A cross-sectional study of alexithymia in patients with relapse remitting form of multiple sclerosis

Stojanov J, Stojanov A¹

ABSTRACT
Background: Alexithymia is one’s incapacity to identify, comprehend, and describe emotions. There is almost no literature data about the levels of alexithymia among patients with relapse remitting type of multiple sclerosis.
Aim: The objective of the present study was to assess the levels of alexithymia in patients with relapse remitting type of multiple sclerosis in relation to their sociodemographic variables and clinical characteristics of the disease.
Methods: This cross-sectional study included 106 consecutively assessed patients with relapse remitting type of multiple sclerosis. In addition to the data regarding disease duration, number of demyelinating relapses, and degree of neurological disability, assessed by the expanded disability scale score (EDSS), we used Toronto alexithymia scale (TAS), fatigue severity scale (FSS) and, Hamilton scale for the assessment of anxiety and depression and sociodemographic questionnaire.
Results: Study included 74 female and 32 male patients, with a median age of 44 years, median disease duration 90 months, and median EDSS 4. About 29.55% of patients had alexithymia and borderline alexithymia was observed in 31.15% patients. Alexithymia correlated with anxiety and depression (P < 0.01) on all TAS subscales. Higher levels of neurological disability based on EDSS, severe fatigue based on FSS scores, and severe relapse remitting type of multiple sclerosis with more relapses and longer disease duration correlated with alexithymia (P < 0.01), depression (P < 0.01), and anxiety (P < 0.01). Higher rates of alexithymia were noticed in older, unemployed, single patients, and those having fewer children.
Conclusions: Alexithymia was found in a relatively high percentage in patients with relapse remitting type of multiple sclerosis.

KEY WORDS: Alexithymia, anxiety, depression, multiple sclerosis

Introduction
Multiple sclerosis (MS) is a chronic autoimmune, inflammatory, and neurodegenerative disease of the central nervous system (CNS). Prevalence of patients with MS is rising from lowest 0.22/100,000 in South Africa to more than 200/100,000 in Northern Europe.¹² The prevalence of MS in the whole of Europe is 127/100,000.¹³

Up to 85% of MS patients are characterized by the relapsing-remitting phenotype of multiple sclerosis (RRMS), which implies the emergence of new or worsening recurrent neurological problems that have a complete or partial recovery, lasting from several days to several weeks.¹⁶ MS starts most often in young adults (average age 20–40), and it is characterized by repetitive inflammatory demyelination attacks and axonal loss, affecting different parts of the CNS at different time intervals. These lesions have been associated with cognitive and affective impairments commonly seen in MS.¹⁵

Inability to acknowledge emotional facial expressions, to sense and realize what others think or feel, accepted as a process of...
perspective-taking or theory of mind, more sophisticated form of empathy, has been reported in patients with MS. This inability, especially its cognitive aspect was pointed out as the earliest indication of neurodegeneration in MS patients. Importantly it is the ability to recognize one’s own emotions, the inability of which could be called “alexithymia”. Alexithymia is a personality trait that depicts one’s incapacity to identify, comprehend, and describe their proper and other’s emotions and distinguishing them from bodily sensations. Lesions and atrophy in prefrontal cortices, affecting ventromedial and dorsolateral regions have been connected with emotion processing, alexithymia, and empathy in MS patients. Prevalence of alexithymia in the general population is up to 20%, while in MS varies even up to 40%. Available literature indicates that there is a high percentage of psychiatric comorbidity in MS patients, particularly depression and anxiety. Alexithymia was found to be a major predictor to the development of mood disturbance.

The objective of the present study was to assess the levels of alexithymia in RRMS patients regarding sociodemographic and clinical characteristics of the disease.

Methods

This cross-sectional study included 106 consecutively assessed patients between January 2016 and January 2019. Only patients aged >18 years with RRMS according to Mac Donald criteria, without any known psychiatric comorbidity were included in the study. The exclusion criteria were also patients with a primary or secondary progressive type of the MS as well as patients with other chronic illness (diabetes, asthma, hypertension, heart failure, renal, and hepatic insufficiency) and patients with a history of addiction. All patients had an MMSE score >24 and have been receiving immune-modulatory therapy (interferon beta or glatiramer acetate) at the time inclusion in the study. Based on prestudy sample size calculation, the approximate number of patients to be recruited was 35 patients/group (α = 0.05; β = 0.20).

We collected sociodemographic data about current age, gender, place of residence, current partner status, number of children, profession and employment status, presence of psychiatric disease in the family, history of addiction, as well as clinical characteristics of the disease such as disease duration in months and number of relapses.

The study included a single application of Toronto alexithymia scale (TAS), fatigue severity scale (FSS), and Hamilton scale for the assessment of anxiety (HAM-A) and depression (HAM-D). Questionnaires were assigned to patients only after carrying out a complete neurological examination and collecting epidemiological data, three or more months after administrating last pulse corticosteroid therapy for the relapse of the disease.

For the assessment of current disability status, we used an expanded disability status scale (EDSS). EDSS is the standard measure of physical disability in addition to disease progression and the degree of neurological impairment, often used in clinical practice. It is divided into eight functional systems (FS), and the total score ranges from 0–10. Patients with a score of ≤3.5 are treated ambulatory.

TAS is widely used reliable and refined self-reported 20-item measure of alexithymia, with a 5-choice scale. TAS total score indicates the general level of alexithymia, the sum of three independent scores that measure difficulty in identifying feelings (DIF), difficulty in communicating feelings (DCF), and externally oriented thinking (EOT). International cutoff values are the following: no-clinical alexithymic (scores ≤51), borderline alexithymic (scores of 52-60), or alexithymic (scores >60). For the purpose of this study, we used a validated and standardized Serbian version of the TAS.

FSS is a 9-items self-rated questionnaire for describing fatigue in MS, and the final score consists of calculating each item score. Seven-point Likert scale assess patient’s agreement ranging from 1 (strongly agree) to 7 (strongly disagree). If the total FSS score was ≥4, patients were considered to be fatigued.

HAM-D measures the intensity of depression, and the values are interpreted as follows: 0–9 (without depression), 10–15 (mild depression), 16–24 (mild-to-moderate depression), and 25 or more (moderate-to-severe depression). HAM-A measures the intensity of anxiety, where the ultimate values below 17 indicate absence or mild anxiety, values between 18–24 on mild-to-moderate anxiety, and values between 25–60 on moderate-to-severe anxiety.

The study was conducted in accordance with all applicable guidelines, including the basics of good clinical practice, the Helsinki Declaration, and the Law on Health Care of the Republic of Serbia, with verbal and written consent prior to enrollment and treatment with respect, protection of the participants’ personality, and data obtained in the research. Local review board gave their ethical approval for the conduction of this study.

All data were statistically processed by IBM SPSS statistical software (version 21) for windows operative system. P values of less than 0.05 were regarded as statistically significant. Numerical data are presented as medians and interquartile range (IQR) for nonparametric data and as mean ± standard deviation (SD) for parametric data. The Mann-Whitney test was used to compare continuous variables between two groups, and the Kruskal-Wallis test was used to compare more than two groups. Correlations were assessed using Pearson’s correlation coefficients or Spearman’s correlation coefficients.

Results

The study included 106 consecutively assessed patients (74 female and 32 male patients), with a median age of 44 years (IQR 18–65). The median disease duration was 90 months (IQR 8–186) and median EDSS was 4 (IQR 1–6.5). About 29.55% of patients had alexithymia and borderline alexithymia was observed in 31.15% patients. RRMS patient demographics,
Alexithymia was identified in 47.1% of patients with depression (scores ≥10 on HAM-D) and 36.8% of patients with anxiety (scores ≥18 on HAM-A). There was a significant positive correlation of alexithymia with anxiety and with depression in patients with RRMS (P < 0.01). Patients with higher scores on depression and anxiety scales had higher alexithymia scores on all TAS subscales [Table 2].

Higher levels of neurological disability based on EDSS, severe fatigue based on FSS scores, more relapses and longer disease duration were also in positive correlation with higher scores on TAS (P < 0.01) [Table 3]. Patients with severe RRMS, patients with more relapses, longer duration of disease, and severe fatigue on FSS also had higher degrees of depression (P < 0.01) and anxiety (P < 0.01).

Higher rates of alexithymia were noticed in higher age, actively unemployed, being single and having fewer children [Table 4]. For individuals with RRMS, no statistically significant influence of sex, place of residence, educational level or presence of psychiatric disorders in the family was noticed.

**Discussion**

Our results show the correlation between several sociodemographic and clinical characteristics of RRMS and levels of alexithymia. Alexithymia correlated with anxiety and depression, higher levels of neurological disability based on EDSS, severe fatigue based on FSS scores, and severe relapse remitting type of multiple sclerosis with more relapses and longer disease duration. Higher rates of alexithymia were noticed in older, unemployed, single, and with fewer children.

Using a 60-point cutoff score on the TAS, 29.55% of patients scored for alexithymia, which is within the scope of the findings by other authors, from as low as 10% to up to 40%. A higher percentage of patients were borderline alexithymic (31.15%) then alexithymic, which is consistent with the results of other research.  

Severe MS with more relapses and longer duration of disease was associated with high levels of alexithymia. In our study, a significant positive correlation was found between severe RRMS on EDSS score with more relapses and longer duration of disease with depression, anxiety, and alexithymia. In addition, high levels of neurological disability were associated with the presence of alexithymia, more relapses and longer duration of RRMS.

Some studies did not find any difference in MS duration, EDSS score, or a number of relapses between alexithymic and non-alexithymic MS patients or relative to age, gender, education, or even disease type. We found a correlation between higher age, being single, and having fewer children with high rates of alexithymia in RRMS. High physical disability and fatigue, progressive development of the disease and the presence of cognitive impairment have been connected with unemployment in MS. We found a correlation between current unemployment and high rates of alexithymia in RRMS.

Available literature indicates an established relationship between alexithymic MS patients and mood disorders. Our finding also shows that high levels of depression and anxiety, correlate with high levels of alexithymia, as well as between alexithymia and non-alexithymic MS patients or relative to age, gender, education, or even disease type.

**Table 1: Demographic and clinical characteristics of patients with relapse remitting form of multiple sclerosis (n=106)**

| Age in years | 44.10 (18-65) |
|-------------|---------------|
| Female gender | 74 (69.8%) |
| Disease duration in months | 90.23 (8-186) |
| EDSS* | 3.89 (1-6.5) |
| Number of relapses | 4.06±1.89 |
| Education |  |
| Primary studies | 28 (26.4%) |
| Secondary studies | 49 (46.3%) |
| University degree | 29 (27.3%) |
| Partner status: married or cohabitant | 66 (62.3%) |
| Occupational status: employed (including students) | 48 (45.2%) |
| Number of children |  |
| Zero | 37 (34.9%) |
| One or two | 53 (50%) |
| Three or more | 16 (15.1%) |
| Psychiatric disease in family | 21 (19.9%) |
| FSS* | 46.81±12.15 |
| HAM-A* | 17.10±4.50 |
| HAM-D* | 17.72±4.75 |
| TAS | 58.77±11.15 |
| DCF** | 15.25±4.76 |
| DIF** | 19.23±3.88 |
| EOT** | 23.57±5.34 |

| Mean±standard deviation for parametric data, frequency (%) and median (interquartile range) for nonparametric data are reported; |  |
| *Expanded Disability Status Scale; | °Fatigue Severity Scale; | Hamilton scales for the assessment of anxiety; | Hamilton scales for the assessment of depression; | Toronto Alexithymia Scale; | **Difficulty in Communicating Feelings; | Difficulty in Identifying Feelings; | Externally Oriented Thinking |

**Table 2: Correlations between TAS score and subscores and HAM-D and HAM-A (n=106)**

| DCF† | \( R_p \) | \( P \) | DIF† | \( R_p \) | \( P \) | EOT† | \( R_p \) | \( P \) | TAS** | \( R_p \) | \( P \) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| HAM-A* | 0.287 | <0.01** | 0.347 | <0.01** | 0.175 | <0.05* | 0.350 | <0.01** |
| HAM-D* | 0.197 | <0.05* | 0.376 | <0.01** | 0.167 | <0.05* | 0.322 | <0.01** |

\( P<0.01**; \ P<0.05*; \) Hamilton scales for the assessment of anxiety; Hamilton scales for the assessment of depression; Difficulty in Communicating Feelings; Difficulty in Identifying Feelings; Externally Oriented Thinking; Toronto Alexithymia Scale
with anxiety and alexithymia with depression in RRMS patients. Scores on different subscales of TAS-20 (DIF, DCF, EOT), show that all three subscales correlate with anxiety and depression. Other authors found that DIF correlated with both anxiety and depression, DCF only with anxiety, and for EOT there was not any correlation with any of the mood scales.\[26\]

So far scientific literature has related alexithymia with depression and fatigue.\[22\] Chronic and high-intensity pain, lower educational level, and high levels of depression can affect the self-perceived state of health and affect existence as well as the level of alexithymia.\[27\] The perception and intensity of fatigue and its relationship with alexithymia in MS patients were noticed which is consistent with our findings that severe fatigue on FSS scale correlates with depression, anxiety, and alexithymia.\[28,29\]

All three components of behavior cognitive, emotional, and physiological are important for MS outcome.\[30,31\] A study showed a dissociation between behavioral and neurophysiological response in RRMS patients with undamaged cognitive functioning, and another found a connection between physical disability and self-reported physical activity among MS patients.\[32,33\] In MS patient’s theory of mind is impaired, and social cognitive disorders may occur apart from behavioral disorders.\[5,14\]

If we start from the assumption that individual emotion experience determines empathic reaction and social cognition, within is expected that a high levels of alexithymia could reduce the ability to adequately assess the situation and engagement in active problem solving with empathy towards others and could have negative consequences in assessment and a realistic picture of the disorder, as well as on prognosis of RRMS.\[35\]

We would like to emphasize that literature data on this subject are scarce and that this is one of the few studies in MS patients, which examines the correlation of various sociodemographic factors and clinical characteristics to the levels of alexithymia. Moreover, this is the first study of alexithymia conducted only on a subpopulation of RRMS patients, whose degree of neurodegeneration is generally lower than in patients with primary progressive MS. We believe that the results of our study significantly complement the already existing knowledge of high levels of alexithymia in patients with MS, provide the necessary information about the levels of alexithymia in so far unexamined RRMS and open up some new questions and opportunities for further research on this topic. Obtained data can also be of great importance in the prevention, treatment process, and prognosis outcome of RRMS.

Limitations of our study were that it was performed on a relatively small sample, that we did not include healthy controls, with no correlation with magnetic resonance findings, and patients were not monitored over time. We also did not consider the use of different immunomodulatory drugs and their potential impact on alexithymia.

### Conclusion

Results of our study show that the prevalence of alexithymia in RRMS patients is relatively high. High levels of alexithymia correlate with depression and anxiety, some clinical characteristics such as high levels of neurological disability, more relapses, longer duration of disease and severe fatigue, as well as some sociodemographic characteristics such as higher age, current unemployment, being single, and having fewer children in RRMS patients. Alexithymia and social cognition are still an under-researched; they pose challenges and difficulties to patients with RRMS. Since little evidence exists on the progression of alexithymia over time, particularly in RRMS patients, it is our suggestion that scale for alexithymia should be integrated with the daily clinical work, as well as correlated with findings of clinical disease progression and MR imaging in future studies.

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### Conflicts of interest
There are no conflicts of interest.

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### Table 3: Correlations between TAS scores and EDSS, FSS, number of relapses and disease duration (n=106)

|         | EDSS* | FSS* | Relapses | Duration |
|---------|-------|------|----------|----------|
| TAS*    |       |      |          |          |
| R       | 0.275 | 0.432| 0.298    | 0.225    |
| P       | <0.01** | <0.01** | <0.01** | <0.01** |

P<0.01**, *Toronto Alexithymia Scale; †Expanded Disability Status Scale; ‡Fatigue Severity Scale

### Table 4: Correlation between TAS scores and sociodemographic characteristics of the disease (n=106)

|         | Age | Employment | Partner | Number of children |
|---------|-----|------------|---------|--------------------|
| TAS*    |     |            |         |                    |
| R       | 0.164 | -0.187 | -0.193 | -0.210 |
| P       | <0.05* | <0.05* | <0.05* | <0.05* |

P<0.05*; *Toronto Alexithymia Scale
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