Depression in patients with multiple sclerosis

Depresija kod oboljelih od multiple skleroze

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──────────────── **Summary** ────────────────

Objective: The aim of the study was to determine the prevalence of depression in patients with multiple sclerosis (MS) and to analyze the link between depression and patient sex, age, clinical course of MS, disease duration, antidepressant intake, and degree of disability.

Patients and methods: The study was conducted on 102 MS patients that had undergone inpatient rehabilitation at the Lipik Hospital in the period from May 15, 2015 to September 15, 2015. Data on patient age, sex, degree of disability, clinical course of MS, antidepressant use, and time elapsed from MS diagnosis were collected. The diagnosis of depressive syndrome was made using the Patient Health Questionnaire-nine (PHQ-9). Study patients were divided into two groups according to the depressive syndrome absence or presence.

Results: The total number of respondents was 102, of which 31 (30.4%) met the criteria for depressive syndrome diagnosis. 10 (32.3%) out of the 31 patients were taking antidepressants. There was a statistically significant positive correlation between the presence of depressive syndrome and higher level of disability (P = 0.028), whereas there was no correlation between the presence of depression and sex (P = 0.429), age (P = 0.652), disease duration (P = 0.549), and disease course (P = 0.326).

Conclusion: The high rate of patients screened positive for depression and the fact that only one-third of these patients were taking antidepressants call for an active approach to diagnosis and the treatment of depression in MS patients.

Key words: multiple sclerosis, depression, PHQ-9 questionnaire

──────────────── **Sažetak** ────────────────

Cilj rada: Cilj rada je bio odrediti učestalost depresije kod oboljelih od multiple skleroze (MS) i analizirati povezanost depresije sa spolom bolesnika, dobi, kliničkim oblikom MS, trajanjem bolesti, uzimanjem antidepresiva i stupnjem onesposobljenosti.

Ispitanici i metode: Studija je obuhvatila 102 oboljelih od MS koji su u razdoblju od 15. svibnja 2015. do 15. rujna 2015. provodili stacionarnu rehabilitaciju u Specijalnoj bolnici za medicinsku rehabilitaciju Lipik. Prikupljeni su podaci o spolu i dobi ispitanika, stupnju onesposobljenosti, kliničkom obliku MS, uzimanju antidepresiva i vremenu proteklom od postavljana dijagnoze MS. Dijagnoza depresivnog sindroma postavljena je pomoću upitnika PHQ-9. Ispitanici su podijeljeni u dvije skupine, ovisno o prisutnosti ili odsutnosti depresivnog sindroma.

Rezultati: Ukupan broj ispitanika bio je 102, od kojih je 31 (30,4%) ispunilo kriterije za dijagnozu depresivnog sindroma, a 10 njih (32,3%) uzimalo je antidepresive. Nađena je statistički značajna povezanost između prisutnosti depresivnog sindroma i višeg stupnja onesposobljenosti (P = 0,028), dok nije nađena između prisutnosti depresivnog sindroma u odnosu na spol (P = 0,429), životnu dob (P = 0,652), trajanje bolesti (P = 0,549) i klinički tijek bolesti (P = 0,326).

Zaključak: Visoka učestalost bolesnika pozitivnih na testu probira na depresiju i činjenica da samo trećina njih uzima antidepresive zahtijeva aktivan pristup u dijagnostici i liječenju depresije kod oboljelih od MS.

Ključne riječi: multipla skleroza, depresija, upitnik PHQ-9

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Introduction

Mood disorders (e.g., depressed mood, anxiety) in MS patients have a multifactorial etiology including disease-related processes resulting in neural damage, genetic and environment-related predispositions, normal grieving, and adjustment to loss.[1] Depression can also be a psychological reaction to lifestyle changes that occur when patients face the reality of living with a chronic disease, as well as the lack of social support.[2,3] If left untreated, depressive symptoms in MS patients may worsen over time.[4] Depressive symptoms are strongly associated with worse self-reported functioning and low health-related quality of life.[5,6] MS patients who suffer from depression have a lower coping capacity, higher levels of fatigue and reduced adherence to disease-modifying therapy.[7-9] Studies evaluating the prevalence of depression in MS patients vary in the methods used to identify depression. Some use formal diagnostic interviews, others diagnoses abstracted from administrative databases, and still others screening questionnaires or a combination of methods. Based on diagnoses conferred by interviews or obtained from data sources other than questionnaires, the prevalence of depression ranges from 3.80% to 68.4%.[10] When screening questionnaires were used to identify depression, the prevalence ranged from 6.94% to 70.1%.[10] The estimated prevalence of depression using a mixture of methods ranged from 4.98% to 58.9%, and the summary estimate was 23.7% (95% CI: 17.4%-30.0%).[10] Only a few previous studies analyzed the link between the presence of depression and patient age, clinical course of MS, disease duration, and degree of disability.[11-13]. The presence of depression was found to be significantly associated with older age,[11] but there were no correlations with disease duration or disability as measured by EDSS.[12] The SPMS course was found to be the most common course of disease in depressed MS patients,[13] while disease duration and the clinical course of MS were unrelated to major depressive episodes.[14] In some studies, depression was more common in women,[15,16] in others in men,[17] or the prevalence rate was similar in both sexes.[7,18] Depression is recognized to affect the MS population more often than the general population.[19] Patients suffering from other chronic neurological diseases also have a high prevalence of depression. The prevalence rate in patients with Alzheimer's disease is up to 50%, Parkinson's disease 35%, epilepsy 30%-35%, and myasthenia gravis 26%.[20-23] Depression is frequently underdiagnosed and undertreated in MS patients, with reported rates of missed diagnosis of 23-30%,[24,25] and inadequate treatment between 20%-36% of those reporting depression.[24,26]

In studies using screening questionnaires aiming at detecting possible depression, a variety of instruments are employed.[27-31] In our study, we used the Patient Health Questionnaire-nine (PHQ-9) as a measuring instrument.[29] In recent years, the PHQ-9 has been widely used to measure depression in MS patients,[32-37] as well as in patients with other chronic neurological disorders.[38]

Due to a wide range in the prevalence of depression observed in previous studies and the high rates of missed diagnosis, the aim of the study was to determine the prevalence of depression in MS patients and to analyze the association between depression and patient sex, age, clinical course of MS, disease duration, degree of disability, and use of antidepressants.

Patients and Methods

The study included 102 patients with MS that underwent inpatient rehabilitation at Lipik Special Hospital for Medical Rehabilitation in the period from May 15, 2015 to September 15, 2015. Participating in the study were patients older than 18 and diagnosed with MS according to the revised McDonald criteria.[39] The exclusion criterion was serious cognitive impairment, corticosteroid treatment, or any other medical complication in the previous three months. Data on patient age, sex, degree of disability, clinical course of MS, antidepressant use, and time elapsed from MS diagnosis were collected. The diagnosis of depressive syndrome was made by use of the PHQ-9 questionnaire.[29] The PHQ-9 is a multiple-choice self-report inventory screening tool for depression. Its nine items pertain to the DSM IV[40] criteria for major depressive disorder: (1) Anhedonia, (2) Depressed mood, (3) Trouble sleeping, (4) Feeling tired, (5) Change in appetite, (6) Guilt, self-blame or worthlessness, (7) Trouble concentrating, (8) Feeling slowed down or restless, and (9) Thoughts of being better off dead or hurting oneself. Each item is rated on a 4-point scale from 0 to 3 (0-Never; 1-Several days; 2-More than half the days; and 3-Nearly every day). Major depressive syndrome is diagnosed if 5 or more of the 9 depressive symptom criteria have been present at least "more than half the days" in the past 2 weeks, and 1 of the symptoms is depressed mood or anhedonia. Other depressive syndrome is diagnosed if 2, 3, or 4 depressive symptoms have been present at least "more than half the days" in the past 2 weeks, and 1 of the symptoms is depressed mood or

anhedonia. One of the 9 symptom criteria ("thoughts that you would be better off dead or of hurting yourself in some way") counts if present at all, regardless of duration. Additionally, the PHQ-9 has established construct validity as a measure of depression severity (scores of 5, 10, 15, 20 represent cutpoints for mild, moderate, moderately severe and severe depression, respectively), making it useful for serial monitoring of depressive symptom burden and depression treatment outcome[41]. As a screening instrument, PHQ-9 provides diagnosis of major depressive syndrome and other depressive syndrome. The diagnosis of major depressive disorder and other depressive disorder requires structured psychiatric interviews to confirm the diagnoses of depressive syndrome in the screening test.

Study patients were divided into two groups, according to the presence or absence of the depressive syndrome. The group with present depressive syndrome included those with major as well as other depressive syndromes. The degree of disability for all study subjects was based on the Expanded Disability Status Scale (EDSS),[42] and assessment of cognitive status was performed using the Mini Mental Status Exam (MMSE).[43] The study was approved by the Hospital Ethics Committee and patients were required to provide written consent for their participation. Statistical analysis was performed using the SOFA Stats. Comparison of the variables was conducted using the Student's t-test and Pearson's correlation test.

Results

The study included 102 patients, 77 (75.5%) female and 25 (24.5%) male, mean age 51.4 years, age range 25-80 years. The mean time elapsed from MS diagnosis was 14.7 years (range, 6 months to 62 years). The relapsing-remitting course of the disease (RRMS) was experienced by 47 (46.1%), secondary progressive MS (SPMS) by 51 (50.0%), primary progressive (PPMS) by 3 (2.9%) and benign by 1 (1.0%) patient. The mean EDSS was 5.3, range 1.5 to 9. Out of 102 study patients, 31 (30.4%) screened positive for depressive syndrome, with the mean PHQ-9 score of 14.1 (SD 4.9). Of these 31 patients, 10 (32.3%) were taking antidepressants. Out of 31 patients screened positive for depressive syndrome, 18 (58.1%) had major and 13 (41.9%) other depressive syndrome. Patient characteristics according to the presence/ absence of depressive syndrome are shown in Table 1. In the group of patients with depressive syndrome, there was a statistically significantly higher proportion of patients with higher level of disability compared with the group of patients without depressive syndrome (P = 0.028). There were no statistically significant between-group differences according to sex (P = 0.429), age (P = 0.652), disease duration (P = 0.549) and disease course (P = 0.326). Due to small number of patients that suffered from PPMS and benign MS course, only patients with RRMS and SPMS were included in the analysis of the relationship of depression and MS course.

Table 1 Characteristics of patients screened positive and negative for depressive syndrome
Tablica 1. Karakteristike pacijenata s pozitivnim i negativnim ishodom na sindrom depresije

Characteristics *Karakteristike*	Screened positive for depression *Pozitivni na depresiju*	Screened negative for depression *Negativni na depresiju*
n (%)	31 (30.4)	71 (69.6)
Age (yrs), $\overline{X} \pm$ SD /*Starost*	52.2 ± 9.78	51.0 ± 12.56
Female, n (%) / *Žensko*	25 (80.7)	52 (73.2)
Male, n (%) /*Muško*	6 (19.3)	19 (26.8)
EDSS, $\overline{X} \pm$ SD	5.9 ± 1.92	4.9 ± 1.83
MS course, n (%)		
RRMS	12 (38.7)	35 (49.3)
SPMS	17 (54.8)	34 (47.9)
PPMS	2 (6.5)	1 (1.4)
Bening MS	0 (0.0)	1 (1.4)
Time elapsed from MS diagnosis (yrs), $\overline{X} \pm$ SD /*vrijeme od dijagnoze MS (god.)*	13.7 ± 8.50	15.1 ± 11.90

EDSS = Expanded Disability Status Scale; MS = multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis; PPMS = primary progressive multiple sclerosis; Bening MS = benign multiple sclerosis

Discussion

In our study, the prevalence of depressive syndrome in MS patients was 30.4%. The prevalence of depression in patients with MS varied significantly in published studies. Heterogeneous results in various literature reports could be due to differences in the methods of data collection, small sample size, study design, and differences in the socioeconomic or cultural context.[10,12] The summary estimate of depression prevalence in MS patients is 23.7%,[10] which is comparable to our results.

A limitation of the study was the fact that using the PHQ-9 or any other questionnaire does not set a definitive diagnosis of depression, but provides screening instead. Therefore, positive patients require further psychiatric assessment.

The proportion of patients screened positive for depression who reported ongoing use of antidepressants was low (32.3%). Such findings are in concordance with the results reported elsewhere.[24,26]

We found no significant between-group sex difference. In the studies by Gottberg et al.[7] and Chwastiak et al.,[18] there were no differences in the prevalence of depression between men and women either, whereas Hakim et al.[17] reported a higher prevalence in men. In two studies by Patten et al., depression was more common in women.[15,16] As other factors that may influence sex difference in the prevalence of depression were not analyzed in these studies, the reasons for different findings remain unknown.

In our study, patients with depressive syndrome had a higher level of disability as measured by EDSS score compared with patients without depression, whereas we found no association of the presence of depressive syndrome with age, disease duration and disease course. Positive correlation between depression and higher disability level was also observed in the studies that analyzed depression prevalence in various chronic medical conditions, and could be the result of numerous effects of physical disability on various aspects of patient life, e.g., employment, self-care, social interaction, etc.[44,45] Opposite to the aforementioned findings, in a study by Dahl et al. there was no association between the prevalence of depression and level of disability in MS patients.[12] In their study, there was no difference in disease duration between depressed and non-depressed MS patients,[12] whereas Seyed Saadat et al. and Montel et al.[11,13] reported on older age and SPMS course as risk factors for developing depression. These diverse findings in the studies assessing the link between the presence of depression and disease-related or epidemiological parameters may be explained by different study designs (e.g., patient selection from administrative databases or community sample, usage of diagnostic questionnaires or formal diagnostic interviews), different sample size, and regional and cultural differences.[11-14] Unlike the aforementioned studies, in our study respondents were MS patients referred for inpatient rehabilitation, which could also have an impact on the results. The latter means that the analysis excluded some of those with short disease duration associated with low functional deficit, younger age, and relapsing-remitting course because these patients are rarely treated as inpatients.

Despite these limitations, the results of our study indicated the prevalence of depression to increase with the increasing degree of disability irrespective of age, sex or MS course.

Conclusions

In the present study, the prevalence of depression based on the PHQ-9 questionnaire in patients with MS was 30.4%. Considering the high prevalence of depression on the screening test and the fact that only one-third of depression positive patients were taking antidepressants, there is a need to actively look for depression symptoms in patients with MS.

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