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Clinical study

Prevalence, severity, outcomes, and risk factors of COVID-19 in multiple sclerosis: An observational study in the Middle East

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ABSTRACT

A cross-sectional hospital records-based study was conducted to evaluate the prevalence, severity, outcomes, and identify demographic and clinical risk factors of coronavirus disease (COVID-19) in patients with MS. The study was conducted at multiple clinics in Oman, Kuwait, and the United Arab Emirates (UAE) from March 2020 to February 2021. The association of patient demographics, MS disease characteristics, and use of disease-modifying therapies with outcomes of COVID-19 illness were evaluated using odds ratio. A total of 134 MS patients with COVID-19 (prevalence rate of 3.7%) having a median age of 35.5 years were analyzed in the study. A majority (126 [94.0%]) of patients had mild COVID-19 illness and 122 (91.0%) made a full recovery, while 1 (0.7%) patient died. The median EDSS score reported in the study was low (1.0). Univariate regression analysis showed high EDSS scores, progressive MS disease, and use of anti-CD20 therapy such as rituximab as risk factors for moderate to severe COVID-19 requiring hospitalization. Comorbidities were associated with a higher risk of non-recovery from COVID-19 in both univariate and multivariate analyses. Age, sex, smoking history, and duration of MS did not show a significant association with severity or adverse COVID-19 disease outcome. Identification of risk factors can aid in improving the treatment and monitoring of pwMS and COVID-19.

1. Introduction

The emergence of the coronavirus disease 2019 (COVID-19) pandemic has raised substantial concerns regarding its impact on populations affected by auto-immune diseases. Multiple sclerosis (MS), an autoimmune neurodegenerative disorder of the central nervous system, is being studied for its correlation with COVID-19 [1–3].

MS patients are considered a high-risk population for COVID-19, due to the high prevalence of disability and widespread use of immunosuppressive disease-modifying therapy (DMT) [4]. Among MS patients, those who belong to an older age group or have a more progressive form of the disease have been shown to develop complications in addition to respiratory tract symptoms during a COVID-19 infection [5].

Indeed, MS patients are found to be at a greater risk of exacerbations and relapses due to this viral infection [4,6].

The exact relationship between COVID-19 and MS is still unclear. There are contradictory reports regarding the relation between COVID-19 severity/risk and immunosuppressive medications. The primary aim of our study was to evaluate the prevalence, severity, and outcomes of COVID-19 and to identify demographic and clinical risk factors in pwMS from three countries in the Middle East, namely Oman, Kuwait, and the United Arab Emirates.

Abbreviations: coronavirus disease 2019, COVID-19; United Arab Emirates, UAE; Multiple Sclerosis, MS; Disease-modifying therapy, DMT.

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2. Methodology

This was a retrospective, cross-sectional, observational study conducted in one MS clinic in Oman (Khaoula hospital, Muscat), three clinics in Kuwait (Ibn Sina hospital, Amiri hospital, Jahra hospital), and one clinic in the United Arab Emirates (Rashid hospital, Dubai). The study was conducted from March 2020 to February 2021. The data was collected from hospital records. MS was diagnosed according to the revised 2010 McDonald criteria. Before the application of these criteria, the diagnosis of MS was based on previously accepted diagnostic criteria. Demographic data including patient's age, gender, date of MS onset (date of first clinical event) and diagnosis, presentation at onset, disease duration (time in years since the first clinical event), type of MS, expanded disability status scale (EDSS) scores, and the use of disease-modifying therapies (DMTs) was extracted from the records. Data of MS patients who were diagnosed with COVID-19 were also extracted from the records. The data were confirmed by either contacting patients by phone or when they visited the clinics for their routine scheduled visits or due to their concern about their DMTs. The patients were asked to complete a self-administered survey sent via email or filled at the clinic that retrospectively collected details of the course of their COVID-19 illness such as symptoms, investigations performed, and requirement of hospitalization. Information was also obtained from their medical records. The severity of COVID-19 was categorized as mild (not requiring hospitalization), moderate (hospitalized), and severe (requiring intensive care). MS patients older than 18 years of age with the following diagnoses were included: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), or primary progressive MS (PPMS). Diagnosis of COVID-19 was done either through PCR, serology, or chest imaging. The endpoints for this study were the prevalence rate of COVID-19 in the studied MS cohort and measures of association of COVID-19 severity, hospitalization, and outcome with key demographic and clinical variables of MS.

2.1. Statistical analysis

The prevalence of COVID-19 in MS patients was estimated by dividing the number of confirmed COVID-19 cases in the cohort by the total number of MS patients as per the hospital records. This was compared to the COVID-19 prevalence in the general population of that country/city. Descriptive statistics were used to compare demographics, disease characteristics, and the severity of MS. Univariate logistic regression models were performed on identified variables, namely, COVID-19 outcome (recovery or non-recovery), COVID-19 severity (mild or non-mild [moderate/severe]), and hospital admission (Yes/No) to assess their association with covariates such as age (<45 or ≥ 45), gender, smoking, EDSS score (0–4.5 or 5–9.5), comorbidities, MS diagnosis (RRMS/CIS or progressive [SPMS/PPMS]), MS disease duration, (≤ 10 years or >10 years), On/Off DMTs, duration of current DMT (≤ 5 years or >5 years), and type of DMT. Pearson's chi-squared test, Fisher's exact test, Student's *t*-test, and the Mann–Whitney *U* test were used for comparisons as appropriate. Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated with a logistic regression model. A multivariate logistic regression analysis was performed using the same variables used in the univariate analysis.

3. Results

As of February 26, 2021, a total of 3624 pwMS were reported in the records of previously specified clinics and hospitals of Kuwait (2334), Dubai, UAE (1050), and Oman (240). Of these, 134 patients (Kuwait: 92 (3.9%), Dubai, UAE: 36 (3.4%), Oman: 6 (2.5%)) had tested positive for COVID-19 with an overall prevalence rate of 3.7% in the total analyzed MS population. Demographics and clinical characteristics of the cohort of 134 patients are presented in Table 1. Ninety-eight patients (73.1%) were female, with the median age of the cohort being 35.5 years, and a mean (SD) disease duration of 8.83 (6.0) years. Non-smokers accounted for 88.8% of the total cohort with 91% reporting no morbid obesity. Relapsing-remitting MS accounted for 86.6% of all types of MS patients analyzed in the cohort. The majority (90.3%) had no comorbidities. Hypertension/cardiovascular disease (5 [3.7%]), malignancy in remission (2 [1.5%]), renal disease (1 [0.7%]), and liver disease (1 [0.7%]) were few co-morbidities reported. The median EDSS score (1.0) was in the range of 0–4.5 for 127 (94.8%) patients while 7 (5.2%) patients reported a score in the range of 5–9.5 [Table 1].

A total of one twenty-eight (95.5%) patients were diagnosed by polymerase chain reaction, four (3.0%) patients had a positive serology, and one (0.7%) patient had chest imaging showing typical lesions for COVID-19, while the diagnostic methodology was unknown for one patient. Overall, 127 (94.8%) patients were on DMTs; the four most common DMTs being used were fingolimod (26.9%), ocrelizumab (15.7%), and rituximab and natalizumab (10.4% each), with 5.2% reporting no MS treatment [Table1]. The majority (94.0%) of patients reported mild COVID-19, 3.7% reported moderate severity of infection, while 1.5% reported severe COVID-19, and one (0.7%) patient was in a life-threatening condition. Patients presented with typical symptoms for COVID-19. Notably, fever (temperature more than 38 °C), fatigue, dry cough, and sore throat were more frequent in patients, along with anosmia. Eight (6.0%) patients were hospitalized; of these, 3 (2.2%) were in the intensive care unit and 2 (1.5%) required ventilator support. In evaluating COVID-19 outcome in terms of recovery and non-recovery, we found that 122 (91.0%) patients recovered, and one (0.7%) patient died. At the time of writing this manuscript, 9 (6.7%) patients had an ongoing COVID-19 infection, and the outcome was unknown in 2 (1.5%) patients.

To estimate the risk factors associated with COVID-19 severity, hospitalization, and outcomes, we calculated the odds ratios (ORs) from univariate and multivariate logistic regression models. Since all moderately ill patients were also hospitalized, the statistical results of the association of various covariates were similar for both, hospitalization, and COVID-19 severity. Univariate analysis showed a statistically significant higher risk of moderate/severe COVID-19 severity and hospitalization in patients with higher EDSS scores (OR: 8.06; 95% CI 1.290–50.453, $p = 0.026$) and in patients with progressive disease (OR 8.85; 95% CI 1.786–43.855, $p = 0.008$) [Table 2]. The association between age and COVID-19 severity was found to be non-significant ($p = 0.082$) with a 3.8 times higher risk of moderate/severe disease and hospitalization in patients aged 45 and above.

The presence of at least one comorbidity was significantly associated with a 5.3 times higher risk of non-recovery from COVID-19 (95% CI 1.174–24.225, $p = 0.03$) [Table 3]. Univariate analysis of DMT use showed a statistically significant higher risk of developing moderate/severe COVID-19 and consequent hospitalization in patients on rituximab (6.2 times higher risk) (95% CI 1.319–29.830, $p = 0.021$). However, patients on other DMTs including ocrelizumab did not show an association with COVID-19 severity. The category of anti-CD20 therapy (rituximab and ocrelizumab combined data) showed significant association with COVID-19 severity (5.3 times higher risk) (95% CI 1.203–23.639, $p = 0.028$) [Table 4]. There was no association between DMT use and the outcome of COVID-19 ($p > 0.05$).

Multivariate regression analysis did not show a significant association of any of the covariates tested with the severity of COVID-19 or hospitalization [Table 5]. However, similar to univariate analysis, a significant association of non-recovery was found with the presence of comorbidities. There was a significant 1.5 times higher risk of non-recovery in patients with any comorbid condition, eliminating the effect of all other covariates (95% CI 1.073–2.134, $p = 0.018$) [Table 6].

4. Discussion

This hospital records-based observational study analyzed cohorts of MS patients from three clinics in Kuwait and one clinic each in UAE and

Table 1
The distribution of demographic and clinical variables for COVID-19 MS patients.

Demographic and Clinical Characteristics		N = 134
Age	Median	35.5
	Mean (SD)	36.1 (9.7)
	< 45	114
	≥ 45	20
Sex, n (%)	Male	36 (26.9)
	Female	98 (73.1)
Smoking, n (%)	Yes	15 (11.2)[a]
Obesity, n (%)	Yes	12 (9.0)[a]
Pregnancy, n (%)	Yes	2 (1.5)[a]
Comorbidities, n (%)	No	121 (90.3)
	CVS/HTN	5 (3.7)
	Malignancy in remission	2 (1.5)
	Renal function	1 (0.7)
	Liver disease	1 (0.7)
	Others	1 (0.7)
Diagnosis, n (%)	CIS	7 (5.2)
	RRMS	116 (86.6)
	SPMS	7 (5.2)
	PPMS	4 (3.0)
Disease Duration	Mean (SD)	8.83 (6.0)
	≤ 10 years	91 (67.9)
	> 10 years	43 (32.1)
On/Off DMT, n (%)	Off DMT	7 (5.2)
	On DMT	127 (94.8)
Current DMT, n (%)	No	7 (5.2)
	IFNB	12 (9.0)
	GA	1 (0.7)
	Teriflunomide	7 (5.2)
	DMF	11 (8.2)
	Fingolimod	36 (26.9)
	Natalizumab	14 (10.4)
	Alemtuzumab	4 (3.0)
	Ocrelizumab	21 (15.7)
	Rituximab	14 (10.4)
	Cladribine tablets	4 (3.0)
	Others	3 (2.2)
Duration of Current DMT, n (%)	≤ 5 years	109 (81.3)
	> 5 years	23 (17.2)
Diagnosis of COVID-19, n (%)	PCR	128 (95.5)
	Serology	4 (3.0)
	Typical chest imaging	1 (0.7)
COVID-19 Symptoms, n (%)	No	12 (9.0)
	Yes	122 (91.0)
Symptoms, n (%)	Fever	105 (78.4)
	Fatigue	86 (64.2)
	Dry cough	74 (55.2)
	Sore throat	70 (52.2)
	Anosmia	47 (35.1)
	Pain	22 (16.4)
	Pneumonia	6 (4.5)
	Diarrhea	8 (6.0)
Severity, n (%)[b]	Mild	126 (94.0)
	Moderate	5 (3.7)
	Severe	2 (1.5)
	Life threatening	1 (0.7)
Hospital Admission, n (%)	Yes	8 (6.0)
ICU Admission, n (%)	Yes	3 (2.2)[a]
Ventilator Required, n (%)	Yes	2 (1.5)
ECMO required, n (%)	Yes	1 (0.7)
	Unknown	2 (1.5)
COVID-19 Outcomes, n (%)	Ongoing	9 (6.7)
	Recovery	122 (91.0)
	Death	1 (0.7)
EDSS Score, n (%)	0–4.5	127 (94.8)
	5–9.5	7 (5.2)
EDSS Score, median		1.0
Country, n (%)	Kuwait	92 (68.7)
	Dubai	36 (26.9)
	Oman	6 (4.5)

CIS, clinically isolated syndrome; COVID-19, coronavirus disease 2019; CVS, cardiovascular system; DMF, dimethyl fumarate; DMT, disease modifying therapy; ECMO, extracorporal membrane oxygenation; EDSS, Expanded Disability Severity Scale; GA, glatiramer acetate; HTN, hypertension; ICU, intensive care unit; IFNB, interferon beta; MS, multiple sclerosis; PCR, polymerase chain reaction; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

[a] Contains some missing values.

[b] Severity definitions: mild- those not requiring hospitalization, moderate- those requiring hospitalization, severe- those requiring admission to intensive care unit, life-threatening- those whose COVID-infection was life-threatening.

Table 2
Summary of univariate logistic regression models for the COVID-19 MS patients in relation to COVID-19 severity.

Variables	Categories	Odds Ratio	95% CI		P-Value[a]
			Lower Bound	Upper Bound	
Age Group	≥ 45 < 45	3.847	0.842	17.587	0.082
Gender	Female Male	0.591	0.134	2.612	0.488
Smoker	Yes No	1.133	0.130	9.898	0.910
EDSS	High (5–9.5) Low (0–4.5)	8.067	1.290	50.453	**0.026**
Comorbidities	Any co-morbid condition No comorbidity	2.130	0.231	19.668	0.505
MS Diagnosis	Progressive disease (PPMS + SPMS) Non-progressive disease (RRMS + CIS)	8.850	1.786	43.855	**0.008**
Current DMT Duration	> 5 years ≤ 5 years	0.662	0.078	5.660	0.707
Disease Duration	> 10 years ≤ 10 years	1.290	0.294	5.65	0.736

CI, confidence interval; CIS, clinically isolated syndrome; COVID-19, coronavirus disease 2019; DMT, disease modifying therapy; EDSS, Expanded Disability Severity Scale; MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

[a] p value is significant at <0.05.

Oman for eleven months. The prevalence rate of COVID-19 (3.7%) in the analyzed MS cohort is marginally lower than the overall prevalence of COVID-19 in the general population of Kuwait (5.3%), Dubai (4.75%), and Oman (4.07%) [7]. A few similar studies investigating the effects of COVID-19 in MS patients have been reported in literature. A study early on in the pandemic carried out in Italy reported similar prevalence of COVID-19 among MS patients as in the general population [8]. Zabalza et al. reported on the incidence of COVID-19 in MS patients followed at a center in Barcelona, Spain. The incidence of confirmed COVID-19 among MS patients (6.3%) was found to be similar to that in the general population of the Catalan region of Spain (6.1%) [1]. Similarly, Sepulveda et al conducted a cross-sectional study to investigate the incidence of COVID-19 in a cohort of MS patients at a single center in Barcelona, Spain. The study found that the cumulative incidence of confirmed COVID-19 cases (1.27%) was similar to that of the general population (1.32%) [3]. The results of these studies corroborate our findings of similar or only slightly lower prevalence of COVID-19 in MS patients compared to that in the general population of that region or country.

The hospitalization rate (6.0%), the requirement of intensive care (2.2%), and the mortality rate (0.7%) in our cohort were low. It could be possible that the younger age (median age, 35.5 years) of the patients with no comorbidities being reported in a majority of them (90.3%) and their low physical disability status (median EDSS score 1.0) may have contributed to mitigating their COVID-19 course. The lower rates of

Table 3
Summary of univariate logistic regression models for the COVID-19 MS patients in relation to COVID-19 outcome.

Variables	Categories	Odds Ratio	95% CI		P-Value[a]
			Lower Bound	Upper Bound	
Age Group	≥ 45 < 45	1.156	0.234	5.715	0.859
Gender	Female Male	0.711	0.200	2.523	0.598
Smoker	Yes No	0.695	0.083	5.797	0.737
EDSS	High (5–9.5) Low (0–4.5)	1.758	0.194	15.949	0.616
Comorbidities	Any co-morbid condition No comorbidity	5.333	1.174	24.225	**0.030**
MS Diagnosis	Progressive disease (PPMS + SPMS) Non-progressive disease (RRMS + CIS)	2.511	0.476	13.247	0.278
On/Off DMT	On DMT Off DMT	0.569	0.063	5.163	0.616
Current DMT Duration	> 5 years ≤ 5 years	2.658	0.727	9.718	0.139
Disease Duration	> 10 years ≤ 10 years	2.297	0.695	7.594	0.173

CI, confidence interval; CIS, clinically isolated syndrome; COVID-19, coronavirus disease 2019; DMT, disease modifying therapy; EDSS, Expanded Disability Severity Scale; MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.
[a] p value is significant at <0.05.

Table 4
Summary of univariate logistic regression models for the current DMT use among the COVID-19 MS patients in relation to COVID-19 severity.

Variables[b]	Odds Ratio	95% CI		P-Value[a]
		Lower Bound	Upper Bound	
Fingolimod	0.371	0.044	3.129	0.362
Natalizumab	1.242	0.141	10.903	0.845
Ocrelizumab	1.877	0.352	10.002	0.461
Rituximab	6.273	1.319	29.830	**0.021**
Anti-CD20 (rituximab + ocrelizumab)	5.333	1.203	23.639	**0.028**

CD20, cluster of differentiate 20; COVID-19, coronavirus disease 2019; DMT, disease modifying therapy; MS, multiple sclerosis.
[a] p value is significant at <0.05.
[b] Four DMDs most commonly used by patients in the study have been listed over here. DMDs not listed in this table have a low number of patients and give skewed results.

hospitalization and deaths in our study are also similar to those reported in other studies that have a low percentage of confirmed cases of COVID-19 in MS patients. For example, a UK community-based study with 15.6% of confirmed cases of COVID-19 in MS patients reported 1.3% of hospitalizations and no deaths [9]; a European and US study with 17% of confirmed cases of COVID-19 in MS patients described 5.6% of hospitalizations and no deaths [10], and an Italian program with 24.5% of confirmed cases reported 4% of patients with mild disease and 2.1% of mortality [11]. In contrast, higher rates of hospitalization (21.0%–25.6%) were found in studies with a higher proportion of confirmed cases [5,12,13].

Clinical characteristics of COVID-19 in MS patients in our study do

Table 5
Summary of multivariate logistic regression models for the COVID-19 MS patients in relation to severity.

Variables	Categories	Odds Ratio	95% CI		P-Value[a]
			Lower Bound	Upper Bound	
Age Group	≥ 45 < 45	1.797	0.217	14.899	0.587
Gender	Female Male	0.520	0.075	3.629	0.509
Smoker	Yes No	0.728	0.052	10.297	0.815
EDSS	High (5–9.5) Low (0–4.5)	7.828	0.182	336.513	0.284
Comorbidities	Any co-morbid condition No comorbidity	1.218	0.751	1.977	0.424
MS Diagnosis	Progressive disease (PPMS + SPMS) Non-progressive disease (RRMS + CIS)	1.007	0.033	30.687	0.997
Current DMT Duration	> 5 years ≤ 5 years	1.100	0.099	12.246	0.938
Disease Duration	> 10 years ≤ 10 years	0.962	0.131	7.049	0.970

CI, confidence interval; CIS, clinically isolated syndrome; COVID-19, coronavirus disease 2019; DMT, disease modifying therapy; EDSS, Expanded Disability Severity Scale; MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.
[a] p value is significant at <0.05.

Table 6
Summary of multivariate logistic regression models for the COVID-19 MS patients in relation to COVID-19 outcome.

Variables	Categories	Odds Ratio	95% CI		P-Value[a]
			Lower Bound	Upper Bound	
Age Group	≥ 45 < 45	0.699	0.113	4.308	0.699
Gender	Female Male	0.564	0.125	2.536	0.455
Smoker	No Yes	0.408	0.038	4.382	0.46
EDSS	High (5–9.5) Low (0–4.5)	1.334	0.038	46.821	0.874
Comorbidities	Any co-morbid condition No comorbidity	1.513	1.073	2.134	**0.018**
MS Diagnosis	Progressive disease (PPMS + SPMS) Non-progressive disease (RRMS + CIS)	2.632	0.155	44.709	0.503
Current DMT Duration	> 5 years ≤ 5 years	3.295	0.689	15.751	0.135
Disease Duration	> 10 years ≤ 10 years	1.156	0.246	5.43	0.855

CI, confidence interval; CIS, clinically isolated syndrome; COVID-19, coronavirus disease 2019; DMT, disease modifying therapy; EDSS, Expanded Disability Severity Scale; MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.
[a] p value is significant at <0.05.

not differ greatly from those in the general population and are similar to those seen in other published articles [14–16]. In our cohort, fever, fatigue, dry cough, and sore throat were the most common symptoms.

In univariate analyses, higher EDSS scores (≥5) and progressive disease were identified as risk factors for increased COVID-19 severity and consequent hospitalization, while risk factors for an unfavorable outcome in terms of recovery and non-recovery were the presence of comorbid conditions. A similar multicenter, retrospective, observational cohort study was conducted by Louapre et al. to evaluate risk factors and outcomes of COVID-19 in MS patients in France. The study used the Covisep registry and identified greater age, male sex, comorbidities, progressive disease, and higher EDSS as risk factors for increased COVID-19 severity in their univariate analyses [5].

In the general population, the risk for severe COVID-19 illness increases with age, and older adults are at the highest risk [16]. In our study, we found age to be a risk factor with 3.8 times higher risk of moderate/severe COVID-19 in MS patients who are above the age of 45 years, but this association was not statistically significant. This may be attributed to a lower number of patients (20) in the older age group (≥45) in our cohort. In the study conducted by Parotta et al., critically ill COVID-19 infected MS patients were older (mean age of 57.7 years) [12].

It is established that respiratory dysfunction is common in pwMS an EDSS of 7 or more and is linked to impairment of expiratory muscles [17]. In our univariate analyses, EDSS was an independent risk factor for a severe form of COVID-19. The cohort we analyzed had a low level of neurological disability as assessed by EDSS scores, with 94.8% reporting scores between 0 and 4.5; however, higher disability scores [5–9.5] had a significant association with increasing severity of COVID-19 infection. The association between COVID-19 severity and EDSS has been previously reported only by Louapre et al.; COVID-19 patients with severity scores of 3 or more (moderate/severe) on the COVID-19 ordinal scale had higher EDSS (median EDSS, 6.0) [5]. The identification of higher EDSS as a risk factor for severe COVID-19 and increased risk of hospitalization should lead to the adoption of sufficient and sustainable precautionary measures for limiting COVID-19 infection in these patients.

Certain comorbid conditions in COVID-19 are known to increase the risk for severe illness. pwMS frequently have several comorbidities that have been related to a worse COVID-19 prognosis [5]. Univariate and multivariate analysis in our study also showed the presence of comorbidities as an independent risk factor for COVID-19 outcome with a higher chance of non-recovery. Due to the insufficient number of patients, we were unable to establish the association of specific comorbidities with COVID-19 severity or outcome.

Relapsing-remitting MS is typically known to be the most common type of MS and most patients are diagnosed initially with this type. The disease takes a more progressive course after several decades. The majority of patients in our cohort had RRMS (86.6%). Considering the lower age of the participants, this is understandable. Progressive disease was associated with increased COVID-19 severity in our cohort. This was similar to the results of studies conducted by Louapre et al. and Parotta et al. that found progressive MS to be a risk factor for developing more severe COVID-19 [5,12].

Disease-modifying therapies are known to modify the risk of COVID-19 infection based on their mechanisms of action. In our study, we found a statistically significant higher risk of developing moderate/severe COVID-19 and consequent hospitalization in patients on rituximab (6.3 times higher risk) and anti-CD20 therapy (5.3 times higher risk). However, a few studies have found that the type/class of DMT is not a predictor for increased severity of COVID-19 or of poor outcome [3,5,8,12,18,19]. A large electronic health record-based observational study conducted by Reder et al. in 2021 found that pwMS taking interferons and glatiramer acetate had the lowest risk of COVID-19 whereas patients receiving anti-CD20 therapies had the highest risk [20]. Another study by Fragoso et al. carried out using data from five Latin American countries in patients with MS and confirmed diagnosis of COVID-19 reported the use of anti-CD20 therapies as the only risk factor associated with hospitalization and death [21]. Other studies including one with a large multinational sample of MS patients have also implicated anti-CD20 therapy (either rituximab or ocrelizumab) in increasing the risk of severe COVID-19 and hospitalization/ICU admission [22–24]. The results of these studies corroborate our results and can be explained by the fact that anti-CD20 therapies impact the humoral immune response and decrease the levels of IgG and IgM over time [25]. However, any association with DMTs should be inferred with caution as results may be attributed to inadequate sample size and may vary if a larger cohort with the use of any of the DMTs is analyzed. A study by Zabalza et al. [1] found longer MS disease duration to be a risk factor for COVID-19; however, this association was not seen in our study.

Our study has several notable limitations that include the lack of a structured pre-defined data collection format; it also involved voluntary reporting by health care professionals, which may have led to biased reporting towards more severe cases. Considering the retrospective nature of the study there may also be some amount of recall bias. The small sample size does not let an appropriate assessment of the DMT-related COVID-19 risk of infection. The study did not use the WHO-recommended COVID-19 eight-category ordinal scale for describing disease severity. The lack of a non-infected cohort makes it difficult to make any assumptions and comparisons between MS characteristics in COVID-19 patients and among those in the general MS population. An adequate number of patients were not included in the analysis in Oman due to the lack of a comprehensive follow-up protocol and the prevailing COVID scenario. The strength of the study is that it is one of the few studies on MS patients with COVID-19 from the Middle East and can provide valuable insights on risk factors leading to more severe disease and consequent adverse outcomes in this patient population.

5. Conclusions

The prevalence of COVID-19 in the MS patient cohort from the Middle East is marginally lower than that in the general population. COVID-19 severity and outcome in this cohort are largely dependent on a few key indicators such as the presence of co-morbidities, higher scores of disabilities, presence of progressive forms of MS, and the use of anti-CD 20 DMTs. The prognosis of COVID-19 is generally favorable in a majority of COVID-19 pwMS.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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