ORIGINAL ARTICLE

Clinical and Radiological Evaluation of Movement Disorders in Multiple Sclerosis

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Abstract

Background: ***Movement disorders (MDs) are among the numerous symptoms of multiple sclerosis (MS), a neurodegenerative, inflammatory disease.***

Aim of the work: ***We conducted this study to determine the prevalence of MDs in patients with MS (PwMS), to know the clinical type of MDs occurring with PwMS, and the MRI finding of those patients.***

Patients and Methods: ***This was a cross-sectional study that screened PwMS between September 2022 and September 2024. We assessed the prevalence of MDs, their clinical phenotypes, and the MRI findings for those patients.***

Results: ***Out of 320 screened PwMS, 76 (24%) experienced MDs. Mean age was 27.76; 58% were female, and 84% were urban residents. Most of the patients (64.5%) had one MD. The first exhibited MDs were as follows: ataxia (42%), extensor spasms (17%), tremors (13%), and restless legs syndrome (11%). The percentage of extensor spasms (3.9%) and ataxia (6.6%) decreased if presented as a second MD. All patients had periventricular lesions; juxtacortical (92%), cortical (32%), frontal subcortical (44%), and lentiform nucleus lesions (43%) were common. Bilateral lesions were frequent, especially in frontal subcortical regions (69.7%). Infratentorial lesions, mainly in the pons (66.2%), also involved the midbrain and cerebellum. We noted peri-ependymal brainstem lesions (38.1%) and cervical spine abnormalities (80.3%).***

Conclusion: ***Our study revealed that MDs are prevalent among PwMS. Different MDs may occur including ataxia and RLS, and tremors. Additionally, we observed significant diversity in the location of MS lesions in the brain, which presumably contributes to the varied clinical presentations of the MDs.***

Keywords: Multiple sclerosis; Movement disorders; Ataxia; Extensor spasm; restless leg syndrome; Radiological; Supratentorial; Infratentorial

1. Introduction

Multiple sclerosis (MS) is an immune-mediated disease that affects the neurological system of the body, leading to myelin degeneration and axonal injury in the brain and spinal cord. It is a significant cause of non-traumatic brain injury in young people. The latest account of multiple sclerosis cases globally is 2.8 million, with a prevalence rate of 35.9 per 100,000 individuals.[1,2] Demyelinating diseases (DDs) have demonstrated an association with movement disorders (MDs).[3] The precise frequency and prevalence of MDs in MS remain ambiguous due to previous research primarily being retrospective, relying on brief case series or review papers .[4] Furthermore, there is an inconsistency among authors on the diagnosis of MDs in multiple sclerosis, with some focusing exclusively on typical extrapyramidal diseases while others include tonic spasms, cerebellar tremors, spasticity, and ataxia. This resulted in considerable variability in the reported rates across multiple studies. Moreover, MDs not associated with multiple sclerosis, such as essential tremors, may have undermined the findings of previous studies.[5] In PwMS, the appearance of MDs may be related, either causally or coincidentally. [6]

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A prior study revealed that tremor is the most prevalent movement disorder in multiple sclerosis (MS), while additional movement disorders have been documented in approximately 1.6% of MS patients .[6] Other MDs, such as tonic spasms and paroxysmal focal dystonia, may occur as the initial presentation of the disease.[5] Moreover, variable other MDs might occur, including paroxysmal hemi-kinesigenic dyskinesia (PHKD), restless leg syndrome (RLS), myoclonus, fasciculations, tics, and hemifacial spasm (HFS). .[7,8]

MDs often occur due to the lack of myelin or neurodegenerative sequelae linked to MS. The varied processes and pathways involved allow us to assess this link individually.[9] MDs may manifest rapidly after MS attacks in the spinal cord, brainstem, or cerebellum. Also, in certain instances, they may serve as the initial manifestation of an MS attack.[8,10] MS lesions that cut off the extrapyramidal system in different locations can cause MDs in PwMS by changing the plasticity of neurons.[6] Myelin-covered axons cover many areas of subcortical grey matter, and the brainstem, striatum, pallidum, and thalamus are the primary locations for plaques associated with MDs. However, the majority of recorded cases did not identify a link between lesion placement and MDs. [9,11] Therefore, we conducted this study to determine the prevalence of MDs among MS patients. We also aim to understand the specific clinical types of MDs that PwMS experienced, as well as the MRI results for those patients.

2. Patients and methods

Study Design and Setting:

We performed a cross-sectional study on diagnosed multiple sclerosis patients exhibiting movement disorders throughout their disease course. We studied the prevalence of movement disorders in MSM.S. patients, the clinical type of movement disorder, and their MRI findings. Data collected from patients admitted or following up at Al-Azhar University hospitals at Al-Hussein and El-Sayed Galal hospitals during the study period from September 2022 to September 2024.

Ethical considerations:

All procedures conducted in studies that involved study participants adhered to the institutional and/or national research committee's ethical standards, as well as the 1975 Helsinki Declaration and its subsequent amendments or comparable ethical standards .[12] We obtained written informed consent from all patients who were enrolled in the study. We conducted the study in accordance with the recommendations of our institutional ethical committee and the Institutional Review Board (IRB) Neuro-Med._0000044. All participants received clear illustrations of all clinical interventions prior to the study's processing.

Participants Selection and Data Collection:

Included patients:

The study included diagnosed MS patients, depending on the revised McDonald criteria for MS 2017.[13] We studied the prevalence of MDs among the screened PwMS. We also reported on the various clinical types of MDs in PwMS. We conducted an epidemiological evaluation including demographic information such as age, sex, residence, occupation, education level, marital status, co-morbid medical conditions, and MS type. We also evaluated the MDs by taking a history, which included the clinical phenotype of the movement (which was done by an oral quick survey for the PwMS). We also reported the MRI lesions in those patients.

Excluded patients:

We excluded individuals with multiple sclerosis mimicking conditions that cause MDs, such as systemic lupus, overlap syndromes, CNS infections, or Behcet's disease. We also excluded individuals with systemic illnesses that cause MD, such as hepatic failure, renal failure, and hyperthyroidism. We also excluded participants with primary movement disorders or other neurodegenerative diseases.

Sample size calculation:

We calculated the sample size for movement disorders, specifically abnormal or involuntary movements, in a clinically presented sample of multiple sclerosis patients. As reported in Abboud et al.8, to be able to reject the null hypothesis with 90% power at the $\alpha = 0.05$ level using one-way analysis of variance and test ratio, and with a 15% dropout rate considered, we found that the minimum sample size was 57 people. We used G*Power software version 3.1.2 for Microsoft Windows to calculate the sample size. [14]

Statistical Analysis:

We compiled a comprehensive summary of all assessment data, including demographics, using descriptive techniques tailored to the data type. We summarized the quantitative variables using the mean, standard deviation, and the 2-sided 95% confidence interval (CI) of the mean, median, minimum, and maximum. We summarized the qualitative variables using counts, percentages, and the number of non-missing data. In the non-paired comparison, we carried out independent t-tests. We conducted categorical data analysis using the chi-square test. We employed SPSS version 25.0 to conduct all data analyses .[15] P-values <0.05 were specified as the threshold for statistical significance.

3. Results

The prevalence of movement disorders among PwMS

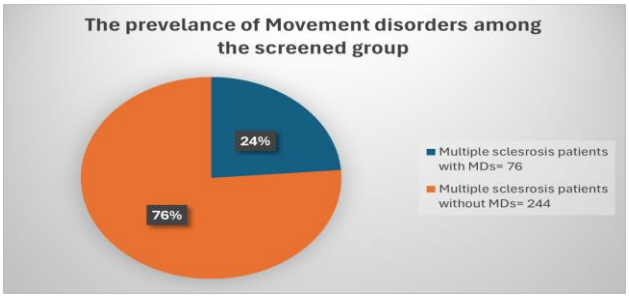

Figure 1. showed the prevalence of movement disorders among the screened group

Among 320 screened MS patients, this cross-sectional study included 76 patients with multiple sclerosis who experienced MDs. Thus, the prevalence rate was (24%).

Demographic Characteristics

Table 1. Demographic characteristics of the included multiple sclerosis patients.

DEMOGRAPHIC CHARACTERISTIC	N = 76
[1]AGE, [YEARS]	27.76 ± 9.392
GENDER	
FEMALE	44 (58%)
MALE	32 (42%)
RURAL/ URBAN	
RURAL	12 (16%)
URBAN	64 (84%)
OCCUPATION	
NOT WORKING	8 (11%)
HOUSEWIFE	17 (22%)
STUDENT	26 (34%)
WORKING	25 (33%)
MARITAL STATUS	
DIVORCED	3 (3.9%)
MARRIED	30 (39%)
SINGLE	43 (57%)
COMORBIDITY	
NO	68 (89%)
DM	2 (2.6%)
SMOKING	6 (7.9%)

[1]MEAN ± SD. [2]MEDIAN [IQR]. * MEDIAN [RANGE].
MS; MULTIPLE SCLEROSIS.

The 76 included patients had a mean age of 27.76 years and a majority of women (58%). Most patients were in urban areas (84%), with rural areas having only 16%. The occupations of patients are mainly students (34%), employed (23%), housewives (22%), and unemployed (11%). Most patients were unmarried (57%), married (39%), and divorced (4%). Most patients do not have any documented comorbidities, but a minority suffer from diabetes mellitus (2.6%) and a subset of current smokers (7.9%).

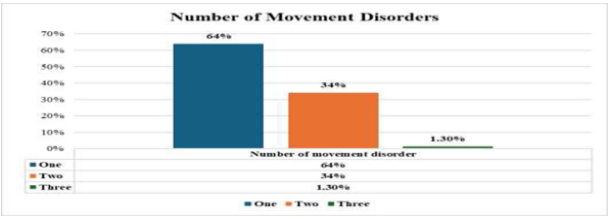

Figure 2. Number of Movement Disorders (MDs) among participants.

Among the 76 included participants, 64.5% (49) had one MD, 34.2% (26) had two MDs, and 1.3% had three MDs.as shown in figure 2.

Movement Disorders (MDs) characteristics:

Table 2. Frequency of Movement Disorders among participants

	1ST MD	2ND MD
MD	N = 76	N = 76
EXTENSOR SPASM		
NO	63 (83%)	73 (96%)
YES	13 (17%)	3 (3.9%)
ATAXIA		
NO	44 (58%)	71 (93%)
YES	32 (42%)	5 (6.6%)
RLS		
NO	68 (89%)	72 (95%)
YES	8 (11%)	4 (5.3%)
TREMORS		
NO	66 (87%)	70 (92%)
YES	10 (13%)	6 (7.9%)
CHOREA		
NO	76 (100%)	75 (99%)
YES	0	1 (1.3%)
DYSTONIA		
NO	75 (99%)	75 (99%)
YES	1 (1.3%)	1 (1.3%)
DYSTONIC TREMORS (DT)		
NO	76 (100%)	75 (99%)
YES	0	1 (1.3%)
EPILEPSY		
NO	72 (95%)	75 (99%)
YES	4 (5.3%)	1 (1.3%)
SPASTICITY		
NO	74 (97%)	75 (99%)
YES	2 (2.6%)	1 (1.3%)
PHKD		
NO	75 (99%)	75 (99%)
YES	1 (1.3%)	1 (1.3%)
HFS		
NO	75 (99%)	75 (99%)
YES	1 (1.3%)	1 (1.3%)
FUNCTIONAL MD		
NO	74 (97%)	76 (100%)
YES	2 (2.6%)	0
PSEUDOATHETOSIS		
NO	75 (99%)	75 (99%)
YES	1 (1.3%)	1 (1.3%)
NYSTAGMUS		
NO	74 (97%)	76 (100%)
YES	2 (2.6%)	0
FASCICULATION		
NO	0	74 (97%)
YES	0	2 (2.6%)

[1] N (%)

The most prevalent MD as a 1st occurring MD was extensor spasm, affecting 17% of participants. Ataxia was also relatively common, occurring in 42% of cases. Restless Legs Syndrome (RLS) was present in 11% of individuals. 13% of participants exhibited tremors. Notably, chorea, dystonia, and dystonic tremors were extremely rare, with each affecting less than 2% of the group. Epilepsy and spasticity were present in a small proportion of

participants, at 5.3% and 2.6%, respectively. Other MDs are with less variability, as shown in Table 2.

Participants with a second MD displayed a distinct pattern of MD frequency. Extensor spasm was significantly less common in this group, affecting only 3.9% of participants. Ataxia was exceptionally rare, with only 6.6% of individuals experiencing it. RLS, tremors, and chorea also showed lower prevalence compared to the 1st MD group. Dystonia and dystonic tremors were slightly more common in the 2nd MD group but still affected less than 2% of participants. Epilepsy and spasticity were rare, with rates like the 1st MD group. PHKD, HFS, and functional movement disorder were absent in this group. 1.3% of participants showed pseudoathetosis, while Nystagmus was absent. Interestingly, fasciculation was present in 2.6% of the 2nd MD group, unlike the 1st MD group, where it was completely absent, as shown in Table 2.

General MRI findings for supratentorial area in MS patients

Table 3. General MRI findings for supratentorial area in MS patients.

LESION SITE	N = 76	
SUPRA TENTORIAL PERIVENTRICULAR	76 (100%)	
SUPRA TENTORIAL CORTICAL	24 (32%)	
SUPRA TENTORIAL JUXTACORTICAL	70 (92%)	
ARE THERE SUPRATENTORIAL SPECIFIC AREAS	75 (99%)	
LENTIFORM NUCLEUS	33 (43%)	
LENTIFORM LATERALITY (SIDE) (N= 33)		
BILATERAL		17 (51.5%)
LEFT		13 (39.4%)
RIGHT		3 (9.1%)
FRONTAL SUBCORTICAL	33 (44%)	
FRONTAL SUBCORTICAL LATERALITY (N= 33)		
BILATERAL		23 (69.7%)
LEFT		7 (21.2%)
RIGHT		3 (9.1%)
PARIETAL SUBCORTICAL	29 (38%)	
PARIETAL SUBCORTICAL LATERALITY (N= 29)		
BILATERAL		15 (51.7%)
LEFT		4 (13.8%)
RIGHT		10 (34.5%)
TEMPORAL SUBCORTICAL	18 (24%)	
TEMPORAL SUBCORTICAL LATERALITY (N= 18)		
BILATERAL		10 (13%)
LEFT		3 (3.9%)
RIGHT		5 (6.6%)
OCCIPITAL SUBCORTICAL	19 (27%)	
OCCIPITAL SUBCORTICAL LATERALITY (N= 19)		
BILATERAL		3 (15.8%)
LEFT		6 (31.6%)
RIGHT		10 (52.6%)
CAUDATE NUCLEUS	4 (5.3%)	
CAUDATE NUCLEUS LATERALITY (N= 4)		
BILATERAL		1 (25%)
LEFT		2 (50%)
RIGHT		1 (25%)
INTERNAL CAPSULE	7 (9.2%)	
WHICH PART OF INTERNAL CAPSULE AND LATERALITY (N= 7)		
LEFT GENU		1 (14.3%)
LEFT POSTERIOR LIMB		3 (42.8%)
POSTERIOR LIMB		1 (14.3%)
RIGHT ANTERIOR LIMB		1 (14.3%)
RIGHT POSTERIOR LIMB		1 (14.3%)
THALAMUS	23 (30%)	
THALAMUS LATERALITY (N= 23)		
BILATERAL		9 (39.1%)
LEFT		6 (26.1%)
RIGHT		8 (34.8%)
SUBTHALAMUS	3 (3.9%)	
SUBTHALAMUS LATERALITY (N= 3)		
BILATERAL		1 (33.3%)
RIGHT		2 (66.7%)
CORONA RADIATA (N= 5)	5 (6.6%)	
CORONA RADIATA LATERALITY		
BILATERAL		1 (20%)
LEFT		4 (80%)
CORPUS CALLOSUM	5 (6.6%)	
DEEP CORTICAL LESIONS	2 (2.6%)	
DEEP CORTICAL LESION SIDE (N= 2)		
RIGHT PARIETAL		1 (50%)
RIGHT TEMPORAL		1 (50%)
CORTICAL LESIONS	4 (5.3%)	
CORTICAL LESIONS LATERALITY (N= 4)		
FRONTAL		2 (50%)
PARIETAL AND TEMPORAL		2 (50%)

[1] N (%)

All patients (100%) exhibited periventricular lesions, while a substantial proportion displayed cortical (32%), juxtacortical (92%), and frontal subcortical (44%) lesions. Parietal subcortical, temporal subcortical, occipital subcortical, and lentiform nucleus involvement were less frequent, occurring in 38%, 24%, 27%, and 43% of patients, respectively. Regarding laterality, bilateral lesions were common in most subcortical regions, with

the frontal subcortical area showing the highest prevalence of bilateral involvement (69.7%). The caudate nucleus, internal capsule, thalamus, and subthalamus were affected by a smaller percentage of patients, with varying laterality distributions. Notably, corona radiata lesions were present in 6.6% of patients, predominantly on the left side. Deep cortical lesions were rare, affecting only 2.6% of patients. The complete details are described in Table 3.

General MRI findings for infratentorial and spine cervical areas in MS patients

Table 4. General MRI findings for infratentorial and spine cervical areas in MS patients

1. LESION SITE	OVERALL (N=76)	
INFRATENTORIAL MID BRAIN LESIONS	20 (26.3%)	
INFRATENTORIAL MID BRAIN LESIONS LATERALITY (N=20)		
BILATERAL		7 (35%)
LEFT		8 (40%)
RIGHT		5 (25%)
INFRATENTORIAL PONTINE LESIONS	49 (66.2%)	
INFRATENTORIAL PONTINE LESIONS LATERALITY (N=49)		
BILATERAL		16 (32.6%)
LEFT		17 (34.7%)
RIGHT		16 (32.6%)
INFRATENTORIAL MEDULLARY LESIONS	8 (10.7%)	
INFRATENTORIAL MEDULLARY LESIONS LATERALITY (N=8)		
BILATERAL		2 (25%)
LEFT		3 (37.5%)
RIGHT		3 (37.5%)
INFRATENTORIAL CRUS CEREBRI LESIONS	6 (7.9%)	
INFRATENTORIAL CRUS CEREBRI LATERALITY (N=6)		
BILATERAL		1 (16.7%)
LEFT		4 (66.6%)
RIGHT		1 (16.7%)
INFRATENTORIAL SUPERIOR CEREBELLAR PEDUNCLE (SCP) LESIONS	1 (1.3%)	
INFRATENTORIAL MIDDLE CEREBELLAR PEDUNCLE (MCP) LESIONS	47 (61.8%)	
INFRATENTORIAL MCP LESIONS LATERALITY (N=47)		
BILATERAL		26 (55.3%)
LEFT		17 36.2%)
RIGHT		4 (8.5%)
INFRATENTORIAL INFERIOR CEREBELLAR PEDUNCLE (ICP) LESIONS	8 (10.5%)	
INFRATENTORIAL ICP LESIONS LATERALITY (N=8)		
LEFT		3 (37.5%)
RIGHT		5 (62.5%)
INFRATENTORIAL CEREBELLAR HEMISPHERE LESIONS	24 (31.6%)	
INFRATENTORIAL CEREBELLAR HEMISPHERE LESIONS LATERALITY (N=24)		
BILATERAL		11 (45.9%)
LEFT		5 (33.3%)
RIGHT		8 (33.3%)
INFRATENTORIAL CEREBELLAR VERMIS LESIONS	5 (6.6%)	
INFRATENTORIAL PERI EPENDYMAL BRAIN STEM LESIONS	24 (31.6%)	
ARE THERE ANY MRI SPINE CERVICAL LESIONS	61 (80.3%)	

The data showed a high prevalence of infratentorial lesions, with the pons being the most commonly affected area (66.2%). The midbrain and cerebellum (including hemispheres, vermis, and peduncles) were also frequently involved, though to a lesser extent. Notably, there was a relatively balanced distribution of lesions between the left and right hemispheres in most infratentorial regions. Peri ependymal brain stem lesions were observed in 38.1% of cases. Regarding the cervical spine, MRI evidence of lesions was found in 80.3% of patients. The severity of these lesions was categorized as high, low, or moderate, with moderate being the most common category (46.1%). The complete details are described in Table 4.

4. Discussion

Movement problems are thought to be less common in people with multiple sclerosis (MS) than in others .[3] The true frequency and incidence of MS and MDs are unclear because most previous research on the subject has relied on retrospective studies, small case series, or review papers.[4] This inconsistency could be caused by the use of retrospective data in the research, the small sample size, and the inclusion of concurrent MDs unrelated to MS.[3] Certain MDs have symptoms that clearly suggest the presence of multiple sclerosis (MS), prompting an immediate diagnosis and treatment. PwMS often have problems with their movements. Thus, we conducted this study to determine the prevalence of movement disorders in MS patients. Also, to know the clinical type of movement disorders occurring with multiple sclerosis patients and the MRI findings of those patients.

We included 76 MS patients, with a prevalence rate (24%), while the prevalence rate of the Abboud et.al. study was (30.3%).[8] The mean age of the study group was 27.76 years, which is

consistent with the previous study of Romero-Pinel L, which reports the occurrence of MS between 20 and 40 years of age.[16] The female percentage was 58% which went with previous observations of other published studies. [17,18]. In our study, we observed ataxia in 28% of PwMS, while only 2.6% of the cohort displayed RLS and tremors. This is opposed by other studies in which tremors were the most prevalent, either Abboud et.al.,[8] or Nociti et.al. [6]

Ataxia was the most common MD in our study. This result aligns with the retrospective study that describes MDs in MS and other demyelinating diseases.[19] Studies reporting the prevalence of ataxia in patients with MS are lacking. However, studies suggest that ataxia can occur at a prevalence rate of up to 80%, with symptoms being more common in patients with progressive disease.[20,21] However, other studies showed that RLS is the commonest demyelination-related movement disorder.8 Furthermore, one study reported that tremors were more prevalent in MS, with reported prevalence percentages ranging between 25% and 58% in PwMS.[22] Our study found that RLS had a low prevalence of just 2.6% among individuals with MS. However, the prevalence of RLS in MS is inconsistent in the previous research, ranging from 13% to 65%. [23–25]

Our study found that tremors were not common in individuals with MS, with a prevalence rate of only 2.6%. Pittock et al. found that the prevalence of severe tremors in MS patients was 3%.[26] Shalash et al. found that 14.4% of a group of 250 Egyptian patients with relapse-remitting MS had tremors .[27] We can attribute this disparity to the diversity of tremors observed in different forms of MS among our study group and Shalash's study group. [27]

Our study's MRI scans showed that all MS patients had periventricular lesions, confirming the typical imaging pattern associated with the condition. According to the Revised McDonald Criteria for Multiple Sclerosis, the presence of a periventricular lesion (PVL) is a defining feature of the condition.[13] Consistent with MS's known preference for white matter regions close to the cortex, juxtacortical lesions were also very common (92%). The widespread nature of MS disease was highlighted by the observation of subcortical lesions in several locations, with the frontal subcortical area exhibiting the highest bilateral involvement at 69.7 percent.[28] Interestingly, a significant proportion of patients exhibited lesions in the lentiform nucleus (43%) and other deep gray matter structures, though the caudate nucleus, internal capsule, thalamus, and subthalamus were less frequently affected. This distribution suggests a predilection for both white and gray matter involvement in MS, which may contribute to the diverse clinical manifestations observed in these patients.[29] Those affected areas have also been reported in prior studies.[9] Lesions in the corona radiata were relatively uncommon, seen in only 6.6% of patients, predominantly on the left side, indicating a possible lateralization preference in lesion development.[29] The presence of infratentorial lesions was notably high, with the pons being the most frequently affected area (66.2%). The involvement of the midbrain and cerebellum, including its various components, further highlights the widespread nature of MS lesions beyond the supratentorial regions.

4. Conclusion

Our study showed the prevalence of MDs in PwMS. Also, it showed the frequency and clinical phenotypes of those MDs with higher prevalence of ataxia, RLS and low prevalence of tremors. This had an impact on the motor function of PwMS. Finally, it showed the higher variability and wide spread of MS lesions at multiple locations in the brain which reflected the higher discrepancy of disease lesions and its presentations.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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