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Relationship between disability and psychiatric outcome in multiple sclerosis patients and its determinants

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Abstract

Background Multiple sclerosis (MS) is an inflammatory demyelinating central nervous system disease with diverse clinical manifestations. The present study aimed to compare the psychiatric outcomes of MS patients with full ambulatory versus impaired ambulatory function and identify the potential risk factors for disability in MS. Seventy MS patients were classified into two groups based on their Expanded Disability Status Scale (EDSS) scores, Group A: full ambulatory (EDSS ≤ 4.5) ($N=48$), Group B: impaired ambulatory (EDSS ≥ 5) ($N=22$). All participants were evaluated by the Socioeconomic Scale, Hamilton Anxiety Scale, Hamilton Depression Scale, Brief Psychiatric Rating Scale, and The Pittsburgh Sleep Quality Index.

Results In the total cohort ($N=70$), females represented (77.1%). The mean age was 31.16 ± 6.46, the mean age of onset was 26 ± 6.083, and the mean disease duration was 5.33 ± 3.653 years which was less in Group A than in Group B. Relapsing–remitting multiple sclerosis (RRMS) was the most common presentation (80%), representing 93.6% of Group A. Group A reported more severe depression and anxiety, while Group B had more poor sleep quality. Correlation analysis showed increased relapses, progressive-relapsing multiple sclerosis (PRMS), cervical or dorsal plaques, sensory or motor manifestations, and precipitancy increased disability, while RRMS type decreased disability.

Conclusions Full ambulatory MS patients had high anxiety and depression, while impaired ambulatory MS patients had poor sleep quality. Associated factors for disability were frequent relapses, plaque location, MS subtype, sphincter, and sensory symptoms.

Trial registration clinicaltrials.gov, NCT05029830. Registered: September 01, 2021, https://clinicaltrials.gov/ct2/show/NCT05029830

Keywords Multiple sclerosis, EDSS, Psychiatric manifestations, Quality of life

Background

Multiple sclerosis (MS) is an inflammatory demyelinating central nervous system disease characterized by various heterogeneous clinical manifestations not limited to symptoms but related to other factors, including the neuroradiologic and histologic presentations of lesions and responsiveness to therapy [1]. MS has several disabling symptoms, including pain, fatigue, sensory and visual impairment, urinary and bowel incontinence, spasticity, tremors, and cognitive and sexual dysfunction. The

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disease's course is highly unpredictable and typically marked by relapses and remissions [2].

Moreover, MS is associated with various psychiatric disorders, including depression, manic-depressive illness, anxiety disorders, euphoria, pathological laughing and crying, and psychosis [3]. Mood disorders (MD) are the most prevalent type of psychiatric illness. They are more common in people with MS than in the general population, with a higher annual prevalence ratio of depressive and anxiety symptoms compared to people of similar socioeconomic status, age, sex, and geographic location [4]. Several studies investigated the correlation between MD and MS therapy's adverse effects [5]. Many disease-modifying therapies (DMTs), particularly interferon beta, have been linked to the emergence of depressive symptoms [6]. Nonetheless, several studies have shown that past therapy for depression can predict the development of depressive syndrome in MS patients while receiving DMTs [7]. Since the development of depression and anxiety under DMTs may diminish treatment adherence, identifying and treating MD in MS patients is essential for enhancing patient compliance [8].

MS is a chronic neurological disorder that can compromise patients' quality of life (QoL) due to different factors, including disability degree, MS subtype, and personal factors like social support, education, age, and employment [9]. The QoL encompasses numerous aspects of a person's life, such as their overall health, including mental, physical, and social functions. The impairment of QoL in people with MS cannot be fully explained by neurological dysfunction, highlighting the inadequacies of measuring disability with the Expanded Disability Status Scale (EDSS) alone [10]. Additionally, psychiatric comorbidity with MS leads to reduced QoL, increased fatigue levels, and decreased adherence to DMTs [11].

Several studies investigated the psychiatric symptoms in patients with MS [11–13], but few studies have been conducted to detect the relationship between psychological factors and disability in MS [14]. Moreover, few studies investigated the psychiatric manifestations of Egyptian MS patients [15]. The present study aimed to compare the psychiatric outcomes of MS patients with full ambulatory versus impaired ambulatory function and identify the potential risk factors for disability in MS.

Methods

Study design and setting

A cross-sectional study was conducted at the Neurology department in the Neurology, Psychiatry, and Neurosurgery Hospital, Assiut University Hospitals, from September 2021 to October 2022.

Participants and clinical data collection

In total, 70 participants were recruited for the study. The inclusion criteria were: (a) a diagnosis of multiple sclerosis according to the revised McDonald criteria for 2017, regardless of therapy; (b) an age range between 18 and 40 years; and (c) both genders were included. The exclusion criteria were as follows: (a) age below 18 or over 40, (b) a history or current substance use, (c) a history of previous psychiatric disorders before MS onset, (d) a history of suggestive or diagnosed collagen disease such as Bechet disease, and (e) a history suggestive of other neurological or medical diseases.

All eligible participants underwent a comprehensive medical history, physical and neurological examinations, and psychiatric evaluation. Diagnostic and Statistical Manual of Mental Disorders-5th Edition (DSM-5) (American Psychiatric Association, 2013) [16] was used to diagnose the psychiatric disorders by using the Structured Clinical Interview for DSM-5 Disorders—Clinician Version (SCID-5-CV) during the psychiatric interview [17]. Also, the revised McDonald Criteria 2017 [18] was used to diagnose multiple sclerosis. The disease course was classified as relapsing–remitting MS (RRMS), primary progressive MS (PPMS), progressive relapsing MS (PRMS), and secondary progressive MS (SPMS), as well as a clinically isolated syndrome (CIS), based on revised McDonald criteria from 2017 [18].

Neurophysiological and imaging data collection

Visual evoked potential (VEP)

VEP was used to confirm the presence of visual pathology or to discover subclinical asymptomatic visual pathway involvement [19]. VEP was done with the Nihon Kohden MEB-7102 (Nihon Kohden Corp., Tokyo, Japan) according to the technical parameters recommended by the American Society for Clinical Evoked Potentials and International Federation of Clinical Neurophysiology for visual system testing [20, 21]. VEP was recorded for each eye averaging 200 responses using surface recording electrodes over the occipital lobe using stimulation with a shift of a checkerboard pattern (black and white), and the checkerboard pattern is reversed (black to white to black) at a rate of 1 or 2 per second. Each eye was examined multiple times. After storing the data, the peak latencies of N75, P100, and N145 were determined. According to the department's normative data, the average VEP P100 latency was (94 ± 8) milliseconds. The VEP variables were considered abnormal if at least one of the patient's eyes had a delayed P100 latency.

MRI data collection and interpretation

Brain and spine MRIs were performed on all patients using a 1.5 Tesla (Magnetom Sempra, Siemens, Erlangen, Germany) and reassessed at the evaluation time. The images were analyzed by a radiologist with experience in neuroradiology who was blind to the patient's clinical presentation and the outcomes of the paraclinical testing. On a T2-weighted MRI, the MS lesions were recognized as regions of focal hyperintensity (T2, T2-FLAIR, or similar). These patches are rounded to oval in shape, and their sizes range in diameter from a few millimeters (mm) to more than one or two centimeters. Their long axis must be at least 3 mm to satisfy diagnostic requirements, although topography must also be considered. Lesions were classified into five categories based on their anatomical locations: infratentorial, juxtacortical, subcortical, periventricular, and cortical [22].

Scales and questionnaires

The participants were classified into two groups based on their EDSS scores; Group A: full ambulatory (EDSS $\leq$ 4.5) (N=48), Group B: impaired ambulatory (EDSS $\geq$ 5) (N=22). In addition, every participant filled out the socioeconomic scale (SES), the Hamilton Anxiety Scale (HAM-A), the Hamilton Depression Scale (HAM-D), the Brief Psychiatric Rating Scale (BPRS), and the Pittsburgh Sleep Quality Index (PSQI).

Expanded Disability Status Scale (EDSS)

EDSS is a method for measuring disability based on a clinician's neurological examination [23]. The EDSS measures disability by assigning a Functional System Score (FSS) to each of the eight Functional Systems (FS). It is a ranking system with 0.5-point increments from 0 (normal neurological examination) to 10 (death due to MS). Lower values on the EDSS scale represent neurological impairments, while higher values (> EDSS 6) represent the disabilities of MS patients. The difference between EDSS 4 and 6 largely depends on a person's walking ability [24]. Because walking is affected by up to 89%, as measured by an EDSS score between 4.5 and 5 [25, 26], the EDSS could be classified into two levels; the first levels, 1.0 to 4.5, corresponding to people with full ambulatory ability, and the subsequent levels 5.0 to 9.5 represent a loss of ambulatory ability [23, 27].

Socioeconomic Scale (SES)

We determined the social burden and socioeconomic classes using the Arabic version of the socioeconomic scale [28]. It includes four primary variables: the educational level of the father and mother, their occupation, the total family income, and the family's lifestyle.

Hamilton Anxiety Scale (HAM-A)

A 14-item scale measures the level of a patient's anxiety. Each item has multiple symptoms, and each group of symptoms is rated on a scale from 0 to 4, with a score of 4 representing the most severe condition. These scores generate an overall anxiety severity score ranging from 0 to 56 [29]. The degree of anxiety severity is extracted according to the following criteria: scores (14 to 17, mild anxiety); (18 to 24, moderate anxiety); and (25 to 30, severe anxiety) [30].

Hamilton Depression Scale (HAM-D)

The 17-item scale was designed to measure the severity of depressive symptoms, such as low mood, insomnia, agitation, anxiety, and weight loss [31]. The degree of depression severity is extracted according to the following criteria: (0 to 7 normal scores), (8 to 13 mild depression), (14 to 18 moderate depression), (19 to 22 severe depression), (23 and above very severe depression) (31).

Brief Psychiatric Rating Scale (BPRS)

BPRS is one of the most widely used instruments for rapid screening for the presence and severity of psychiatric disorders [32]. The 24-item BPRS (version 4.0) evaluated 24 psychiatric symptoms [33]. The presence and severity of each psychiatric symptom were rated on a scale from 1 (absent) to 7 (extremely severe). Thus, scores can range from 24 to 168, with lower scores indicating less severe psychopathology [32].

The Pittsburgh Sleep Quality Index (PSQI)

It is a self-reported questionnaire that assesses sleep quality and disturbances over one month. Nineteen items yield seven "domains" sleep-related scores on subjective sleep quality, latency, duration, habitual efficiency, disturbances, use of sleeping medications, and daytime dysfunction. The total PSQI score ranges from 0 to 21, with higher scores reflecting a poorer night-time sleep quality [34]. A cut-off value of > 5 indicates poor sleep quality and is a sign of relevant sleep disturbances in at least two sub-scales or moderate problems in more than three sub-scales [34]. For this reason, the optimal cut-off score (separating good from poor sleepers) is 5 [35].

Statistical analysis

Statistical analysis was conducted using Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 26.0; Armonk, NY: IBM Corp.). A frequency and proportion analysis was performed for qualitative variables, while quantitative variables were presented as (mean ± SD). The Pearson Chi-square test was used to compare categorical variables, Mann–Whitney U-test was used to compare the mean values of two

independent groups with skewed data, and the Student's *t*-test for the normal distributed mean value. Spearman correlation was applied, and a point-biserial correlation coefficient was utilized to correlate dichotomous and continuous variables. Multivariate linear regression was used to identify possible risk factors for disability and psychiatric problems in MS. The *p*-value of < 0.05 was considered statistically significant.

Result

Sociodemographic data of studied groups

A total of 70 patients who met the inclusion requirements were identified. Table 1 summarizes the sociodemographic characteristics. There was no statistically significant difference between the studied groups regarding socioeconomic status. Most participants were married females with middle socioeconomic status (Table 1).

Clinical and imaging data of studied groups

Table 2 summarizes the studied groups' clinical characteristics, clinical presentations, imaging, and visual evoked potential findings. There were no statistically significant differences in the age of onset and the mean duration of illness between both groups. 80% of the participants had RRMS, with a higher significant percentage (93.8%) in Group A. PRMS had a higher percentage in Group B than in Group A. There was a statistically significant difference in the number of relapses in Group B compared to Group A (p value ≤ 0.0001*). 41.4% of participants (29/70) received DMT, with interferons being the most used (28.6%), with no significant difference between groups (Table 2).

Regarding clinical presentations, there was a statistically significant difference between groups for all clinical manifestations except cerebellar manifestation. All participants in Group B had motor manifestations, while about a third of Group A (37.5%) did not. In Group B, the percentage of participants who complained of sensory affection and sphincter manifestations was significantly higher than in Group A (95.5% vs. 72.9%, 50% vs. 14.6%, respectively). In Group B, bilateral optic affection was more prevalent (27.3%) than in Group A (4.2%) (Table 2).

Regarding the distribution of MS plaque in the MRI, the juxta cortical distribution was significantly higher in

Table 1 Sociodemographic data of the studied groups

	Total participants ($N=70$)	Group A ($N=48$)	Group B ($N=22$)	X^2 or *t* or *z* value	*p*-value
Age (mean ± SD)	31.16 ± 6.46	31.06 ± 6.49	31.36 ± 6.52	0.032	0.858#
Gender					
Male	16 (22.9%)	11 (22.9%)	5 (22.7%)	0.0001	0.986
Female	54 (77.1%)	37 (77.1%)	17 (77.3%)		
Level of education					
Illiterate	8 (11.4%)	7 (14.6%)	1 (4.5%)	5.502	0.138
Primary education	1 (1.4%)	1(2.1%)	0 (0%)		
Secondary education	28 (40%)	15 (31.3%)	13 (59.1%)		
University	33 (47.1%)	25 (52.1%)	8 (36.4%)		
Marital state					
Single	15 (21.4%)	11 (22.9%)	4 (18.2%)	4.55	0.207
Married	53(75.7%)	37 (77.1%)	16 (72.7%)		
Divorced	1(1.4%)	0 (0%)	1 (4.5%)		
Widow	1 (1.4%)	0 (0%)	1 (4.5%)		
Medical comorbidity					
Diabetes mellitus	5 (7.1%)	4 (8.3%)	1 (4.5%)	0.326	0.495
Hypertension	3 (4.3%)	2 (4.2%)	1 (4.5%)	0.005	0.684
Cardiac disease	1 (1.4%)	1 (2.1%)	0 (0%)	0.465	0.686
Family history of psychiatric disorders	2 (2.9%)	1 (2.1%)	1 (4.5%)	0.329	0.533
Cigarette Smoking	2 (2.9%)	1 (2.1%)	1 (4.5%)	0.329	0.533
Socioeconomic status (mean ± SD)	112.27 ± 33.65	107.24 ± 27.055	123.265 ± 43.57	3.54	0.064#
Low	5 (7.1%)	4 (8.3%)	1 (4.5%)	0.707	0.702
Middle	60 (85.7%)	40 (83.3%)	20 (90.9%)		
High	5 (7.1%)	4 (8.3%)	1 (4.5%)		

Group A: full ambulatory (EDSS ≤ 4.5), Group B: impaired ambulatory (EDSS ≥ 5). DMT: disease-modifying therapy. #By Student's *t*-test

Table 2 Clinical characteristics, clinical presentations, imaging, and visual evoked potential of the studied groups

	Total participants (*N* = 70)	**Group A (*N* = 48)**	**Group B (*N* = 22)**	***p*-value**
Age of onset (mean ± SD)	26 ± 6.083	26.27 ± 5.76	25.38 ± 6.86	0.828
Duration of illness (mean ± SD)	5.33 ± 3.653	4.79 ± 3.313	6.57 ± 4.154	0.128
Type of MS				
RRMS	56 (80%)	44 (93.6%)	11 (50%)	0.001*
PRMS	13 (18.6%)	3 (6.4%)	10 (45.5%)	
PPMS	1 (1.4%)	0 (0%)	1 (4.5%)	
Number of relapses (mean ± SD)	2.77 ± 1.024	2.42 ± 0.895	3.55 ± 0.858	< 0.0001*
DMT				
No DMT (steroid only)	41 (58.6%)	29 (60.4%)	12 (54.5%)	0.849
Interferons	20 (28.6%)	13 (27.1%)	7 (31.8%)	
Fingolimod	8 (11.4%)	5 (10.4%)	3 (13.6%)	
Rituximab	1 (1.4%)	1 (2.1%)	0 (0%)	
Motor system manifestations				
No symptoms	18 (25.7%)	18 (37.5%)	0 (0%)	0.001*
Present motor system affection				
1. Hemiparesis or hemiplegia				
Rt side	15 (21.4%)	11 (22.9%)	4 (18.2%)	
Left side	15 (21.4%)	10 (20.8%)	5 (22.7%)	
2. Spinal affection				
Paraparesis or paraplegia	10 (14.3%)	6 (12.5%)	4 (18.2%)	
Quadriparesis or quadriplegia	9 (12.9%)	1 (2.1%)	8 (36.4%)	
Monoparesis	3 (4.3%)	2 (4.2%)	1 (4.5%)	
Cerebellar manifestations				
No symptoms	53 (75.7%)	35 (72.9%)	18 (81.8%)	0.295
Present cerebellar manifestations				
Unilateral ataxia	10 (14.3%)	6 (12.5%)	4 (18.2%)	
Bilateral ataxia	2 (2.9%)	2 (4.2%)	0 (0%)	
Truncal ataxia	5 (7.1%)	5 (10.4%)	0 (0%)	
Sphincter manifestations				
No	52 (74.3%)	41 (85.4%)	11 (50%)	0.006*
Present sphincter manifestations				
Precipitancy	15 (21.4%)	7 (14.6%)	8 (36.4%)	
Hesitancy	2 (2.9%)	0 (0%)	2 (9.1%)	
Retention	1 (1.4%)	0 (0%)	1 (4.5%)	
Sensory manifestations				
No	14 (20%)	13 (27.1%)	1 (4.5%)	0.001*
Present sensory manifestations				
Heminumbness	39 (55.7%)	29 (60.4%)	10 (45.5%)	
Sensory level	17 (24.3%)	6 (12.5%)	11 (50%)	
Optic manifestations				
No symptoms	36 (51.4%)	25 (52.1%)	11 (50%)	0.030*
Present optic manifestations				
Right (RT) optic affection	14 (20%)	11 (22.9%)	3 (13.6%)	
Left (LT) optic affection	12 (17.1%)	10 (20.8%)	2 (9.1%)	
Bilateral optic affection	8 (11.4%)	2 (4.2%)	6 (27.3%)	
MRI brain				
Periventricular	43 (61.4%)	27 (56.3%)	16 (72.7%)	0.290
Cerebellum	19 (27.1%)	15 (31.3%)	4 (18.2%)	0.386
Juxtacortical	30 (42.9%)	25 (52.1%)	5 (22.7%)	0.036*

Table 2 (continued)

	Total participants (*N* = 70)	Group A (*N* = 48)	Group B (*N* = 22)	*p*-value
MRI spine				
Cervical plaque	10 (14.3%)	3 (6.3%)	7 (31.8%)	0.008*
Dorsal plaque	15 (21.4%)	8 (16.7%)	7 (31.8%)	0.210
Lumber	10 (14.3%)	5 (10.4%)	5 (22.7%)	0.268
The visual evoked potential				
Normal	29 (41.4%)	21 (43.8%)	8 (36.4%)	0.61
Abnormal	41 (58.6%)	27 (56.3%)	14 (63.6%)	

Group A: full ambulatory (EDSS ≤ 4.5), Group B: impaired ambulatory (EDSS ≥ 5), relapsing–remitting multiple sclerosis (RRMS), progressive-relapsing multiple sclerosis (PRMS), primary progressive MS (PPMS), disease-modifying therapy (DMT)

Group A, and the cervical distribution was significantly higher in Group B. The distribution of periventricular plaques was higher in Group B (72.7%) than in Group A (56.3%), but this difference was not statistically significant. The cervical, dorsal, and lumbar plaques were more prevalent in Group B than in Group A (Table 2).

Concerning VEP findings, there was no statistically significant difference between groups; however, Group B had a higher percentage of abnormal VEP (63.6%) than Group A (56.3%) (Table 2).

Results of psychiatric questionnaires

Table 3 shows the psychiatric questionnaire results. There was a statistically significant difference between the groups regarding the total Hamilton Anxiety Scale Score and its categorical classification, with moderate and severe anxiety occurring more frequently in Group A than in Group B. (47.9% vs. 22.7%, and 27.1% vs. 0%, respectively). There was a significant difference between the studied group regarding Hamilton's depression categorical classification. The incidence of severe depression in Group A was more significant (66.7%) than in Group B (50%). There was no significant difference between the groups regarding sleep. However, poor sleep quality was more prevalent in Group B (50%) than in Group A (43.8%) (Table 3).

Table 3 Results of psychiatric questionnaires among the studied groups

	Total participants (*N* = 70)	Group A (*N* = 48)	Group B (*N* = 22)	*p*-value
Hamilton Anxiety Rating Scale (HAM-A)				
Normal	4 (5.7%)	2 (4.2%)	2 (9.1%)	**0.001***
Mild	25 (35.7%)	10 (20.8%)	15 (68.2%)	
Moderate	28 (40%)	23 (47.9%)	5(22.7%)	
Severe	13 (18.6%)	13 (27.1%)	0 (0%)	
Total score of (HAM-A) (mean ± SD)	31.76 ± 10.596	35.38 ± 9.531	23.86 ± 8.391	**0.0001#**
Hamilton Depression Rating Scale (HDRS)				
Normal	3 (4.3%)	0 (0%)	3 (13.6%)	**0.001***
Mild	13 (18.6%)	5 (10.4%)	8 (36.4%)	
Moderate	11 (15.7%)	11 (22.9%)	0 (0%)	
Severe	43 (61.4%)	32(66.7%)	11(50%)	
Total score of (HDRS) (mean ± SD)	28.56 ± 7.125	28.83 ± 5.567	27.95 ± 9.844	0.635#
The Pittsburgh Sleep Quality Index (PSQI)				
Good sleep quality	38 (54.3%)	27 (56.3%)	11 (50%)	0.797
Poor sleep quality	32 (45.7%)	21 (43.8%)	11 (50%)	
Total score of (PSQI) (mean ± SD)	6.74 ± 4.699	6.94 ± 4.493	6.32 ± 5.204	0.612#

Group A: full ambulatory (EDSS ≤ 4.5), Group B: impaired ambulatory (EDSS ≥ 5)

[#] By Student's t-test

Table 4 The distribution of The Brief Psychiatric Rating Scale (BPRS) among the studied groups

	Total participants (*N* = 70)	Group A (*N* = 48)	Group B (*N* = 22)	*p*-value
Somatic concern	5.94 ± 1.238	5.98 ± 1.263	5.86 ± 1.207	0.619
Anxiety	5.26 ± 1.180	5.29 ± 1.11	5.18 ± 1.368	0.798
Depression	4.87 ± 1.372	4.79 ± 1.352	5.05 ± 1.430	0.430
Suicidality	4.30 ± 1.526	4.46 ± 1.271	3.95 ± 1.963	0.586
Guilt	5.40 ± 1.439	5.44 ± 1.367	5.32 ± 1.615	0.907
Hostility	4.99 ± 1.527	5.00 ± 1.384	4.95 ± 1.838	0.731
Elated mode	2.67 ± 1.259	2.65 ± 1.229	2.73 ± 1.352	0.866
Grandiosity	1.49 ± 0.737	1.50 ± 0.825	1.45 ± 0.510	0.826
Suspiciousness	5.03 ± 1.383	5.17 ± 1.136	4.73 ± 1.804	0.733
Hallucination	4.11 ± 1.575	4.08 ± 1.485	4.18 ± 1.790	0.499
Thought content	5.26 ± 1.348	5.13 ± 1.378	5.55 ± 1.262	0.220
Bizarre behavior	1.50 ± 0.913	1.46 ± 0.922	1.59 ± 0.908	0.531
Self-neglected	5.81 ± 1.333	5.79 ± 1.254	5.86 ± 1.521	0.498
Disorientation	4.89 ± 1.470	4.79 ± 1.501	5.09 ± 1.411	0.427
Conceptual disorganization	4.71 ± 1.416	4.71 ± 1.414	4.73 ± 1.453	0.926
Blunted affect	5.01 ± 1.508	5.06 ± 1.435	4.91 ± 1.688	0.725
Emotional withdrawal	4.99 ± 1.637	5.00 ± 1.611	4.95 ± 1.731	0.995
Motor retardation	5.33 ± 1.709	5.40 ± 1.783	5.18 ± 1.563	0.294
Tension	5.69 ± 1.518	5.71 ± 1.611	5.64 ± 1.329	0.539
Uncooperativeness	5.40 ± 1.377	5.40 ± 1.284	5.41 ± 1.593	0.662
Excitement	3.13 ± 1.215	3.13 ± 1.16	3.14 ± 1.356	0.906
Distractibility	5.13 ± 1.372	5.15 ± 1.304	5.09 ± 1.540	0.896
Motor hyperactivity	1.51 ± 0.676	1.48 ± 0.618	1.59 ± 0.796	0.702
Mannerism and posturing	2.07 ± 0.997	2.06 ± 0.976	2.09 ± 1.065	0.979
Total score of brief psychotic scale	98.67 ± 18.64	98.81 ± 17.32	98.36 ± 21.68	0.904

Table 4 shows no statistically significant difference between both groups regarding the brief psychiatric rating scale and its sub-scales (Table 4).

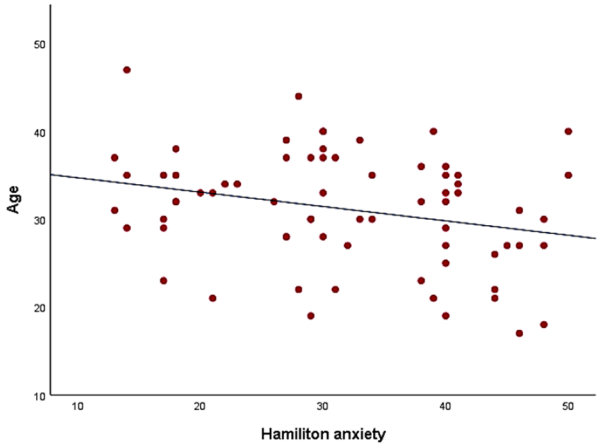
Correlative studies

Correlation between EDSS, psychometric scales score, and other parameters was performed (Additional file 1: Table S1). Total anxiety score had a negative correlation with age ($r = -0.241$, $p = 0.044$) (Fig. 1A), cigarette smoking ($r = -0.236$, $p = 0.049$), number of attacks ($r = -0.293$, $p = 0.014$) (Fig. 1B), PRMS subtype ($r = -0.311$, $p = 0.009$) while there was a positive association with RRMS subtype ($r = 0.362$, $p = 0.002$), presence of depression ($r = 0.639$, $p = 0.0001$) (Fig. 1C), and poor quality of sleep ($r = 0.286$, $p = 0.016$) (Fig. 2B). According to depression scores, there was a positive association between the presence of dorsal plaques ($r = 0.237$, $p = 0.049$) and bad sleep quality ($r = 0.370$, $p = 0.002$) (Fig. 2C). The total PSQI score positively correlated with the duration of illness ($r = 0.276$, $p = 0.022$) (Fig. 2A).

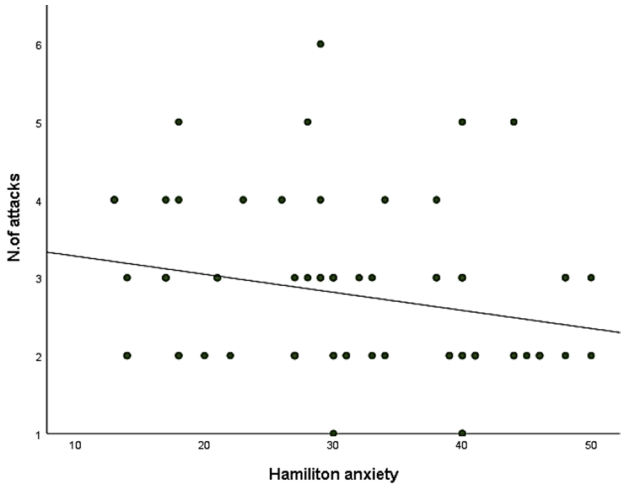
Total BPRS was associated with cerebellar manifestations ($r = 0.244$, $p = 0.042$). Regarding the EDSS, patients with more disability had an increased number of attacks ($r = 0.538$, $p = 0.0001$) (Fig. 3A), had PRMS type ($r = 0.387$, $p = 0.001$), presence of sensory ($r = 0.370$, $p = 0.002$) (Fig. 3B), motor ($r = 0.591$, $p = 0.0001$) (Fig. 3C), or sphincter manifestations ($r = 0.342$, $p = 0.004$), presence of cervical ($r = 0.360$, $p = 0.002$), or dorsal plaques in MRI ($r = 0.308$, $p = 0.010$), while having RRMS was associated with less disability ($r = -0.430$, $p = 0.0001$).

Linear regression

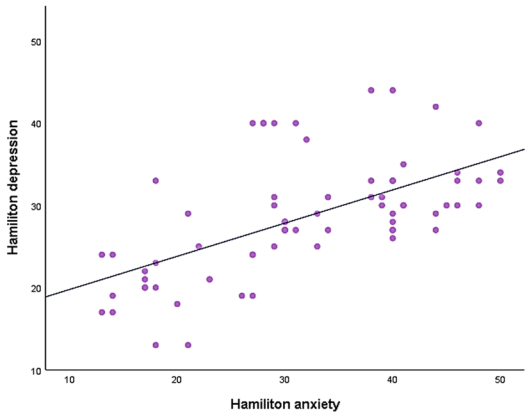
Multivariate regression models were done to evaluate possible risk factors of disability and psychiatric problems in MS patients (Additional file 1: Tables S2, S3, S4, S5, and S6). Patients with more disability had motor manifestations ($p = 0.046$). MS patients who are cigarette smokers were more likely to have more depression ($p = 0.027$) and less anxiety ($p = 0.037$). MS patients with anxiety were more vulnerable to depression ($p = 0.001$) and less likely to have high BPRS scores ($p = 0.030$).



(A) Correlation between age and Hamilton anxiety



(B) Correlation between the number of attacks and Hamilton anxiety



(C) Correlation between Hamilton depression and Hamilton anxiety

Fig. 1 Scattered plot showing Spearman correlation between Hamilton anxiety and other clinical and psychometric scales

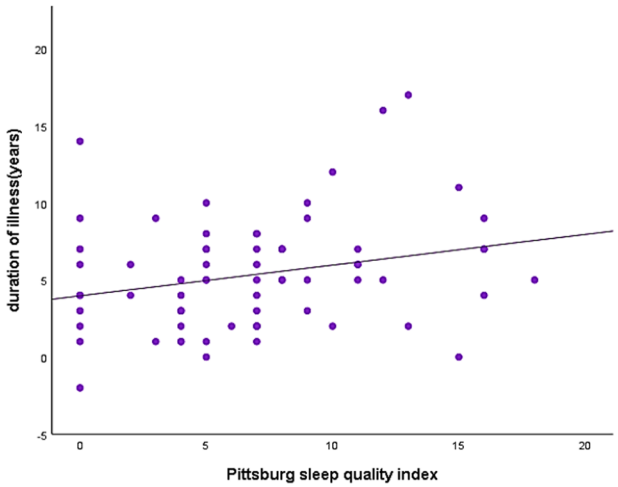
Discussion

MS is a chronic neurological disorder with various symptoms and an unclear prognosis that can compromise QoL [9]. Patients with MS have a high prevalence of psychiatric disorders, resulting in poor QoL and severe distress [11, 12]. The early diagnosis and treatment of psychiatric disorders in MS patients are advantageous for enhancing the quality of life of patients and carers [7]. The present study aimed to compare the psychiatric outcomes of MS patients with full ambulatory versus impaired ambulatory function and identify the potential risk factors for disability in MS.

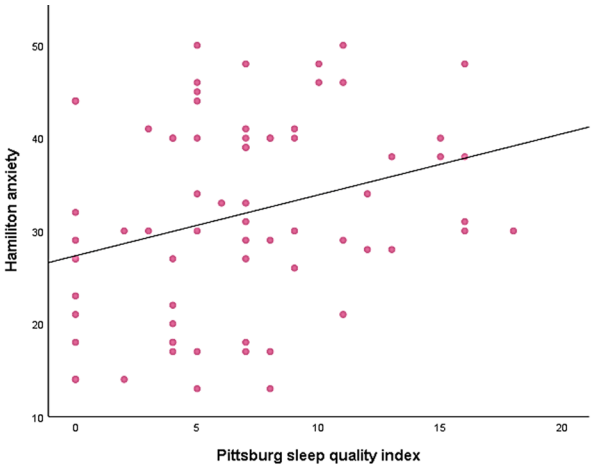
In the current study, females represented 77.1% of the participants, with a female-to-male ratio of 3.31:1, consistent with previous studies [36–38]. Zakaria et al. in Egypt [39] reported that 72% of their patients were female, with a female-to-male ratio of 2.57:1. This disparity may be due to the small sample size and age restrictions of the present study.

In this study, the mean age of onset of MS was 26 ± 6.08 years, consistent with earlier studies in Egypt, UAE, and Kuwait [39–41]. In contrast, it was younger than that (30.2 ± 10.2) recorded by research on the Lebanon population [42]. Moreover, it was younger than the average age of onset in Western populations, which was 30.5 years in Italy [43], 32.5 years in France [44], and 30.0 years in the UK [45]. This variation in age of onset may be attributed to different genetic characteristics compared to other Arabic and Western countries.

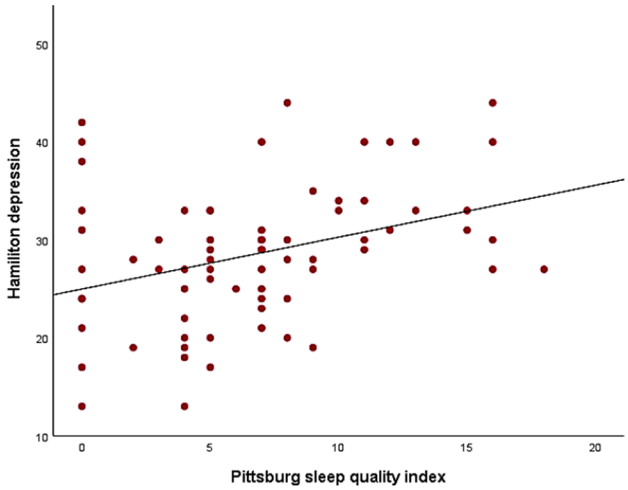
In the current study, there was no significant difference in age of onset between the full and impaired ambulatory groups, which indicates that the age at onset alone



(A) Correlation between duration of illness and PSQI



(B) Correlation between Hamilton anxiety and PSQI



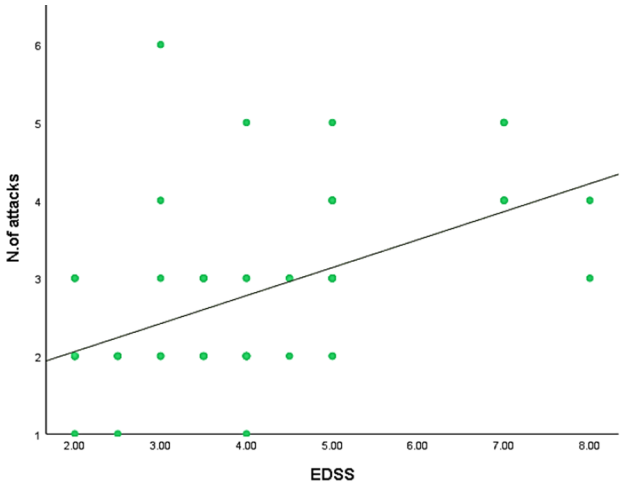
(C) Correlation between Hamilton depression and PSQI

Fig. 2 Scattered plot showing Spearman correlation between PSQI and other clinical and psychometric scales

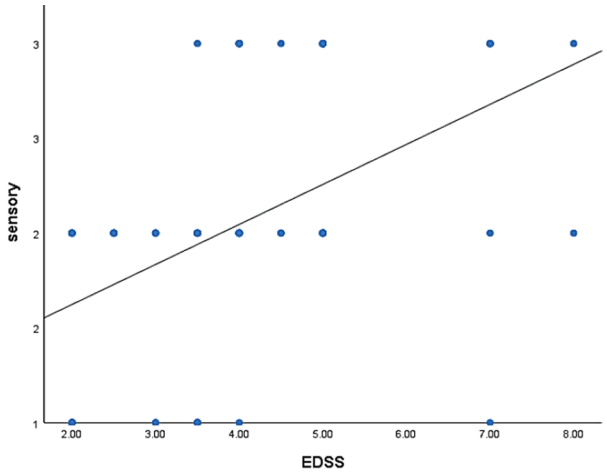
could not be a risk of being more disabled. This finding is consistent with a previous study by Tremlett et al. [46], which reported that older age of onset was unrelated to worse outcomes. In contrast, Scalfari et al. [47] found that older age at the onset of relapsing–remitting disease was associated with higher EDSS scores.

In the present study, RRMS was the most common MS presentation, with a significantly higher percentage in the full ambulatory group. However, the impaired ambulatory group exhibited equal proportions of PRMS and RRMS subtypes. The current results were consistent with a previous study by Mahmoud Afifi et al. [48], which found that 78% of the patients had RRMS and 2% had PPMS. Comparable findings were reported in other studies [39, 49]. However, the current percentage of RRMS exceeded the 60% reported in Saudi Arabia and Iraq [50]. Variations in the frequencies of RRMS may be attributable to differences in sample sizes and ethnic and genetic backgrounds in different populations. This phenotype is characterized by relapses followed by complete remission, allowing the patient to continue walking, which explains the higher prevalence of RRMS in the full ambulatory group.

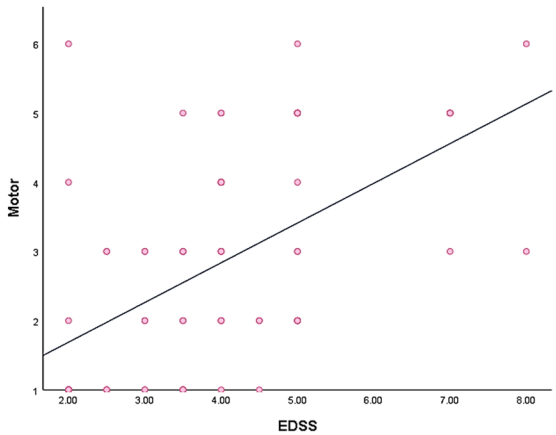
In this study, all clinical manifestations except ataxia were statistically different between the two groups. The impaired ambulatory group had a higher motor weakness with more spinal affection, sensory affection, significant sphincteric affection, and bilateral optic affection than the full ambulatory group. The current findings were consistent with those reported by El-Salem et al. [36],



(A) Correlation between the number of attacks and EDSS



(B) Correlation between sensory manifestation and EDSS



(C) Correlation between motor manifestation and EDSS

Fig. 3 Scattered plot showing Spearman correlation between EDSS and other clinical and psychometric scales

who found that motor symptoms (30.8%) were the most prevalent, followed by visual and sensory complaints (20.1% and 19.6%, respectively). Globally, Browne et al. [51] reported that motor weakness and spasticity (50%), sensory problems (40%), visual disturbances (31%), balance (22%), bladder and bowel (17.5%) were the most frequently reported MS presenting symptoms worldwide.

In the current study, anxiety was detected in 94.3% of the MS patients, with a significantly higher level in the full ambulatory group. This percentage is much higher than that reported in other studies [15, 52–54], which reported that 14–41% of MS patients had anxiety disorders. The different evaluation methodologies, sample sizes, and populations could explain the variations in frequency. Additionally, this study found that moderate-to-severe anxiety is more prevalent in the full ambulatory group, which agrees with Beiske et al., who reported anxiety was associated with lower disability (EDSS < 3). They observed that individuals with less disability had a greater risk of anxiety than those with more disability, but this risk decreased over time [53]. The higher frequency of anxiety in the full ambulatory group may be attributable to their reaction to their new diagnosis and the onset of the disease [55], as well as the consequences of their illness regarding treatment costs, worry about their children's futures, and marriage prospects, preoccupations, and fears regarding death and dying [14]. However, the impaired ambulatory group experienced less worry as they reached the stage of disease acceptance [56].

In the current study, depression presented in 95.7% of the MS patients, with a significantly higher percentage in the full ambulatory group. The current findings showed higher figures than those reported in previous studies [15, 52–54], which ranged from 17.6% to 79%. The disparities in numbers may be attributed to disparities in evaluation methods, demographic, and sample size.

In this study, severe depression was more prevalent in the full ambulatory group (66.7%) than in the impaired ambulatory Group B (50%); nevertheless, the mean total HDRS score was nearly identical across the two groups. This finding is consistent with that reported by Dalos et al. [57], who stated that the frequency or severity of depressive episodes in MS patients is independent of the severity of their disease. Also, Possa and colleagues reported that the risk of depression was higher among patients in the first few years after MS diagnosis [58]. In contrast, the previous Egyptian study by Abdel Sayed et al. [15] reported a correlation between depression and disability and found that the severity of depression is proportional to the severity of the disability. In addition, another study found a 3- to 6-fold rise in the prevalence of depressive symptoms among MS patients with intermediate and advanced disease [56]. The higher prevalence of depression in the full ambulatory group may be attributable to their anticipation of the long-term consequences of their illness and the losses they expect due to their anticipated disability, including the loss of their active lifestyle, employment, and economic burden they will face.

In the present study, there was no statistically significant difference in sleep quality between the two groups; however, 45.7% of the current MS participants reported poor sleep quality. This percentage was in line with 47.5% reported by Merlino et al. [59] and higher than the 38% reported by Čarnická et al. [60]. Sleep problems in MS have the potential to impact the disease, hence increasing the disability of MS patients and limiting their quality of life [61–63].

According to the correlation study for disability in MS patients, the current study revealed that MS patients with increased relapses, PRMS subtype, cervical or dorsal plaques, sensory or motor manifestations, and precipitancy had increased disability. In contrast, the RRMS subtype was associated with decreased disability. These findings are partially consistent with a systematic review [64], which reported that long-term disability in RRMS was associated with sphincter symptoms at onset and early disease course outcome. However, relapse frequency alone is an inadequate predictor of long-term disability in RRMS.

Based on the correlation study for psychiatric disorders in MS patients, the current study revealed no correlation between EDSS scores and depression, anxiety, and sleep quality. These findings agree with the results reported by Alsaadi et al. [52] and Dahl et al. [65]. In contrast, Sarısoy et al. found a correlation between psychopathology prevalence and psychological distress in MS patients and disability [13]. However, according to the present data, anxiety was negatively correlated with age, cigarette smoking, number of attacks, and PRMS subtype and positively correlated with RRMS subtype, depression, and poor sleep quality. These findings agree with a previous study that reported that MS patients with less disability, as in RRMS, had a higher risk of anxiety than those with more disability, but this risk decreased over time [53]. This finding was often noticed after MS patients were notified of their diagnosis and early after the disease onset [55], and could be explained by the fact that patients with RRMS were anxious about future attacks; however, the more disabled individuals had reached a level of acceptance and adaption to their illness by time [56]. Also, the present study found a significant correlation between depression and a dorsal spinal lesion location that could not be explained.

In the current study, motor manifestations were identified as a potential risk factor for having more disability, consistent with a previous study that reported pyramidal presentation in clinically isolated syndrome considered a risk factor for disability progression [66]. In addition, cigarette smoking was identified as a potential risk factor for depression and anxiety in MS patients, consistent with the findings of a recent systematic review conducted by Vong et al. in 2023, which provided significant evidence for an increased prevalence of depression in MS patients who are either current or former smokers. However, only current smoking was linked to a higher incidence of anxiety [67]. Also, a previous systematic review [68] in the general population revealed associations between smoking and depression and anxiety; however, the included studies have not established whether anxiety and depression cause smoking or vice versa due to inconsistency in the direction of the association. Thus, future research should examine this association using different approaches that allow stronger causal inferences [68].

Furthermore, in the current study, MS patients with anxiety were more vulnerable to depression, consistent with previous findings [69], indicating considerable comorbidity. This association necessitates the early identification of anxiety to provide social support as a therapeutic approach to treating and preventing anxiety and depression symptoms [69].

This study has some limitations that need to be addressed in future research. First, the most disabling symptoms, such as fatigue, cognitive dysfunction, and

lesion load impact, were not evaluated. In addition, the current sample size was relatively small. Thirdly, this study had no age- and gender-matched comparator group.

Conclusion

Our study confirmed that MS patients with full ambulation had a high prevalence of psychiatric disorders such as anxiety and depression, whereas those with impaired ambulation had more poor sleep quality. Diagnosing and treating these disorders is essential to improve patients' quality of life. In addition, increased relapses, PRMS, cervical or dorsal plaques, sensory or motor manifestations, and precipitancy increased disability, whereas RRMS type decreased disability.

Abbreviations

BPRS	Brief Psychiatric Rating Scale
DMTs	Disease-modifying therapies
EDSS	Expanded Disability Status Scale
HAM-A	Hamilton Anxiety Scale
HAM-D	Hamilton Depression Scale
mm	Millimeters
MD	Mood disorders
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
PSQI	Pittsburgh Sleep Quality Index
PRMS	Primary relapsing multiple sclerosis
QoL	Quality of life
RRMS	Relapsing–remitting multiple sclerosis
SES	Socioeconomic Status Scale
VEP	Visual evoked potential

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41983-023-00702-x.

Additional file 1. Supplemental Data. **Table S1**. Correlation of EDSS, psychometric scales score and other parameters. **Table S2**. Multivariate linear regression for EDSS with other parameters. **Table S3**. Multivariate linear regression for anxiety with other parameters. **Table S4**. Multivariate linear regression for depression with other parameters. **Table S5**. Multivariate linear regression for sleep with other parameters. **Table S6**. Multivariate linear regression for brief psychotic scale with other parameters.

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Author contribution

SSH: study conceptualization and design, manuscript reviewing and editing. ESD: study conceptualization and design, manuscript reviewing and editing. GKA: study conceptualization and design, data analysis, manuscript reviewing and editing. SRA: data collection, manuscript reviewing and editing. NAH: data analysis, writing the original draft, manuscript reviewing and editing. All authors gave final approval of the manuscript version to be published.

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Availability of data and materials

The data set of this work is available and uploaded with this article.

Declarations

Ethics approval and consent to participate

The study was approved by the ethical committee of the Faculty of Medicine, Assiut University, with Institutional Review Board (IRB) Number: 17101339. This study was registered on a clinical trial with registration Number: NCT05029830. The research complied with the World Medical Association Declaration of Helsinki. A written informed consent was obtained from all participants to participate in the study after explaining all the study points before the start of the study. The informed consent was clear and indicated the purpose of the study, and their freedom to participate or withdraw at any time without any obligation. Furthermore, participants' confidentiality and anonymity were assured by assigning each participant with a code number for the purpose of analysis only. The study was not based on any incentives or rewards for the participants.

Consent for publication

Not applicable.

Competing interests

The authors declared no potential conflicts of interest concerning this article's research, authorship, and/or publication of this article.

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