COGNITIVE AND DEPRESSIVE DISORDERS IN MULTIPLE SCLEROSIS

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SUMMARY – Among other symptoms, multiple sclerosis can also produce symptoms of affective and cognitive disorders. The majority of patients have certain cognitive dysfunctions, and the most common affective disorder is reactive depression. The aim of the study was to determine the correlation of the Mini-Mental State (MMS) and Beck Depression Inventory (BDI) scale scores with the Expanded Disability Status Scale (EDSS) score in patients with multiple sclerosis treated at University Department of Neurology, Sarajevo University Clinical Center in Sarajevo. We evaluated 50 randomly selected patients with various types of multiple sclerosis using the MMS, BDI and EDSS instruments. The study included 33 women and 17 men (66% : 34%), mean age 40.74 years (SD 9.236). The mean value of EDSS score was 3.98, ranging from 1.0 to 8.5 in women and from 1.0 to 6.5 in men. BDI scale scores showed a mean value of 12.56. The mean MMS score in baseline sample was 26.88. Statistically significant positive correlation was found between age and EDSS score, and negative correlation between EDSS and MMS, as well as between BDI and MMS. Study results indicated older patients with multiple sclerosis to have a higher EDSS score with more pronounced cognitive disturbances. There was no statistically significant correlation between EDSS score and depression.

Key words: Multiple sclerosis, psychology; Depressive disorders – diagnosis; Cognitive disorders – diagnosis; Disability – evaluation

Introduction

Multiple sclerosis (MS) is a chronic inflammatory, noncontiguous, progressive, multifocal demyelinating and autoimmune disease of the central nervous system (white brain mass and spinal cord; CNS), which can manifest with various neurologic signs. MS can also produce symptoms of affective and cognitive disorders. Cognitive dysfunctions, which are usually irreversible, affect 40%-60% of patients[1]. The most common cognitive dysfunctions are those involving attention, memory, speed of information processing, visual spatial per-ception and learning. These dysfunctions are closely related to the number and location of CNS lesions[2].

In January 2002, the New York City Chapter of the National Multiple Sclerosis Society convened a panel of experts to review the issue of depressive affective disorders associated with MS. This Goldman Consensus Conference Study Group provides recommendations for improvement of diagnosis, screening, and clinical management for depressive disorders among patients suffering from MS. The prevalence of depressive disorders is between 27% and 75%, and according to Fisher *et al.*, it is present in 47% to 54% of MS patients[3,4]. Reactive depression is the most common affective disorder[5]. Depression and cognitive dysfunctions in MS patients have negative impact on their working ability, social relationships and quality of life.

The aim of this study was to determine the correlation of the Mini-Mental State (MMS) and Beck De-

pression Inventory (BDI) scale scores with the score of Expanded Disability Status Scale (EDSS) in MS patients treated at University Department of Neurology, Sarajevo University Clinical Center in Sarajevo.

Material and Methods

We evaluated 50 randomly selected patients with various types of MS. All patients had Poser criteria for definitive diagnostic categories of MS: consistent course (relapsing/remitting) with at least 2 bouts by at least 1 month apart; or slow, stepwise progressive course for at least 6 months, documented neurologic signs of lesions in more than one area (functional system) of the brain or spinal cord white matter, onset of symptoms at age between 10 and 50 years, and absence of another more likely neurologic explanation[6,7].

MMS is a current screening test used to evaluate a wide spectrum of cognitive functions. It contains 30 short questions, and each positive answer carries 1 point. A total score between 28 and 30 points is considered as normal, between 24 and 28 indicates mild cognitive impairment, and a score below 24 indicates diffuse cognitive impairments and requires additional diagnostic evaluation.

BDI contains 21 category attitudes related to depression and each one is assessed by the four-grade severity scale. A BDI score between 1 and 10 is interpreted as normal mood, between 11 and 16 as mild mood disorder, 17 to 20 as borderline depression, 21 to 30 as mild depression, 31 to 40 as severe depression, and a score above 40 as extremely pronounced depression.

EDSS is a unified scale for the assessment of functioning in MS patients, which includes exploration of impairment in several functional systems. Total score on EDSS scale can be between 0.0 (normal neurologic status) to up to 10.0 (lethal outcome due to MS).

Selected patients were clinically followed at the outpatient department for demyelinating disorders of the University Department of Neurology. The instruments used in the study were MMS, BDI and EDSS. Statistical significance of differences was determined by use of Student's t-test and correlation between study variables by Spearman correlation coefficient with the level of significance set at $P<0.05$.

Results

The study included 50 patients, 33 women and 17 men (66%: 34%), mean age 40.74 years (SD 9.236).
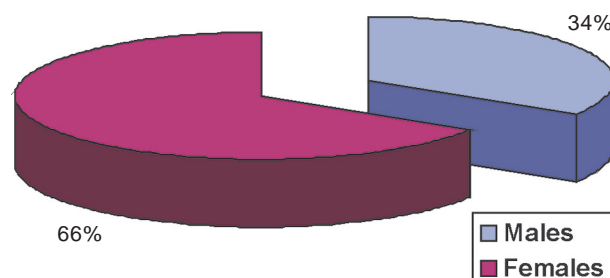

Fig. 1. Sex distribution of patients with multiple sclerosis.

There was a statistically significant sex difference in favor of female patients (P=0.0257), but there was no statistically significant age difference (t=0.0042; P=0.756) (Figs. 1 and 2).
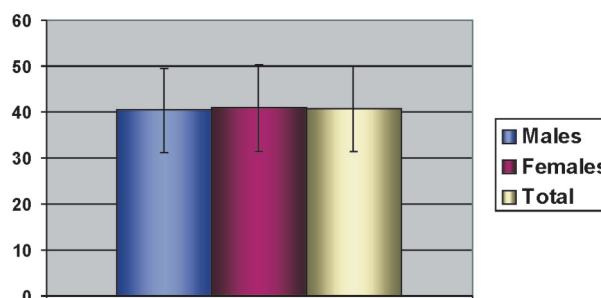

Fig. 2. Patient distribution according to sex and age groups.

The mean value of EDSS score was 3.98, with variations from 1.0 to 8.5 among women and from 1.0 to 6.5 among men. According to this, an average patient was fully mobile without any assistance, independent for more than 12 hours *per* day and able to walk without assistance or rest for approximately 500 meters. Statistical analysis by Student's t-test indicated that there was no significant sex difference in EDSS score (t=0.00012; P=0.876) (Fig. 3).
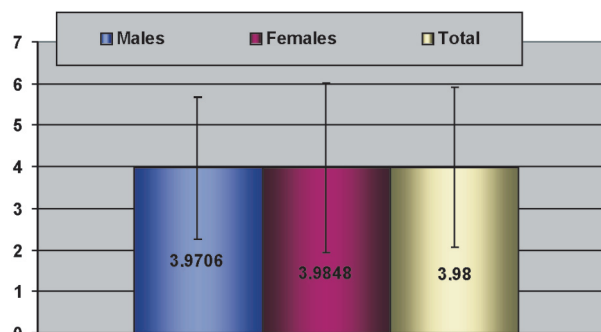

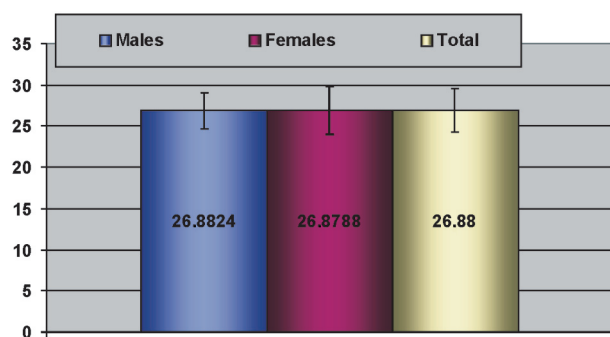
Fig. 3. Mean values of EDSS score.

Fig. 4. Mean values of BDI scale score.

BDI scale yielded a mean score of 12.56. The mean BDI score showed some sex differences with slightly higher values in male patients, however, the difference did not reach statistical significance (t=0.0526; P=0.286) (Fig. 4).
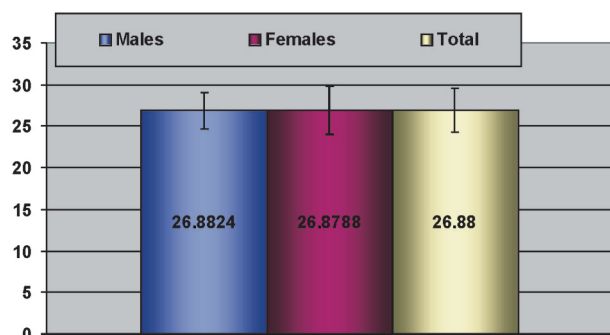

Fig. 5. Mean values of MMS scale score.

In our sample, the mean MMS score was 26.88, with nearly identical values in male and female patients: (26.8824 and 26.8788, respectively). According to this, Student's t-test indicated that there was no significant between-group difference (t=0.000154; P=0.982 (Fig. 5).

We correlated EDSS, BDI, MMS and age by use of Spearman matrix. EDSS score showed negative, statistically non-significant correlation with age (Spearman
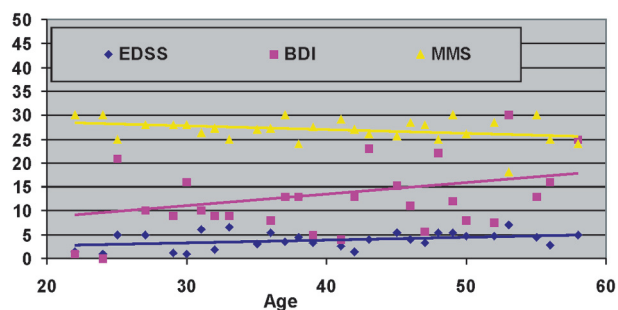

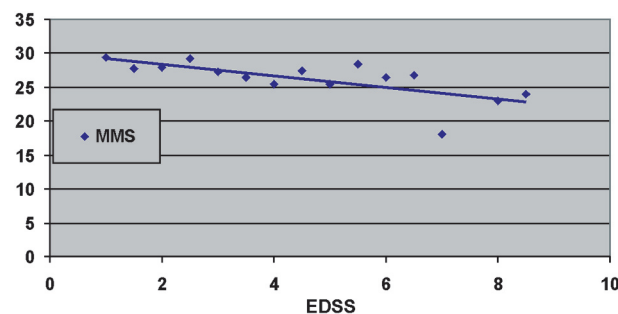*Fig. 6. Correlation between EDSS, BDI, MMS scores and age.*

Fig. 7. Correlation between EDSS and MMS.

rho=-0.186; P=0.156). BDI scale score yielded positive correlation with patient age (Spearman rho=0.653; P=0.0487). Correlation analysis of age and MMS score indicated that age had almost no influence on MMS score (Spearman rho=0.0084; P=0.726) (Fig. 6).

We also correlated EDSS with MMS and BDI with MMS. Both correlations yielded negative, statistically significant correlation coefficients (EDSS to MMS: rho=-0.725; P=0.0026; and BDI to MMS: rho=-0.589; P=0.0429) (Figs. 7 and 8).
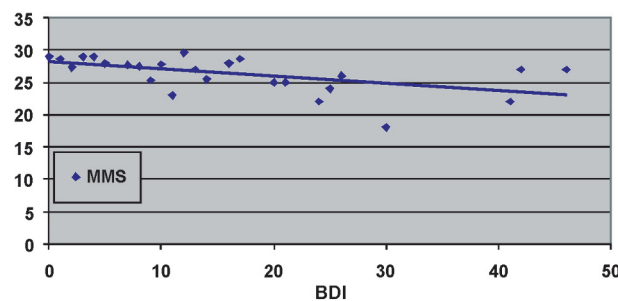
Fig. 8. Correlation between BDI and MMS.

Discussion

This study raised a question of relation between neurologic impairment in MS and mental disorders, among which this study was focused on the symptoms of cognitive and emotional deficits. Our study included 33 women and 17 men (66%:34%), mean age 40.74 years (SD 9.236), which is comparable to the study reported by Birnboim and Miller, who had 60% of female and 40% of male patients, mean age 39.06 years (SD 8.09)[8].

It is well known that cognitive dysfunction is a major cause of disability in patients with MS and it profoundly undermines the patient's quality of life[9]. Cognitive disorders are present in 13%-72% of patients with MS, and can be found in 43%-46% of cases on an average, rarely in the early stage of disease. MS involves

specific cognitive problems in the domain of attention, memory (short-term and long term), speed of information processing, abstract thinking, visuospatial perception and learning. Cognitive deficit does not correlate with physical disability, fatigue or depression, but there is a significant connection with cortical or subcortical lesion recorded on MRI. Cognition impairment need not be irreversible, often relapsing disease, and glucocorticoid therapy may lead to transient deterioration. MMS is a modern "screening" test for assessing the wide spectrum of cognitive functions. It contains 30 short questions and each accurate answer is 1 point. A total score of 28 to 30 points is considered to be normal, 24-28 indicates mild cognitive impairment, and score below 24 indicates diffuse cognitive damage and requires additional testing. The mean MMS score in a baseline sample was 26.88, which means that the average patient had mild cognitive problems and the variations in MMS score ranged from normal results to diffuse cognitive dysfunction. There was no statistically significant sex difference in terms of cognitive problems. We used MMS, but in our future studies we will have to use the Perceived Deficits Questionnaire of Multiple Sclerosis Quality of Life Inventory (PDQ), which accurately measures self-reported symptoms of psychological impairment[10].

Depression is the most common disorder that can be found in 27%-75% of MS patients, followed by euphoria in 25%, mainly in patients with progressed brain atrophy and with sparse cognitive and neurologic finding.

BDI is a measure for the general depressive symptoms, which contains 21 categories of attitudes, and each is estimated on four-grade scale representing the degree of disturbance severity. A BDI score 1-10 is considered as normal mood, 11-16 as mild mood disorder, 17-20 indicates borderline clinical depression, 21-30 moderate depression, 31-40 severe depression, and score over 40 is extremely pronounced depression. Our patients had a mean BDI score of 12.56, which indicates the existence of mild depression symptoms, without statistically significant sex differences. The Goldman Group expressed general agreement that some sort of scale-based assessment of depression in MS population would be helpful in screening of these depressive disorders. Our results of the mean BDI score were within the current gold standard for the diagnosis of depressive disorders in MS population (Goldman Consensus Group)[11].

EDSS is a unified scale for assessing disability in MS patients, which includes exploration of impairments in multiple functional systems. The total score on the EDSS scale ranges from 0.0 (normal neurologic status) to up to 10.0 (death due to MS). EDSS as an indicator of the extent of disablement showed a wide range, with a mean value of 3.98 and mean age 40.74, which explains the negative statistical correlation between MMS, BDI, MMS and EDSS in our material, with a remark that the goal of the study was to determine depressive and affective disorders in our sample of 100 patients, thus to provide projections for our future approach in the management of these patients with medication, psychotherapy and sociotherapy, tending to complete the multimodal approach to this category of patients.

Our results of EDSS with a mean EDSS of 3.98 in our patients are comparable to those reported by Werf *et al.* in 1998[12] and by Birnboim and Miller with EDSS of 4.37[8]. In our study, there was no statistically significant correlation between EDSS and BDI. This could be explained by the significant cognitive dysfunction in patients with higher EDSS score. We found a statistically significant positive correlation between age and EDSS score, whereas negative correlation was recorded between EDSS and MMS, and between BDI and MMS. Our results of negative correlation between EDSS and BDI are consistent with the results reported by Moller *et al.*, according to which the presence of depressive symptomatology did not correlate with the severity of neurologic disability[13].

The results of the present study explicitly indicated that mental disorders should be considered and psychiatric therapy administered during the treatment of MS, which is often neglected[14]. In 2008, Siepman *et al.* reported the results of their study designed as a study of mutual correlation of the level of disablement, depression and cognitive impairments in 101 patients with MS. They found that cognitive dysfunction was significantly more present among patients with depressive disorders in comparison to those free from depression on the depression scale, and that the level of disablement could progress in the very early stage after detection of the disease (in two years)[15].

Cognitive impairment in patients with MS further complicates diagnostic evaluation[16]. In our patient sample, Spearman test identified a statistically significant positive correlation between age and EDSS score (rho=0.287; $P<0.05$) and negative correlation between EDSS and MMS (rho=-0.442; $P<0.01$) as well as between BDI and MMS (rho=−0.382; $P<0.01$). In January 2009, Christodoulou *et al.* published the results of a longitudinal study performed in 38 patients with MS

and found that negative affect could be a predictor of cognitive impairment, especially in the area of vertebral and visuospatial functioning[17].

The etiology of depression in these patients is not well understood and has been varyingly attributed to emotional reaction to the diagnosis or disability associated with the neurologic condition, the anatomical and/or neurochemical outcomes of neurodegeneration, and the influence of other disease factors. Beyond the inherent burden depression places upon patients and caregivers, it increases cognitive and functional disability and, depending on MS, poorer treatment adherence and recovery, earlier institutionalization, and an increased risk of suicidal behavior[16].

Little is known about the perception of body image in women diagnosed with relapsing remitting MS (RRMS). There are some studies of correlation between body image and depression in women diagnosed with RRMS. Kindrat reports that there are important psychological aspects which clinicians might need to attend when working with women with RRMS[18]. Because of the high prevalence and implications for the quality of life and possibly disease progression, depression has been studied in MS. Yet, publications of theoretical work attempting to explain depression in a comprehensive way are scarce[19]. Our results of the moderately present depressive affect in our sample are comparable to the results reported by Beiske *et al*., demonstrating a significant statistical correlation between depression and MS, with a note that these authors found a relatively high score of anxiety of 19.3% among younger patients[20]. A number of studies suggest that depression in MS patients responds to antidepressant medication and occasionally to psychotherapeutic approaches[18].

Conclusions

Results of this study indicated that older patients with MS had a higher EDSS score with more pronounced cognitive disturbances. We found no statistically significant correlation between physical impairment and depression. Both cognitive and depressive disorders were equally present in both sexes. Cognitive dysfunctions were more pronounced in later stage of the disease. The frequency and severity of depressive symptoms did not correlate with physical impairment. Prompt detection and treatment (both neurologic and psychiatric) of cognitive and affective mental functions improve rehabilitation and quality of life in patients with multiple sclerosis.

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Sažetak

SPOZNAJNI I DEPRESIVNI POREMEĆAJI KOD MULTIPLE SKLEROZE

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Među drugim simptomima multipla skleroza može uzrokovati i simptome afektivnih i spoznajnih poremećaja. Većina bolesnika ima određene spoznajne disfunkcije, dok je najčešći afektivni poremećaj reaktivna depresija. Cilj studije bio je utvrditi korelaciju vrijednosti dobivenih pomoću ljestvica *Mini-Mental State* (MMS) i *Beck Depression Inventory* (BDI) s vrijednosti na ljestvici *Expanded Disability Status Scale* (EDSS) u bolesnika s multiplom sklerozom liječenih na Neurološkoj klinici Kliničkog bolničkog centra u Sarajevu. Procjena je obuhvatila 50 nasumce izabranih bolesnika s različitim tipovima multiple skleroze uz primjenu MMS, BDI i EDSS. Bilo je 33 žena i 17 muškaraca (66%:34%) srednje dobi od 40,74 (SD 9,236) godine. Srednja vrijednost EDSS bila je 3,98, u rasponu od 1,0 do 8,5 kod žena te od 1,0 do 6,5 kod muškaraca. Na ljestvici BDI srednja vrijednost je bila 12,56, dok je srednja vrijednost za MMS u ispitanom uzorku bila 26,88. Utvrđena je statistički značajna pozitivna korelacija između dobi i vrijednosti EDSS, dok je negativna korelacija utvrđena između EDSS i MMS te između BDI i MMS. Rezultati ovoga ispitivanja pokazali su da stariji bolesnici s multiplom sklerozom imaju višu vrijednost EDSS uz jače izražene kognitivne smetnje. Nije bilo statistički značajne korelacije između vrijednosti EDSS i depresije.

Ključne riječi: *Multipla skleroza, psihologija; Depresivni poremećaji – dijagnostika; Spoznajni poremećaji – dijagnostika; Invalidnost – procjena*