

Evaluation of quality of life in multiple sclerosis patients: impact of fatigue, anxiety and depression

Avaliação da qualidade de vida em portadores de esclerose múltipla: impacto da fadiga, ansiedade e depressão

Evaluación de la calidad de vida en portadores de esclerosis múltiple: impacto de la fatiga, ansiedad y depresión

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ABSTRACT | This study aims to assess the perception of quality of life in patients with multiple sclerosis (MS) and to verify if there is an association with fatigue, anxiety and depression. This is a cross-sectional study with a sample composed by 100 individuals with a diagnosis of MS enrolled in the *Centro de Referência para Atenção ao Paciente Portador de Doença Desmielinizante do Hospital da Restauração*. The Functional Determination Scale for Quality of Life in Multiple Sclerosis (DEFU), the Modified Fatigue Impact Scale (MFIS-BR), and the Hospital Anxiety (HADS-S) and Depression Scale (HADS-D) were applied. Patients with a Primary progressive clinical form presented worse perception of quality of life (66.90 ± 3.47) when compared to the Secondary progressive (71.65 ± 5.92) and Relapse-remitting (79.00 ± 6.62) forms, with Significant difference ($p < 0.001$). There was a strong positive correlation between the DEFU and the MFIS-BR scores ($r = 0.84$), and a strong negative correlation between DEFU and HADS-A ($r = -0.85$), and DEFU and HADS-D ($r = -0.82$). The decrease in the perception of quality of life in patients with multiple sclerosis is more critical in progressive forms of the disease and is associated with the presence of fatigue, depression and anxiety.

Keywords | Multiple Sclerosis; Quality of Life; Fatigue; Depression; Anxiety.

RESUMO | O objetivo do estudo foi avaliar a percepção da qualidade de vida em pacientes com esclerose múltipla (EM) e verificar se há associação com fadiga, ansiedade e depressão. Trata-se de um estudo transversal com

amostra composta por 100 indivíduos com diagnóstico de EM cadastrados no Centro de Referência para Atenção ao Paciente Portador de Doença Desmielinizante do Hospital da Restauração. Foram aplicadas: a escala de determinação funcional da qualidade de vida na EM (Defu), a escala modificada do impacto da fadiga (MFIS-BR) e a escala hospitalar de ansiedade (HAD-a) e depressão (HAD-d). Os pacientes com a forma clínica primariamente progressiva apresentaram pior percepção da qualidade de vida ($66,90 \pm 3,47$) quando comparados às formas secundariamente progressivas ($71,65 \pm 5,92$) e remitente-recorrente ($79,00 \pm 6,62$), com diferença estatística significativa ($p < 0,001$). Houve forte correlação positiva entre os escores da Defu e da MFIS-BR ($r = 0,84$), e forte correlação negativa entre Defu e HAD-a ($r = -0,85$) e Defu e HAD-d ($r = -0,82$). A diminuição da percepção da qualidade de vida em pacientes com EM é mais crítica nas formas progressivas da doença e tem associação com a presença de fadiga, depressão e ansiedade.

Descritores | Esclerose Múltipla; Qualidade de Vida; Fadiga; Depressão; Ansiedade.

RESUMEN | El objetivo del estudio fue evaluar la percepción de calidad de vida en pacientes con esclerosis múltiple (EM) y verificar si existe una asociación con fatiga, ansiedad y depresión. Este es un estudio transversal con una muestra de 100 individuos diagnosticados con EM, registrados en el Centro de Referencia para Atención al Paciente con Enfermedades Desmielinizantes en el Hospital da Restauração. Aplicamos: la Escala de Determinación Funcional de Calidad de Vida en

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EM (Defu), la Escala de Impacto de Fatiga Modificada (MFIS-BR) y la Escala de Ansiedad Hospitalaria (HAD-a) y Depresión (HAD-d). Los pacientes con la forma clínica primaria progresiva tenían una peor percepción de la calidad de vida ($66,90 \pm 3,47$) en comparación con la forma secundaria progresiva ($71,65 \pm 5,92$) y recurrente-remitente ($79,00 \pm 6,62$), con una diferencia estadísticamente significativa ($p < 0,001$). Hubo una fuerte correlación positiva entre los puntajes

Defu y MFIS-BR ($r=0,84$), y una fuerte correlación negativa entre Defu y HAD-a ($r=-0,85$) y Defu y HAD-d ($r=-0,82$). La disminución de la percepción de la calidad de vida en pacientes con EM es más crítica en las formas progresivas de la enfermedad y se asocia con la presencia de fatiga, depresión y ansiedad.

Palabras clave | Esclerosis Múltiple; Calidad de Vida; Fatiga; Depresión; Ansiedad.

INTRODUCTION

Considered the most common demyelinating disorder of the central nervous system, multiple sclerosis (MS) is characterized by repeated episodes of neurological dysfunction with variable remission¹. This disease is presented under three main types: Relapse-remitting (RRMS), Secondary progressive (SPMS) and Primary progressive (PPMS)².

In the case of RRMS, the individual presents clearly defined outbreaks with complete or incomplete remission, maintaining periods without progression between outbreaks. In SPMS, the individual presents an initial process type RRMS, which is subsequently succeeded by progression with or without occasional outbreaks, discrete remissions and plateaus. And in PPMS, the individual presents a progressive process from the beginning, with occasional plateaus and/or discrete fluctuations³.

The disease and the side effects of medications impact negatively in the health and well-being of these individuals, interfering in their quality of life (QoL)⁴. According to the World Health Organization, QoL is defined as the individual's perception of their position in life, in the cultural context and in the system of values in which they live and in relation to their goals, expectations, standards and desires⁵. In the biomedical area, health-related quality of life (HRQoL) refers to satisfaction regarding health status, a combination of health status and affective response to this condition⁶. Among the groups of chronic patients, HRQoL is used to compare its relationship with the physical and psychological disabilities caused by these diseases and to assess the effects of certain types of treatments⁷.

The MS triggers a set of very common damage, as fatigue⁸, pain⁹ and alterations of motricity and sensitivity³, being the fatigue the most frequent and disabling symptom of the disease¹⁰, occur in 75% to 96% of disease carriers¹¹. In Brazil, it is estimated that between 66.7% and 86.7%

of the carriers present this condition¹². The impact of this symptom highlights the importance of its assessment and diagnosis¹³.

Among the set of psychological complications originating in MS the depression is one of the most common symptoms¹⁴. This illness affects between 27% and 54% of patients, although lower rates have been estimated, and symptoms are described as moderate or severe¹⁵. In a Canadian multicenter study, with 3,125 patients, it was observed that depression rate is 7.5 times greater than that of the general population for the same age, and suicidal ideation is present in 28.6% of patients with MS¹⁶.

Anxiety in patients with MS also tends to present higher scores in anxiety assessment scales when compared to anxious patients who do not have this disease¹⁷. Fear of pain, disability and unpredictability of this disease can intensify anxiety symptoms¹⁸.

The study aims to assess the perception of QoL in patients with MS and to verify if the disease is associated with fatigue, anxiety and depression.

METHODOLOGY

Cross-sectional study whose sample was composed by 100 individuals diagnosed with MS registered in the *Centro de Referência para Atenção ao Paciente Portador de Doença Desmielinizante do Hospital da Restauração (CRAPPDD/HR)*, located in Recife (PE), in the period between May, 2014 and April, 2016.

The inclusion criteria for the study were: patients aged 18 years or older, clinical diagnosis of MS confirmed by neurologist, and registration at CRAPPDD/HR. The exclusion criteria were: schooling below four years, presence of other associated neurological diseases, use of antidepressants and/or anti-anxiety medications in the last three months, use of immunotherapy or

immunosuppressive drugs, an antecedent of abusive use of drugs and alcohol, refusal to participate in the study.

Personal, socioeconomic, and clinical data of the disease were collected. The sample characterization is presented in Table 1, according to the clinical forms of

the disease. There was a predominance of RRMS cases (60%). The SPMS and PPMS forms represented equally 40% of the remaining cases. The mean age of patients with PPMS at the onset of signs and symptoms was higher than in the RRMS and SPMS groups ($p < 0.001$).

Table 1. Characterization of patients with MS by clinical form of the disease

Characterization	Clinical form of the disease			p-value*
	RRMS	SPMS	PPMS	
	Mean±SD	Mean±SD	Mean±SD	
Current Age	37.58±2.55	40.45±3.73	41.65±4.06	<0.001 ^{a,b}
Age at onset of symptoms	29.56±2.36	29.46±2.46	34.60±2.03	<0.001 ^{b,c}
	No. (%)	No. (%)	No. (%)	p-value**
Sex				
Female	47 (78.3)	15 (75.0)	16 (80.0)	0.925
Male	13 (21.7)	5 (25.0)	4 (20.0)	
Race				
White	15 (25.0)	5 (25.0)	6 (30.0)	0.988
Brown	40 (66.7)	13 (65.0)	12 (60.0)	
Black	5 (8.3)	2 (10.0)	2 (10.0)	
Marital status				
Single	24 (40.0)	8 (40.0)	9 (45.0)	0.996
Married	30 (50.0)	10 (50.0)	9 (45.0)	
Divorced	6 (10.0)	2 (10.0)	2 (10.0)	
Schooling				
Elementary school	14 (23.3)	5 (25.0)	6 (30.0)	0.928
High school	36 (60.0)	13 (65.0)	11 (55.0)	
Higher education	10 (16.7)	2 (10.0)	3 (15.0)	

*Kruskal-Wallis test; **Test χ^2 or Fisher's exact test; ^astatistically significant difference between the RRMS and SPMS forms; ^bstatistically significant difference between the RRMS and PPMS forms; ^cstatistically significant difference between SPMS and PPMS forms; RRMS: Relapse-remitting multiple sclerosis; SPMS: Secondary progressive multiple sclerosis; PPMS: Primary progressive multiple sclerosis; SD: Standard deviation; No.: Frequency.

Spinal cord symptoms/initial signs were more common in individuals with the PPMS clinical form ($p=0.003$) compared to the RRMS and SPMS forms. No statistically significant difference was recorded for the other initial and evolutionary symptoms/signs (Table 2).

Then, the patients responded to a version of the Functional Assessment of Multiple Sclerosis (FAMS) scale, translated and validated for the Portuguese language named DEFU (*Determinação Funcional de Qualidade de Vida*), composed by 44 items divided into 6 domains valid for analysis: mobility, symptoms, emotional well-being, general contentment, thinking and fatigue, and family/social well-being. Higher scores reflect better QoL. The 5 domains with 7 items allow scores ranging between 0 and 28; the domain with 9 items (thinking and fatigue) has its scores ranging between 0 and 36, and the total score varies from 0 to 176¹⁹.

The Modified Fatigue Impact Scale (*Escala Modificada do Impacto da Fadiga* — MFIS-BR) was also used in the translated version to Portuguese and validated for the Brazilian population. The instrument is composed by 21 items stratified in three subscales: physical, cognitive and psychosocial subscales. The total score is given by the sum of the three subscales and ranges between 0 and 84;

values below 38 correspond to the absence of fatigue, and values above represent the presence of fatigue²⁰.

Table 2. Presence of initial and evolutionary symptoms/signs for each clinical form of the disease

Symptoms and Signs	Clinical form of the disease			p-value*
	RRMS	SPMS	PPMS	
	No. (%)	No. (%)	No. (%)	
Initial				
Pyramidal	7 (11.7)	3 (15.0)	3 (15.0)	0.889
Spinal cord-related	12 (20.0)	5 (25.0)	12 (60.0)	0.003 ^{a,b}
Optic	11 (18.3)	6 (30.0)	1 (5.0)	0.120
Sensory	18 (30.0)	2 (10.0)	1 (5.0)	0.090
Torso	7 (11.7)	3 (15.0)	1 (5.0)	0.580
Cerebellar	5 (8.3)	2 (10.0)	1 (5.0)	0.834
Evolutionary				
Pyramidal	36 (60.0)	11 (55.0)	11 (55.0)	0.884
Spinal cord-related	41 (68.3)	15 (75.0)	16 (80.0)	0.570
Optic	30 (50.0)	11 (55.0)	7 (35.0)	0.398
Sensory	32 (53.3)	12 (60.0)	11 (55.0)	0.874
Torso	19 (31.7)	5 (25.0)	7 (35.0)	0.779
Cerebellar	17 (28.3)	7 (35.0)	9 (40.0)	0.594

*Test χ^2 or Fisher's exact test; ^astatistically significant difference between RRMS and PPMS; ^bstatistically significant difference between SPMS and PPMS; RRMS: Relapse-remitting multiple sclerosis; SPMS: Secondary progressive multiple sclerosis; PPMS: Primary progressive multiple sclerosis; No.: Frequency.

Finally, the Hospital Anxiety and Depression Scale (HADS) was used, also translated and validated for the Portuguese language, developed for hospitalized patients or those with chronic diseases, avoiding questions that can be attributed to both depression and symptoms of MS. This questionnaire is composed by 14 items, subdivided into 2 subscales, of which 7 assess the symptoms of depression (HADS-D) and 7 the symptoms of anxiety (HADS-A). It is considered that the score equal to or greater than 8 is a indicative of anxiety or depression, for this is the most sensitive score to detect the symptoms²¹.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software v. 20.0 for Windows. The Kolmogorov-Smirnov test was used to analyze data distribution, and Bartlett's test, to verify the homogeneity of variances. The Kruskal-Wallis test was used to analyze the differences in DEFU scores among the subgroup of carriers, according to the clinical forms of the MS.

For categorical variables, Pearson's chi-squared test and Fisher's exact test were used. The Spearman's correlation index was used to analyze the correlation between the variables DEFU and MFIS-BR, DEFU and HADS-D, and DEFU and HADS-A. The significance level was considered at 5%.

RESULTS

According to the mean scores obtained in the DEFU scale, patients with the PPMS clinical form presented worse perception of QoL (66.90±3.47) when compared to SPMS (71.65±5.92) and RRMS (79.00±6.62), with a statistically significant difference (p<0.001). For all DEFU domains, higher mean scores were recorded in the RRMS clinical form, with a statistically significant difference when compared to the two other types. Only for the domain thinking and fatigue there was statistical difference between the SPMS and PPMS clinical forms (Table 3).

It was verified that, according to the scores obtained in the MFIS-BR scale, 63% of the individuals in the sample presented fatigue, with a mean score equal to 41.53±0.84. Regarding the scores recorded in the HADS, 43% of the participants presented anxiety, and 48% depression. The mean score of HADS-A was 9.79±2.97, and the HADS-D mean was 10.0±3.06. There was a strong positive correlation between the DEFU and MFIS-BR scores (r=0.84) showed in Figure 1 and a strong negative correlation between DEFU and HADS-A (r=-0.85) presented at Figure 2, and DEFU and HADS-D (r=-0.82) as shown in Figure 3.

Table 3. DEFU scale domains by clinical form of the disease

DEFU Domains	Clinical form of the disease			p-value*
	RRMS	SPMS	PPMS	
	Mean±SD	Mean±SD	Mean±SD	
Mobility	14.08±1.27	12.75±1.33	11.95±0.94	<0.001 ^{a,b}
Symptoms	12.00±1.17	10.85±0.81	10.20±0.41	<0.001 ^{a,b}
Emotional well-being	9.35±0.93	8.15±0.87	7.55±0.51	<0.001 ^{a,b}
General Contentment	15.56±1.21	14.2±1.00	13.4±0.59	<0.001 ^{a,b}
Thinking and fatigue	13.43±1.18	12.25±1.40	11.2±0.83	<0.001 ^{a,b,c}
Family/Social well-being	14.56±1.06	13.45±0.75	12.6±0.59	<0.001 ^{a,b}

*Kruskal-Wallis; ^astatistically significant difference between RRMS and SPMS; ^bstatistically significant difference between RRMS and PPMS; ^cstatistically significant difference between SPMS and PPMS; RRMS: Relapse-remitting multiple sclerosis; SPMS: Secondary progressive multiple sclerosis; PPMS: Primary progressive multiple sclerosis; SD: Standard deviation.

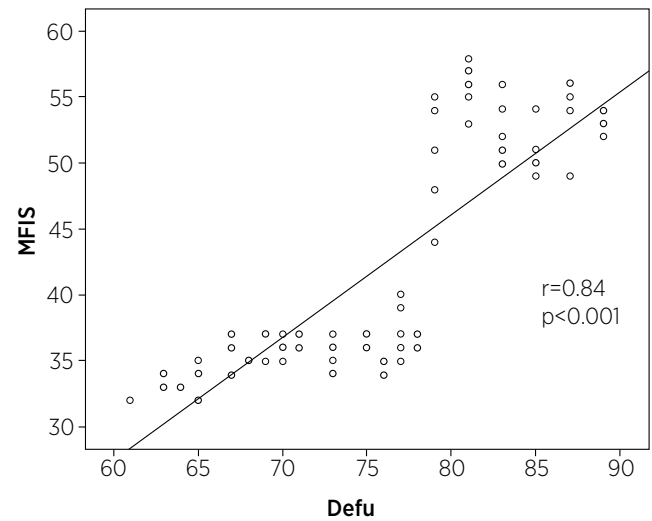


Figure 1. Correlation between DEFU and MFIS-BR scores
r: Spearman's correlation

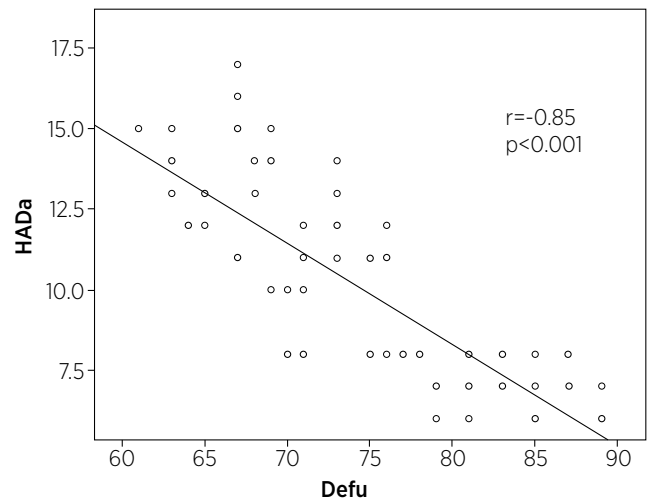


Figure 2. Correlation between DEFU and HADS-A scores
r: Spearman's correlation

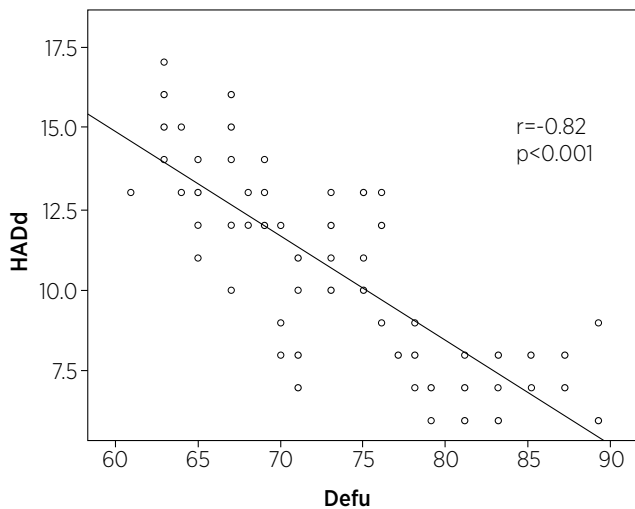


Figure 3. Correlation between DEFU and HADS-D scores
r: Spearman's correlation

DISCUSSION

This study aims to assess the perception of QoL in patients with MS and to verify if the disease is associated with fatigue, anxiety and depression. The results suggest that individuals with MS experience decreased QoL perception. Evidence of previous research corroborate this finding and emphasize its association with the presence of fatigue and psychological symptoms²²⁻²⁷.

It is believed that people with MS present a reduction in the perception of QoL due to the clinical alterations of the disease and the side effects of the medications used, being associated with the presence of fatigue, anxiety and depression.

It is evident that patients with this disease have a wide range of initial and evolutionary symptoms/signs that affect their QoL. In this study, was registered an association between the presence of initial symptoms/signs with sping cord origin and the clinical form of PPMS. Spinal cord involvement can represent an important marker of chronicity and worse prognosis of this disease, which seems true, since individuals with PPMS had lower mean score in the DEFU scale when compared to individuals with the other forms²⁸.

For all domains of the DEFU scale, lower mean scores were recorded in individuals with progressive clinical forms, since there are no obvious remissions in these cases, with the most significant deficits in comparison with those who have periods of remission. The domains related to physical aspects seem to be associated with fatigue, depression and anxiety²⁹⁻³¹.

Fatigue was recorded in 63% of the study participants. Due to the damage in different regions of the brain, thinking and activities require greater energy than before, besides the greater need for strength to perform physical activities by the fact that the muscles with spasticity work against each other³². The demyelination makes the action of sending signals more difficult for neurons, and it is necessary to increase neuronal activity in cell tissues to compensate for this deficit, which gradually leads to weakness of physical capacities and results in the exhaustion of physical components in patients with MS³³.

Anxiety was recorded in 43% of the patients with MS in the research. Previous studies have confirmed an association between anxiety and a reduction in the perception of QoL^{34,35}. The anxiety of patients with MS can be explained by the theory of natural etiology or by biobehavioral approaches, which consider anxiety as an endogenous product that is created to face dangerous stimuli and is naturally produced in situations which the self is in danger — a mechanism that leads to a reduction in physiological functions and, therefore, decrease in the indicators associated with QoL in patients³¹.

Depression was recorded in 48% of the patients in the sample. The literature reports that depression is a significant predictor for the mental aspects that compose the perception of QoL³⁶⁻³⁸. The depression harms the motivation, interest and collaboration of the patient and, consequently, may affect the emotional state, personal satisfaction and social situation. Another interpretation is that depression can distort people's views on the world and their health, and change them in a way that deteriorates their assessment of themselves³⁹.

One of the results of depression is the sensation of lack of energy, which negatively influences the patient's ability to withstand physical pressures. It is probably associated with focal demyelinating lesions and immune system malfunction⁴⁰. These complications can lead to functional limitations and generalized disorders in physical and psycho-emotional components of QoL.

The study did not consider the level of disease severity and the family/social support style, factors that may influence the symptoms presented and in QoL perception of patients with MS. Some data presented are self-reported, which increases the possibility of biased responses. Another limitation of this research is the reduced size of the sample that may affect the results. It is suggested a prudent generalization of the results.

It is also suggested the realization of future research that take into consideration possible mechanisms contributing to the alteration of patients with MS QoL, as follow-up with an interdisciplinary health team, including the realization of physical therapeutic and psycho-therapeutic treatment, quality of family/social support, employment and levels of coping.

FINAL CONSIDERATIONS

The decrease in the perception of QoL in patients with MS is more critical in the progressive forms of the disease and it is associated with the presence of fatigue, depression and anxiety.

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