Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Correspondence

Characteristics of COVID-19 disease in multiple sclerosis patients

Dear Editor

We read the study by Safavi et al. (2020) in a recent issue of Multiple Sclerosis and Related Disorders with great interest. They reported a cross-sectional study among multiple sclerosis (MS) patients to identify suspected COVID-19 cases and the factors associated with it. They suggested that most MS patients have a mild course of CVID-19 infection.

The novel coronavirus disease (COVID-19) is in the pandemic stage with significant concerns for individuals with an underlying health-related condition (Richardson et al., 2020). Multiple sclerosis (MS) patients on immunosuppressive/immunomodulatory disease modifying therapies (DMT) are generally at increased risk of infections raising concern related to different risk or outcome in case of infection with COVID-19. It is still uncertain, however, whether immunosuppressive agents increase or decrease the severity of COVID-19 infection in MS patients (Ritchie and Singanayagam, 2020). So, we designed this study to assess characteristics and outcome of COVID-19 disease in our MS patients.

Our MS clinic is a major tertiary referral center affiliated with Isfahan University of Medical Sciences, Isfahan, Iran. We contacted our MS patients from April 13 to May 13 via their mobile or/and cell phones. We contacted once again (about one week later) to patients who didn't not respond to the first attempt to contact them. We asked about the presence of COVID-19 symptoms, admission in the hospital, and use of diagnostic procedures related to COVID-19 (chest computed tomographic [CT] scan and transcription polymerase chain reaction [RT-PCR]). We evaluated the medical records for diagnosis confirmation of COVID-19 infection (chest CT or RT-PCR). The severity of COVID-19 infections were classified as asymptomatic, mild (no need for hospitalization), moderate (reporting shortness of breath and requiring hospitalization), severe (reporting pneumonia), and critical (need to admission in intensive care). The patients' contact information, demographic (age, gender), and clinical features (course of MS, severity of the disease, duration of disease, and DMT) were extracted from our database (it was described previously) (Mirmosayyeb et al., 2020).

Out of 743 contacted cases, 543 answered. The mean (standard deviation [SD]) age was 35.28 (8.11) years and 81.2% (n = 441) of patients were female. The median (interquartile range [IQR]) for EDSS score and disease duration were 0.0 (0.0, 2.0) and 7.0 (4.5, 10.0), respectively. Fifty-six (10.3%) patients were on no disease modifying therapy, 296 (54.4%) interferon beta, 35 (6.5%) glatiramer acetate, 55 (10.1%) fingolimod, 27 (5.1%) dimethyl fumarate, 20 (3.7%) teriflunomide, 42 (7.7%) rituximab, and 12 (2.2%) natalizumab. In terms of clinical course of the disease, 435 (80.1%) patients had relapsing-remitting (RR) course, 43 (7.9%) secondary-progressive, 12 (2.2%) primary-progressive, and 53 (9.8%) clinically isolated syndrome.

Of 543 patients, 66 cases reported symptoms suspicious for COVID-19 infection including dyspnea in 33, (50.0%), sore throat in 30 (50.0%) anosmia or dysgeusiain 25 (37.9%), cough in 20 (30.3%), gastrointestinal symptoms in 19 (28.8%), and fever in 10 (16.7%). Twelve patients performed chest computed tomography (CT) scan or were tested for COVID-19 (RT-PCR). COVID-19 disease was diagnosed in 9 patients (7 patients based on typical chest CT findings and 2 based on upper respiratory tract RT-PCR), 4 patients were on interferon beta, 2 on no DMT, and one patient on each of the following: fingolimod, glatiramer acetate, and rituximab. Seven patients had a mild course of infection, one patient (treated with fingolimod) had severe course, and one patient (treated with rituximab) had a critical course resulting in patient demise (Table 1).

Although limited by small number of subjects our study on effect of DMTs on the COVID-19 disease outcome in our survey appears to be consistent with previous studies (Sormani, 2020;Barzegar et al., 2020;Montero-Escribano et al., 2020). It seems that patients on treatment with interferon beta or glatiramer acetate developed mild CIVID-19 without severe respiratory and neurological complications. The effect of fingolimod on COVID-19 is complex. Although fingolimod is currently being investigated as a potential treatment for COVID-19 infection (ClinicalTrials.gov identifier NCT04280588), some case studies, as well as single case suggests a more severe COVID-19 infection in fingolimod-treated MS patients (Barzegar et al., 2020;Valencia-Sanchez and Wingerchuk, 2020;Foerch et al., 2020). Some studies proposed that anti-CD20 monoclonal antibodies such as ocrelizumab and rituximab may have protective role against COVID-19 disease (Ghajarzadeh et al., 2020;Novi et al., 2020;Montero-Escribano et al., 2020). However, Safavi et al. suggested that anti-CD20 monoclonal antibodies can increase the susceptibility of MS patients to COVID-19 infection (Safavi et al., 2020). In our study, one patient treated with rituximab developed severe COVID-19 disease and succumbed to the infection.

Our study has some limitations. The study design was not appropriate to assess the prevalence of COVID-19 disease in MS patients. However, explaining this issues is not in the scope of this study. There is the possibility that the asymptomatic patients or cases with mild disease-related symptoms had COVID-19 infection, but they didn't visit a doctor or undergo additional assessment. On the other hand, it is possible that some patients with severe or critical course of disease could not respond to our attempts to contacts them. Therefore, the effect of specific DMTs on the severity of COVID-19 should be interpreted cautiously. Notwithstanding these limitations, the study suggests that most MS patients developed uncomplicated COVID-19 infection. Further work is needed to understand the implications of specific DMTs on COVID-19 disease fully.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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Table 1
Description of confirmed cases.

	Age	Sex	Disease duration, y	MS course	Comorbidity	More recent EDSS	DMTs	Treatment duration	COVID-19 symptoms	Severity of COVID-19	Outcomes
1	36	Female	6	RRMS	Hashimoto's disease	0	Fingolimod	6	Fever, dyspnea, Sore throat, diarrhea	Severe	Recovering
2	39	Female	14	RRMS	Epilepsy	0	Interferon beta- 1b	5	Fever, dyspnea	Mild	Recovered
3	37	Male	10	RRMS	–	0	Interferon beta- 1a	10	Cough, dyspnea	Mild	Recovered
4	50	Female	3	RRMS	Amnesia	0	Interferon beta- 1b	2	Cough	Mild	Recovered
5	46	Female	27	SPMS	–	8	No treatment	–	Fever, Sore throat	Mild	Recovered
6	33	Female	7	RRMS	–	0	Glatiramer acetate	5	Fever, dyspnea	Mild	Recovered
7	34	Female	1	CIS	–	0	No treatment	–	Sore throat, anosmia, diarrhea	Mild	Recovered
8	29	Female	7	RRMS	–	2	Interferon beta- 1b	3	Cough, dyspnea	Mild	Recovered
9	43	Female	18	SPMS	Hypothyroidism	6.5	Rituximab	4	Fever, cough, dyspnea	Critical	Death

Note: y: year, DMTs: disease-modifying therapies, EDSS: Expanded Disability Status Scale, RRMS: relapsing-remitting MS (RR) SPMS: secondary-progressive MS, PPMS: primary-progressive MS, CIS: clinically isolated syndrome.

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