Sedimentation Rate
TGL: Triglyceride
HDL: High density lipoprotein
IgG: Immunoglbulin G

Table (7): Distribution of symptoms among different types of disease:

Variables	CIS	RRMS	SPMS	PPMS		
	N (n=9)	N (n=199)	N (n=44)	N (n=6)	x2	P value
Brain stem (n=38)	**(5.26)2**	**(47.36) 18**	**(42.1) 16**	**(5.26)2**	**23.5**	***0.001>**
Cerebellar (n=14)	**-**	**(71.42) 10**	**(28.57) 4**	**-**	**2.6**	**0.456**
Combined (n=15)	**(20) 3**	**(60) 9**	**(13.3) 2**	**(6.66) 1**	**14.47**	***0.002**
Motor (n=58)	**(1.8) 1**	**(81.03) 47**	**(16.36) 9**	**(1.8) 1**	**0.73**	**0.866**
Sensory (n=44)	**-**	**(93.1) 41**	**(2.27) 1**	**(4.54) 2**	**9.71**	***0.021**
Focal spinal (n=36)	**-**	**(77.77) 28**	**(22.22) 8**	**-**	**0.598**	**0.896**
visual (n=53)	**(5.7) 3**	**(86.8) 46**	**(7.5) 4**	**-**	**5.2**	**0.157**
x2 Chi square test * significant <0.05						

RRMS: Relapsing remittent multiple sclerosis
PPMS: Primary progressive multiple sclerosis
SPMS: Secondary progressive multiple sclerosis
CIS: Clinical isolated sclerosis

Table (8): Radiological finding among different disease types:

MRI findings		Types of MS				x2	P value
		CIS (n=9)	RRMS (n=199)	SPMS (n=44)	PPMS (n=6)		
		(%) N	(%) N	(%) N	(%) N		
Presence of T1 black holes		**(0) 0**	**(8.1) 16**	**(63.63) 28**	**(33.3) 2**	**76.3**	***0.001>**
Sites of lesions	**Juxtacortical**	**(33.3) 3**	**(80.9) 161**	**(61.36) 27**	**(83.3) 5**	**16.9**	***0.001>**
	Periventricular	**(77.77) 7**	**(92.96) 185**	**(56.82) 25**	**(33.3) 2**	**49.9**	***0.001>**
	Infratentorial	**(0) 0**	**(16.08) 32**	**(54.54) 24**	**(33.3) 2**	**31.3**	***0.001>**
Activity	**Enhancement**	**(33.3) 3**	**(40.2) 80**	**(31.81) 14**	**(0) 0**	**2.87**	**0.410**
	New T2 lesions	**(0.0) 0**	**(29.14) 58**	**(29.54) 13**	**(100) 6**	**11.9**	***0.007**
MRI brain	**Active**	**(0.0) 0**	**(40.7) 81**	**(95.45) 42**	**(100) 6**	**52.25**	***0.001>**

DISCUSSION

Multiple sclerosis is the most common neuroimmunological disorder in young adults [13]. The aim of this study was to evaluate the clinical characteristics of multiple sclerosis patients in Sharkia Governorate. Zagazig University medical center is the tertiary referral center in Sharkia Governorate, so data from this center represent the frequency and characteristics of MS disease in Sharkia Governorate. In our study the percentage of MS in Sharkia Governorate was 3.376/100,000 population which is considered lower than that recorded by different studies about the prevalence of MS in Egypt (14.1/100,000 population) [9]. The explanation to this difference may be due to the higher number of population in Sharkia Governorate as it is the third governorate regarding the number of population in Egypt (about 7.64 million population) [14]. Also, there is inadequate medical knowledge about MS disease between

general practitioner doctors. In our study the female: male ratio was 2.03:1 and this is in accordance with a previous Egyptian study that reported a ratio of 2.57:1 [15]. Our result was higher than that in some Middle East countries as in Iraq (1.2:1) [16], Kingdom of Saudi Arabia (1.32:1) [16], and Qatar (1.33:1) [17]. The mean age of our patients was 33.2 years. This is in agreement with the Egyptian study which was 31 years [15]. The mean age of onset of the disease was 27 ± 4.3. Five cases (1.94%) of our patients have a family history of MS, this result is lower than that of the other Egyptian studies 6% of positive family history recorded by Zakaria et. al. 2016 [15] while Hamdy, et al. (2017) found positive family history to be 2.28% in patients attending four tertiary referral MS centers in Cairo [18]. A larger proportion with this risk factor for MS was observed in Qatar (17%); KSA (21%)(24),, and Dubai (19%), which may be related to consanguineous marriages [19]. Relapsing remitting multiple sclerosis was the most common MS presentation in our study (77.1%), which was approximately similar to data recorded by Ain Shams University study in Egypt (75%) [15] and other Arab countries as Dubai [19], Kuwait and Qatar (77–83%) [20]. However, it was lower than that reported in Jordan (90%) but higher than in KSA (60%) and Iraq (60%) [16 & 20]. Data from other countries are variable, suggesting a prevalence of RRMS of 63% in Greece, 64% in Austria, 65% in Colombia or 84% in Sweden [21]. In the present study, the most frequent presenting symptoms overall were motor symptoms (21.3%), followed by the visual (20.5%) then sensory symptoms (17%). A motor presentation was also the common presentation in other Egyptian studies (20.9 %) followed by visual (20.5%) then sensory (17%) [15]. Sensory symptoms were more common as presenting symptoms in studies from Qatar and Kuwait [16 & 17]. The Expanded Disability Severity Scale (EDSS) remains the gold-standard measure for assessing the level of disability in MS [22]. The mean EDSS score of our patients was 2.17 ± 1.87, this is in accordance with other studies from Dubai (2.4) [19] and KSA (2.5) [20]. Our result was lower than other Egyptian studies 3.6 [15]; and some Arab countries such as Jordan (3.9) [21], but was slightly lower than that in Qatar (2.7) [17].

In our patients there was no statistically significant difference between male and female patients regarding biomarkers results, but there was significant difference regarding IgG index in CSF and oligoclonal bands being higher in female patients. The same results were found by Florian and his colleagues [23].

CONCLUSION

We concluded that the frequency of MS in Sharkia Governorate was 3.376 /100,000 population. The female: male ratio is 2.03:1; while the mean age of onset of the disease is 27 ± 4.3. RRMS was the most common MS presentation in our study (77.1%). The most frequent presenting symptoms overall are motor symptoms (22.48%), followed by the visual (20.5%) then sensory symptoms [17]. The mean EDSS score of our patients was 2.17 ± 1.87. Recommendation: We recommend that it is mandatory to increase awareness among medical students and general practitioners regarding clinical manifestations and diagnosis of multiple sclerosis and notify the increasing prevalence of this disease in our governorate.

Conflict of interest: None.

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To Cite:
Ramadan, B., Fahmi, R., Soliman, A., Hassan, M., Almotaym, A., Sarhan, N. Multiple Sclerosis in Sharkia Governorate through Patients Attending Zagazig University Multiple Sclerosis Unit. *Zagazig University Medical Journal*, 2023; (1044-1050): -. doi: 10.21608/zumj.2022.117321.2458