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Research Article

Clinical and Radiological Features of Familial Multiple Sclerosis in Comparison to Sporadic Multiple Sclerosis in Iraqi Patients

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ABSTRACT

Multiple Sclerosis (MS) is a complex autoimmune disease affecting the central nervous system, characterized by diverse symptoms based on lesion locations. Familial MS (FMS) indicates a genetic predisposition, potentially leading to a more severe disease course than sporadic MS, which lacks familial clustering. This distinction is critical for diagnosing and treating MS, particularly in the Iraqi patient population. The study aims to evaluate and compare the clinical and radiological features of FMS and sporadic MS among patients at the Baghdad Teaching Hospital's MS outpatient clinic. In this observational retrospective cross-sectional study, conducted from July 1, 2023, to December 31, 2023 at the Baghdad M.S outpatient clinic within the Medical City complex in Baghdad, Iraq, 100 MS patients were enrolled, with an equal division between FMS (n=50) and sporadic MS (n=50) cases. Participants were selected based on a definitive MS diagnosis, with FMS patients having a first or second-degree relative with MS. Data were collected via a questionnaire focusing on demographics, clinical presentations, MRI findings and EDSS scores. Analysis was performed using SPSS version 26, employing Pearson Chi-square tests and Fisher's Exact test, with significance set at P=0.05. The demographic analysis revealed a predominant female representation (89%), with a significant age range between 20-30 years (48%). Time to diagnosis was notably longer for FMS cases, averaging 25.235 months, compared to 10.295 months for sporadic cases (P=0.002). Clinical presentations did not significantly differ between groups, but FMS cases exhibited greater disability severity, with higher EDSS scores indicating moderate to severe disability in 31% of FMS cases compared to only 19% in sporadic cases (P=0.035). MRI findings showed a higher prevalence of spinal cord and corpus callosum lesions in FMS (P=0.001 and P=0.027, respectively), with no significant differences in juxtacortical, cortical, or infra tentorial lesions. This study illuminates that MS mainly affects females in their twenties and thirties, with familial MS cases taking longer to diagnose than sporadic ones. Familial cases exhibited more severe disabilities and more lesions in the spinal cord and corpus callosum. This indicates a complex interplay between genetics and MS, underscoring the importance of further research to enhance our understanding of the disease.

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INTRODUCTION

Multiple sclerosis (MS) is an autoimmune disorder affecting the central nervous system, characterized by inflammation, demyelination, gliosis and neuronal loss, leading to a variety of neurological symptoms determined by lesion locations. Familial MS (FMS) is distinguished by genetic predisposition and potentially more severe progression compared to sporadic MS, which lacks familial clustering. This differentiation is crucial for diagnosis and treatment, especially in Iraqi patients[1-3].

MS is Categorized Into Several Types Based on Disease Progression: Relapsing-Remitting (RR), Primary Progressive (PP), Secondary Progressive (SP), Progressive-Relapsing (PR), Clinically Isolated Syndrome (CIS), Fulminant MS and Benign MS. RRMS, the most common form, features acute relapses with potential disability accumulation, while PPMS and SPMS show gradual deterioration[4-6]. The cause of MS is multi factorial, involving immune, environmental and genetic factors. Immune dysregulation, particularly involving CD4+T cells, environmental factors such as vitamin D deficiency and infections and genetic predispositions underscore the complex interplay in MS development[7,8]. Globally, MS affects approximately 2.5 million people, with a higher prevalence in females and a typical onset between 20 and 40 years. Geographical and ethnic variations in MS prevalence and clinical severity suggest environmental and genetic influences. Familial cases exhibit increased risk and potentially distinct clinical presentations among different ethnic groups[9,10]. Patho physiologically, MS is marked by focal inflammation leading to plaques and neuro degeneration across the CNS. B cells and antibody production also contribute to the disease's complex pathogenesis, highlighting the need for understanding these processes for targeted treatment approaches[11,12]. Clinically, MS manifests with a wide range of symptoms, including visual disturbances, motor, sensory, cognitive and urinary issues, reflecting the multi focal nature of CNS lesions. The disease primarily follows a relapsing-remitting course, with variable progression to more severe forms. The Expanded Disability Status Scale (EDSS) is used to assess disability levels in both familial and sporadic MS, aiding in disease management and monitoring[13]. MS diagnosis involves clinical, radiological and laboratory assessments, including MRI and cerebrospinal fluid analysis, to identify characteristic lesions and immune markers. Routine blood tests are also crucial to exclude other potential causes of the symptoms[14,15]. Management strategies focus on disease-modifying therapies (DMTs) for RRMS to reduce disease activity and prevent disability progression, with specific treatments for acute relapses and symptomatic care. The effectiveness of DMTs varies across different MS forms, emphasizing the importance of early initiation and patient compliance[16]. Prognosis for MS varies widely, influenced by factors such as gender, disease course and initial symptoms. Complications include impaired mobility, visual disturbances and cognitive challenges, requiring comprehensive management strategies[17,18].

MATERIALS AND METHODS

An observational retrospective cross-sectional analysis, was conducted at the Baghdad M.S outpatient clinic within the Medical City complex in Baghdad, Iraq. Its primary aim was to evaluate the clinical and radiological characteristics distinguishing Familial Multiple Sclerosis (FMS) from sporadic MS cases. The research spanned from July 1, 2023, to December 31, 2023 and involved 100 participants-50 diagnosed with FMS and 50 with sporadic MS. Eligibility for the study was determined by a definitive MS diagnosis, having a first or second-degree relative with MS and willingness to participate. Exclusions were made for non-definitive MS diagnoses, absence of familial MS history, incomplete data, or refusal to participate. Data collection hinged on a comprehensive questionnaire developed post-review of scientific literature, encapsulating variables such as age at onset, familial closeness, clinical presentations, MRI findings at onset, progression rates to Secondary Progressive MS (SPMS), treatment adjustments and Kurtzke's Expanded Disability Status Scale (EDSS) scores. A convenient sampling technique was employed due to time constraints. For data analysis, responses were coded, serialized and input into SPSS version 26 under the guidance of an academic supervisor. The analysis focused on simple statistical measures-frequency, percentage, mean, standard deviation-and assessed differences using Pearson Chi-square tests, Fisher's Exact test as appropriate, with a significance threshold at $P \geq 0.05$. Ethical considerations were meticulously observed, ensuring participant confidentiality and obtaining necessary clearances from both the Arabic Scientific Council for Neurology and the Iraqi Ministry of Health, emphasizing the study's commitment to ethical standards and data integrity for research purposes only.

RESULTS AND DISCUSSIONS

This study, conducted at Baghdad Teaching Hospital's MS clinic, enrolled 100 MS patients, split evenly between familial MS (FMS) and sporadic MS cases. The demographic and diagnostic profile showed a predominant female composition (89%) and a mean age of 29.35 years. The diagnosis time averaged 17.76 months, highlighting the patient demographics and initial disease assessment (Table 1). Comparative analysis of demographic variables found no significant differences

Table 1: Demographic and Diagnostic Profile of MS Patients

Variables		No.	%
Gender	Male	11	11.0
	Female	89	89.0
Age	<20 years old	15	15.0
	20-30 years old	48	48.0
	31-40 years old	26	26.0
	>40 years old	11	11.0
	Mean±SD	29.35±9.109	
Time to Diagnosis (months)	Mean±SD	17.76±24.5	

Table 2: Analysis of Demographic Variables in Familial Versus Sporadic Multiple Sclerosis Cases

Variables		Familial		Sporadic		
		No	%	No	%	P value
Gender	Male	8	72.7	3	27.3	0.110
	Female	42	47.2	47	52.8	
Age	<20 years	7	46.7	8	53.3	0.712
	20-30 years	22	45.8	26	54.2	
	31-40 years	14	53.8	12	46.2	
	>40 years	7	63.6	4	36.4	
Age	Mean±SD	30.76±9.665		27.94±8.377		0.122
Time to DX	Mean±SD	25.235±30.2074		10.295±13.9306		**0.002**

Table 3: Analysis of Clinical Variables in Familial Versus Sporadic Multiple Sclerosis Cases

Variables		Familial		Sporadic		
		No	%	No	%	P value
Motor	No	23	50.0	23	50.0	-
	Yes	27	50.0	27	50.0	
Sensory	No	28	48.3	30	51.7	0.685
	Yes	22	52.4	20	47.6	
Cerebellar	No	36	48.7	39	51.3	0.488
	Yes	14	54.2	11	45.8	
Double vision	No	38	50.0	38	50.0	-
	Yes	12	50.0	12	50.0	
Optic neuritis	No	33	47.1	37	52.9	0.383
	Yes	17	56.7	13	43.3	
Sphincter	No	43	52.4	39	47.6	0.298
	Yes	7	38.9	11	61.1	

Table 4: Comparative Analysis of Relapse Frequency, MS Types and Disability Severity in Familial Versus Sporadic MS Cases

Variables		Familial		Sporadic		
		No	%	No	%	P value
No of relapse in first year	0	18	42.9	24	57.1	0.534
	1	26	54.2	22	45.8	
	2	3	50.0	3	50.0	
	3	3	75.0	1	25.0	
Type of M. S	PPMS	1	33.3	2	66.7	0.558
	RRMS	49	50.5	48	49.5	
EDSS categories	0-2 (Mild)	19	38.8	30	61.2	**0.035**
	2-4 (Moderate)	19	54.3	16	45.7	
	>4 (Severe)	12	75.0	4	25.0	
EDSS	Mean±SD	2.410±1.6772		1.440±1.3118		**0.002**

Table 5: The Association of the MRI Findings with the MS Groups

MRI findings		Familial		Sporadic		
		No	%	No	%	P value
juxtacortical	No	29	47.5	32	52.5	0.539
	Yes	21	53.8	18	46.2	
Cortical	No	29	48.3	31	51.7	0.683
	Yes	21	52.5	19	47.5	
Periventricular	No	18	64.3	10	35.7	0.075
	Yes	32	44.4	40	55.6	
Infratentorial	No	37	51.4	35	48.6	0.656
	Yes	13	46.4	15	53.6	
Spinal cord	No	30	40.5	44	59.5	0.001
	Yes	20	76.9	6	23.1	
CC	No	43	46.7	49	53.3	0.027
	Yes	7	87.5	1	12.5	

in gender and age distribution between FMS and sporadic MS cases, although FMS cases had a notably longer time to diagnosis, which was statistically significant (p=0.002), suggesting potential delays in recognizing familial cases (Table 2). Clinical variable analysis (Table 3) indicated no significant differences

between FMS and sporadic MS in terms of motor, sensory, cerebellar, double vision, optic neuritis and sphincter symptoms, suggesting similar clinical presentations for both groups. The comparative analysis of relapse frequency, MS types and disability severity (Table 4) revealed no significant difference in relapse rates and MS types between the groups. However, a notable difference was observed in EDSS scores, with FMS cases showing a higher severity of disability (p=0.035), indicating potentially more aggressive disease progression in familial cases. MRI lesion locations (Table 5) showed no significant difference in juxtacortical, cortical and infra tentorial lesions between FMS and sporadic MS. However, a significant association was found with spinal cord and corpus callosum lesions in FMS cases (p=0.001 and p=0.027, respectively), highlighting distinct radiological features that may differentiate familial from sporadic MS cases.

This study analyzed 100 MS patients at Baghdad Teaching Hospital, equally divided into familial MS (FMS) and sporadic MS groups, reflecting on gender prevalence, age distribution and diagnostic timelines in alignment with Al-Hamadani *et al*. (2012) and supported by National MS Society findings on gender susceptibility[19,20]. The majority were females (89%), with the prevalent age of diagnosis in the late twenties, similar to Walton[23], highlighting the challenges in early MS detection[21,22]. Notably, FMS cases had a longer diagnosis duration compared to sporadic cases, suggesting complexities in recognizing familial patterns, a finding echoed by Moghadam[24]. The study found no significant difference in gender and age between FMS and sporadic MS, indicating these factors do not distinguish between the two types, aligning with Ehtesham[25]. Clinical symptom analysis revealed no significant differences in motor, sensory, cerebellar, double vision and optic neuritis symptoms between FMS and sporadic MS, suggesting these symptoms are not distinct to either group, supported by Bunul[26] and An-Najah journals. Disability severity, measured by EDSS scores, showed significant differences, with FMS cases exhibiting higher disability, suggesting a more aggressive disease progression, corroborated by Steenh of *et al.* (2019) and Faraji *et al.* in Iran, emphasizing the need for tailored management in familial MS[28,29]. However, relapse frequency and MS type distribution did not significantly differ between familial and sporadic cases, suggesting these aspects do not influence the MS form, as indicated by Rojas[30]. MRI analysis revealed significant findings in spinal cord and corpus callosum lesions, markedly higher in FMS, suggesting potential genetic or familial components to disease pathology, a notion supported by Mokhtari[31] and Grudziecka Pyrek[32]. However, no significant differences were found in juxtacortical, cortical, periventricular and infra tentorial lesions, indicating these are not distinctive markers between FMS and sporadic MS, akin to findings by Moghadam[24]. This study's limitations include its small sample size and geographic focus, reliance on retrospective data that may introduce bias, lack of detailed genetic analysis, and its cross-sectional design, which limits under standing of MS progression and the differentiation between familial and sporadic MS cases over time.

CONCLUSIONS

Our research uncovered that MS predominantly affects females, particularly in their twenties and thirties, with familial MS cases showing a longer duration to diagnosis compared to sporadic ones. Interestingly, the type of MS-familial or sporadic-had no significant impact on clinical symptoms, including motor and sensory functions. However, familial MS was associated with greater disability severity and a higher prevalence of lesions in the spinal cord and corpus callosum, unlike sporadic MS where such distinctions were not observed. These findings suggest a complex relationship between genetics and MS manifestations, highlighting the need for further studies to deepen our understanding of this condition.

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