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EXPLORING COMMON PSYCHOLOGICAL SYMPTOMS IN MULTIPLE SCLEROSIS PATIENTS: SINGLE CENTER SAUDI EXPERIENCE

Running Title: Psychological symptoms in multiple sclerosis

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Abstract:
Background: *Multiple sclerosis (MS) is a destructive and incurable disease, mostly accompanied with disability; therefore, it demonstrates significant psychological symptoms that may impact seriously the socioeconomic status, autonomy, dignity and overall quality of life of the affected patients.*
Objectives: *To explore prevalence and associated factors of depression, anxiety and stress among patients with MS.*
Subjects and methods: *A cross-sectional study was conducted at Neurology department, Al-Hada Armed Forces hospital, Taif city, Saudi Arabia. All patients diagnosed with MS for at least 6 months throughout the period between November, 2025 and January, 2026 and attended for follow-up were eligible for inclusion in the study. A questionnaire was used for data collection, which composed of two main parts. The first part included demographic and medical characteristics of the participants and the second part was the Depression Anxiety and Stress Scale (DASS-21) to assess depression, anxiety and stress.*
Results: *A total of 84 patients with MS were included in the study. Almost two-thirds (54; 64.3%) were females. Their age at onset of the disease ranged between 14 and 56 years with a mean±SD of 30.8±9.5 years. Majority of them (65; 80.2%) had Relapsing-remitting MS (RRMS) and only 11 (13.6%) had clinically isolated syndrome (CIS). Duration of the disease ranged between one and 35 years with a mean±SD of 7.6±6.0 years. Severe depression was observed among 30 patints (35.7%) while severe anxiety was reported by 43 patients (51.2%). Severe stress was observed in 31 patients (36.9%). Multivariate logistic regression analysis (fixed model) revealed no significant determinants for the development of psychological problems among patients with MS; mostly due to relatively small sample size.*
Conclusion: *Psychological sysptoms of depression, anxiety and stress are common among patients with MS, with no difference between them as regards demographic and disease-related characteristics.*
Keywords: *Multiple sclerosis, depression, Anxiety, Stress, Psychological symptoms*

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INTRODUCTION:

Multiple Sclerosis (MS) is the commonest inflammatory, chronic, autoimmune disease affecting the Central Nervous System (CNS) of young adults, mainly females of approximately 30 years of age.[1]

MS is characterized by a variable and unpredictable course.[2] There are four types of Ms, which are Relapsing-remitting MS (RRMS), Clinically isolated syndrome (CIS), Primary progressive MS (PPMS) and Secondary progressive MS (SPMS).[1]

MS is a destructive and incurable disease, mostly accompanied with disability; therefore, it demonstrates significant psychological symptoms including depression, anxiety and stress that may impact seriously the socioeconomic status, autonomy, dignity and overall quality of life of the affected patients.[2]

Depression is a common associate with MS patients with a Lifetime prevalence range between 30% and 40%,[3, 4] which has an adverse impact in reducing the quality of life of those patients as well as it reduces treatment adherence and enhances the risk of disease relapse.[5] Depression in MS may be produced by a combination of nurological changes in mood-regulating circuits, psychological stressors or inflamatory cytokines.[2]

Anxiety disorders affects about 36% of patients with MS,[6] with about from 34% to 70% of early diagnosed patientd experiencing anxiety.[7] It results from a combination of biological and psychosocial factors.[8, 9]

Association between stress and MS is presented in controversial results in literature; while some studies observed an association between them,[10, 11] some others didn`t find this association.[12, 13] These conflicting findings was explained by heterogeneity in study design[14] and by the indirect way through which stress affects MS.[15]

Despite the fact that patients with MS are often subjected to uncertainty in their life and dramatic life changes, that may lead to high levels of psychiatric problems in the form of depression, anxiety and stress, these disorders are often unrecognized and undertreated by many physicians. Therefore, this study aimed to address these psychological problems in those patients, which could have benefits for their management and improving their life quality.

Subjects and methods

A cross-sectional study was conducted at Neurology department, Al-Hada Armed Forces hospital, Taif city, Western Saudi Arabia which is a tertiary care military hopital with 415 bed capacity. All patients diagnosed with multiple sclerosis for at least 6 months who attending the out patient MS clinic and medical day care unit, Al-Hada Armed Forces hospital, Taif city throughout the period between November, 2025 and January, 2026 for follow-up were eligible for inclusion in the study. Patients with severe cognitive impairment, severe psychiatric or medical impairment and those who refused to participate in this study were excluded.

Online Roasoft sample size calculator was utilized to calculate the minimum required sample size according to the assumption of having 115 eligible patients. So, with considereing a prevalence of depression as 19.7% according to a recent similar Saudi study,[16] 5% margins of errors and 95% confidence interval, the required sample will be 79 patients. Convenient non-random sample technique was applied to select consecutive eligible patients till the required sample size has been achieved.

A questionnaire was used for data collection, which composed of two main parts. The first part included demographic and medical characteristics of the participants including gender, age, educational level, current marital status, employment status, type of the disease, and duration of the disease in years. The second part was the Depression Anxiety and Stress Scale (DASS-21), which is a 21-item questionnaire include three self-report scales created to assess the states of depression, anxiety, and stress. Each of the three scales contains seven items. Respondents are asked to use 4-point severity/frequency scales to rate the extent to which they have experienced each state over the past week.[17] This scale was validated to the Arabic culture by Taouk et al.[18] The final score was interpreted to give severity of illness regarding depression, anxiety and stress. The final score of each subscale was doubled as the original tool included 42 items. Then, categorization was done as for depression; score 0–9 means no depression, 10–20 means mild to moderate depression and 20+means severe depression. For anxiety, score 0–7 means no anxiety, 8–14 means mild to moderatee anxiety while 15+ means severe anxiety. As for the stress, score 0–14 means no stress, 15–25 means mild to moderate stress while 26+ indicates severe stress.[19]

Demographic and medical characteristics were collected by the treating physicians and data collectors during the visit while the DASS-21 was self-administered tool as the questionnaires were distributed by the researcher to all the eligible patients during their waiting for the follow up appointment.

Approval from the regional Research and Ethical Committee- Al-Hada Armed Forces Hospital Taif,

Saudi Arabia was obtained before data collection (No. 2025-1130 and dated 30 November, 2025).

Data were statistically analyzed by using Statistical Package for Social Sciences (SPSS) software, version 28. Categorical data were described in the form of frequency and percentages whereas continuous variables were described in the form of mean, range and standard deviation (SD). Chi-square test was applied to test for the association between categorical variables. One-way analysis of variance (ANOVA) test was used to compare a numerical variable between more than two different groups. Patients who expressed at least one the studied psychological problems (depression, anxity and stress) were treated as cases and investigated aganst thoe without any of these problems in a multivariate logitic regression analysis (fixed model) to identify factors associated with the development of psychological problems among patient with multiple sclerosis; results were presented as adjusted odds ratio (aOR) and their 95% confidence intervals (CI) and p-value less than 0.05 was considered for statistical significance.

Results

A total of 84 patients with MS were included in the study. Table 1 summarizes their demographic and disease-related characteristics. Almost two-thirds (54; 64.3%) wre females and 48; 57.1% were secondary school/below educated. Their age at onset of the disease ranged between 14 and 56 years with a mean±SD of 30.8±9.5 years. As regards employment status, 50; 59.5% were not working. Two-thirds of patients were married (current or ever) (56; 66.7%). Majority of them (65; 80.2%) had Relapsing-remitting MS (RRMS) and only 11 (13.6%) had clinically isolated syndrome (CIS). Duration of the disease ranged between one and 35 years with a mean±SD of 7.6±6.0 years.

Severe depression was observed among 30 patints (35.7%) as seen in Figure 1 while severe anxiety was reported by 43 patients (51.2%) as displayed in Figure 2. Severe stress was observed in 31 patients (36.9%). Figur 3

Severe depression was more observed in female compared to male patients (38.9% versus 30%), p=0.020. Also, severe depression was more reported among university/above educated patients as opposed to secondary school/below educated patients (47.2% versus 27.1%), p=0.011. Other studied demgraphic factors (age, age at diagnosis, employment status and marital status) as well as disease-related factors (disease type and duration) were not significantly associated with depression severity. Table 2

None of the studied demographic factors (gender, age, age at diagnosis, educational level, employment status and marital status) and disease-related factors (disease type and duration) was significantly associated with severity of anxiety and stress among the participants as clear from Table 3 and Table 4, respecively.

Multivariate logistic regression analysis (fixed model) revealed no significant determinants for the development of psychological problems among patients with MS. Table 5

Discussion

MS often results in cognitive disability as well as deterioration of physical and motor abilities of the affected patients and in addition, the disease itself is characteriuzed by lacking of good prognosis, and definitive treatment which all could lead to psychiatric problems, including depression, anxiety and stress.[20] Furthermore, MS patients are more likely to be affected by psychological disorders as a result of alterations in brain structure or in immunological as well as inflammatory pathways.[20-23]

Some previous studies demonstrated that depression, anxiety and stress risks are higher in MS patients than in healthy individuals.[16, 24, 25, 26] In the present study and in agreement with the aforementioned statements and studies, depression was detected in 46.4% of patients and was severe in 35.7% of them while anxiety was reported in 59.5% of patients and was severe in 51.2% of them. Also, stress was observed in 46.4% of patients and severe in 36.9% of patients. Comparable findings were reported in various local and international tudies. In Riyadh (Saudi Arabia; 2022), the prevalence of anxiety was 35.3% whereas that of depression was 19.7%.[17] Also in Riyadh (Saudi Arabia; 2022), the prevalence of anxiety was 42.9% wherea that of depression was 58.8%.[27] Earlier in Riyadh (Saudi Arabia; 2020), moderate to severe anxiety were observed in 51.1% of patients while depression was reported in 64% of them; 28.9% had mild to moderate levels.[28] In Iran (2022), almost half (48.6%) of MS patients did not express depressive symptoms and the remaining reported some degrees of depression.[29] Peres et al (2022) performed a systematic review and meta-analysis study and revealed an overall prevalence of depression in MS patients as 27%, 15.8% in RRMS, and 19.1% in PPMS and an overall prevalence of anxiety as 35.2%; 21.4% in RRMS, and 24.1% in PPMS.[30] In United States of America (2021), results showed high prevalence of both severe depression (24%) and severe anxiety (22%).[6] In Argentina (2020), the prevalence of anxiety was 45%.[31] In Iran (2020), moderate depression, moderate anxiety and moderate stress were observed among 47.1%,

39.1%, and 44.8% of patients, respectively.[25] In Canada (2018), the prevalence of anxiety was 30%.[24] In another Canadian study (2017), as opposed to control subjects, MS patients expressed higher annual prevalence ratio of depression (1.77) and anxiety disorders (1.46).[26] Boeschoten et al (2017) conducted a systematic review and meta-analysis and showed a pooled mean prevalence of depression of 30.5% whereas that of anxiety of 22.1% and reported that prevalence of a depresion was relatively lower in European studies than others.[3] In Oman (2015), prevalence of anxiety and depression were nearly 35% and 51%, respectively.[32] In Australia (2013), the prevalence of anxiety was 44.5% while that of depression was 18.5%.[33] Comparison between the previous studies including the present one should be taked in the light of using different tools to assess depression, anxiety and stres as well as the difference in the demographic and disease-related characteristics of the patients. However, higher rates in MS patients than control subjects were evident.

In the univariate analyis of the present study, severe depression was significantly more observed in female compared to male patients and in more educated as opposed to lower educated patients. However, multivariate analysis showed no significant determinants for psychological problems among patients with MS. In other similar local and international studies, some determinants were identified. In Riyadh (Saudi Arabia, 2022), significant predictors for depression were male gender, low education, unemployment, physical inactivity, and fatigue while significant predictors for anxiety were region, unemployment, short duration since last MS relapse, physical inactivity, and fatigue.[16] In another Saudi study (2022), significant predictors for both disorders were low education and having partial to severe disability. Females were more likely to have anxiety than males.[27] Also, in Saudi Arabia (2020), patients aged between 53 and over 60 years expressed higher levels of mild anxiety (76.3%) and higher level of mild to moderate depression (53.6%) while patients younger than 53 years expressed higher levels of moderate to severe anxiety (60.7%) and depression (62.3%). Poor health status (37.6%) was associated with a higher prevalence of depression and not currently married patients had significant depression levels. Female older patients and those with poor general health state were more prone to have anxiety.[28] In Iran (2022), in a binary logistic regression analysis, level of education, marital status, and number of hospital admissions due to MS relapses were significant predictors for depression while in the logistic regression analysis, expanded disability status scale (EDSS) was ignificant predictor for anxious symptoms.[29] In United States (2021), significant predictors of both problems (depression and anxiety) were lack of social support, younger age, shorter disease duration, lower education and substance use.[6] In Argentina (2020), univariate analyis revealed that younger patients, those with shorter duation since diagnosis, patients with a history of psychiatric disorders, depressed, and thoe who had worse health-related quality of life were more likely compared to their peers to develpe anxiety while in multivariate analysis, only depresion and worse health-related quality of life remained significant after controlling for confounders.[32] In Iran (2020), significant determinants for depression were job, education, and economic status of the patients and the only significant determinant for anxiety was economic status while there was no significant determinant for stress among the studied variables.[25] Again having different risk factors for development of psychological problems in patients with MS in different studied could be explained by difference in dmographic and disease-related characteristics of the participants in addition to their cultural background.

The present study had some important limitations. First of all, the present study followed a cross-sectional design, so it was impossible to detect the cause and effect relationship between the independent and depndent variables. Second, data were collected by self-administered tool, which might impact the results validity due to measurement bias. Third, the possibility of type 1 error could reduce the results validity. Fourth, conduction of the study in one healthcare facility couls impact the generalizability of findings. Some important variables such as disability severity, relapse frequency, treatment type, magnetic resonant imaging (MRI) findings, fatigue severity, socioeconomic status, social support, and psychiatric medication history were not included due to missing information in most cases regarding these variables. :Finally, relatively small lows ample size could limit the precision of results.

CONCLUSIONS:

Psychological sysptoms of depression, anxiety and stress are common among patients with MS, with no difference between them as regards demographic and disease-related characteristics. Threfor, physicians should pay attention to screening for symptoms of depression, anxity and stress among patints with MS during their regular clinic visits with referral of affcted patients to psychologists.

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Table 1: Demographic and medical characteristics of the participants (n=84)

Variables	Frequencuy	Percentage
Gender		
Male	30	35.7
Female	54	64.3
Age in years		
Range	20-65	
Mean±SD	38.4±11.0	
Age at onset in years		
Range	14-56	
Mean±SD	30.8±9.5	
Educational level		
Secondary school/below	48	57.1
University/above	36	42.9
Employment status		
Not working	50	59.5
Working	21	25.0
Student	8	9.5
Others	5	6.0
Marital status		
Unmarried	28	33.3
Married (current or ever)	56	66.7
Disease type (n=81)		
Relapsing-remitting MS (RRMS)	65	80.2
Clinically isolated syndrome (CIS)	11	13.6
Primary progressive MS (PPMS)	5	6.2
Duration of the disease (years)		
Range	1-35	
Mean±SD	7.6±6.0	

SD: Standard deviation

Table 2: Factors associated with depression severity among patients with multiple sclerosis

Variables	Depression			p-value
	No N=45 N (%)	Mild/moderate N=9 N (%)	Severe N=30 N (%)	
Gender				
Male (n=30)	14 (46.7)	7 (23.3)	9 (30.0)	
Female (n=54)	31 (57.4)	2 (3.7)	21 (38.9)	0.020*
Age in years				
Mean±SD	38.6±10.7	39.1±8.5	37.9±12.2	0.942**
Age at onset in years				
Mean±SD	30.8±9.8	34.4±8.1	29.7±9.4	0.419**
Educational level				
Secondary school/below (n=48)	26 (54.2)	9 (18.8)	13 (27.1)	
University/above (n=36)	19 (52.8)	0 (0.0)	17 (47.2)	0.011*
Employment status				
Not working (n=50)	27 (54.0)	4 (8.0)	19 (38.0)	
Working (n=21)	13 (61.9)	3 (14.3)	5 (23.8)	
Student (n=8)	3 (37.5)	0 (0.0)	5 (62.5)	
Others (n=5)	2 (40.0)	2 (40.0)	1 (20.0)	0.166
Marital status				
Unmarried (n=28)	16 (57.2)	2 (7.1)	10 (35.7)	
Married (current or ever) (n=56)	29 (51.8)	7 (12.5)	20 (35.7)	0.741*
Disease type (n=81)	N=44	N=9	N=28	
Relapsing-remitting MS (RRMS) (n=65)	34 (52.3)	6 (9.2)	25 (38.5)	
Clinically isolated syndrome (CIS) (n=11)	8 (72.7)	1 (9.1)	2 (18.2)	
Primary progressive MS (PPMS) (n=5)	2 (40.0)	2 (40.0)	1 (20.0)	0.173*
Duration of the disease (years) Mean±SD	7.8±5.7	4.7±2.2	8.2±7.0	0.283**

***Ch-square test** ****One-way analyis of variance (ANOVA)**

Table 3: Factors associated with anxiety severity among patients with multiple sclerosis

Variables	Anxiety			p-value
	No N=34 N (%)	Mild/moderate N=7 N (%)	Severe N=43 N (%)	
Gender				
Male (n=30)	12 (40.0)	2 (6.7)	16 (53.3)	
Female (n=54)	22 (40.7)	5 (9.3)	27 (50.0)	0.905*
Age in years				
Mean±SD	39.9±11.3	37.4±9.8	37.5±10.9	0.623**
Age at onset in years				
Mean±SD	31.6±10.5	32.0±9.2	30.0±8.8	0.725**
Educational level				
Secondary school/below (n=48)	23 (47.9)	3 (6.3)	22 (45.8)	
University/above (n=36)	11 (30.6)	4 (11.1)	21 (58.3)	0.254*
Employment status				
Not working (n=50)	24 (48.0)	4 (8.0)	22 (44.0)	
Working (n=21)	6 (28.6)	2 (9.5)	13 (61.9)	
Student (n=8)	3 (37.5)	0 (0.0)	6 (62.5)	
Others (n=5)	1 (20.0)	1 (20.0)	3 (60.0)	0.577*
Marital status				
Unmarried (n=28)	13 (46.4)	4 (14.3)	11 (39.3)	
Married (current or ever) (n=56)	21 (37.5)	3 (5.4)	32 (57.1)	0.191*
Disease type (n=81)	N=34	N=7	N=40	
Relapsing-remitting MS (RRMS) (n=65)	25 (38.5)	7 (10.8)	33 (50.7)	
Clinically isolated syndrome (CIS) (n=11)	7 (63.6)	0 (0.0)	4 (36.4)	
Primary progressive MS (PPMS) (n=5)	2 (40.0)	0 (0.0)	3 (60.0)	0.453*
Duration of the disease (years)				
Mean±SD	8.3±6.3	5.4±1.4	7.5±6.2	0.512**

***Ch-square test** ****One-way analyis of variance (ANOVA)**

Table 4: Factors associated with stress severity among patients with multiple sclerosis

Variables	Stress			p-value
	No N=45 N (%)	Mild/moderate N=8 N (%)	Severe N=31 N (%)	
Gender				
Male (n=30)	14 (46.7)	4 (13.3)	12 (40.0)	
Female (n=54)	31 (57.4)	4 (7.4)	19 (35.2)	0.536*
Age in years				
Mean±SD	38.6±11.2	36.0±10.8	38.8±10.9	0.807**
Age at onset in years				
Mean±SD	31.2±10.3	31.3±9.4	30.2±8.3	0.893**
Educational level				
Secondary school/below (n=48)	26 (54.2)	6 (12.5)	16 (33.3)	
University/above (n=36)	19 (52.8)	2 (5.6)	15 (41.7)	0.488*
Employment status				
Not working (n=50)	28 (56.0)	3 (6.0)	19 (38.0)	
Working (n=21)	11 (52.4)	3 (14.3)	7 (33.3)	
Student (n=8)	4 (50.0)	2 (25.0)	2 (25.0)	
Others (n=5)	2 (40.0)	0 (0.0)	3 (60.0)	0.542*
Marital status				
Unmarried (n=28)	15 (53.6)	3 (10.7)	10 (35.7)	

Married (current or ever) (n=56)	30 (53.6)	5 (8.9)	21 (37.5)	0.961*
Disease type (n=81)	N=44	N=7	N=30	
Relapsing-remitting MS (RRMS) (n=65)	35 (53.8)	7 (10.8)	23 (35.4)	
Clinically isolated syndrome (CIS) (n=11)	7 (63.6)	0 (0.0)	4 (36.4)	
Primary progressive MS (PPMS) (n=5)	2 (40.0)	0 (0.0)	3 (60.0)	0.583*
Duration of the disease (years) Mean±SD	7.4±5.7	4.8±2.4	8.6±6.8	0.258**

***Ch-square test** ****One-way analysis of variance (ANOVA)**

Table 5: Determinants of psychological problems among patients with multiple sclerosis: Multivariate logistic regression analysis (Fixed model)

Independent variables	aOR	95% CI	p-value
Gender			
Male[a]	1.0		
Female	0.84	0.26-2.66	0.763
Age in years	0.97	0.89-1.06	0.480
Age at onset in years	1.00	0.91-1.10	0.977
Educational level			
Secondary school/below[a]	1.0		
University/above	1.64	0.56-4.80	0.367
Employment status			
Not working[a]	1.0		
Working	1.16	0.31-4.34	0.821
Student	0.73	0.09-5.78	0.765
Others	0.39	0.26-31.10	0.386
Marital status			
Unmarried[a]	1.0		
Married (current or ever)	0.88	0.24-3.14	0.837
Disease type (n=81)			
Relapsing-remitting MS (RRMS)[a]	1.0		
Clinically isolated syndrome (CIS)	0.30	0.07-1.31	0.108
Primary progressive MS (PPMS)	0.56	0.07-4.25	0.576
Duration of the disease (years)	0.98	0.90-1.07	0.666

[a]: Reference catgory
CI: Confidence interval
aOR: Adjusted odds ratio

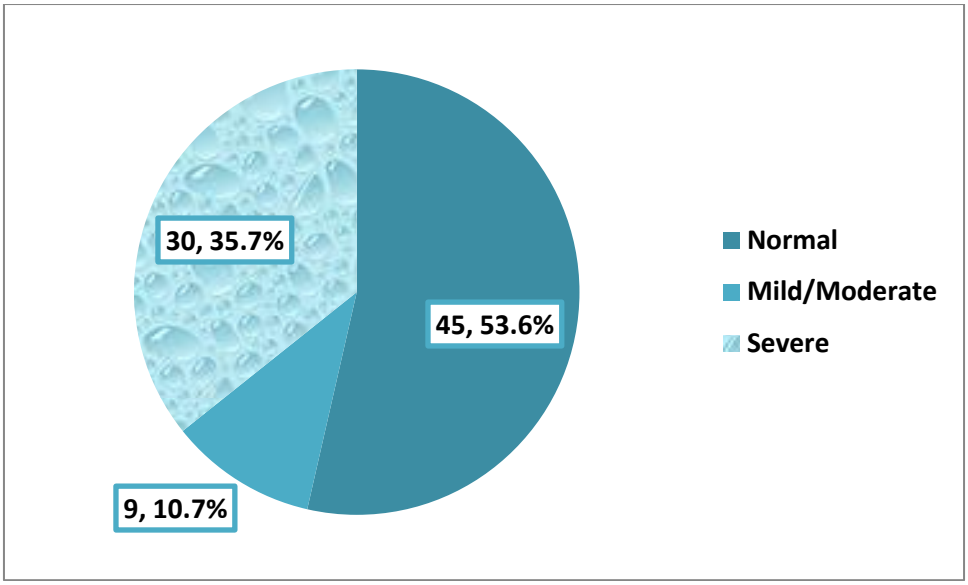

Figure 1: Depression among patients with multiple sclerosis

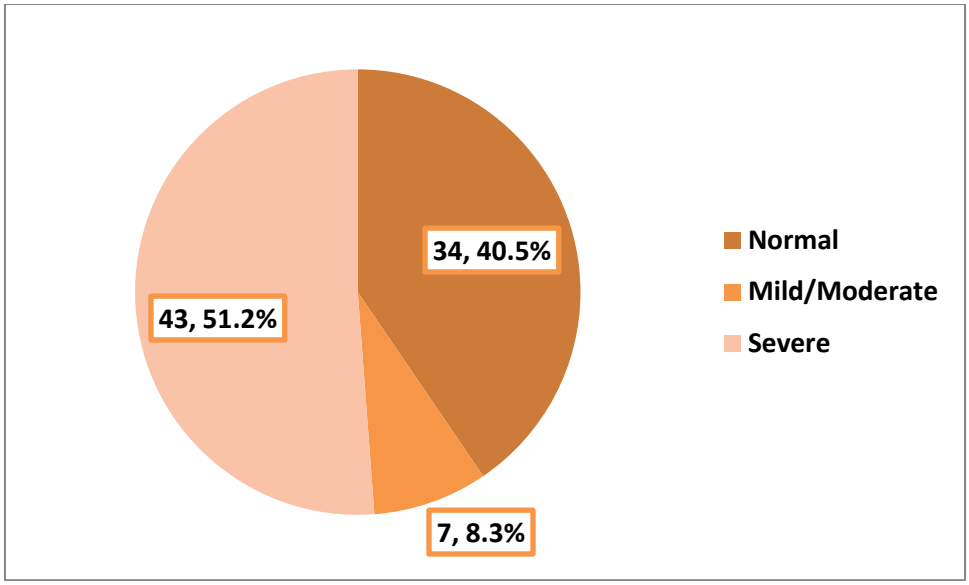

Figure 2: Anxiety among patients with multiple sclerosis

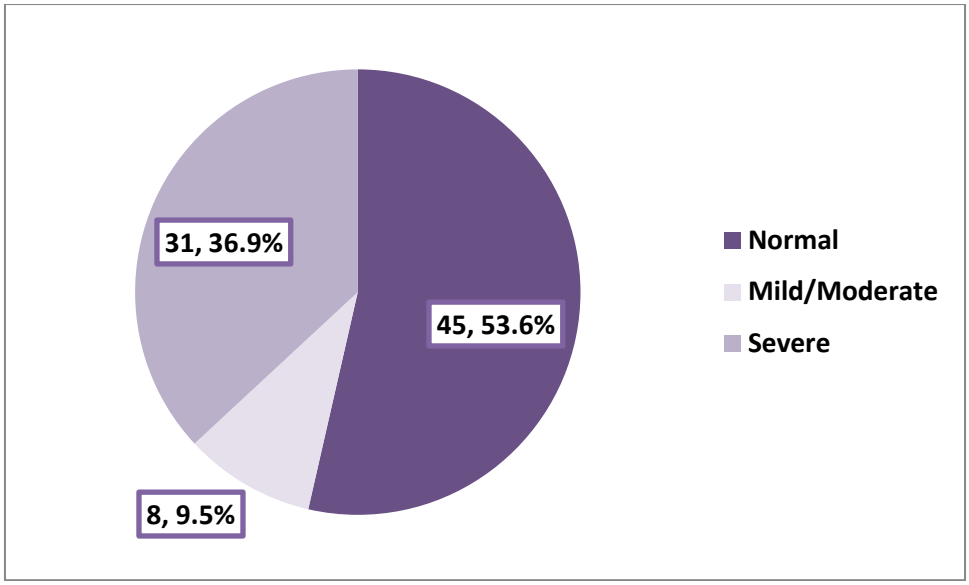

Figure 3: Stress among patients with multiple sclerosis