

Social anxiety disorder among patients with multiple sclerosis: a population-based case-control study in Ecuador

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Introduction. Several studies have found that individuals with multiple sclerosis (MS) experience relatively high rates of anxiety and depression; however, there are few reports about social anxiety in individuals with MS.

Aim. To analyze the prevalence of social anxiety disorder and other psychiatric comorbidities in MS patients compared to matched controls.

Subjects and methods. We included 50 patients with MS that were seen during regularly scheduled visits and 50 sex- and age-matched participants from the general population within a six-month interval. All included participants completed the Social Phobia Inventory (SPIN) and the Depression, Anxiety and Stress Scale with 21 items (DASS-21). We defined clinically significant social anxiety symptoms as SPIN scores ≥ 19 .

Results. The MS patients' mean age was 41.9 years (54% female). The self-reported psychosocial assessments showed that MS participants were more likely to present positive social anxiety symptoms (OR = 7.37; 95% CI = 1.99-27.30; $p < 0.001$), depression (OR = 3.76; 95% CI = 1.41-10.10; $p = 0.006$), stress (OR = 2.67; 95% CI = 1.09-6.52; $p = 0.029$), and general anxiety (OR = 4.70; 95% CI = 1.93-11.40; $p < 0.001$) than the general population. There were moderate correlations between social anxiety and depression ($p = 0.006$), general anxiety ($p = 0.001$), and stress ($p < 0.001$) in MS patients.

Conclusions. Patients with MS had a higher risk of presenting social anxiety symptoms than a matched control group in a Hispanic population.

Key words. Autoimmune disorders. Depression. Multiple sclerosis. Social anxiety. Social phobia. Stress.

Introduction

Multiple sclerosis (MS) is an autoimmune chronic inflammatory disease of the central nervous system that causes demyelination without a known etiology. [1] The demyelination of the central nervous system can cause sensory and motor changes depending on the location of the lesions in the brain and spinal cord. [2] In addition, patients present symptoms such as asthenia, gastrointestinal and bladder impairments, vision abnormalities, sexual dysfunction and neuropsychiatric disorders [3-5].

Neuropsychiatric symptoms are common in patients with MS, and they have important implications for functioning and quality of life. The leading psychiatric disorders in patients with MS are depression and anxiety making them a prevalent topic in the literature, in contrast to specific anxiety disorders in MS patients that have restricted data [6,7].

Depression and anxiety are common in the general population. The presence of both psychiatric disorders with other comorbidities is associated with worse outcomes in patients with chronic degenerative diseases. Social anxiety disorder (SAD)

is a disabling disorder in which patients suffer with considerable morbidity that often precedes the development of other psychiatric disorders. The development of comorbidity adds to the severity of the disorder, increases the risk of suicide attempts, and increases the overall burden of the disease for both the patient (greater disability) and the health care service (greater use of medical services) [8]. Little is known about the prevalence of this psychiatric disorder in MS and the effect that it has on the disease. We hypothesized that Ecuadorian patients with MS would be higher at risk of presenting SAD along with other psychiatric comorbidities due to the variety of symptoms (changes in sensation, visual problems, muscle weakness, depression, difficulties with coordination and speech, severe fatigue, cognitive impairment, etc.) that can cause impaired mobility and disability over the years.

In this study we focused on assessing the prevalence of SAD in patients with MS, and its association with psychiatric comorbidities such as depression, general anxiety and stress, and we established a comparison between MS patients and the general population in Ecuador.

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Subjects and methods

Study design

This is a case-control study that consisted on an interview of 1-hour duration, conducted by a trained resident and a neurologist. Using the same protocol for all the participants, a brief interview was conducted, and a battery of standardized self-reported questionnaires was administered. Other clinical information was collected through medical records.

Participants

This is a population-based, prospective, observational and cross-sectional study conducted at Teodoro Maldonado Carbo Hospital (TMCH) in Guayaquil, Ecuador. The TMCH is one of the main specialist hospitals serving people with MS in the Coast Region of Ecuador which has a population approximately of 8,496,542.

A total of 50 randomly selected MS patients and 50 participants from the general population, matched by age and gender, participated in this study. Patients with a diagnosis of MS according to the 2017 McDonald criteria, this includes clinically isolated syndrome (individuals with an episode of neurologic symptoms for the first time that lasts at least 24 hours and is caused by inflammation or demyelination in the central nervous system and that present with MRI findings or oligoclonal bands in cerebrospinal fluid) [9], over age 18 who visited the neurology outpatient department or hospitalized between November 01, 2017 and April 30, 2018 were recruited.

Those whose cognitive capacity measured with the Mini Mental State Examination (MMSE) [10] was considered likely to prevent them from understanding and filling out the questionnaires (i.e. MMSE < 27) and patients enrolled in clinical trials were excluded. The control group was obtained through local advertisement.

All patients included in the study gave verbal consent to be part of the study.

The sample size was obtained from the following formula:

$$\text{Sample size: } \frac{1,96^2 \times 0,5 \times (1-0,5)}{0,08^2} = 50$$

$$1 + \frac{1,96^2 \times 0,5 \times (1-0,5)}{0,08^2 \times 74}$$

Measures

Information about age, gender, social habits, education, civil, and employment status as well as clinical features such as MS subtype, years of MS and treatment were obtained from medical record. Current neurological disability on the Expanded Disability Status Scale (EDSS) [11] was measured at the time of the interview.

Psychosocial measures

Symptoms of social anxiety were assessed using the Social Phobia Inventory (SPIN). The questionnaire is a 17-item self-assessment scale with three subscales of fear (6 items), avoidance (7 items) and physiological discomfort (4 items). Each item is rated on a 5-point Likert scale, ranging from 0 (not at all) to 4 (extremely). The total points for each of the items were summed up to create a score between 0 and 68 points. The SPIN distinguishes socially anxious individuals from normal controls by using a 19-point cut-off and is a reliable valid measure for evaluating treatment change in social anxiety symptoms [12].

We used the Depression, Anxiety and Stress Scale with 21 items (DASS-21) to evaluate the presence of depression, general anxiety and stress symptoms. This measure employs a 4-point Likert scale and relate to perceived stress in addition to depression and anxiety (7 items/subscale) over the preceding seven days. Higher scores indicate greater distress. Internal consistency for the DASS-21 and concurrent validity have been found to be excellent. Clinical range, based on normative data, is defined as scores ≥ 16.57 for stress, ≥ 12.75 for anxiety, and ≥ 9.26 for depression [13-15].

Other study measures

The CAGE [16] questionnaire was used to screen for alcohol abuse and alcohol dependence. It was initially validated by Mayfield and colleagues in a psychiatric service in 1970 [17], and later in different countries and populations [18,19]. The CAGE is an acronym for each of four questions. The questionnaire can be administered in less than 60 s and is generally used with a threshold of two or more positive answers.

Statistical analysis

The data were analyzed with SPSS v. 25.0 and JAMOVI v. 0.9.2.3 software. Descriptive analyses were performed as absolute and relative proportions for categorical data, mean and standard deviation for

continuous variables with approximately normal distribution and median with interquartile range (IQR) if not fulfilling these criteria. To make comparisons between groups, independent *t*-tests or Mann-Whitney were used for continuous variables and chi-square test for categorical variables; *p* values of < 0.05 were considered statistically significant. Correlations between continuous variables in the MS group were calculated using Spearman's correlation test to examine associations between the SPIN, DASS-21 Depression, DASS-21 Anxiety, DASS-21 Stress and EDSS.

Results

All patients that were offered the opportunity to be included in the study accepted. Basic demographic information and morbidity ratings for the two groups are summarized in table I. In general, the MS participants and the general population were comparable. The mean age in the MS group was 41.9 ± 13.7 and it was 41.4 ± 13.2 years for the control group ($p = 0.85$). The frequency of distribution of sex, civil status, social habits (alcohol and tobacco) and education in the two groups of MS and general population did not differ significantly ($p > 0.05$). The results showed that there was a significant difference in employment status between the two groups ($p = 0.003$). The mean time since diagnosis of multiple sclerosis (by a neurologist) was 10.04 years with a median of 7 years (IQR: 3-14). The reported types of MS were: 8% primary progressive, 82% relapsing-remitting, 8% secondary progressive, and 2% clinically isolated syndrome. 22% of the MS group presented dysarthria, 6% tremor, 22% bowel or bladder dysfunction, 6% visual problems, 22% ataxia, and 54% gait difficulties.

Table II describes the odds ratios (ORs) of psychiatric comorbidities in patients with MS and controls. The prevalence of depression on MS patients was 38%, stress 40%, general anxiety 54%, and social anxiety 32%. Analyses revealed that patients with MS were more likely than the matched population to have depression (OR = 3.76; 95% CI = 1.41-10.1), stress (OR = 2.67; 95% CI = 1.09-6.52), general anxiety (OR = 4.70; 95% CI = 1.93-11.4), and social anxiety disorder (OR = 7.37; 95% CI = 1.99-27.3). These results were significantly different according to chi-square tests.

Table III presents the sociodemographic and clinical characteristics of the low and high SPIN subgroups. No significant associations were found between these subgroups.

Table IV presents self-reported symptoms of depression, general anxiety and stress in MS patients with high and low SPIN scores. There was a significant association between social anxiety social anxiety symptoms and DASS-21 cutoff scores for depression, general anxiety and stress. Patients with MS and co-morbid social anxiety were more likely to have depression (OR = 11.6; 95% CI = 2.84-47.1), stress (OR = 6.11; 95% CI = 1.66-22.5), and general anxiety (OR = 3.80; 95% CI = 1.02-14.2).

Associations between self-reported social anxiety symptoms, co-morbid psychiatric symptoms and neurologic disability were examined through spearman correlations (Figure; Table V).

We found significant and moderate correlations between SPIN and DASS-21 Depression, DASS-21 General Anxiety and DASS-21 Stress scores; however, there was not a significant correlation between the neurologic disability measured by the EDSS and SPIN scores. DASS-21 Depression scores were significant correlated with neurologic disability.

Discussion

More than 30% of the MS patients had positive social anxiety symptoms. This number is nearly five times higher as the corresponding proportion in the general population. The few known studies that have focused on MS patients and SAD have not addressed comorbidities in Hispanic populations. In one study by Poder et al [20], the prevalence of SAD in patients with MS was studied in a clinical setting and not compared to the GP. In a more recent study [21], the prevalence of psychiatric comorbidities in MS patients were also studied in an Indian population. Another study examined psychiatric comorbidities in chronic physical conditions, one of them being MS, but did not compare it to the general population [22].

Although Korostil and Feinstein [23] showed that the prevalence of social phobia in patients with MS were similar to those found in the general population using the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV); our study showed a significant difference between the MS group and the general population group regarding social anxiety symptoms measured by the SPIN.

The fact that the symptoms of social anxiety were not significantly associated with sociodemographic characteristics such as gender, age, marital status, employment status, social habits; and clinical features including years with MS, neurological

Table 1. Sociodemographic and clinical characteristics of multiple sclerosis (MS) patients and general population.

		MS patients (n = 50)	General population (n = 50)	<i>p</i>
Age (mean ± standard deviation)		41.9 + 13.7	41.4 + 13.2	0.853
Sex	Male	23 (46%)	22 (44%)	0.841
	Female	27 (54%)	28 (56%)	
Level of education	Less than high school	2 (4%)	0	0.165
	High school diploma	13 (26%)	7 (14%)	
	Unfinished college education	6 (12%)	5 (10%)	
	Professional degree	29 (58%)	38 (76%)	
Civil status	Single	20 (40%)	15 (30%)	0.670
	Civil union	3 (6%)	4 (8%)	
	Married	21 (42%)	20 (40%)	
	Separated or divorced	5 (10%)	9 (18%)	
	Widowed	1 (2%)	2 (4%)	
Employment status	Employed	27 (18%)	42 (10%)	0.003 ^a
	Pension	14 (54%)	3 (84%)	
	Other	9 (28%)	5 (6%)	
Alcohol abuse	CAGE ≤ 1	47 (94%)	47 (94%)	1.000
	CAGE ≥ 2	3 (6%)	3 (6%)	
Smoking frequency	None	46 (92%)	43 (86%)	0.577
	Smokes 1-5 cigarettes per day or rarely	3 (6%)	6 (12%)	
	Smokes 6-15 cigarettes per day	1 (2%)	1 (2%)	
Years of MS (mean and interquartile range)		10.04 (3-14)	N/A	N/A
Medication	Interferon β-1a (Rebif [®]) ^b	18 (36%)		N/A
	Fingolimod	18 (36%)	N/A	
	Interferon β-1a (Avonex [®]) ^c	12 (24%)		
	Other	2 (4%)		
Class of MS	Relapsing-remitting	41 (82%)		N/A
	Secondary progressive	4 (8%)	N/A	
	Primary progressive	4 (8%)		
	Clinically isolated syndrome	1 (2%)		
EDSS (mean ± standard deviation)		4.1 ± 2.37	N/A	N/A
Neurological symptoms	Dysarthria	11 (22%)	N/A	N/A
	Tremor	3 (6%)	N/A	N/A
	Bladder/bowel dysfunction	11 (22%)	N/A	N/A
	Visual problems	3 (6%)	N/A	N/A
	Ataxia	12 (24%)	N/A	N/A
	Gait difficulties	27 (54%)	N/A	N/A

EDSS: Expanded Disability Status Scale; N/A: not applicable. ^a*p* < 0.05; ^b Interferon β-1a 22 µg or 44 µg subcutaneously three times a week; ^c Interferon β-1a 30 µg intramuscular once a week.

disability, subtype of MS, treatment and specific neurological symptoms such as ataxia, tremor, gait difficulty, dysarthria, bladder/bowel dysfunction, among others, was an unexpected finding. These data relate to a study conducted by Poder et al [20], however, in that study neurological symptoms were not studied separately.

It is important to mention the significant associations between SAD and other psychiatric comorbidities such as depression, general anxiety and stress in people with MS. Davidson et al [24] and colleagues showed that much of the impairment associated with social anxiety disorder is attributable to comorbid disorders in a nonclinical population sample. They proposed that social anxiety disorder without comorbid depression or anxiety may be a milder form of the disorder. Wittchen et al [25] study of a nonclinical sample of patients with social anxiety disorder also demonstrated significantly more impairment among patients with comorbid disorders than among those with 'pure' social anxiety disorder.

Inflammation has been described as a significant contributing factor in psychiatric disorders. Thus, the distribution and number of brain lesions might be etiologically associated with the emergence of social anxiety disorder and psychiatric comorbidities in patients with MS. Previous studies have addressed the effects of neuroinflammation on the presence of general anxiety and depression [26]. Stress management therapy is able to reduce the gadolinium-enhancing lesions over a period of 24 months, therefore decreasing disease burden and inflammation itself [27].

Thus, social anxiety disorder may have its greatest adverse impact on function and quality of life through its association with the development of comorbid pathology. Although SAD has been described to precede other psychiatric comorbidities in the general population, we cannot assure address this possibility in this cross-sectional study. However, studies have proposed that the development of complications due to comorbid disorders among patients with social anxiety disorder may be preventable if social anxiety disorder is detected and treated early [28].

This study was based on self-reported information and the respondents were not necessarily a fully representative sample of people with MS. Another limitation of the present study is that because of the cross-sectional study only correlations but not causal associations can be described, e.g., between neurologic disability and the level of social anxiety, depression, general anxiety and stress.

Table II. DASS-21 and SPIN scores of MS patients and general population.

		MS patients (n = 50)	General population (n = 50)	Odds ratio (95% CI)	p
DASS-21	Depression	Normal/mild	31 (62%)	3.76 (1.41-10.10)	0.006 ^a
		Moderate/severe	19 (38%)		
DASS-21	Stress	Normal/mild	30 (60%)	2.67 (1.09-6.52)	0.029 ^a
		Moderate/severe	20 (40%)		
DASS-21	General anxiety	Normal/mild	23 (46%)	4.70 (1.93-11.40)	< 0.000 ^a
		Moderate/severe	27 (54%)		
SPIN	Social anxiety	SPIN < 19	34 (68%)	7.37 (1.99-27.30)	< 0.000 ^a
		SPIN > 19	16 (32%)		

CI: confidence interval; DASS-21: Depression Anxiety and Stress Scales; MS: multiple sclerosis; SPIN: Social Phobia Inventory. ^ap < 0.05.

The findings convincingly demonstrate that clinicians need to screen for social anxiety and psychiatric comorbidities in patients with MS, and that appropriate management decisions have to be made. Although there is scant evidence regarding the treatment of psychiatric disturbances in patients with MS [29], psychosocial interventions, and even anxiolytic drugs, should be considered [30].

Patients with MS have many impediments that limit their quality of life such as ataxia, gastrointestinal and bladder impairments and other sensory and motor changes. This quality of life obstructions that are observed in patients with MS could be a potential reason for neuropsychiatric disorders. Social boundaries, social unacceptance, association with current and subsequent symptoms and domain functions could be potential reasons why there is a prevalence of SAD in MS patients.

Further studies on social anxiety and other psychiatric comorbidities in MS patients should control for disease activity and sociodemographic factors. Not only depression, but also social anxiety, general anxiety and stress should be studied as a potential risk for relapses and neurological disability progression.

In conclusion, there is a high prevalence of social anxiety disorders, as well as other psychiatric comorbidities in patients with MS rather than in the general population, and these disorders are often underdiagnosed and undertreated. This study showed

Table III. Sociodemographic and clinical characteristics of MS patients with high versus low SPIN scores.

		SPIN < 19 (n = 34)	SPIN ≥ 19 (n = 16)	p	
Sociodemographic characteristics	Age (mean ± standard deviation)	40.5 ± 13.3	45.0 ± 14.6	0.281	
	Sex	Male	14 (41.2%)	9 (56.3%)	0.318
		Female	20 (58.8%)	7 (43.7%)	
	Level of education	Less than high school	2 (5.8%)	0	0.493
		High school diploma	7 (20.6%)	6 (37.5%)	
		Unfinished college education	4 (11.8%)	2 (12.5%)	
		Professional degree	21 (61.8%)	8 (50%)	
	Civil status	Single	14 (41.2%)	6 (37.5%)	0.642
		Civil union	1 (2.9%)	2 (12.5%)	
		Married	14 (41.2%)	7 (43.7%)	
		Separated or divorced	4 (11.8%)	1 (6.3%)	
		Widowed	1 (2.9%)	0	
	Employment status	Employed	22 (64.7%)	5 (31.3%)	0.083
		Pension	7 (20.6%)	7 (43.7%)	
		Other	5 (14.7%)	4 (25%)	
	Alcohol abuse	CAGE ≤ 1	31 (91.2%)	16 (100%)	0.220
		CAGE ≥ 2	3 (8.8%)	0	
	Smoking frequency	None	32 (94.1%)	14 (87.4%)	0.336
Smokes 1-5 cigarettes per day or rarely		2 (5.9%)	1 (6.3%)		
Smokes 6-15 cigarettes per day		0	1 (6.3%)		
Years of MS (mean and interquartile range)		8.59 (3.0-11.8)	13.1 (5.0-19.0)	0.123 ^a	
Medication	Interferon β-1a (Rebif®) ^b	13 (38.2%)	5 (31.25%)	0.775	
	Fingolimod	13 (38.2%)	5 (31.25%)		
	Interferon β-1a (Avonex®) ^c	7 (20.6%)	5 (31.25%)		
	Other	1 (2.9%)	1 (6.25%)		
Class of MS	Relapsing-remitting	30 (88.2%)	11 (68.7%)	0.282	
	Secondary progressive	2 (5.9%)	2 (12.5%)		
	Primary progressive	2 (5.9%)	2 (12.5%)		
	Clinically isolated syndrome	0	1 (6.3%)		
EDSS (mean and interquartile range)		3.65 (1.5-6.0)	5.06 (3.75-6.50)	0.085 ^a	
Neurological symptoms	Dysarthria	6 (17.6%)	5 (31.3%)	0.279	
	Tremor	2 (5.9%)	1 (6.3%)	0.279	
	Bladder/bowel dysfunction	6 (17.6%)	5 (31.3%)	0.279	
	Visual problems	3 (8.8%)	0	0.220	
	Ataxia	7 (20.6%)	5 (31.3%)	0.410	
	Gait difficulties	17 (50%)	10 (62.5%)	0.408	

EDSS: Expanded Disability Status Scale; SPIN: Social Phobia Inventory. ^a $p < 0.05$; ^b Interferon β-1a 22 µg or 44 µg subcutaneously three times a week; ^c Interferon β-1a 30 µg intramuscular once a week.

Figure. Correlation matrix of Spearman coefficients between DASS-21, SPIN and EDSS. DASS.DEP: depression according to DASS questionnaire; DASS.GAN: general anxiety according to DASS questionnaire; DASS.STR: stress according to DASS questionnaire; SPIN.SP: social phobia according to SPIN; EDSS: Expanded Disability Status Scale.

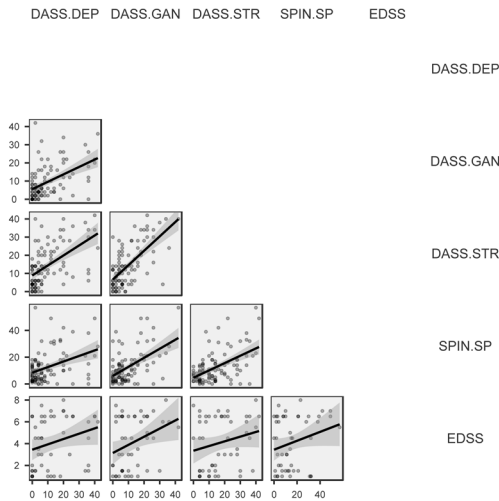


Table IV. Self-reported psychosocial assessments comparing patients with high versus low SPIN scores.

		SPIN < 19 (n = 34)	SPIN ≥ 19 (n = 16)	Odds ratio (95% CI)	p
DASS-21	Depression	Normal/mild 27 (79.4%)	4 (25%)	11.6 (2.84-47.10)	< 0.001 ^a
	Moderate/severe	7 (20.6%)	12 (75%)		
DASS-21	Stress	Normal/mild 25 (73.5%)	5 (31.3%)	6.11 (1.66-22.50)	0.004 ^a
	Moderate/severe	9 (26.5%)	11 (68.7%)		
DASS-21	General anxiety	Normal/mild 19 (55.9%)	4 (25%)	3.80 (1.02-14.20)	< 0.041 ^a
	Moderate/severe	15 (44.1%)	12 (75%)		

CI: confidence interval; DASS-21: Depression Anxiety and Stress Scales; SPIN: Social Phobia Inventory. ^ap < 0.05.

Table V. Spearman correlation coefficients between DASS-21, SPIN and EDSS.

		DASS-21 General anxiety	DASS-21 Stress	SPIN Social anxiety	EDSS
DASS-21 Depression	Spearman's rho	0.268	0.444 ^a	0.384 ^a	0.341 ^b
	p	0.060	0.001	0.006	0.015
DASS-21 General anxiety	Spearman's rho	–	0.532 ^a	0.441 ^a	0.268
	p	–	< 0.001	0.001	0.060
DASS-21 Stress	Spearman's rho	–	–	0.509 ^a	0.199
	p	–	–	< 0.001	0.167
SPIN Social anxiety	Spearman's rho	–	–	–	0.165
	p	–	–	–	0.253

DASS-21: Depression Anxiety and Stress Scales; EDSS: Expanded Disability Status Scale; SPIN: Social Phobia Inventory. ^aCorrelation is significant at the 0.01 level (2-tailed); ^bCorrelation is significant at the 0.05 level (2-tailed).

that SAD is significantly associated with psychiatric such as general anxiety, stress, and depression among people with multiple sclerosis. However, considering the limitations of this study, in order to judge and generalize the results of this research, further studies are required with a larger sample.

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Trastorno de ansiedad social en pacientes con esclerosis múltiple: estudio poblacional de casos y controles en Ecuador

Introducción. Varios estudios han encontrado que individuos con esclerosis múltiple (EM) presentan tasas altas de ansiedad y depresión; sin embargo, hay pocos informes sobre ansiedad social en individuos con EM.

Objetivo. Analizar la prevalencia del trastorno de ansiedad social y otras comorbilidades psiquiátricas en pacientes con EM en comparación con los controles pareados.

Sujetos y métodos. Durante un intervalo de seis meses, incluimos a 50 pacientes con EM que fueron observados durante visitas programadas regularmente y a 50 participantes de la población general pareados por sexo y edad. Todos los participantes completaron el inventario de fobia social (SPIN) y la escala de depresión, ansiedad y estrés de 21 ítems. Definimos síntomas de ansiedad social clínicamente significativos los que tenían un resultado en el SPIN mayor o igual a 19.

Resultados. La edad media de los pacientes con EM era de 41,9 años (el 54%, mujeres). Las evaluaciones psicológicas notificadas demostraron que los participantes con EM tenían más probabilidad de presentar síntomas positivos de ansiedad social (OR = 7,37; IC 95% = 1,99-27,30; $p < 0,001$), depresión (OR = 3,76; IC 95% = 1,41-10,10; $p = 0,006$), estrés (OR = 2,67; IC 95% = 1,09-6,52; $p = 0,029$) y ansiedad general (OR = 4,70; IC 95% = 1,93-11,40; $p < 0,001$) que la población general. Se observaron correlaciones moderadas entre ansiedad social y depresión ($p = 0,006$), ansiedad general ($p = 0,001$) y estrés ($p < 0,001$) en los pacientes con EM.

Conclusiones. Los pacientes con EM tienen un riesgo más elevado de presentar síntomas de ansiedad social que la población hispana en general.

Palabras clave. Ansiedad social. Depresión. Esclerosis múltiple. Estrés. Fobia social. Trastornos autoinmunes.