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Neuropsychiatric changes during the COVID-19 pandemic in multiple sclerosis patients

Alterações neuropsiquiátricas durante a pandemia de COVID-19 em pacientes com esclerose múltipla

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ABSTRACT

Background: This study reported on a variety of psychological reactions related to anxiety, sleep quality, depression, fatigue, and quality of life in individuals with multiple sclerosis (MS), related to the Covid-19 quarantine experience. **Objective:** The aim of this study was to investigate the neuropsychiatric effects of the COVID-19 pandemic in MS patients and to analyze the risk factors contributing to psychological stress. **Methods:** The study was designed as a prospective, cross-sectional survey study. Multiple assessment tools that are used in neurological practice, including Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Fatigue Impact Scale (FIS), Pittsburgh Sleep Quality Index (PSQI), and Multiple Sclerosis Quality of Life-54 (MSQOL-54) were administered prospectively both during the early and the peak stages of COVID-19 outbreak (ESO and PSO, respectively). The survey forms were designed using SurveyMonkey and the participants were participating in the survey via a web link and QR code. **Results:** Fifty patients were included in the study. BDI scores, PSQI and FSI measurements, cognitive and social subscale scores and total FIS score, MSQOL-54 measurements, physical and mental subscale scores, and total MSQOL-54 score at PSO were significantly different than those at ESO. The body mass index values of the patients increased significantly at PSO compared to those measured at ESO. **Conclusions:** The results provide a basis for the development of psychological interventions that could minimize the prevalence of sleep disorders and depression and could improve patients' quality of life during the outbreak.

Keywords: Coronavirus Infections; Pandemics; Social Isolation; Multiple Sclerosis.

RESUMO

Introdução: Este estudo relatou uma variedade de reações psicológicas relacionadas a ansiedade, qualidade do sono, depressão, fadiga e qualidade de vida em indivíduos com esclerose múltipla (EM), relacionadas à experiência de quarentena de COVID-19. **Objetivo:** O objetivo deste estudo foi investigar os efeitos neuropsiquiátricos da pandemia de Covid-19 em pacientes com EM e analisar os fatores de risco que contribuem para o estresse psicológico. **Métodos:** O estudo foi desenhado como um estudo prospectivo e transversal. Várias ferramentas de avaliação usadas na prática neurológica, incluindo Inventário de Depressão de Beck (Beck Depression Inventory — BDI), Inventário de Ansiedade de Beck (Beck Anxiety Inventory — BAI), Escala de Impacto de Fadiga (Fatigue Impact Scale — FIS), Índice de Qualidade de Sono de Pittsburgh (Pittsburgh Sleep Quality Index — PSQI) e Qualidade de Vida da Esclerose Múltipla-54 (Multiple Sclerosis Quality of Life-54 — MSQOL-54) foram administrados prospectivamente durante o estágio inicial do surto de COVID-19 (EIS) e o estágio de pico do surto de COVID-19 (EPS). Os formulários da pesquisa foram projetados usando o *SurveyMonkey* e os participantes participaram da pesquisa por meio de um *link* da *web* e código QR. **Resultados:** Foram incluídos 50 pacientes no estudo. Os escores BDI, PSQI, FSI, subescala cognitiva e social e escore total do FIS, MSQOL-54, subescala física e mental e MSQOL-54 total no PSO foram significativamente diferentes dos do EIS. Os valores do índice de massa corporal dos pacientes aumentaram significativamente na EPS em comparação com os medidos na EIS. **Conclusões:** Nossos resultados são uma base para o desenvolvimento de intervenções psicológicas que podem minimizar a prevalência de distúrbios do sono e depressão e melhorar a qualidade de vida dos pacientes durante o surto.

Palavras-chave: Infecções por Coronavírus; Pandemias; Isolamento Social; Esclerose Múltipla.

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Authors' contributions: CFD was responsible for the selection of patients in accordance with the inclusion criteria, as well as for the planning and design of the study, the analysis of the data, and the writing of the article. F Bilek did the planning and design of the study, the analysis of the data, and the writing of the article. F Balgetir carried out the planning and design of the study, the upload and distribution of surveys to the online system, the analysis of the data, and the writing of the article.

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INTRODUCTION

Multiple sclerosis (MS) is a chronic, inflammatory, and autoimmune disease of the central nervous system (CNS) that is triggered by environmental factors and characterized by multifocal zones of inflammation, demyelination, relapse, and remission. The spread of coronavirus disease 2019 (COVID-19) has brought about extensive restrictions that were designated to minimize contact among individuals and have also led to access to health systems, provision of basic needs and travel for the majority of the world population. Patients with chronic diseases, such as MS, were among the first groups subjected to restrictions such as curfews and restricted access to in-hospital services, since these patients had and increased risk of being infected with COVID-19. Both qualitative and quantitative studies have reported on various psychological reactions associated with the Covid-19 quarantine experience, including anxiety, sense of loneliness, sleep deprivation, anger, stress, and concerns about the health of family members[1-6]. Moreover, a previous study indicated that the hospital staff who were quarantined due to the possibility of a contact with suspected severe acute respiratory syndrome (SARS) cases had an increased prevalence of acute stress disorder[3]. On the other hand, patients with chronic diseases such as MS are known to be affected more severely by natural disasters and crises[7]. In such patients, the psychological and cognitive deterioration associated with numerous factors including keeping abreast of morbidity and mortality rates on a daily basis, social isolation and sense of loneliness, minimal access to all services including healthcare services and clinical visits, termination of public transport modes, and the challenges in access to drugs and in drug management have reached an alarming level. These challenges in access to drugs and in drug management are particularly important because patients with chronic diseases, particularly MS patients, are highly vulnerable and most of these patients suffer from multiple diseases and weakness. Accordingly, these patients need continuous follow-up to ensure their physical and psychological integrity[2,6].

To our knowledge, there are very few studies reporting on the impact of the COVID-19 pandemic on fatigue, sleep quality, depression, anxiety, quality of life, and cognitive functions in MS patients[7,8]. The aim of this study was to investigate the neuropsychiatric effects of the COVID-19 pandemic in MS patients and to analyze the risk factors contributing to psychological stress.

METHODS

Study design

The study was designed as a prospective, cross-sectional survey study. Multiple assessment tools that are used in neurological practice, including the Beck Depression Inventory (BDI), the Beck Anxiety Inventory (BAI), the Fatigue Impact Scale (FIS), the Pittsburgh Sleep Quality Index (PSQI), and the Multiple Sclerosis Quality of Life-54 (MSQOL-54) were administered prospectively both during the early stage of COVID-19 outbreak (ESO) and the peak stage of COVID-19 outbreak (PSO). The study was approved by Local Ethics Committee (Approval No: FÜ- 2020/07-07) and was conducted in accordance with the Declaration of Helsinki.

The ESO data were collected on January 15th, 2020 (*i.e.*, 13 days after the outbreak of Covid-19 was declared a PHEIC) when there were no national measures taken against the pandemic in Turkey and the PSO data were collected on April 23rd, 2020 when the pandemic had its peak effects and strict restrictions such as curfews were being imposed by the government in Turkey[9]. PSO data began to be collected 3 months after the collection of the ESO data.

Eligibility

Inclusion criteria were: age 18–45 years, voluntary participation in the study, being followed with a diagnosis of relapsing-remitting MS (RRMS) or secondary progressive MS, an Expanded Disability Status Scale (EDSS) score of ≤4.0[10], and no history of attacks/relapse within the last four weeks. Exclusion criteria were: use of medication for fatigue, ongoing treatment for major sleep disorder, clinical depression, hypothyroidism, and vitamin B12 deficiency, severe balance disorders (cerebrovascular event, peripheral neuropathy, Meniere's vertigo), history of corticosteroid treatment within the last four weeks, pregnancy, cardiovascular disease, hypertension, and orthopedic problems that could restrict mobility. EDSS assessment was performed in single rooms in non-COVID-19 areas reserved for Neurology patients by a neurologist certified in EDSS (FB; https://www.neurostatus.net).

Data collection

The survey was administered online to avoid face-to-face contact and due to the travel restrictions imposed by the government. The survey form was designed using SurveyMonkey and participants were invited to participate in the survey via a web link and QR code[11]. Participants filled out the survey form easily and safely by using their computers, smartphones, and tablet devices. Employing an online survey due to the nationwide isolation and the risk of Covid-19 infection during the pandemic provided numerous advantages such as time efficiency due to the rapid access to participants. The mean time to complete the survey was 16 min.

Data collection tools

The BDI is a 21-item, self-report inventory used to measure characteristic attitudes and symptoms of depression. In this inventory, a score of ≤9 indicates 'no depression', 10–16 indicates 'mild depression', 17–23 indicates 'moderate depression', and ≥24 indicates 'severe depression'[12].

The BAI is a 21-item, self-report inventory used to identify anxiety symptoms and to quantify their intensity. Total score ranges from 0 to 63 and higher total scores indicate more severe anxiety. The clinical classification of scoring results is as follows: 8–15 suggests mild anxiety, 16–25 suggests moderate anxiety, and 26–63 suggests severe anxiety[13,14].

The FIS is a self-report 40-item questionnaire used to assess functional limitations attributed to fatigue in MS patients. FIS assesses the physical, cognitive, and social impacts of fatigue during the past month. The total score ranges between 0 and 160, and higher total scores indicate greater impact of fatigue[15,16]

The PSQI is a self-rated 19-item questionnaire assessing participants' sleep quality, sleep duration, and sleep disturbances and their severity during the past month. Total score ranges between 0 and 21, which consists of seven sub-scores. Participants with a PSQI ≤5 are classified as 'good sleepers' and participants with a PSQI >5 are classified as 'bad sleepers'[17,18].

The MSQOL-54 is a generic scale used to assess the health-related quality of life in individuals with MS. The summary scores are the physical health composite summary and the mental health composite summary, and higher total scores indicate better quality of life[19,20].

Statistical analysis

Data were analyzed using SPSS for Windows, version 22.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Continuous variables were expressed as mean±standard deviation and categorical variables were expressed as frequencies (n) and percentages (%). The ESO and PSO values of the parameters were compared using paired-samples t-test. A p value of <0.05 was considered significant.

RESULTS

Table 1 presents the demographic and clinical characteristics of the 50 patients included in the study. Two patients were excluded from the study since they did not complete the survey. The EDSS score was 2.5 in one patient and ≤2 in the remaining patients (Table 1).

BDI scores at PSO were significantly higher than those at ESO (p<0.01). Additionally, a strong correlation was found between the BDI scores measured at these two stages (r=0.93; p<0.01). However, no significant difference was found between the BAI scores measured at ESO and PSO (15.63±11.27 *vs.* 18.22±10.53) (p>0.05) (Table 2).

In FSI measurements, the cognitive and social subscale scores and the total FIS score were significantly higher at PSO compared to ESO (p<0.01 for all), whereas no significant difference was found with regard to the physical subscale scores (p>0.05). Moreover, a strong correlation was found between the FSI scores measured at ESO and PSO with regard to the cognitive (r=0.91), physical (r=0.92), and social (r=0.97) subscale scores and the total FSI score (r=0.96) (p<0.01 for all) (Table 2).

In MSQOL-54 measurements, a negative correlation was found between the measurements performed at ESO and PSO with regard to the physical (r=0.91) and mental (r=0.85) subscale scores and the total MSQOL-54 score (r=0.93) (p<0.01 for all). Although a significant difference was found between the MSQOL-54 measurements performed at ESO and PSO with regard to the mental subscale scores and the total MSQOL-54 score (p<0.01 for both), no significant difference was found with regard to the physical subscale scores (p>0.05) (Table 2).

The PSQI measurements indicated that the sleep quality of the patients deteriorated significantly (p<0.01). Moreover, a positive correlation was found between the PSQI scores measured at ESO and PSO (r=0.94; p<0.01) (Table 2).

On the other hand, the body mass index (BMI) values of the patients increased significantly at PSO compared to

Table 1. Demographic and clinical characteristics of patients.

		n=50	%
Gender	Female	42	84
	Male	8	16
	X±SD	min	max
Age (years)	30.02±7.01	19	43
EDSS	1.1±0.46	0.5	2.5

X: mean; SD: standard deviation. Continuous variables are presented as mean±standard deviation and categorical variables are presented as n (% of group); EDSS: Expanded Disability Status Scale.

Table 2. Neuropsychiatric parameters and body mass index values.

	ESO X±SD	PSO X±SD	p-value
BDI	12.64±8.16	16.40±9.48	0.000**
BAI	17.63±9.27	18.12±8.53	0.087
FIS			
Cognitive	12.24±9.23	14.18±10.71	0.004**
Physical	13.12±8.51	13.64±9.21	0.311
Social	19.82±16.16	23.22±17.49	0.000**
Total	45.18±32.24	51.12±35.89	0.000**
MSQOL-54			
Physical	57.23±9.26	55.57±10.98	0.015*
Mental	64.44±9.87	60.49±10.73	0.000**
Total	60.84±8.86	58.03±9.45	0.000**
PSQI	8.27±1.36	8.78±1.49	0.000**
BMI	24.07±4.59	24.21±4.53	0.005**

X: mean; SD: standard deviation; ESO; early stage of COVID-19 outbreak; PSO: peak stage of COVID-19 outbreak; BDI; Beck Depression Inventory; BAI; Beck Anxiety Inventory; FIS; Fatigue Impact Scale; MSQOL-54; Multiple Sclerosis Quality of Life-54; PSQI: Pittsburgh Sleep Quality Index; BMI; body mass index; *p<0.05; **p<0.01.

those measured at ESO (p<0.01) and a positive correlation was found between the measurements performed at these two stages (r=0.91; p<0.01) (Table 2).

DISCUSSION

To our knowledge, there has been no study investigating the neuropsychiatric impact of COVID-19 pandemic in MS patients. Moreover, most studies evaluating MS patients during the pandemic have focused on the treatment of MS with immunomodulatory and/or immunosuppressive agents[21,22], epidemiology of infected patients[23], clinical characteristics of COVID-19, and the challenges experienced by MS patients[24]. The present study aimed to investigate the neuropsychiatric effects of the COVID-19 pandemic in MS patients and the risk factors that contribute to psychological stress. Accordingly, the findings of the study will provide useful information to healthcare professionals for preserving the neuropsychosocial wellbeing of MS patients during the COVID-19 pandemic.

Anxiety disorder is an anticipated affective disorder in the context of a pandemic. A previous Chinese study reported that most of their patients had moderate and severe anxiety during the pandemic[24]. In the present study, however, the anxiety levels in MS patients showed no significant increase during the pandemic, which could be attributed to the fact that our patients and their relatives had not been diagnosed with COVID-19 throughout this period. On the other hand, the increased anxiety levels in the Chinese study could be explained by the military state of emergency declared by the Chinese Government to control the rapid spread of the pandemic[25].

The COVID-19 pandemic has been shown to cause depression in a large number of individuals due to its unique environmental stress factors[26]. The present study, similarly to other ones[25,26], revealed that the depression levels of MS patients increased significantly during the pandemic. On the other hand, in the context of a pandemic, many individuals may suffer significant personal losses and grieving reactions. Additionally, long-term self-isolation, which is mostly the primary strategy employed to minimize the spread of the pandemic, adds up an additional risk layer for depression. Accordingly, the individuals may not be able to tolerate this social deprivation for a long time. In particular, patients with chronic diseases such as MS, who have minimal access to social services, are at greater risk of depression. Moreover, in families in which family members need to live together in the same house for a long time may have frequent arguments. Therefore, they may be at a greater risk of depression. In addition, other stress factors, such as economic loss, can add up another risk layer.

The neuropsychiatric state of MS patients in the context of a pandemic can be overlooked due to their social and internal conflicts, which may lead to the overlooking of their emerging emotions. Physical parameters are the primary factors in the assessment of disability in MS patients. Nevertheless, the evaluation of neuropsychiatric parameters in such patients tends to be more important in the context of traumatic periods such as pandemics, since the symptoms of these patients are often emotional because they are often caused by psychological conflicts[27]. In the present study, the MSQOL-54 scores indicated that mental deterioration was more prevalent than physical in our patients. Additionally, the quality of life also decreased in our patients during the pandemic. In long-term traumatic periods such as pandemics, MS patients need to be provided with strategies that could allow them to have a different perspective in terms of interpreting their emotions, thoughts, awareness, and the events occurring in their environment in order to minimize the impact of this exposure. In the present study, the FSI measurements indicated that patients deteriorated in terms of cognitive and social subscales while no significant difference was found with regard to the physical subscale during the pandemic. Knowledge of these factors may help MS patients in their struggle against their illnesses and in reducing their perceived stress[28-31].

Stress may not be the sole cause of sleep deprivation in the context of a pandemic[32,33]. To date, there have been numerous studies investigating the prevalence and psychological effect of sleep deprivation during the Severe Acute Respiratory Syndrome (SARS) pandemic[34]. However, to our knowledge, there has been no study reporting on sleep quality in MS patients during the COVID-19 pandemic. In our study, MS patients were found to have reduced sleep quality during the COVID-19 pandemic, which was consistent with the findings presented by recent studies conducted with healthy individuals[35-37]. Reduced sleep quality may aggravate the symptoms of chronic diseases as well as reduce treatment response[38]. Accordingly, multidimensional and multistage studies are needed to investigate sociopsychological factors that could increase sleep quality. It is an undeniable fact that the Covid-19 pandemic has brought about numerous ambiguities, particularly in the realm of healthcare, as well as in the social, psychological, and economic areas.

Interestingly, the BMI values of our patients showed a significant increase over the short period between ESO and PSO (24.07±0.65 *vs.* 24.21±0.64). When COVID-19 began to spread across the world, people began to consume ultra-processed, high-calorie, and long shelf-life foods. Additionally, opportunities for physical exercise were reduced due to the implementation of restrictions such as social distancing and curfews[39]. Accordingly, the decreased physical activity and increased food intake during the COVID-19 pandemic could explain the increased BMI in our patients. On the other hand, the causes of increased BMI during the COVID-19 pandemic and the measures that need to be taken could be a research topic for further studies.

In the present study, no patient was diagnosed or suspected with COVID-19 or was in direct or indirect contact with infected patients, nor had undergone any medical consultation regarding COVID-19. Additionally, patients stated having strictly obeyed the curfews and having not left home even for their basic needs throughout the pandemic. In this case, it clearly indicates that they had limited access to daily essentials as well as healthcare services and drugs. The findings of the present study revealed that the patients had increased levels of depression and mental fatigue and decreased quality of life during the COVID-19 pandemic. These findings will provide useful solutions for the development of strategies regarding psychological support and the identification of priority areas in the regions most severely affected by the COVID-19 pandemic. On the other hand, medical and psychological readiness of the general population and a well-established healthcare system are of prime importance in the fight against the pandemic[40]. Accordingly, our findings have both clinical and political implications. First and foremost, health authorities need to identify high-risk groups based on the sociodemographic profiles of patients in order to be able to perform early psychological interventions. Secondly, the content of psychological interventions should be modified according to the needs of the general population, mainly because the prevalence of neuropsychiatric disturbances increases in the context of a pandemic.

Our study was limited in several ways. First, as the study had a cross-sectional design, the data and analyses derived from the study may not be sufficient for obtaining causal inferences. Second, the study might have a sampling bias, since the participants consisted of volunteers that participated in an online survey. Third, participants with severe fatigue, sleep disorders, psychological comorbidities, and high EDSS were excluded from the study. This causes the population to be more homogeneous than in real life.

In conclusion, our results are likely to form a basis for the development of psychological interventions that could minimize the prevalence of sleep disorders and depression and could improve patients' quality of life during the Covid-19 pandemic. Our results can also be used to help formulate neuropsychiatric interventions.

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Compliance with ethical standards: our study was approved according to the local ethical committee. All patients gave their informed written consent to be enrolled in the study according to the Declaration of Helsinki.

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