

The Possible Direct Correlation between Cognitive Impairment and Fear of Catching COVID-19 among Patients with Multiple Sclerosis

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Abstract

Objective: The prevalence of cognitive impairment in multiple sclerosis (MS) is significant and it is estimated that 40% to 70% of patients with MS suffer from this impairment. COVID-19 is also a new infectious disease. The symptoms of this disease, which include fever, shortness of breath, and cough, can be mild to severe and can even lead to death. Due to the use of immunosuppressive drugs by Patients with MS, they might be at greater risk of catching COVID-19. Thus, patients with MS may be more afraid of catching the virus. One of the important factors is the relationship between cognitive deficit and the increase in patients' fear of COVID-19. The aim of this study was to assess the relationship between fear of catching COVID-19 and cognitive impairment in patients with MS.

Method: This cross-sectional study was conducted at the MS Clinic, Sina hospital, Tehran University of Medical Sciences, Tehran, Iran. Our participants in this project were Patients with MS who were over 18 years old and had no history of other neurological and psychiatric diseases. In addition to obtaining demographic and clinical information, we measured the fear of catching the COVID 2019 via Fear of COVID-19 Scale (FCV-19S), which is 7-item questionnaire. We also used Multiple Sclerosis Neuro Psychological Screening Questionnaire (MSNQ) to assess memory and information processing speed in Patients with MS.

Results: After adjustment for age, gender, disease duration, highest level of education, MS type, and EDSS in linear regression model, as well as the MSNQ total score and fear score of catching coronavirus, the results demonstrated a significant positive correlation with P value of 0.00 and β : 0.024.

Conclusion: The present study showed a direct relationship between cognitive disorder and level of fear regarding COVID-19. Patients with more cognitive disorders were more afraid of COVID-19.

Key words: COVID-19; Cognitive Impairment; Fear; Multiple Sclerosis

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Multiple Sclerosis (MS) is an immune mediated disorder recognized by central nervous system involvement. The disease causes a range of symptoms, including motor, somatosensory, visual, cognitive, and psychiatric disorders (1). Different studies suggest that the prevalence of cognitive involvement in MS is significant and 40% to 70% of patients with MS suffer from these impairments (2). Even in the early stages of the disease, cognitive deficit can be seen in patients with MS (3). Physical symptoms of the disease are not an accurate predictor of cognitive impairment in Patients with MS. For example, patients suffering from severe physical symptoms may have fewer complaints of cognitive impairment or, conversely, patients with severe cognitive problems may have fewer physical symptoms. (4). Attention, memory, visual abilities, speed of information processing and executive functions are most significant cognitive abilities that are commonly involved in patients with MS (5).

Meanwhile, COVID-19 is a new infectious disease that originated in Wuhan, China, in early December 2019 and spread rapidly around the world in late January 2020. The symptoms of this disease can be mild to severe and can even lead to death. The most common symptoms include fever, cough, and shortness of breath, which may appear 2 to 14 days after exposure to the virus (6). Based on available data, the elderly and people with underlying and chronic medical conditions may be at greater risk for severe complications of COVID-19 (7).

Given the immunosuppressive effects of some MS medications, patients are possibly at higher risk of infections. Thus, the fear and anxiety of coronavirus is more common among them. Fear of illness or health anxiety is a complex condition that includes symptoms of distress psychological, physical arousal, cognitive errors, avoidance, and other defensive behaviors (8). With the spread of COVID-19 in the world, in addition to the physical, social, and economic problems associated with it, many people are suffering from many psychological pressures, such as anxiety, depression, insomnia, despair, and fear of getting infected (9, 10). Considering the possible side-effects of medications, patients with MS are more afraid of catching COVID-19. Thus, it is very important for them to be able to overcome this fear and find ways to adapt to it. Cognitive impairment in patients with MS is 1 of the issues that can cause problems in adapting to existing conditions and may lead to more anxiety and fear. Accordingly, the aim of this study was to investigate the relationship between fear of catching COVID-19 and cognitive impairment in patients with MS.

Materials and Methods

Participants

This cross-sectional study was conducted at the MS Clinic, Sina hospital, Tehran University of Medical Sciences, Tehran, Iran. Patients with MS whose disease diagnosis had been confirmed by a neurologist according to 2017 McDonald criteria for MS, participated in our study. Inclusion criteria included age 18 and above, no chronic psychiatric disorders such as bipolar disorder or psychosis, and no use of corticosteroids in the last 3 months. The participant's demographic and clinical information included age, gender, marital status, education, employment status, MS type, expanded disability status scale (EDSS), and duration of disease.

Ethical Consideration

In this study, we first provided the participants with the necessary explanations about the importance of implementing this research project and obtained their satisfaction to participate in this research project. Then, the patients were given a written consent form before the main questionnaires.

Data Collection Tools

FCV-19S

The Fear of COVID-19 Scale (FCV-19S) is a 7-item unidimensional tool with strong psychometric properties developed by Ahorsu et al (10). This instrument has validity and reliability in measuring the fear of COVID-19 across the general population. The minimum possible score for each question is 1 and the maximum is 5. By collecting the scores of each question, the total score can be calculated. A higher score indicates that the patient is more fearful of the corona virus .

MSNQ

Multiple Sclerosis Neuro Psychological Screening Questionnaire (MSNQ) is a brief self-administered test with 15 questions that reflect the neuropsychological ability during activities of daily living. MSNQ is a cost-effective assessment tool to identify cognitive impairment in patients with multiple sclerosis (MS). The questions in this questionnaire measure information processing speed and memory in less than 5 minutes. In 2003, Benedict et al designed this questionnaire to identify cognitive impairment early in patients with MS within the shortest time and cost-effectively with also acceptable validity and reliability. Each question has 5 options: never, rarely, sometimes, often, and always. The score on each question can range from 0 to 4. The maximum score of the patient in this questionnaire can be 60, with higher total scores obtained by the patient indicating more cognitive impairment (11).

Unfortunately, this questionnaire has not been standardized in Iran, but from this questionnaire with Persian translation, several good Iranian researches have been done (12-14). We have used this translation in our study.

Data Analysis

Qualitative and quantitative data were presented as number (percentage) and mean (standard deviation), respectively. The differences of MSNQ total score and fear score between the 2 subgroups of qualitative data were analyzed using independent samples t test; in case of data with more than 2 subgroups, 1-way ANOVA test was used. The correlation between MSNQ total score or fear score and age, highest level of education, EDSS, and disease duration was assessed by Pearson correlation test. In order to evaluate the association between MSNQ total score and fear of catching coronavirus, linear regression model was conducted while adjusting for age, gender, disease duration, highest level of education, MS type, and EDSS.

Results

Study participants included 186 patients with MS with the mean age of 34.38 (8.33) years. Superficially, 143 (76.9%) patients were women, 93 (50.0%) of them were married, and 105 (56.5%) were unemployed. The largest percentage of participants had relapsing-remitting MS (RRMS) diagnosis (109; 58.6%), followed by secondary-progressive MS (SPMS) ([43; 23.1%) and

primary-progressive MS (PPMS) ([11; 5.9%). The mean EDSS and disease duration of participants were 2.66 (1.84) and 7.72 (5.31) years, respectively (Table 1).

There was a significant difference in score of fear of catching coronavirus between females and males ($P = 0.02$). Female participants reported higher fear of catching coronavirus (18.28 (6.28) vs 15.35 (4.74)). The MSNQ total score was significantly different in various types of MS ($P = 0.00$). RRMS patients had 5.84 higher mean score of MSNQ compared to SPMS patients. There was no other significant difference in MSNQ or fear score between subgroups of gender, marital status, employment status, and MS type (Table 2).

A direct significant correlation was found between MSNQ total score with EDSS ($P = 0.01$; $r = 0.18$) and disease duration ($P = 0.02$; $r = 0.18$) of participants. However, the correlation between MSNQ and age or highest level of education was not significant (Table 3).

After adjustment for age, gender, disease duration, highest level of education, MS type, and EDSS in linear regression model, the MSNQ total score and fear score of catching coronavirus revealed a significant positive correlation with P value of 0.00 and β : 0.024 (Table 4 and Figure 1).

Table 1. Demographic and Clinical Characteristics of Patients with MS

Variables	Cases (n=186)	
Age* (years old)	34.38 (8.33)	
Female gender ^{&}	143 (76.9%)	
Marital status ^{&}	Married	93 (50.0%)
	Single	81 (43.5%)
Highest level of education*(years old)	15.22 (2.59)	
Employment status ^{&}	Employed	70 (37.6%)
	Unemployed	105 (56.5%)
MS type ^{&}	RRMS	109 (58.6%)
	SPMS	43 (23.1%)
	PPMS	11 (5.9%)
EDSS*	2.66 (1.84)	
Disease duration* (years)	7.72 (5.31)	

n: number of participants; SD: standard deviation; MS: Multiple sclerosis; RRMS: Relapsing-remitting MS; PPMS: Primary progressive MS; SPMS: Secondary progressive MS; EDSS: Expanded disability status scale

*Data are presented as mean (SD)

[&]Data are presented as n (%)

Table 2. MS Patients' MSNQ Total Score and Fear of Catching the Coronavirus Difference Among Subgroups of Qualitative Variables

Variable	MSNQ Total Score	Fear of Catching the Coronavirus
Gender	Female	16.87 (10.69)
	Male	17.66 (11.41)
	P value [§]	0.72
Marital status	Married	17.71 (11.71)
	Single	16.15 (9.62)
	P value [§]	0.35
Employment status	Employed	15.50 (8.97)
	Unemployed	17.90 (11.74)
	P value [§]	0.13
MS type	RRMS	15.13 (8.95)
	SPMS	20.98 (13.38)
	PPMS	19.09 (12.88)
	P value ^{&}	0.00*

MS: Multiple Sclerosis; MSNQ: Multiple Sclerosis Neuropsychological Questionnaire
Data are presented as mean (SD)

[§] Independent samples t-test; [&] One-way ANOVA

*The difference of MSNQ score between RRMS and SPMS was significant with P value=0.00 and mean difference=5.84.

Table 3. The Correlation between MSNQ Total Score and Fear of Catching the Coronavirus among MS Patients with Quantitative Data

Variable	MSNQ Total Score	Fear of Catching the Coronavirus
Age	0.88 (0.01)	0.41 (-0.06)
Highest level of education	0.15 (-0.11)	0.13 (-0.12)
EDSS	0.01 (0.18)	0.77 (0.02)
Disease duration	0.02 (0.18)	0.70 (0.03)

MS: Multiple Sclerosis; MSNQ: Multiple Sclerosis Neuropsychological Questionnaire

P values were calculated using Pearson correlation test

Data are presented as p value (r)

Table 4. The Association between MSNQ Total Score and Fear of Catching the Coronavirus among Patients with MS

Variable	MSNQ	β
Fear of catching coronavirus among Patients with MS	0.00*	0.24

MS: Multiple Sclerosis; MSNQ: Multiple Sclerosis Neuropsychological Questionnaire

*P value: was calculated using linear regression model adjusted for age, gender, disease duration, highest level of education, MS type and Expanded disability status scale.

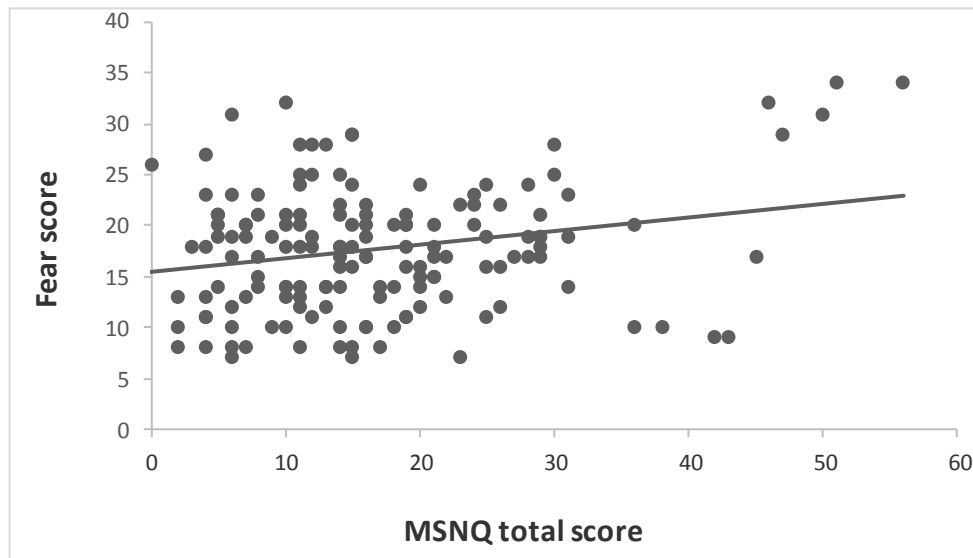


Figure 1. The Association between Multiple Sclerosis Neuropsychological Questionnaire (MSNQ) Total Score and Fear of Catching the Coronavirus among Multiple Sclerosis (MS) Patients: Fear of Coronavirus and MSNQ Total Score Showed a Significant Direct Association, Where Patients with MS with a Higher MSNQ Score Had a Greater Fear for Catching Coronavirus.

Discussion

The present study revealed a direct relationship between cognitive disorder and level of fear regarding COVID-19. Patients with more cognitive disorders were more afraid of COVID-19. Cognitive disorders are a common manifestation in Patients with MS, and according to statistics, 40% to 70% of these patients develop cognitive disorder (15). Cognitive deficits could appear in any stage of the disease (16). These deficits can affect different aspects of patients' function, including employment, daily activity, and social performance (17). Therefore, these cognitive disorders can affect various aspects of their lives (18). One problem is ineffective coping when facing problems. Coping strategies are of great importance in patients' adjustment to the problems that can arise in the course of a chronic illness (19). However, these coping mechanisms can develop problems due to the pathophysiological nature of the disease itself (20). Coping mechanisms are part of cognitive skills that can be impaired along with other cognitive aspects of MS. Studies have shown an association between cognitive disorder and coping mechanisms (21).

A study conducted by Goretti et al (2010) on 63 patients indicated a direct relationship between cognitive disorders, especially with respect to sustained attention, aspects of executive function, and the effective coping rate in these patients (22).

In the study by Calandri et al (2017), 102 patients with relapsing-remitting MS were examined and their coping strategies (problem-solving, emotional release, and avoidance) were assessed. The study found that the better the mental health of the patient, the better he/she

functions in mechanisms such as coping, including problem-solving, emotional release, and avoidance (23). These studies may justify our findings. They show that coping disorders are not only present in patients with MS, but can also be directly related to a person's mental health. It is clear that as the degree of adjustment and coping of patients with the problems increases, their fear and panic will decrease, as they know that they can handle the situation. It seems that cognitive disorder actually makes these coping mechanisms ineffective, and thus the patients get more frightened from the current situation. COVID-19 has resulted in high level of anxiety, depression, and other psychological disorders (24). Many researches have been done on psychiatric disorders caused by the COVID-19 worldwide. In Saudi Arabia, the results of a study showed that the general population has been experiencing moderate to severe psychological problems since this pandemic (25). A Spanish study has confirmed these findings, especially among women and young people who are considered as high-risk patients for COVID-19 (26).

COVID-19 is a problem for everyone, especially those who are more susceptible to infections. MS itself can increase the possibility of developing infections (27). Also, a group of drugs used in MS that suppress the immune system increase the risk of developing or exacerbating COVID-19 in these patients (28). Thus, if a patient could not adapt to the current condition via relying on health care recommendations and using cognitive abilities, he/she would be more afraid of this problem.

The next issue that justifies our findings is the relationship between cognitive disorder and anxiety.

Various studies have shown the effect of anxiety on cognitive abilities. Anxiety can exacerbate individuals' cognitive problems (29). This has also been observed in MS. A study on 141 patients proved that anxiety could directly affect the speed of information processing in patients with MS (30).

Another study on 111 patients demonstrated a direct relationship between anxiety and cognitive disorder in patients with MS (31).

COVID-19 also causes significant anxiety in patients with MS. A study on 33 patients with MS indicated that these patients suffered from high levels of anxiety during coronavirus disease (32). This high anxiety can cause cognitive disorder in these patients (33). In Italy, Francesco Motoles et al conducted a study and demonstrated that patients with MS had more psychological symptoms than the control group in face of COVID-19 (34). In another study with 115 patients with MS, 33 MS caregivers and 129 healthy controls, it was found that patients with MS are more anxious, stressed, and depressed compared to the other 2 groups during COVID-19 pandemic (35).

All these can justify the current findings.

Limitation

The present study had some limitations, the most important of which was the lack of a healthy control group. It is recommended to evaluate and compare the healthy control groups in future studies. Radiological evidence can also help improve our understanding of the findings.

Conclusion

Considering the high prevalence of cognitive dysfunction in patients with MS, this study indicated a direct relationship between cognitive impairment and level of fear catching COVID-19. Patients with MS and with more cognitive deficit were more afraid of COVID-19. Therefore, cognitive rehabilitation should be considered as a potential treatment to reduce this anxiety.

In addition, a combination of cognitive rehabilitation, exercise, and relaxation techniques can be used to reduce cognitive disorders and decrease anxiety and stress in patients, especially during this pandemic.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

References

1. Brassington JC, Marsh NV. Neuropsychological aspects of multiple sclerosis. *Neuropsychol Rev.* 1998;8(2):43-77.
2. McIntosh-Michaelis SA, Roberts MH, Wilkinson SM, Diamond ID, McLellan DL, Martin JP, et al. The prevalence of cognitive impairment in a community survey of multiple sclerosis. *Br J Clin Psychol.* 1991;30(4):333-48.
3. Grant I, McDonald WI, Trimble MR. Neuropsychological impairment in early multiple sclerosis. In: Jensen K, Knudsen L, Stenager E, Grant I (eds) *Mental disorders and cognitive deficits in multiple sclerosis.* London: Libbey; 1989:17-26.
4. Wishart H, Sharpe D. Neuropsychological aspects of multiple sclerosis: a quantitative review. *J Clin Exp Neuropsychol.* 1997;19(6):810-24.
5. Denney DR, Sworowski LA, Lynch SG. Cognitive impairment in three subtypes of multiple sclerosis. *Arch Clin Neuropsychol.* 2005;20(8):967-81.
6. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *Jama.* 2020;323(11):1061-9.
7. Haines S, Caccamo A, Chan F, Galaso G, Catinchi A, Gupta PK. Practical considerations when performing neurodiagnostic studies on patients with COVID-19 and other highly virulent diseases. *Neurodiagn J.* 2020; 60(2):78-95.
8. Özdin S, Bayrak Özdin Ş. Levels and predictors of anxiety, depression and health anxiety during COVID-19 pandemic in Turkish society: The importance of gender. *Int J Soc Psychiatry.* 2020;66(5):504-11.
9. Xiang Y-T, Yang Y, Li W, Zhang L, Zhang Q, Cheung T, et al. Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. *The Lancet Psychiatry.* 2020;7(3):228-9.
10. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet.* 2020;395(10227):912-20.
11. Ahorsu DK, Lin CY, Imani V, Saffari M, Griffiths MD, Pakpour AH. The Fear of COVID-19 Scale: Development and Initial Validation. *Int J Ment Health Addict.* 2020:1-9.
12. Owji M, Sahraian MA, Bidadian M, Ghadiri F, Etesam F, Azimi A, et al. Evaluating the relationship between emotional intelligence and cognitive disorders in patients with Multiple Sclerosis. *Iran J Neurol.* 2018;17(2):78-81.
13. Shahrababak M. COMPARING NEURAL FATIGUE BETWEEN FOUR TYPES OF PATIENTS WITH MULTIPLE SCLEROSIS. *Studies in Medical Sciences.* 2012;23(2):164-71.
14. Mousavi S, Zare H, Etemadifar M, Taher Neshatdoost H. Memory rehabilitation for the

- working memory of patients with multiple sclerosis (MS). *J Clin Exp Neuropsychol*. 2018;40(4):405-10.
15. Benedict RH, Munschauer F, Linn R, Miller C, Murphy E, Foley F, et al. Screening for multiple sclerosis cognitive impairment using a self-administered 15-item questionnaire. *Mult Scler*. 2003;9(1):95-101.
 16. Haines S, Caccamo A, Chan F, Galaso G, Catinchi A, Gupta PK. Practical considerations when performing neurodiagnostic studies on patients with COVID-19 and other highly virulent diseases. *Neurodiagn J*. 2020;60(2):78-95.
 17. Rao SM, Leo GJ, Ellington L, Nauertz T, Bernardin L, Unverzagt F. Cognitive dysfunction in multiple sclerosis. II. Impact on employment and social functioning. *Neurology*. 1991;41(5):692-6.
 18. DeLuca J, Chiaravalloti ND, Sandroff BM. Treatment and management of cognitive dysfunction in patients with multiple sclerosis. *Nat Rev Neurol*. 2020;16(6):319-32.
 19. Moghadasi AN, Pourmand S, Sharifian M, Minagar A, Sahraian MA. Behavioral Neurology of Multiple Sclerosis and Autoimmune Encephalopathies. *Neurol Clin*. 2016;34(1):17-31.
 20. Bond MR. Psychological issues in cancer and non-cancer conditions. *Acta Anaesthesiol Scand*. 2001;45(9):1095-9.
 21. Rabinowitz AR, Arnett PA. Coping in neurological disorders. In *Positive Neuropsychology*. Springer, New York, NY; 2013:13-24.
 22. Goretti B, Portaccio E, Zipoli V, Razzolini L, Amato MP. Coping strategies, cognitive impairment, psychological variables and their relationship with quality of life in multiple sclerosis. *Neurol Sci*. 2010;31(Suppl 2):S227-30.
 23. Calandri E, Graziano F, Borghi M, Bonino S. Improving the quality of life and psychological well-being of recently diagnosed multiple sclerosis patients: preliminary evaluation of a group-based cognitive behavioral intervention. *Disabil Rehabil*. 2017;39(15):1474-81.
 24. Serafini G, Parmigiani B, Amerio A, Aguglia A, Sher L, Amore M. The psychological impact of COVID-19 on the mental health in the general population. *QJM*. 2020;113(8):531-7.
 25. Alkhamees AA, Alrashed SA, Alzunaydi AA, Almohimeed AS, Aljohani MS. The psychological impact of COVID-19 pandemic on the general population of Saudi Arabia. *Compr Psychiatry*. 2020;102:152192.
 26. Rodríguez-Rey R, Garrido-Hernansaiz H, Collado S. Psychological Impact and Associated Factors During the Initial Stage of the Coronavirus (COVID-19) Pandemic Among the General Population in Spain. *Front Psychol*. 2020;11:1540.
 27. Luna G, Alping P, Burman J, Fink K, Fogdell-Hahn A, Gunnarsson M, et al. Infection Risks Among Patients With Multiple Sclerosis Treated With Fingolimod, Natalizumab, Rituximab, and Injectable Therapies. *JAMA Neurol*. 2020;77(2):184-91.
 28. Giovannoni G, Hawkes C, Lechner-Scott J, Levy M, Waubant E, Gold J. The COVID-19 pandemic and the use of MS disease-modifying therapies. *Mult Scler Relat Disord*. 2020;39:102073.
 29. Lester K, Stepleman L, Hughes M. The association of illness severity, self-reported cognitive impairment, and perceived illness management with depression and anxiety in a multiple sclerosis clinic population. *J Behav Med*. 2007;30(2):177-86.
 30. Vissicchio NA, Altaras C, Parker A, Schneider S, Portnoy JG, Archetti R, et al. Relationship Between Anxiety and Cognition in Multiple Sclerosis: Implications for Treatment. *Int J MS Care*. 2019;21(4):151-6.
 31. Marrie RA, Patel R, Figley CR, Kornelsen J, Bolton JM, Graff L, et al. Diabetes and anxiety adversely affect cognition in multiple sclerosis. *Mult Scler Relat Disord*. 2019;27:164-70.
 32. Naser Moghadasi A. One Aspect of Coronavirus disease (COVID-19) Outbreak in Iran: High Anxiety among MS Patients. *Mult Scler Relat Disord*. 2020;41:102138.
 33. Haji Akhoundi F, Sahraian MA, Naser Moghadasi A. Neuropsychiatric and cognitive effects of the COVID-19 outbreak on multiple sclerosis patients. *Mult Scler Relat Disord*. 2020;41:102164.
 34. Motolese F, Rossi M, Albergo G, Stelitano D, Villanova M, Di Lazzaro V, et al. The Psychological Impact of COVID-19 Pandemic on People With Multiple Sclerosis. *Front Neurol*. 2020;11:580507.
 35. Talaat F, Ramadan I, Aly S, Hamdy E. Are multiple sclerosis patients and their caregivers more anxious and more committed to following the basic preventive measures during the COVID-19 pandemic? *Mult Scler Relat Disord*. 2020;46:102580.