ORIGINAL ARTICLE

Addressing the burden of the Coronavirus Disease 2019 pandemic on individuals with multiple sclerosis: a cross-sectional study in Egypt

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Background	The Coronavirus Disease 2019 (COVID-19) pandemic was an ongoing global stress encountered by individuals with preexisting chronic illnesses. This study aimed to evaluate the perceived fears of contracting COVID-19 virus (FCV) infection and to address the associated correlates among patients with multiple sclerosis (MS) during the pandemic.
Patients and Methods	A cross-sectional study included a total of 120 Egyptian patients with MS who were followed up at the Zagazig University Neurology Outpatient Clinics during the COVID-19 outbreak between May 1 and October 31, 2020. The participants, consecutively selected by the convenience sampling method, were interviewed using the Fear of COVID-19 Scale (FCV-19S), Hospital Anxiety and Depression Scale, Expanded Disability Status Scale, and Five-item Modified Fatigue Impact Scale for the assessment of FCV, comorbid anxiety, and depressive symptoms, associated fatigability, and levels of disability, respectively.
Results	Around 58% of patients with MS (*n*= 69) experienced intensified FCV. Those who were unmarried, reporting higher levels of anxiety and depression, diagnosed with primary or secondary progressive MS subtypes, with a longer course of illness, and associated fatigability and disability, were more likely to experience FCV. Comorbid anxiety symptoms were positively correlated with illness duration (*r*= 0.19, *P*= 0.039), increased fatigue (*r*= 0.47, *P* <0.001), and disability (*r*= 0.36, *P* <0.001), while depressive symptoms were positively correlated with increased fatigue (*r*= 0.37, *P* <0.001) and disability (*r*= 0.30, *P* <0.001).
Conclusions	FCV was prevalent among patients with MS. Being unmarried, heightened anxiety, longer duration of illness, and associated fatigability would predict FCV. Both psychological and physical assessment measures of patients with MS should be regularly implemented.
Keywords	Coronavirus Disease 2019 pandemic, Egypt, Fear of Coronavirus Disease 2019 (FCV), Multiple sclerosis.
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INTRODUCTION

The Coronavirus disease 2019 (COVID-19), newly emerged as a worldwide pandemic, is precipitated by the severe acute respiratory syndrome coronavirus type-2 (World Health Organization, 2020; Zhou *et al.*, 2020).

A wide array of psychological symptoms has been documented during the outbreak in different populations, including the intensive worries of contracting an infection, persistent anxiety, or the fear of death as well as feelings

of despair, helplessness, and social isolation (Aljemaiah *et al.*, 2021; Abdelghani *et al.*, 2021a, 2021b). According to the Center for Disease Control and Prevention, those with chronic medical diseases, particularly immunocompromised individuals, are more likely to suffer from a worse course of COVID-19 symptomatology (Kompaniyets *et al.*, 2021). The inclusion of immunocompromised patients among the high-risk groups for COVID-19 was intuitive, as these individuals are at a higher risk to contract an infection and develop disease complications (Möhn *et al.*, 2020).

Multiple sclerosis (MS) is a chronic autoimmune-mediated neurodegenerative demyelinating central nervous system disease, which principally affects young adults (mean age of onset ranges from 20 to 30 years), and can result in physical disability, cognitive impairment, and decreased quality of life (McGinley *et al.*, 2021). Few recent studies have reported that patients with MS did not have a higher incidence of COVID-19 infection, more severe disease, or mortality than individuals with other chronic diseases (Carandini *et al.*, 2020; Capuano *et al.*, 2021); however, the COVID-19 pandemic would be a unique challenge to people with MS given its underlying pathophysiological immune mechanisms, the medications with immunosuppressant or modifying actions, and the need for regular long-term medical service accessibility and follow-up (Sastre-Garriga *et al.*, 2020).

Patients with MS are believed to experience a high incidence of comorbid psychological disorders including, but not limited to, anxiety and depressive disorders (Boeschoten *et al.*, 2017), and their symptoms are likely to be increased by the concomitant fears of contracting coronavirus infection (Chiaravalloti *et al.*, 2021). Studies assessing the psychological burden of the COVID-19 pandemic on the mental well-being of individuals with MS assured that the higher levels of anxiety, depression, distress, and fears observed in patients with MS during the pandemic would be claimed to the pandemic itself, such as social distancing, isolation and quarantines, economic uncertainty, and the uncertainty of contracting the virus (Talaat *et al.*, 2020; Chiaravalloti *et al.*, 2021). Besides, patients with MS may experience excess stressors as disease-modifying therapies would cause significant immune suppression and increase the fear of easily getting sick (Giovannoni *et al.*, 2020). In addition, physical distancing can be an obstacle to the attendance of cognitive and physical rehabilitation and other medical services, which would increase the levels of psychological distress when the patients fail to attain these services (Motolese *et al.*, 2020).

Nonetheless, research investigating the potential psychological and physical impact of the COVID-19 pandemic in individuals with MS in Egypt is still lagging. To our knowledge, this study would be one of few studies, if any, to address the perceived fear of COVID-19 virus (FCV) infection and other associated psychological symptoms secondary to the pandemic and assess their relationship to the disease-related clinical correlates in those populations.

PATIENTS AND METHODS

Study participants and setting

This was a cross-sectional study. The sample size intended to be included was a total of 130 patients with MS who were followed up at the Neurology Outpatient Clinics of Zagazig University Hospitals, the main government general hospitals in Sharkia Province, Egypt, with a population of around 7.5 million people. The sample size was calculated using Epi Info 6.0 at 80% power of the study, 95% confidence level, as the prevalence of anxiety symptoms among patients with MS was 19% (Beiske *et al.*, 2008). All patients were diagnosed with MS according to the 2010 revised McDonald criteria (Polman *et al.*, 2011). We used the convenience sampling method. Respondents of both sexes, all ages, and who accepted to participate and complete the study were recruited. During the data collection, 10(7.4%) patients refused to complete the study. After excluding the incomplete or invalid responses, the final sample size included in the study was 120 (response rate: 92.6%) participants. The survey was conducted from May 1 to October 31, 2020. All participants were interviewed by a face-to-face interview using the study tools and measures with insurance of social distancing and appliance of appropriate precautions.

Data collection and assessment tools
Outcome ascertainment

The main outcome variables were the MS-associated disability and fatigability assessed by the Expanded Disability Status Scale (EDSS) and Five-item Modified Fatigue Impact Scale (MFIS-5), respectively.

Expanded Disability Status Scale

The EDSS was founded by Kurtzke, and utilized to assess neurological deficits in MS. It described illness progression in patients with MS and monitored the treatment effectiveness in clinical trials (Kurtzke, 1983). Eight functional systems (FS) were included in the EDSS scoring system: pyramidal, cerebral, brain stem, cerebellar, sensory, visual, bowel and bladder, and others. Each separate system impairment was graded, and all systems' scores were collectively calculated. The EDSS scores ranged from 0 (normal/average neurological examination) to 10 (death from MS) in 0.5-U increments. The lower values of the EDSS-assessed impairments are based on the neurological examination, while the higher values (> EDSS 6) assessed the handicaps of patients with MS.

Five-item modified fatigue impact scale

The MFIS-5 was the shortened version of the 21-item MFIS, which had three dimensions (physical, cognitive, and psychosocial) (D'Souza, 2016). The MFIS-5 five items were derived from the former scale: two items from the cognitive subscale (#1 and #19), two items from the physical subscale (#10 and #17), and the fifth item from the psychosocial subscale (#9). Each item was scored on a five-point Likert scale from 0 (never) to 4 (almost always), with the total score ranging from 0 to 20. Higher scores indicated more severe fatigue. The MFIS-5 had shown proven psychometric properties regarding its test–retest and internal reliability and sensitivity to change (Meca-Lallana *et al.,* 2019).

Exposure ascertainment

The primary exposure was measured by the Fear of COVID-19 Scale (FCV-19S) to assess the perceived FCV infection in patients with MS.

Fear of COVID-19 Scale

The FCV-19S was a newly emerging seven-item psychometric tool composed of seven questions with responses of 'strongly disagree,' 'disagree,' 'neither agree nor disagree,' 'agree,' and 'strongly agree' scored from 1 to 5 for each question (Ahorsu *et al.,* 2020). The higher values indicated greater FCV infection. A cutoff point score of 16.5 or higher was adopted denoting a significant level of intensified FCV (Nikopoulou *et al.,* 2020). We used the Arabic version of this scale, which had shown good reliability and validity (Alyami *et al.,* 2021).

Covariates

Demographic and clinical variables and comorbid psychological symptoms were examined as potential confounders. A semistructured checklist was formulated to collect both demographic and clinical data. Sociodemographic data included age, sex, marital status, and working status, while clinical data included questions about MS subtypes, current MS medications, and illness course duration. The Hospital Anxiety and Depression Scale was used as a screening tool for associated symptoms of depression and anxiety among the participants (Zigmond and Snaith, 1983).

The Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale included 14 questions; seven questions investigated depressive symptoms, and the other seven asked for anxiety symptoms, with a score of each question from 0 to 3. The total score of each subscale ranged from 0 to 21. Valid cases of depression and anxiety were considered if scores of greater than equal to 11, for each, were recorded. In the current study, we used the Arabic version which proved good reliability and validity (El-Rufaie and Absood, 1987).

Ethical considerations

The study protocol was approved by the Zagazig University Institutional Review Board (IRB no. 9810/28.9.2022), assuring that this study was conducted according to the ethical guidelines outlined in the Declaration of Helsinki. After discussing the study objectives, and confirming confidentiality, written consent was obtained from all participants.

Data analyses

Statistical Package for the Social Sciences (SPSS), version 20.0 was utilized to analyze the collected data. Qualitative variables were expressed by frequency distributions, and the χ^2 test was used to compare the proportions of categorical data. Quantitative variables were expressed by means and SD, and the independent sample *t* test was used to compare the means of the two groups. Mann–Whitney *U* test was applied for data not normally distributed. Pearson correlation coefficient was applied to evaluate the relationship between two linear variables. The multivariate logistic regression analysis was applied to obtain odds ratios and 95% confidence intervals of FCV among study participants. All results were considered significant when their probability was below 5% ($P < 0.05$).

RESULTS

This study included a total of 120 Egyptian patients diagnosed with MS who were followed up at the Neurology Outpatient Clinics of Zagazig University Hospitals. Of these patients, 83(69.2%) were females, 69(57.5%) were married, 58(48.3%) were jobless. The means of age, associated anxiety, and depressive symptoms were 29.5±7.4, 11.2±3.8, and 10.9±2.7 years, respectively. Those who reported intensified levels of FCV infection represented 57.5% (*n*= 69) of all participants.

The association between the mean score of FCV (measured by the FCV-19S) and demographic and clinical variables are displayed in Tables 1 and 2. Those with higher levels of FCV were more likely to be unmarried (*t*= 2.42, *P* <0.001), experiencing higher levels of anxiety (*t*= -6.13, *P* <0.001) and depressive symptoms (*t*= -4.18, *P* <0.001), diagnosed with primary progressive MS or secondary progressive multiple sclerosis subtypes (χ^2= 8.19, *P*= 0.004), of longer illness course duration (*z*= -5.11, *P* <0.001), and likely reporting associated fatigability (*t*= -7.77, *P* <0.001) and disability (*z*= -5.12, *P* <0.001).

Table 3 describe the results from the logistic regression after adjustment for all significant variables to identify the potential predictors of FCV among patients with MS. Those who were unmarried had higher anxiety scores; longer course duration, and associated fatigability showed greater odds of FCV (odds ratios: 5.6, 1.25, 1.28, and 1.4, respectively).

Table 4 illustrate the correlation between emotional symptoms and MS-related clinical variables. The associated anxiety symptoms were found to be positively correlated with illness course duration ($r= 0.19$, $P= 0.039$), associated fatigue ($r= 0.47$, $P <0.001$), and disability ($r= 0.36$, $P <0.001$), while depressive symptoms were correlated with only associated fatigue ($r= 0.37$, $P <0.001$) and disability ($r= 0.30$, $P <0.001$).

Table 1: Association between perceived fear of Coronavirus Disease 2019 infection, and demographic and clinical factors of patients with multiple sclerosis:

Variable	Normal stress reaction	Intensified FCV	Total	χ^2	P value
		n(%)			
Sex				0.83	0.363
Male	18(35.3)	19(27.5)	37(30.8)		
Female	33(64.7)	50(72.5)	83(69.2)		
Marital status				2.42	<0.001
Married	42(82.4)	27(39.1)	69(57.5)		
Not married	9(17.6)	42(60.9)	51(42.5)		
Working status				0.75	0.461
Working	24(47.1)	38(55.1)	62(51.7)		
Not working	27(52.9)	31(44.9)	58(48.3)		
		Mean(SD)		*t* test	
Age	28.2(7.1)	30.5(7.6)	29.5(7.4)	−1.68	0.097
HADS scoring					
Anxiety	9.1(2.8)	12.8(3.6)	11.2(3.8)	-6.13	<0.001
Depression	9.8(2.1)	11.7(2.8)	10.9(2.7)	-4.18	<0.001

FCV, Fear of Coronavirus Disease 2019 Virus; HADS, Hospital Anxiety and Depression Scale. Bold text indicates statistical significance where *P* value less than 0.05.

Table 2: Association between perceived fear of Coronavirus Disease 2019 infection and disease-related clinical factors of patients with multiple sclerosis:

Variable	Normal stress reaction	Intensified FCV	Total	χ^2	P value
		n(%)			
MS subtype				8.19	0.004
PRMS	47(92.2)	49(71.0)	96(80.0)		
PPMS or SPMS	4(7.8)	20(29.0)	24(20.0)		
		Mean(SD)		*t* test	
MFIS-5 Scoring (fatigue)	6.6(2.3)	10.6(3.1)	8.9(3.4)	-7.77	<0.001
		Mean (SD) Range		**MWU**	
MS course duration (years)	4.4(3.4)	9.2(5.6)	7.2(5.4)	-5.11	<0.001
	1.0–13.0	2.0–22.0	1.0–22.0		
EDSS scoring (disability)	1.0(0.7)	2.3(1.7)	1.8(1.5)	-5.12	<0.001
	0.5–3.0	0.5–6.0	0.5–6.0		

EDSS, Expanded Disability Status Scale; MFIS-5, Five-item Modified Fatigue Impact Scale; MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; PRMS, primary relapsing multiple sclerosis; SPMS, Secondary progressive multiple sclerosis. Bold text indicates statistical significance where *P* value less than 0.05.

Table 3: Predictors of perceived fear of Coronavirus Disease 2019 infection in patients with multiple sclerosis:

Variable	B	SE	Wald	*P* value	OR	CI (95%)	
Marital status (unmarried)	1.73	0.68	6.37	0.012	5.61	1.47	21.44
Associated anxiety	0.23	0.10	5.02	0.025	1.25	1.03	1.53
Associated depression	0.15	0.13	1.16	0.281	1.16	0.89	1.51
MS subtype (PPMS or SPMS)	1.04	1.31	0.63	0.427	2.83	0.22	36.95
MS course duration	0.24	0.09	7.96	0.005	1.28	1.08	1.51
MFIS-5 Scoring (fatigue)	0.36	0.15	5.97	0.015	1.44	1.07	1.92
EDSS scoring (disability)	0.12	0.56	0.05	0.827	1.13	0.38	3.38

Bold text indicates statistical significance where 95% confidence intervals do not include the null value (1.00).

Table 4: Correlation between associated emotional symptoms, and disease duration, associated fatigability, and disability in patients with multiple sclerosis:

Variable	HADS score (anxiety)	HADS score (depression)
	Pearson correlation, *P* value	
MS course duration (years)	0.19, 0.039	0.15, 0.098
MFIS-5 scoring (fatigue)	0.47, <0.001	0.37, <0.001
EDSS scoring (disability)	0.36, <0.001	0.30, 0.001

Bold text indicates statistical significance where P value less than 0.05.

DISCUSSION

It was stated that patients with chronic diseases, particularly those with autoimmune diseases or receiving immunosuppressants, had higher levels of fear and health anxiety because they were at higher risk of infection with the increased possibility of having severe symptoms and complications if infected (Al-Rahimi *et al.,* 2021). The main findings of this study were that most patients with MS experienced intensified FCV and higher levels of anxiety and depressive symptoms during the pandemic. Consistent with these results, the previous studies confirmed the negative mental health impact of the COVID-19 pandemic in those patients. For example, Yeni *et al.,* (2022) found that compared with healthy individuals, levels of anxiety and depression, but not FCV, were higher among patients with MS who received remote counseling services. Similar studies have reported elevated emotional distress in patients with MS compared with their caregivers and the general population during the COVID-19 pandemic (Costa-Frossard *et al.,* 2020; Demir *et al.*, 2020; Talaat *et al.,* 2020).

These associated emotional disturbances would be related to several reasons. First, the uncertainties about the COVID-19 pandemic were perceived as ongoing stressors that would be associated with disturbed mental health and well-being. Second, economic losses and stigma had been identified as strong constraints for physical or emotional adjustment for mental health problems (Giménez-Llort *et al.,* 2021). Third, significant personal losses, grieving reactions, and long-term self-isolation added up an additional risk layer for mental health problems (Demir *et al.,* 2020). Last, in patients with chronic diseases, particularly those with MS, limited access to social and

medical services, fear of getting infected, fear of death, or worsening of health among these patients and their caregivers would be strong triggers of emotional distress and mental health problems (Demir *et al.,* 2020; Giménez-Llort *et al.,* 2021; Pan *et al.,* 2021).

There were several factors associated with intensified FCV among patients with MS. This study stated that those who were unmarried, and experienced comorbid anxiety, were likely to experience higher levels of FCV. The magnitude of the interaction between marital status, mental health, and chronic illnesses could not be overlooked (Lam and Perales, 2018). In a study conducted on 1030 patients with preexisting chronic diseases in Saudi Arabia, it was reported that those who were unmarried (single or divorced) were more likely to suffer from high levels of FCV (Al-Rahimi *et al.,* 2021). The development of these fears would be related to inadequate care or communication and a low level of family support that unmarried people with chronic diseases might receive. Moreover, various studies have documented the strong association between FCV and associated anxiety and depressive symptoms among patients with MS (Ramezani *et al.,* 2021; Alirezaei *et al.,* 2022). Ahorsu *et al.,* (2020) the developer of FCV-19S, also reported a significant relationship between FCV and depression and anxiety among the general population.

The impact of the COVID-19 pandemic was not limited to the mental well-being, but it would extend to adversely influence the physical status of patients with chronic diseases (Abdelghani *et al.,* 2021a). This study revealed that MS-related variables like course duration and associated fatigability were associated with intensified FCV among MS patients. Besides, associated symptoms

of anxiety and depression were more likely associated with increased fatigability and physical disability. Fatigue was considered by the majority of patients with MS as the most prevalent (87% of patients) and disabling (40% of patients) symptom which would cause significant physical, psychological, emotional, work, and social limitations (Giménez-Llort *et al.,* 2021). It was claimed that comorbid psychological symptoms were found to increase fatigue, disability, relapse rate, disease exacerbations, MRI activity, decreased treatment adherence, more aggressive MS course, and suicidal thoughts and behaviors in patients with MS (McKay *et al.,* 2018; Broche-Pérez *et al.,* 2021; Ramezani *et al.,* 2021).

Consistent with our findings, patients with MS were found to experience higher levels of associated fatigability during the COVID-19 pandemic (Demir *et al.,* 2020; Motolese *et al.,* 2020). Likewise, another study found that during the outbreak, patients with MS complicated with neurotic symptoms like anxiety and/or depression were more likely to report more worsened MS symptoms compared with those without neurotic symptoms (Garjani *et al.,* 2021). It was also reported that there was a significant association between physical disability and symptoms of anxiety and depression among MS patients during the pandemic (Necho *et al.,* 2020). It was argued that the complex interplay between emotional distress and the potential psychological vulnerability of patients with MS would contribute to the perception of symptoms like fatigue (van Kessel and Moss-Morris, 2006). Moreover, functional disability, caused by increased fatigue, was suggested to be associated with worse general mental health (Uhr *et al.,* 2021). In addition, patients with disabilities were particularly impacted by the COVID-19 pandemic due to limited access to health-care facilities (Lebrasseur *et al.,* 2021). Care disruptions were significantly associated with worse health status and fear of MS progression. Moreover, the lack of psychosocial counseling services, during pandemic, would increase the likelihood of stress, and mostly result in MS progression (Manacorda *et al.,* 2021).

This study had a few limitations to be addressed. First, the cross-sectional design would result in difficulty in establishing causal relationships between exposure and outcome variables. Second, the lack of information about the psychiatric status of patients before the pandemic would confuse the readers whether the comorbid psychiatric problems (anxiety and depressive symptoms) occurred as sequelae of the COVID-19 pandemic or MS itself. Third, this study did not include a control group, so it would be difficult to estimate whether the symptoms of depression, anxiety, or FCV were higher or lower than those reported by the general population. Finally, self-report questionnaires and scales would allow for the possibility of social desirability bias among participants. Although these limitations were present, this study was one of the few studies, if any, conducted among patients with MS in Egypt, which would help assess their FCV and its correlates during the current pandemic. Also, this study would draw attention to the necessity of preparedness for future public health crises, with an emphasis on who would be suffering from the highest degree of symptoms based on the disease type, and demographic and socioeconomic correlates.

CONCLUSION AND RECOMMENDATIONS

FCV, and comorbid anxiety and depressive symptoms were prevalent among individuals with MS during the COVID-19 pandemic. Being unmarried, comorbid anxiety, longer course duration of MS, and complicated fatigability were significant risk factors for FCV among patients with MS. It is essential to confirm the need for giving further attention to the patients with chronic medical illnesses in this critical period. Regular follow-up of patients with MS through mobile health anxiety/depression scales and providing psychological counseling services and therapeutic interventions including psychiatric medications when appropriate could be beneficial.

CONFLICTS OF INTEREST
There are no conflicts of interest.

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