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Does anxiety, depression, and sleep levels affect the quality of life in patients diagnosed with multiple sclerosis?

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Abstract. – OBJECTIVE: Multiple sclerosis (MS) is a chronic disease characterized by relapses and remissions, causing physical disability and affecting individuals psychosocially. In this study, we aimed to assess anxiety and depression levels, sleep, and quality of life in MS patients.

PATIENTS AND METHODS: The study included 66 participants, 30 healthy controls, and 36 patients diagnosed with MS. All participants were administered the Sociodemographic and Clinical Data Form, Multiple Sclerosis Quality of Life Instrument (MSQOL-54), Pittsburgh Sleep Quality Index (PSQI), Expanded Disability Status Scale (EDSS), Beck Depression Inventory (BDI), and Beck Anxiety Inventory (BAI).

RESULTS: The PSQI, EDSS, BDI, and BAI scores of MS patients were found to be significantly higher, while the MSQOL-54 score was considerably lower than the healthy control group ($p<0.001$). In the patient group, there was a positive correlation between PSQI score and BDI (r=0.599, $p<0.001$) and BAI (r=0.633, $p<0.001$), while there was a negative correlation between PSQI and MSQOL-54 (r=0.705, $p<0.001$) and the duration of MS diagnosis (r=-0.364, $p=0.029$). A positive correlation was found between the EDSS score and BDI (r=0.401, $p=0.015$) and the number of hospitalizations (r=0.566, $p<0.001$). There was a significant negative correlation observed between MSQOL-54 and BDI (r=-0.807, $p<0.001$) as well as BAI (r=-0.834, $p<0.001$). There is a significant positive relationship between BDI and BAI (r=0.828, $p<0.001$).

CONCLUSIONS: Our research revealed that individuals diagnosed with multiple sclerosis exhibit elevated levels of anxiety and depression symptoms when compared to a healthy control group. Additionally, they tend to experience lower sleep quality and overall quality of life. The provision of necessary psychiatric interventions to these patients following their diagnosis can enable them to accept the disease and actively participate in treatment, thereby positively impacting their quality of life.

Key Words:
Multiple sclerosis, Anxiety, Depression, Sleep, Quality of life.

Introduction

Multiple sclerosis (MS) is a disease of the central nervous system characterized by the development of plaques caused by inflammation. It primarily impacts young adults and can lead to disability by harming the myelin sheath surrounding neurons[1]. Globally, this condition affects 2.3 million individuals and is observed in women twice as frequently as in men[2]. MS has four clinical forms. The most common type, constituting approximately 85% of the cases, is the relapsing-remitting type. It is characterized by distinct attacks that develop over days or weeks and are followed by a period without seizures. Between attacks, the patient's neurological function does not worsen. Relapses and gradual neurological deterioration unrelated to acute attacks characterize the secondary progressive type. A continuous functional decline from the onset of the disease without relapses describes the primary progressive type. The progressive relapsing type is characterized by a steady functional decrease from the beginning of the disease, with acute attacks occurring later and stacking on top of each other[3].

In the clinic, MS, fatigue, walking difficulties, muscle weakness and spasticity, urinary tract disorders, and psychiatric disorders can be observed[4].

Recent studies[5] indicate that individuals with multiple sclerosis (MS) are at risk for sleep disorders, and these disorders contribute to fatigue and other chronic symptoms of MS. Sleep disorders in

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MS patients are often underrecognized and untreated. It is known that over time, depression is more common in multiple sclerosis (MS) disease, but anxiety, bipolar disorder, panic disorder, and suicide attempts also accompany it[6-8]. Research[9] suggests that in addition to the secondary emotional reactions that develop in response to the disabling nature of the disease itself, structural central nervous system damage in MS can also contribute to the development of psychiatric symptoms. It is known that fatigue, along with the disability, depression, and anxiety symptoms observed in the clinical presentation of MS, also reduces the quality of life[10]. Existing studies have not comprehensively evaluated disability status, anxiety, depression, sleep patterns, and quality of life in MS patients.

Patients and Methods

Local ethics committee approval was obtained in 2021 with the reference number 28.09.2021-3968. This study was conducted according to the ethical standards outlined in the revision of the Helsinki Declaration of 1983 and its later amendments. This study calculated the sample size using G*Power version 3.1.9.2 software. The sample size calculation was based on the survey by Kaya et al[11] (Relationship between quality of life, depression, and anxiety in multiple sclerosis). The patient group included 40 individuals who visited the Fethi Sekin City Hospital Neurology Clinic between October 2022 and August 2023 and met the study criteria for a diagnosis of multiple sclerosis. The healthy control group consisted of 35 healthy individuals who visited Fethi Sekin City Hospital annually for regular check-ups and had no medical issues. Participants, who were initially evaluated by a neurologist, later underwent approximately 30-minute structured interviews conducted by a psychiatrist according to DSM-5 criteria. After obtaining signed written consent from all participants, the Sociodemographic and Clinical Data Form, Multiple Sclerosis Quality of Life Instrument (MSQOL-54), Pittsburgh Sleep Quality Index (PSQI), Expanded Disability Status Scale (EDSS), Beck Depression Inventory (BDI), and Beck Anxiety Inventory (BAI) were completed. Our sample group comprised these subtypes because relapsing-remitting and primary progressive types are more commonly seen in MS than other subtypes. The study did not include unstable MS patients with any relapse events in the past 30 days before the survey, individuals unable to answer questions, illiterate participants, those with hearing and speech impairments, individuals with a history of alcohol and substance use in the last six months, those under 18 years of age, and patients with neurological diseases other than MS. Four patients with MS were excluded from the study because they left scale questions unanswered. Five individuals from the healthy group withdrew from participating in the study.

The Scales Used in the Study

Sociodemographic and clinical data form

The Sociodemographic and Clinical Data Form is a semi-structured questionnaire prepared by the researchers, which includes sociodemographic information about the participants such as age, gender, place of residence, economic status, as well as clinical data like disease duration and the presence of other comorbid conditions.

Expanded Disability Status Scale (EDSS)

The most commonly used and well-defined scale for assessing the disability status of MS patients is the Expanded Disability Status Scale (EDSS). The EDSS is an ordinal scale; patients are evaluated on a scale ranging from 0 to 10 points. A score of 0 on the EDSS indicates normal health, while a score of 10 indicates death due to MS, which is rare. In the EDSS, scores increase as multiple sclerosis (MS) worsens. An EDSS score of 2.0 indicates minimal disability, 4.0 indicates moderate disability, but the patient can walk unassisted, 6.0 indicates the need for assistance with walking aids, and 8.0 indicates wheelchair dependence[12]. A Turkish validity and reliability study has been conducted[13]. This study calculated the Cronbach's alpha reliability coefficient for the scale as 0.89.

The Pittsburgh Sleep Quality Index (PSQI)

The Pittsburgh Sleep Quality Index (PSQI) consists of questions about assessing sleep quality over the past month[14]. A total PSQI score of ≤ 5 indicates "good sleep quality", while >5 indicates "poor sleep quality". A Turkish validation and reliability study has been conducted[15]. In this study, the Cronbach's alpha value of the scale was found to be 0.77.

Multiple Sclerosis Quality of Life-54 (MSQOL-54) is one of the most critical scales among this measures[16]. It is a scale created by adding 18 MS-specific items to the SF-36, which contains 36 questions about the overall quality of life. A high scale score indicates a high quality of life.

Turkish validity and reliability studies have been conducted[17]. This study calculated the Cronbach's alpha coefficient for the total scale as α=0.95.

Beck Depression Inventory (BDI)

It was developed to measure the risk of depression, the level of depressive symptoms, and the severity of depressive symptoms in adults[18]. The scale score increases as depressive symptoms increase. Validity and reliability studies[19] have been conducted. In this study, the Cronbach's alpha reliability coefficient for the scale was calculated as 0.74 for the entire scale.

Beck Anxiety Inventory (BAI)

The Beck Anxiety Inventory (BAI), developed by Beck and colleagues in 1988, is a self-assessment scale used to determine the frequency of anxiety symptoms experienced by individuals[20,21]. The scale score increases as anxiety symptoms increase. It has been validated and tested for Reliability in Turkey. In this study, the Cronbach's alpha reliability coefficient for the scale was calculated as 0.86 for the entire scale.

Statistical Analysis

The analyses were conducted using the SPSS 22 software package (Statistical Package for Social Sciences; IBM Corp., Armonk, NY, USA). In the study, descriptive data for categorical variables were presented as n (%); continuous variables were presented as mean ± standard deviation (Mean ± SD). The Chi-square analysis (Pearson Chi-square) was applied to compare categorical variables between groups. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. In comparing binary groups, the Student's *t*-test was used for variables showing normal distribution, and the Mann-Whitney U-test was used for variables not showing normal distribution. Spearman correlation test was used to examine the relationship between continuous variables. The level of statistical significance was set at $p<0.05$.

Results

The study included 66 participants, consisting of 36 patients and 30 controls. In the patient group, 72.2% were female; in the control group, 56.7% were female, and no significant difference was observed ($p=0.187$). The mean age of the patients was 34.3±9.3 years, while the mean age of the control group was 33.3±6.5 years, and no significant difference was observed between them ($p=0.630$). The presence of additional psychiatric disorders ($p<0.001$) and a history of psychiatric treatment ($p=0.004$) were significantly higher in the patient group compared to the control group (Table I).

Of the patients, 86.1% had the Relapsing-Remitting type of MS, while 13.9% had the Primary Progressive type. 69.4% of the patients had an annual attack rate of 1, while 30.6% had two or more attacks. 36.1% of the patients had their most recent attack within 0-6 months, 11.1% had it within 6-12 months, and 52.8% had it more than 12 months ago. 58.3% of the patients have been hospitalized 1-3 times due to MS, while 41.7% have been hospitalized more than three times. The average time elapsed since the diagnosis of multiple sclerosis (MS) stands at 4.2±5.8 years (Table II).

The patient group had significantly higher PSQI, EDSS, BDI, and BAI scores compared to the control group, while the MSQOL-54 score was significantly lower ($p<0.001$) (Table III).

A positive correlation was observed between PSQI score and BDI and BAI in the patient group. In contrast, a negative correlation was observed between PSQI and MSQOL-54 and the duration of MS diagnosis. A positive significant relationship was found between EDSS score and BDI and the number of hospital admissions. There was a negative significant correlation between MSOOL-54, BDI, and BAI. There is a positive, meaningful relationship between BDI and BAI (Table IV).

Discussion

We found that anxiety and depression symptoms were higher in multiple sclerosis patients compared to the healthy control group, and the quality of sleep and life were worse. As multiple sclerosis progresses chronically, the individuals' sleep quality deteriorates; those with poor sleep quality experience increased symptoms of depression and anxiety, ultimately leading to a decreased quality of life. We observed that as disability rates increased in individuals with MS, hospitalization duration increased, and these patients exhibited higher depressive symptoms.

Throughout their lifetime, depression accompanies multiple sclerosis patients at a rate of 30.5%, while anxiety is present at a rate of 22.1%[22]. Depression in MS patients can be attributed to various factors. It may arise from biological factors such as the involvement of plaques[22,23]. However, it can

Table I. Group comparison of sociodemographic and disease-related characteristics.

		Patients (n=36)		Control (n=30)		
		N	%	N	%	p*
Gender	Female	26	72.2	17	56.7	0.187
	Male	10	27.8	13	43.3	
Age, Mean±SD		34.3±9.3		33.3±6.5		0.630**
Marital status	Single	14	38.9	12	40.0	0.927
	Married	22	61.1	18	60.0	
Education status	Elementary school	7	19.4	12	40.0	0.066
	High school and above	29	80.6	18	60.0	
Place of residence	Rural	3	8.3	5	16.7	0.452
	Urban	33	91.7	25	83.3	
Economic status	Low	8	22.2	11	36.7	0.197
	Medium	28	77.8	19	63.3	
Employment status	Yes	21	58.3	19	63.3	0.679
	No	15	41,7	11	36.7	
Comorbid psychiatric disorder	Yes	12	33.3	0	.0	**<0.001**
	No	24	66.7	30	100.0	
Psychiatric treatment history	Yes	13	36.1	2	6.7	**0.004**
	No	23	63.9	28	93.3	
Smoking	Yes	15	41.7	7	23.3	0.116
	No	21	58.3	23	76.7	
Alcohol-substance abuse	Yes	1	2.8	1	3.3	0.896
	No	35	97.2	29	96.7	

*Chi-square analysis, **Student's *t*-test were applied.

Table II. Patients' disease-related characteristics.

		Number	%
Type of MS	Relapsing-remitting	31	86.1
	Primary progressive	5	13.9
Annual attack rate	1	25	69.4
	≥2	11	30.6
Last attack	0-6 month	13	36.1
	6-12 month	4	11.1
	>12 month	19	52.8
Hospitalizations due to MS	1-3 times	21	58.3
	>3	15	41.7
Duration of MS diagnosis, Mean±SD		4.2±5.8	

Table III. Comparison of scale scores between groups.

	Patient Mean±SD	Control Mean±SD	p*
Pittsburgh Sleep Quality Index	6.0±5.2	1.1±1.4	**<0.001**
Expanded Disability Status Scale	2.4±.9	.0±.0	**<0.001**
Multiple Sclerosis Quality of Life Instrument -54	66.1±12.8	83.9±13.3	**<0.001**
Beck Depression Inventory	12.7±10.3	5.1±5.3	**<0.001**
Beck Anxiety Inventory	15.0±12.3	4.7±5.3	**<0.001**

*The Mann-Whitney U test was applied.

Table IV. In the patient group, the correlation of scale scores.

		Pittsburgh Sleep Quality Index	Expanded Disability Status Scale	Multiple Sclerosis Quality of Life Instrument -54	Beck Depression Inventory	Beck Anxiety Inventory
Expanded Disability Status Scale	r	.178				
	p	.298				
Multiple Sclerosis Quality of Life Instrument -54	r	**-.705**	-.241			
	p	**.000**	.156			
Beck Depression Inventory	r	**.599**	**.401**	**-.807**		
	p	**.000**	**.015**	**.000**		
Beck Anxiety Inventory	r	**.633**	.250	**-.834**	**.828**	
	p	**.000**	.142	**.000**	**.000**	
Age	r	.084	.183	-.128	.181	.120
	p	.628	.286	.457	.290	.486
Duration of MS diagnosis	r	**-.364**	.094	.210	-.085	-.241
	p	**.029**	.585	.218	.623	.157
Annual attack frequency	r	.190	.177	-.003	-.058	-.047
	p	.268	.301	.987	.736	.788
The most recent attack	r	-.226	-.021	.116	-.079	-.174
	p	.186	.904	.502	.647	.309
Number of hospitalizations	r	.185	**.566**	-.114	.255	.111
	p	.279	**.000**	.507	.133	.518

also be associated with aspects of the symptoms of this neurological condition, including disability, frequent medical interventions, uncertainty, and a perceived absence of social support[24-26]. It is known that anxiety in MS patients can result from plaques in regions like the amygdala and cerebral cortex and psychosocial factors[27]. As expected, we also found that our patient group's BDI and BAI scale scores were higher than those of the healthy control group. Individuals with mental health disorders typically exhibit poorer sleep quality than the general populace[28]. It is known that sleep disorders, including insomnia, restless legs syndrome, sleep-related movement disorders, and sleep-related breathing disorders, frequently coexist in multiple sclerosis patients[29]. Mosarrezaii et al[30] reported that sleep disorders are present in approximately 70% of MS patients. Zhang et al[31] administered the Pittsburgh Sleep Quality Index (PSQI) to 221 MS-diagnosed patients, and among the 142 patients who correctly completed the scales, three out of four experienced sleep disorders.

Similarly, in a study conducted on MS patients, we observed excessive daytime sleepiness and other sleep-related issues in these patients. We believe this situation may be attributed to sleep problems secondary to anxiety and depression that occur in patients alongside the symptoms of multiple sclerosis, such as spasticity, pain, and fatigue. We believe that sleep disturbances, possibly due to anxiety and depression, may affect the immune system[32], potentially worsening MS symptoms and exacerbating sleep problems.

It is known that individuals with sleep disorders have a lower quality of life[33,34]. MS patients with insufficient sleep often complain of excessive daytime sleepiness, concentration difficulties, memory and learning deficits, mood changes, and fatigue[33,35]. Furthermore, as in our findings, sleep problems tend to increase with the duration of MS disease[36]. Another study[37] involving 152 MS patients found that sleep disorders are common in MS patients, and the presence of sleep disorders (insomnia and daytime sleepiness) significantly affects the quality of life of these patients. We also observed that the patients had poor sleep and low quality of life. Sehanovic et al[38] reported that as disability

increased in MS patients, depressive symptoms increased, and the patient's quality of life deteriorated. It is expected that various factors such as fear, anxiety, loneliness, hopelessness, depression, and sleep problems can negatively affect the quality of life in chronic illnesses[39]. Yeni et al[40] reported in their study with 89 MS patients and 262 healthy control subjects that anxiety, depression, and sleep problems were determinants of physical and mental quality of life. Our data support Yeni et al[40] in this regard.

Our patient group consisted of 72.2% female participants with a mean age of 34.3±9.3 years. It is known that MS is more commonly observed in young adults and females[41]. In our sample group, we observed that MS patients had a history of psychiatric medication use, and some were currently using them. This finding supports the data Marrie et al[42] reported in 2022.

The cross-sectional nature of our study and the use of psychiatric medication by some patients in our sample are among the limitations of our research.

Conclusions

We observed high levels of anxiety and depression, poor sleep, and quality of life in patients with chronic and disabling multiple sclerosis. The symptoms such as fatigue, weakness, and pain observed in the MS clinic can overshadow psychiatric disorders, and unless the patient explicitly mentions them, they may go unnoticed by neurologists. However, anxiety, depression, and sleep disorders also significantly affect patients' quality of life. Our study proves to be vital in increasing awareness among patients and physicians of multiple sclerosis and providing psychosocial support for the detected mental health issues. Following the diagnosis of multiple sclerosis, psychiatric pharmacological and behavioral interventions have the potential to facilitate the formation of cognitive schemas that promote patients' self-awareness regarding their treatment-related strengths. Consequently, this process may contribute to developing a constructive illness perception model, enhancing patients' ability to engage in treatment and adhere to it effectively and actively.

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Conflict of Interest
The authors declare no conflict of interest.

Ethics Approval
Approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Firat University (Approval No.: 28.09.2021-3968).

Informed Consent
Informed consent was taken from all cases and the control group participants before inclusion into the study.

Authors' Contributions
All authors contributed to the planning, designing, literature survey, data collection, and active intellectual support.

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Availability of Data and Materials
All data for this study is presented in this paper.

References

1) Ghasemi N, Razavi S, Nikzad E. Multiple Sclerosis: Pathogenesis, Symptoms, Diagnoses and Cell-Based Therapy. Cell J 2017; 19: 1-10.
2) Browne P, Chandraratna D, Angood C, Tremlett H., Baker C, Taylor BV, Thompson AJ. Atlas of Multiple Sclerosis 2013: a growing global problem with widespread inequity. Neurology 2014; 83: 1022-1024.
3) Loma I, Heyman R. Multiple Sclerosis: Pathogenesis and Treatment. Curr Neuropharmacol 2011; 9: 409-416.
4) Parker LS, Topcu G, De Boos D, das Nair R. The notion of "invisibility" in people's experiences of the symptoms of multiple sclerosis: a systematic meta-synthesis. Disabil Rehabil 2021; 43: 3276-3290.
5) Braley TJ, Boudreau EA. Sleep disorders in multiple sclerosis. Curr Neurol Neurosci Rep 2016; 16: 1-8.
6) Silveira C, Guedes R, Maia D, Curral R, Coelho R. Neuropsychiatric symptoms of multiple sclerosis: state of the art. Psychiatry Investig 2019; 16: 877-882.

7) Boeschoten RE, Braamse AMJ, Beekman ATF, Cuijpers P, van Oppen P, Dekker J, Uitdehaag BMJ. Prevalence of depression and anxiety in Multiple Sclerosis: A systematic review and meta-analysis. J Neurol Sci 2017; 372: 331-341.

8) Marrie RA, Reingold S, Cohen J, Stuve O, Trojano M, Sorensen PS, Cutter G, Reider N. The incidence and prevalence of psychiatric disorders in multiple sclerosis: a systematic review. Mult Scler 2015; 21: 305-317.

9) Menculini G, Mancini A, Gaetani L, Bellingacci L, Tortorella A, Parnetti L, Di Filippo M. Psychiatric symptoms in multiple sclerosis: a biological perspective on synaptic and network dysfunction. J Neurol Neurosurg Psychiatry 2023; 94: 389-395.

10) Berrigan LI, Fisk JD, Patten SB, Tremlett H, Wolfson C, Warren S, Fiest KM, McKay KA, Marrie RA. CIHR Team in the Epidemiology and Impact of Comorbidity on Multiple Sclerosis (ECoMS). Health-related quality of life in multiple sclerosis: Direct and indirect effects of comorbidity. Neurology 2016; 12: 1417-1424.

11) Kaya N, Akpinar Z, Çilli AS. Relationship between depression and anxiety and quality of life in multiple sclerosis. Anadolu Psikiyatri Derg 2003; 4: 220-225.

12) Gulick EE. Model confirmation of the MS-Related Symptom Checklist. J Nurs Res 1989; 38: 147-185.

13) Polat C, Tülek Z, Kürtüncü M, Eraksoy M. Validity and Reliability of the Turkish Version of the Multiple Sclerosis-Related Symptom Checklist. Noro Psikyatr Ars 2017; 54: 131-138.

14) Buysse DJ, Reynolds CF, Monk TH. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989; 28: 193-213.

15) Ağargün MY, Kara H, Anlar O. Pittsburgh Uyku Kalitesi İndeksi'nin Geçerliği ve Güvenirliği. Turk Psikiyatri Derg 1996; 7: 107-110.

16) Vickrey B, Hays RD, Harooni R, Myers LW, Ellison GW. A health-related quality of life measure for multiple sclerosis. Qual Life Res 1995; 4: 187-206.

17) İdiman E, Uzunel F, Özakbaş S, Yozbatıran N, Oğuz M, Çallıoğlu B, Gökçe N, Bahar Z. Cross-cultural adaptation and validation of multiple sclerosis quality of life questionnaire (MSQOL-54) in a Turkish multiple sclerosis sample. J Neurol Sci 2006; 240: 77-80.

18) Beck AT. An inventory for measuring depression. Arch Gen Psychiatr 1961; 4: 561-571.

19) Hisli N. Beck Depresyon Envanteri'nin Üniversite Öğrencileri için Geçerliği, Güvenirliği. Psikoloji Dergisi 1989; 6: 3-13.

20) Beck AT, Epstein N, Brown G, Steer RA. "An inventory for measuring clinical anxiety: psychometric properties". J Consult Clin Psychol 1988; 56: 893-897.

21) Ulusoy M, Sahin NH, Erkmen H. Turkish version of the Beck anxiety inventory: psychometric Properties. J Cogn Psychother Int 1998; 12: 163-172.

22) Fleming WE, Pollak CP. Sleep Disorders in Multiple Sclerosis. Semin Neurol 2005; 25: 64-68.

23) Peres DS, Rodrigues P, Viero FT, Frare JM, Kudsi SQ, Meira GM, Trevisan G. Prevalence of depression and anxiety in the different clinical forms of multiple sclerosis and associations with disability: A systematic review and meta-analysis. Brain Behav Immun Health 2022; 6: 1-16.

24) Berg D, Supprian T, Thomae J, Warmuth-Metz M, Horowski A, Zeiler B, Magnus T, Rieckmann P, Becker G. Pattern in patients with multiple sclerosis and depression. Mult Scler 2000; 6: 156-162.

25) Pujol J, Bello J, Deus J, Cardoner, Ns, Martí-Vilalta, J, Capdevila A. Beck Depression Inventory factors related to demyelinating lesions of the left arcuate fasciculus region. Psychiatry Res 2000; 99: 151-159.

26) Shnek ZM, Foley FW, LaRocca NG, Smith CR, Halper J. Psychological predictors of depression in multiple sclerosis. Neurorehabil Neural Repair 1995; 9: 15-23.

27) Siegert R, Abernethy D. Depression in multiple sclerosis: a review. J Neurol Neurosurg Psychiatry 2005; 76: 469-475.

28) Bystritsky A, Khalsa SS, Cameron ME, Schiffman J. Current diagnosis and treatment of anxiety disorders. P T 2013; 38: 30-38.

29) Lederman O, Ward PB, Firth J, Maloney C, Carney R, Vancampfort D, Stubbs B, Rosenbaum S. Does exercise improve sleep quality in individuals with mental illness? A systematic review and meta-analysis. J Psychiatr Res 2019; 109: 96-106.

30) Mosarrezaii A, Ghasemzadeh N, Rahimi-Golkhandan A, Najafi A, Hashemi S, FazelKia P. Sleep Quality in Patients with Multiple Sclerosis. J Sleep Sci 2018; 3: 17-20.

31) Zhang GX, Zhang WT, Gao SS, Zhao RZ, Yu WJ, Izquierdo G. Sleep disorders in patients with multiple sclerosis in Spain. Neurologia 2021; 5: 213-220.

32) Garbarino S, Lanteri P, Bragazzi NL, Magnavita N, Scoditti E. Role of sleep deprivation in immune-related disease risk and outcomes. Commun Biol 2021; 4: 1304-1308.

33) Bavli S, Inanc Y, Tuncel D. Evaluation of patients with multiple sclerosis and sleep disorders. J Surg Med 2021; 5: 665-669.

34) Ishak WW, Bagot K, Thomas S, Magakian N, Bedwani, D, Larson D, Brownstein A, Zaky C. Quality of life in patients suffering from insomnia. Innov Clin Neurosci 2012; 9: 13-26.

35) Vitkova M, Rosenberger J, Gdovinova Z, Szilasiova J, Mikula P, Groothoff JW, Reijneveld SA, van Dijk JP. Poor sleep quality in patients with multiple sclerosis: gender differences. Brain Behav 2016; 6: 1-9.

36) Garbarino S, Lanteri P, Bragazzi NL, Magnavita N, Scoditti E. Role of sleep deprivation in immune-related disease risk and outcomes. Commun Biol 2021; 4: 1304-1309.

37) Kołtuniuk A, Kazimierska-Zając M, Pogłódek D, Chojdak-Łukasiewicz J. Sleep disturbances, degree of disability and the quality of life in multi-

ple sclerosis patients. Int J Environ Res Public Health 2022; 19: 1-9.

38) Sehanovic A, Kunic S, Ibrahimagic OC, Smajlovic D, Tupkovic E, Mehicevic A, Zoletic E. Contributing factors to the quality of life in multiple sclerosis. Med Arch 2020; 74: 368-372.

39) Akhoundi FH, Sahraian MA, Moghadasi AN. Neuropsychiatric and cognitive effects of the COVID-19 outbreak on multiple sclerosis patients. Mult Scler Relat Disord 2020; 41: 1-8

40) Yeni K, Tulek Z, Terzi M. A year with the fear of COVID-19 in multiple sclerosis patients: examination of depression, sleep quality and quality of life before and after the pandemic. Mult Scler Relat Disord 2022; 57: 1-10.

41) Gammoh OS, Al-Smadi A, Alqudah A, Al-Habahbeh S, Weshah F, Ennab W, Al-Shudifat AE, Bjørk MH. The association between fingolimod and mental health outcomes in a cohort of Multiple Sclerosis patients with stress. Eur Rev Med Pharmacol Sci 2023; 27: 6018-6026.

42) Marrie RA, Fisk JD, Walld R, Bolton JM, Sareen J, Patten SB, Singer A, Lix LM, Hitchon CA, El-Gabalawy R, Katz A, Marriott JJ, Bernstein CN. Use of benzodiazepines and Z-Drugs in multiple sclerosis. Front Neurol 2022; 13: 1-8.