

## Risk factors for suicide in multiple sclerosis: a case-control study

*Fatores de risco para o suicídio na esclerose múltipla: um estudo de caso-controle*

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### ABSTRACT

**Objective:** To evaluate the prevalence and the suicide risk in a Brazilian sample of patients with multiple sclerosis (MS) and to identify potential factors associated with the risk of suicide. A study was performed with outpatient with MS. The risk of suicide and the presence of psychiatric disorders were assessed by version 5.0 of the Mini-International Neuropsychiatric Interview (MINI). The sample of patients at risk for suicide was matched by sex and age to a control group of patients with MS. **Results:** Eight point three percent of the patients had a past history of attempted suicide, and 8.3% had a current suicide risk, totaling 16.6%. The results of this study suggest that the risk factors associated with suicide in this population are depression, marital status single, widowed or divorced, and lower education level.

### Keywords

Suicide, multiple sclerosis, depression.

### RESUMO

**Objetivo:** Avaliar a prevalência e o risco de suicídio em uma amostra brasileira de pacientes com esclerose múltipla (MS) e identificar fatores potenciais associados ao risco de suicídio. Foi realizado um estudo com pacientes ambulatoriais com diagnóstico de esclerose múltipla. O risco de suicídio e a presença de transtornos psiquiátricos foram avaliados pela versão 5.0 do *Mini-International Neuropsychiatric Interview* (MINI). A amostra de pacientes em risco de suicídio foi pareada por sexo e idade a um grupo-controle de pacientes com MS. **Resultados:** Dos pacientes, 8,3% tinham antecedentes de tentativa de suicídio e 8,3% tinham risco de suicídio atual, totalizando 16,6%. Os resultados encontrados neste estudo sugerem que os fatores de risco associados ao suicídio nessa população são: depressão, estado civil solteiro, viúvo ou divorciado e nível de escolaridade mais baixo.

### Palavras-chave

Suicídio, esclerose múltipla, depressão.

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## INTRODUCTION

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system (CNS) that predominantly affects the white matter by promoting the destruction of myelin, oligodendrocytes and axons. Although the etiology is unknown, theories suggest an interaction among immunologic, genetic, environmental and infectious factors. The frequency is higher among females by a ratio of 3:1, and the disease mostly affects individuals between the ages of 20 and 40 years. Clinical manifestations include sensory changes, motor deficits, sphincter changes, optic neuritis, diplopia, cerebellar signs and cognitive dysfunction<sup>1,2</sup>.

The presence of psychiatric symptoms has been known since the first detailed clinical description of *sclérose en plaques* by Charcot at the Hospital Pitié Salpêtrière in the nineteenth century. These symptoms include pathological crying and laughing, euphoria, mania, hallucinations and depression<sup>3</sup>. The presence of psychiatric disorders is frequent in patients with MS, and a higher prevalence of mood and anxiety disorders has been demonstrated in this population. These disorders may occur by a direct or indirect effect of MS treatment on the CNS or may be the result of mental suffering due to this condition. The prevalence of major depression in patients with MS is approximately 50% throughout life. Depression is a major risk factor for suicide. Anxiety disorders, social isolation and recent functional deterioration also appear to be important factors related to suicidal ideation and suicide attempts<sup>4,5</sup>.

Brønnum-Hansen *et al.* found that the risk of suicide in patients with MS is more than double that of the general population in Denmark<sup>6</sup>. Sadovnick *et al.* demonstrated that the proportion of suicide deaths among patients with MS is 7.5 times higher than for the general population in Canada<sup>7</sup>. Feinstein *et al.* evaluated 140 patients with MS and showed that depression, alcohol abuse, and social isolation are important factors related to suicidal ideation and suicide attempts<sup>8</sup>. In this study, the authors detected suicidal ideation in 28.6% of the participants and past suicide attempts in 6.4% of the participants.

The objective of this study was to evaluate the prevalence of suicide risk in a Brazilian sample of patients with MS and to identify potential factors associated with the risk of suicide. The identification of risk factors is essential for the prevention of suicide in this population.

## PATIENTS AND METHODS

A study with a convenience sample of consecutive multiple sclerosis patients was performed at a public university-based outpatient service for Neuroimmunology in Rio de Janeiro, Brazil. Patients with the diagnosis of MS according to the McDonald *et al.* criteria were invited to

participate in this study. The exclusion criteria were patients younger than 18 years or older than 65 years and patients with other neurological diseases that could potentially interfere with the evaluation. A complete medical history, including the course of disease, medication use such as immunomodulators, and socio-demographic data, was collected concurrently. The degree of disability was evaluated by the Expanded State Kurtze of Disability Scale (EDSS), which ranges from 0-10 with increments of 0.5 (half) points; a higher score indicates a greater degree of disability. The neurological exam evaluated eight functional systems: pyramidal, cerebellar, brainstem, sensory, bladder, bowel, visual and mental. The risk of suicide and the presence of psychiatric disorders were assessed by version 5.0 of the Mini-International Neuropsychiatric Interview (MINI), a short structured interview designed to explore each of the necessary criteria for the main diagnoses of the DSM-IV (American Psychiatric Association, 1994). This instrument also contains one specific section that assesses suicide risk. The sample of patients at risk for suicide was matched by sex and age to a control group and patients with MS. The study was approved by the local ethics committee. In the statistical analysis, the Pearson  $\chi^2$  coefficient was calculated for the categorical univariate analysis, and independent samples tests and Mann-Whitney Test were used for the univariate analysis of continuous variables. Pearson's or Spearman's correlations were calculated, as appropriate.  $P < 0.05$  was considered to be statistically significant. SPSS version 18 (SPSS Inc., Chicago, IL, USA) was used to conduct all the analyses.

## RESULTS

The study included 60 patients with MS and detected a suicide risk in 16.6% of the participants. Of these, 8.3% had attempted suicide in the past, and 8.3% were currently at risk of suicide. For those currently at risk, 10% (1 participant) were considered at low risk, 30% (3 participants) were at moderate risk, and 10% (1 participant) were at high risk. All of the patients who committed suicide had done so by intentional overdose of medications or toxic substances: 3 using benzodiazepines, 1 using antihypertensive drugs, and 1 using an organophosphate.

The sample of MS patients at risk for suicide consisted of 7 (70%) female patients and 3 (30%) male patients ranging in age from 22 to 52 years with a mean of 43.7 years ( $SD = 9.8$ ). A sex- and age-matched control group consisting of MS patients without a risk of suicide was used. The control group included 7 (70%) females and 3 (30%) males ranging in age from 23 to 56 years with a mean of 44.7 years ( $SD = 9.8$ ) (Table 1).

The comparison between the two samples detected significant differences for marital status and educational le-

**Table 1.** Demographic and clinical characteristics in patients with multiple sclerosis at risk of suicide (case) and without risk of suicide (controls)

Characteristics	Case N/mean N = 10	Controls N/mean N = 10	
Gender			
Females	7	7	
Males	3	3	
Mean of age in years	43.7 SD = 9.8	44.7 SD = 9.8	
Married	3	8	p = 0.035*
Education (mean years)	10.6 SD = 4.9	14.4 SD = 3.3	p = 0.05**
Disease duration	11.7 SD = 6.6	12.8 SD = 2.4	p = 0.25**
EDSS (mean)	3.4 SD = 2.5	2.4 SD = 1.6	P = 0.12**
Interferon beta 1A	7	9	P = 0.26*
Psychiatric comorbidity			
Depression	6 (60%)	0	p = 0.004**
Bipolar disorder	1 (10%)	0	p = 0.331*
Generalized Anxiety Disorder (GAD)	0	1 (10%)	p = 0.331**
Bulimia	1 (10%)	0	p = 0.331**
Psychotic symptoms	1 (10%)	0	p = 0.331**
Abuse / dependence of marijuana and cocaine	1 (10%)	0	p = 0.331**
Depression + GAD	1 (10%)	0	p = 0.331**

\* Pearson Chi-quadrado; \*\* Mann-Whitney Test.

vel. Patients at risk of suicide were mostly single, widowed or divorced ( $r = 0.503$ ,  $p = 0.024$ ). In contrast, the majority of the participants in the control group were married. Regarding the level of schooling in years of study, the control group had a higher education ( $r = 0.494$ ,  $p = 0.027$ ). However, no significant differences were identified in the degree of disability, disease duration or medications for the treatment of MS when comparing the two groups of MS patients (Table 1).

Comorbidity with major depression was significantly higher in the group with a risk of suicide compared with the control (Pearson correlation  $r = 0.655$ ,  $p = 0.002$ ). Therefore, depression may be an important factor associated with the risk of suicide in patients with MS. An association between MS and other psychiatric disorders such as bipolar disorder (BD), psychotic syndrome, abuse and dependence on drugs such as marijuana and cocaine, and bulimia nervosa was detected in the group with suicide risk. Consequently, these findings suggest that the comorbidity between MS and these disorders are important factors related to the risk of suicide in this population (Table 1).

## DISCUSSION

The findings in this study show that the risk of suicide in patients with MS is high. Of the patients in this study, 8.3% had

a past history of attempted suicide, and 8.3% had a current suicide risk, totaling 16.6%. In this study, we found no significant differences in the duration of disease, disability degree, or beta interferon use when comparing the group of patients with MS and risk of suicide with the control group. However, there were significant differences with respect to marital status. The presence of single, separated or widowed individuals was significantly higher in patients at risk of suicide compared with the control group. The education level was significantly lower in the group with a risk of suicide compared with the control group.

The results of this study suggest that the risk factors associated with suicide in this population are major depression, marital status single, widowed or divorced, and lower education level. The prevalence of major depression in patients with MS is approximately 50%. An epidemiological study conducted by Patten *et al.* revealed that the prevalence of depressive episodes within a twelve-month period is approximately 25.7% in patients with MS and 8.9% in individuals without MS<sup>8</sup>. Sadovnick *et al.* evaluated 221 patients using a structured interview and found that the prevalence of depressive episodes is approximately 50.3% in MS patients<sup>9</sup>. Chwastiak *et al.* conducted an epidemiological study using the Center for Epidemiological Studies Depression Scale (CES-D) and found that 42% of respondents had clinically significant depressive symptoms with 29% scoring in the range of moderate or severe<sup>10</sup>.

The sample of MS patients at risk for suicide met the criteria for other psychiatric disorders such as TB, psychotic syndrome, drug abuse or addiction, and eating disorders. These findings suggest that comorbidity with these disorders increases the risk of suicide in patients with MS.

There are few studies in the literature that evaluated the prevalence and risk factors associated with suicide in clinical samples in MS.

## CONCLUSION

This study is the first of its type to be conducted in Brazil. The results found in this study suggest that the risk of suicide is high and that major depression is the main risk factor associated with suicide. In conclusion, major depression should be systematically investigated in patients with MS<sup>11</sup>. The prevalence of major depression is high in MS patients, and it is the main risk factor associated with suicide in this population.

## INDIVIDUAL CONTRIBUTIONS

All authors had made substantial contributions to the design of the work; substantially contributed for analysis and interpretation of data; critical review of important intellectual

content; attended the final approval of the version to be published; and are responsible for all aspects of work.

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