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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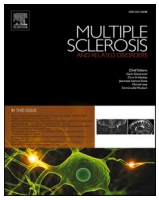

Original article

The disease course of multiple sclerosis before and during COVID-19 pandemic: A retrospective five-year study

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ABSTRACT

Introduction: COVID-19 pandemic is thought to influence the natural history of immune disorders, yet the knowledge on its effect on multiple sclerosis (MS) is unknown and not fully understood for which we conducted this retrospective study.

Methods and materials: We included all patients with MS seen in King Faisal Specialist Hospital and Research Centre in Jeddah, Saudi Arabia, between January 2017 and October 20201. We determined clinical and radiological evidence of disease activities in all patients by the end of the study period, and we compared the disease patterns before and during the pandemic. We also identified patients with COVID-19 since March 2020, who had at least 3 months of follow-up following the infection.

Results: We studied 301 patients; 216 (72%) were women, the mean age was 38 years (range; 16, 73 years), the mean disease duration was 10 years (range; 1, 36 years), and the median EDSS score was 0.5 (range; 0, 8). RRMS accounted for most of the cases (270 patients). MS disease activities were 25% less prevalent during the pandemic compared to the preceding 3 years (26 vs. 51%, respectively, $p < 0.01$). Bivariate analysis showed significant higher disease activities in patients younger than 35 years (73 vs 27%), on DMT (68 vs 32%), and complaint to therapy (69 vs 31%). Multiple logistic regression analysis showed that the likelihood of MS disease activities were 3 times more during the pre-pandemic era (adjusted OR = 3.1, p value < 0.05, 95% CI; 1.4, 7.1). Thirty patients (10%) were infected with COVID-19. All patients reported mild symptoms, and none required hospitalization. COVID-19 was prevalent among younger patients with RRMS, with low EDSS scores, irrespective of DMTs they received. COVID-19 infection was not associated with clinical relapses or MRI changes. Disease activities were dependent on DMT use and not COVID-19 status. Multivariate analyses also confirmed no effect of COVID-19 on disease activities ($p = 0.3$ and 0.4, for clinical and MRI changes, respectively).

Conclusions: MS disease activities did not increase during the pandemic, yet the apparent decrease in the disease activities is probably due to under reporting and not a real decrease in disease activities because of the pandemic. The COVID-19 infection in our MS patients showed a benign disease course, yet standard precautions to reduce the risk of COVID-19 transmission should be applied accordingly.

1. Introduction

Since late 2019, the emergence of COVID-19 in Wuhan, China, evolved in months to a worldwide pandemic, and as of March 20, 2020, more than 190 countries worldwide reported cases of COVID-19, including Saudi Arabia (Paules et al., 2020; Li et al., 2020; WHO, 2020). Furthermore, a growing literature identified high-risk patients for severe COVID-19 infection, including those with diabetes, hypertension, coronary artery disease, and pregnant women (Yang et al., 2020; Guan et al., 2020; Zhang et al., 2020; Qiao, 2020).

The association between human coronaviruses (HCoVs), known neurotropic viruses, and multiple sclerosis (MS) was described in the literature, which raised the potential of COVID-19 for CNS pathology and exacerbation of MS immunopathogenesis during the pandemic (Murray et al., 1992; Murray et al., 1997). Also, patients with immune diseases receiving immune suppressive therapy have their battle with viral infections of different types, which can either alter their disease course or complicate their high-risk immune suppressive therapy

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(Mathew et al., 2014). Early data during the pandemic demonstrated a high risk of severe infection and mortality in immune suppressed patients with malignancy or rheumatological diseases (Sica and Massarotti, 2017; Liang et al., 2020; Fernandez-Ruiz et al., 2021; Akiyama et al., 2021). On the other hand, viral infections exacerbate MS disease activities and relapses (Lucas et al., 2011; Tremlett et al., 2008). With the spread of the pandemic, neurologists were concerned about the risk of severe COVID-19 infection in these patients, particularly those on disease-modifying therapy (DMT) (Berger and Brandstadter, 2020). Nevertheless, evidence also supports a possible safe use of DMTs in MS patients during the pandemic (Louapre et al., 2020). Literature on the impact of the pandemic and COVID-19 infection, on the disease activities of MS is evolving, but still scarce.

In this five-year retrospective cohort study, we aimed to evaluate changes in MS disease course, either clinical or radiological, before and during the pandemic, and the influence of COVID-19 on these parameters that will indicate an active disease course. We will also assess the severity of COVID-19 in patients with MS in our studied population.

2. Methods and materials

2.1. Patients' demographics and characteristics

We retrospectively studied patients with MS seen in King Faisal Specialist Hospital and Research Centre in Jeddah, Saudi Arabia, between January 2017 and October 2021. Our hospital is a tertiary care institution, with multidisciplinary MS clinics. We included patients 18 years and older who were diagnosed with one of the following: relapsing-remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), or clinically isolated syndrome (CIS) (Lublin et al., 2014). Studied patients should also have a baseline MRI of the brain and spine performed during the study period. Patients included in the study should also have data on clinical relapses and MRI brain and spine during the pandemic, and following COVID-19 infection. We collected data on the patient's demographics, including the age, age at the diagnosis, sex, and the presence of other comorbidities (chronic respiratory illness, diabetes, other immune diseases). We identified the disease-modifying therapy (DMT) the patient received, and we classified them as modest, moderate, and high efficacy therapy. Modest efficacy therapy included interferon beta-1a intramuscular, moderate efficacy therapy included teriflunomide 14 mg, dimethyl fumarate, interferon beta-1a 44 mcg, and high efficiency therapy included cladribine, fingolimod, natalizumab, and ocrelizumab (Samjoo et al., 2021).We also considered rituximab as a high efficacy therapy. We determined Expanded Disability Status Scale (EDSS) for the studied patients.

2.2. Comparing the disease activities before and during the pandemic

To assess the impact of the pandemic on MS disease course, we identified patients with either clinically or radiologically active disease in the pre-COVID era, between January 2017 and February 2020. We also identified patients who had active disease during the pandemic, from March 2020 to October 2021. We compared the prevalence of disease activities between the pre-COVID period and during the pandemic until October 2021. Patients who achieved "no evidence of disease activities" (NEDA) during the study period were also determined.

2.3. COVID-19 infection in patients with MS

Since March 2020, we identified MS cases with COVID-19 infection with a confirmed COVID-19 positive PCR. We also collected data on the severity of the infection, the need for hospitalization, and case fatality related to COVID-19 infection.

2.4. Monitoring MS disease activity during the pandemic

We identified whether clinical relapses requiring pulse steroid therapy occurred since March 2020. We also determined radiological evidence of disease activities by the presence of a new lesion or new enhancing lesion in MRI of the brain or spine. To understand any association between COVID-19 and MS disease activities, we identified patients who had any clinical or radiological disease activities following COVID-19 confirmed infection. We reviewed the neurological examinations and estimated EDSS scores during the follow-up visits.

2.5. Data analysis

For data analysis, we used R software. R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/. We performed univariate and bivariate analyses to express descriptive and inferential analyses, including *t*-test and chi-square, and we performed multivariate analysis, using clinical and radiological changes indicating disease activities as the dependent variables separately, and COVID-19 as the independent variable, using other clinical variables as co-variables. We perform survival analysis to estimate clinical and MRI changes following COVID-19 infection. We determined 95% confidence intervals (CI) and interpreted the *P*-value according to the American Statistical Association guidelines (Wasserstein and Lazar, 2016).

3. Results

We included 301 patients, who fulfilled the inclusion criteria. There were 216 women (72%), the mean age was 38 years (SD = 11 years, range; 16, 73 years), and the mean disease duration was 10 years (range; 1, 36 years). The median EDSS score was 0.5 (range; 0, 8). RRMS accounted for most cases (270 patients), followed by SPMS (19 patients), PPMS (10 patients), and CIS was seen in only 2 patients. Eighty-five percent (256 patients) were on DMTs during the study period, where moderate and high efficacy medications were used by three-quarters of our group (231 cases, 77%), and modest efficacy DMT were only used in 25 cases (8%). Thirty-nine patients (16%) reported poor compliance to therapy. Despite the low median EDSS in our group, moderate to high efficacy therapies were the most frequently used regimen in our studied population.

3.1. The impact of the pandemic on MS disease course

From January 2017 through February 2020 (3 years), 154 patients (51%) developed clinical relapses or radiological evidence of disease activities, while from March 2020 to October 2021 (19 months), only 77 patients (26%) reported similar outcomes (OR = 0.26, p value < 0.01). Bivariate analysis, stratified according to patients' characteristics, showed inconsistently significant high disease activities during the pre-COVID era (Fig. 1). Multivariate logistic analysis showed that the odds of disease activities, wither clinical or radiological, were about 3 times more during the pre-COVID period compared to the time of COVID-19 pandemic in our patients (adjusted OR = 3.1, p value = 0.005, 95% CI; 1.41 – 7.14), when age, sex, disease duration, compliance to medications, DMT class according to its efficacy, and EDSS were considered in the regression model (Table 1). By the same token, reporting MS disease activities in our group during the pandemic was 68% less when compared to the pre-COVID era (adjusted OR = 0.32, p value = 0.005, 95% CI; 0.14–0.71). Also, MS disease activities were more prevalent before the pandemic when multiple logistic regression analyses were stratified according to female sex (OR = 4.2, p value < 0.01), age older than 35 years (OR = 6.1, p < 0.01 value), patients with EDDS not more than 1.5 (OR = 4.4, p value < 0.01), DMT use (OR = 3.4, p value < 0.01), and patients who were complaint to therapy (OR = 4.7, p value <0.01). Forty percent of our patients (120 cases) achieved NEDA for almost 5

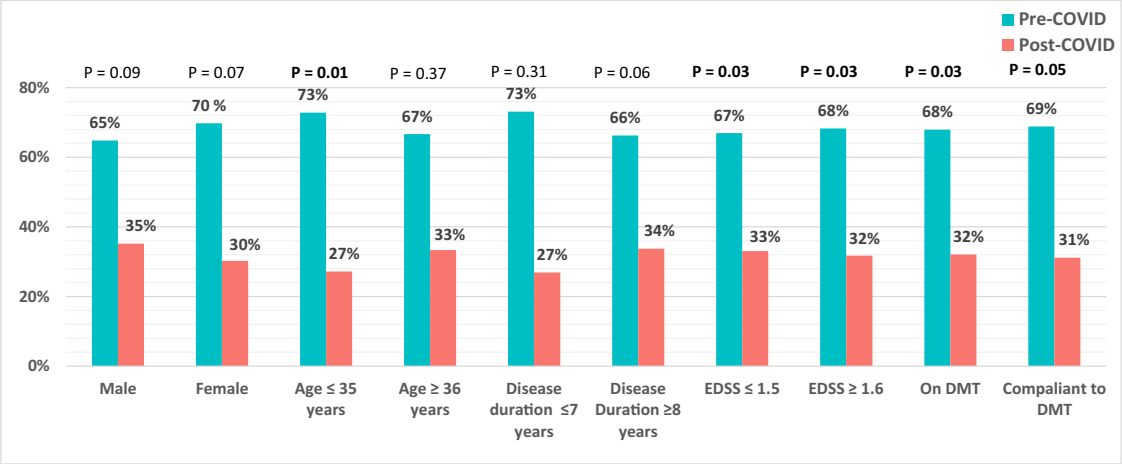

Fig. 1. Bar chart shows MS disease activities before and during the pandemic according to patients' demographics.

Table 1
Multiple logistic regression analysis predicting MS disease activities (clinical relapses or MRI changes) before and during the pandemic.

Predictors	**MS disease activities**			
	Odds Ratios	*Std. Error*[1]	*95% CI*[2]	*P value*
(Intercept)	1.43	1.51	0.18–11.88	0.73
Timing of disease activity [Pre-COVID][3]	3.14	1.30	1.41–7.14	**0.005**
Age	0.99	0.02	0.94–1.03	0.52
Sex [Male]	0.85	0.36	0.38–1.96	0.69
Compliance [No]	2.05	2.92	0.13–56.66	0.61
Compliance [Yes]	1.73	2.56	0.10–52.57	0.71
Disease Duration	0.95	0.04	0.88–1.02	0.18
Medication Efficacy [High]	3.27	4.57	0.12–47.34	0.39
Medication Efficacy [Moderate]	2.54	3.49	0.10–35.06	0.49
Medication Efficacy [Modest]	3.03	4.57	0.10–56.35	0.46
EDSS	1.14	0.12	0.93–1.43	0.22

[1]Std. Error: Standard error
2CI: Confidence interval
3Compared to Post-COVID period

years. Our findings demonstrated that more MS activities were reported before the pandemic, and the pandemic did not appear to be associated with an increase in MS disease activities, even when sex, disease duration, compliance to DMT and EDSS were considered.

3.2. Prevalence and severity of COVID-19 infection

A total of 30 patients (10%) were infected with COVID-19 in patients followed in our MS clinic since the pandemic hit Saudi Arabia in early March 2020. Most of the infections reported were associated with mild symptoms, and none of the patient's required hospitalization or ICU admission. No patients died because of the COVID-19 infection. None of our patients were fully vaccinated by the end of the study period. Therefore, the prevalence of COVID-19 among our MS patients was 10 per 100 cases. Table 2 shows characteristics of COVID-19 positive and negative patients. Apart from the significantly low EDSS in COVID-19 positive MS patients, there were no significant clinical characteristics associated with an increased risk of COVID-19 among our patients MS. With the significant advantage of mobilization and lower EDSS in COVID-19 infected patients, the latter puts these patients at higher risk of exposure to COVID-19, and independent of other MS characteristics. Fig. 2 shows the distribution of COVID-19 according to DMTs.

Table 2
Patients' characteristics of COVID-19 positive and negative MS patients.

	COVID-19 positive *N*=30	**COVID-19 negative *N*=271**	***P* value**
Mean age (range)	34 years (19–60 years)	38 years (16–73 years)	0.052
Sex (men, %)	13 (43%)	72 (27%)	**0.05**
Mean disease duration (range)	8 years (1–25 years)	10 years (1–36 years)	0.4
Median EDSS scale (IQR[4])	0.5 (0–4)	0.6 (0–8)	**0.01**[5]
MS type			
RRMS[6]	30 (100%)	241 (89%)	0.051
Other types	0 (0%)	31 (11%)	
Medication class			
Modest efficacy (INF-β-1a IM)[7]	0 (0%)	25 (9%)	0.8
Moderate efficacy (Dimethyl fumarate, INF-β-1a SC 44 mg, teriflunomide 14 mg)	14 (47%)	101 (37%)	0.3
High efficacy (Cladribine, fingolimod, natalizumab, ocrelizumab, rituximab)	10 (33%)	106 (39%)	0.5
None	6 (20%)	39 (14%)	0.4
Compliance to medications (yes)	21 (70%)	198 (73%)	0.7

[4]IQR: Interquartile
[5]*P* value derived from t test (mean EDDS of 0.6 vs 1.7, respectively)
[6]RRMS: Relapsing remitting multiple sclerosis
[7]INF-β-1a: Interferon beta-1-a intramuscular.

3.3. COVID-19 and clinical relapses

Since March 2020, 25 patients (8%) reported clinical relapses, which required hospital admission and pulse steroid therapy. Only 1 patient (1 out of 30) had COVID-19 prior to the clinical relapse, while 29 of our MS patients with COVID-19 positive PCR never had a clinical relapse during the study period (p-value = 0.3, OR = 0.35, 95% CI; 0.05, 2.72). Therefore, COVID-19 did not appear to be associated with clinical relapses in patients with MS (Fig. 3A). Clinical relapses in our group were only associated with poor compliance to DMTs (p value = 0.01, OR = 4.5, 95% CI; 1.3, 21.9). Accordingly, multivariate regression analysis did not show any association between COVID-19 infection and clinical relapses in our patients with MS (Table 3).

3.4. COVID-19 and radiological activities

The presence of either a new lesion or enhancing lesion was

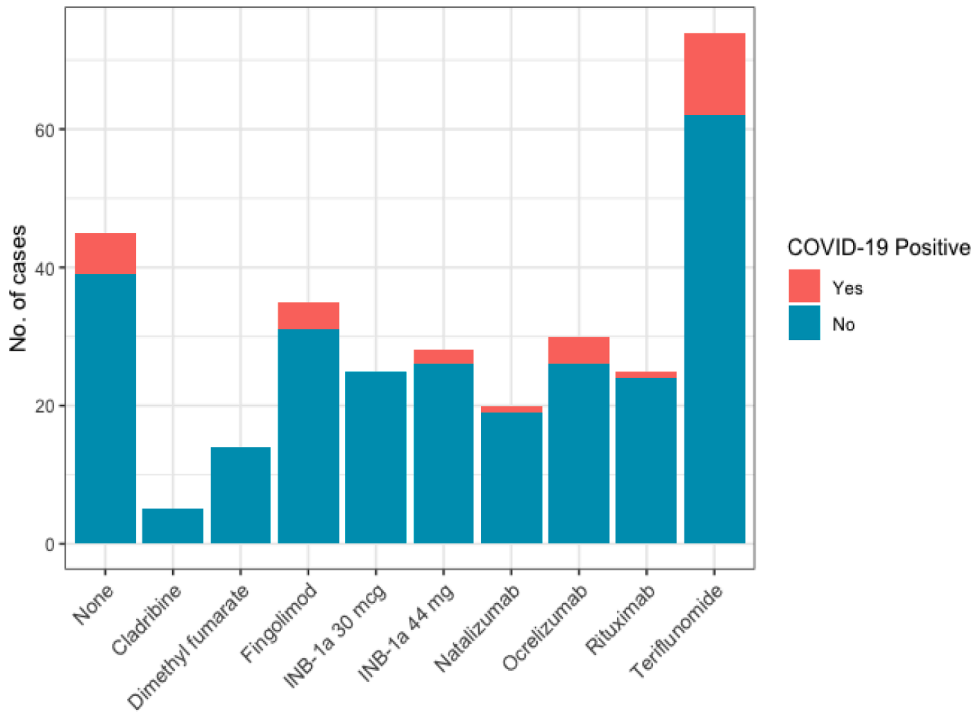

Fig. 2. Bar chart shows COVID-19 status according to disease modifying therapy (DMT).

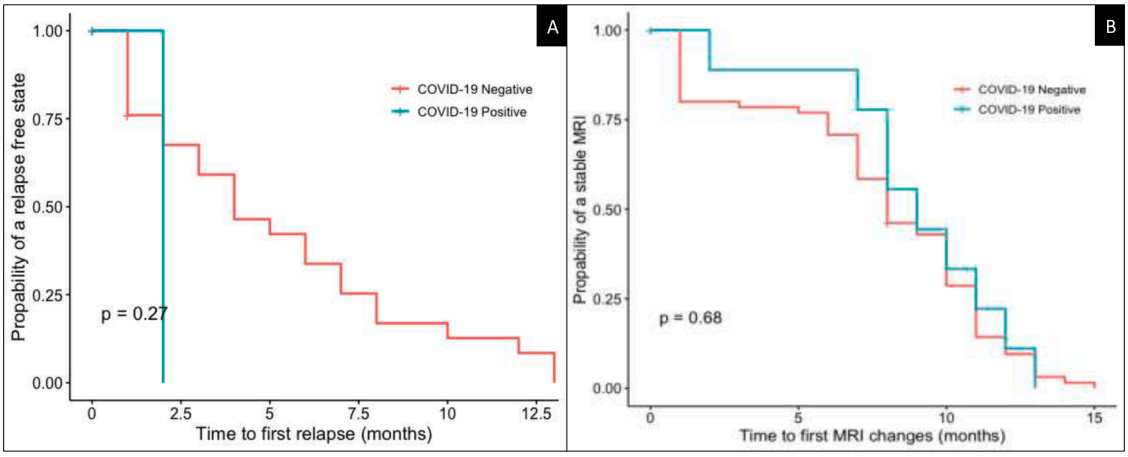

Fig. 3. Kaplan Meir curve shows the probability of MS disease activities following COVID-19 (A: clinical relapses requiring pulse steroid therapy, B: The presence of new lesion or new enhancing lesion in MRI brain or spine).

monitored during the pandemic and following COVID-19 positive PCR. About one-fourth of our group (73 patients) had documented disease activities in MRI of the brain or spine. Only 8 of those patients had COVID-19 positive serology (8 out of 30) preceding the changes seen in the MRI. In the contrary, 22 patients (73%) with COVID-19 had no MRI changes following the infection (p-value = 0.4, OR = 0.7, 95% CI; 0.3, 1.7) (Fig. 3B). These findings also demonstrated no effect of COVID-19 infection on MRI disease activities in our patients with MS. A similar observation was confirmed by multivariate regression analysis (Table 3). MRI changes indicating disease activities were significantly seen in patients not complaint to therapy (p-value < 0.001, OR = 2.1, 95% CI; 4.1, 19.3).

4. Discussion

The prevalence of COVID-19 in patients with neurological diseases varied in literature. For instance, a study conducted in Italy reported 0.9% of patients with Parkinson's disease (PD) infected with COVID-19 (Del Prete et al., 2021), yet pooled analysis estimated a prevalence of up to 8% (Artusi et al., 2021). Similarly, patients with myasthenia graves had a low prevalence of COVID-19 of 1.14% in a highly endemic country (Businaro et al., 2021). In patients with epilepsy, a reported prevalence of 6% was considered high, relative to population prevalence in a hospital-based survey (Bosak et al., 2021). Another study documented only 14 COVID-19 confirmed cases within 5700 patients with epilepsy (Granata et al., 2020). Although contradicting at times, the former reports showed no added risk of COVID-19 in patients with chronic neurological diseases, compared to population prevalence in countries considered highly impacted by the pandemic (Ceylan, 2020; Mantero et al., 2020).

The impact of COVID-19 on exacerbating MS relapses is still unfolding. A study by Barzegar et al. reported an increase in relapses following COVID-19 infection, although methodological flaws and bias could render such a conclusion Barzegar et al. (2021). Another study

Table 3
Multiple logistic regression analysis predicting clinical relapses and MRI changes following COVID-19 infection.

	Clinical relapses				MRI activities			
Predictors	*OR*	*std. Error*	*95% CI*	*P value*	*OR*	*std. Error*	*95% CI*	*P value*
(Intercept)	0.11	0.16	0.01–1.61	0.12	1.06	0.94	0.18–5.96	0.95
COVID [Yes][8]	0.41	0.44	0.02–2.21	0.40	1.01	0.50	0.37–2.55	0.97
AGE	0.96	0.03	0.91–1.01	0.13	0.96	0.02	0.93–0.99	**0.03**
SEX [Male]	0.54	0.29	0.17–1.43	0.24	1.06	0.33	0.56–1.94	0.85
EDSS	1.21	0.13	0.98–1.49	0.06	1.19	0.09	1.02–1.39	**0.03**
Disease Duration	1.02	0.04	0.94–1.10	0.65	0.99	0.03	0.94–1.04	0.72
MS Type [RRMS]	2.51	2.21	0.51–18.84	0.29	1.09	0.60	0.37–3.33	0.88
Medication Efficacy [High]	0.90	0.65	0.24–4.38	0.88	0.55	0.25	0.22–1.38	0.18
Medication Efficacy [Moderate]	1.48	1.04	0.41–7.05	0.57	1.41	0.62	0.61–3.45	0.43
Medication Efficacy [Modest]	0.50	0.61	0.02–4.50	0.56	0.42	0.32	0.08–1.68	0.24

[8]Compared to COVID-19 negative

showed no effect of COVID-19 on MS disease activities, with benign infection outcomes in most cases (Etemadifar et al., 2021). A large cohort from China suggested that relapse rates were determined mainly by MS itself and compliance to medications and not the pandemic (Zhang et al., 2020). Similarly, a study by Zhang reported increased MS relapses during the pandemic mostly in patients with poor compliance to DMT Zhang et al. (2021). Our study demonstrated a reduction in MS disease activities of up to 70% during the pandemic, compared to the three years preceding the pandemic. The apparent "protective" effect of the pandemic in our study can be explained by different reasons. Patients could develop mild attacks that may require visiting emergency room and hospitalization, but because of the fear of hospital acquired infections, particularly COVID-19, they may not seek medical attention. Subsequently, this may underestimate the true prevalence of MS disease activities during the pandemic. Similarly, adapted COVID-19 restrictions during the pandemic, including the lockdown, minimized mobilization between cities, hospitalization, and outpatient investigations, namely MRIs. The lockdown could obligate patients to visit their local hospitals, instead of our institution, in case they develop attacks. Hence, the risk of unreported attacks in our hospital records cannot be disregarded. Furthermore, patients might develop MS disease activity with an unknown COVID-19 status around the time of MS attack or the scheduled follow up MRIs. The aforementioned factors could lead to under reporting of MS attacks during the pandemic. Thus, our findings, along with other reports, did not demonstrate any conclusive evidence of an increase in MS disease activities because of the pandemic. MS disease activities were largely influenced by patients' adherence to DMT use during the pandemic.

Our study showed 10% confirmed COVID-19 cases in our patients with MS, during a strict nationwide COVID-19 preventive measure (Yezli and Khan, 2020; Obied et al., 2020). However, we reported the largest number of cases in the younger population, who had minimal or no disabilities, irrespective of DMTs. Thus, the risk of COVID-19 in our patients with MS was likely related to noncompliance to the preventive measures, as expected in younger patients. Furthermore, our findings were similar to reports published from Saudi Arabia and the region (Alshamrani et al., 2021; Zakaria et al., 2021; Sahraian et al., 2020; Sen et al., 2021). A recent meta-analysis reported a pooled prevalence of 4% of COVID-19 in patients with MS, with 10% hospitalization and pooled death rates of 4% (Moghadasi et al., 2021). Another systematic review showed mild symptoms of fever and cough in MS patients infected with COVID-19, where only 20% of them required hospitalization (OM et al. , 2021). In response to the pandemic, we modified the therapeutic protocols of high efficacy therapy, following published expert opinions aimed to reduce the risk of severe infection in susceptible MS patients (Amor et al., 2020; Reyes et al. , 2021; Sadeghmousavi and Rezaei, 2020; Brownlee et al., 2020; Apostolos-Pereira et al., 2020; Al Jumah et al., 2021). With the wide range of DMTs used in our group, none of them had a severe COVID-19 infection, which is comparable to published reports (Alahmari et al., 2021; Alsofayan et al., 2020; Bsteh et al., 2021; Capasso et al., 2020; Nowak-Kiczmer et al., 2021; Loonstra et al., 2020).

The severity of COVID-19 in patients with MS patients is puzzling. The overstimulation rather than the suppression of the immune system can be the leading cause of the severity or fatality of COVID-19 infected patients (Osuchowski et al., 2021; Dersch et al., 2020; Chiarini et al., 2020; Willis and Robertson, 2020; Iannetta et al., 2020; Zrzavy et al., 2021; Sormani et al., 2021; Cabreira et al., 2021). Patients with MS also have defective interferon signaling and interferon levels, the same system that contributes mainly to the defensive mechanism against COVID-19 (Feng et al., 2019). In the contrary, the immunomodulating effect of interferons and teriflunomide were not linked to an increased risk of systemic infections in MS patients (Luetic et al., 2021; Maghzi et al., 2020; Mantero et al., 2021). Additionally, the immunosuppressive effect of high efficacy therapy, such as ocrelizumab, cladribine, and alemtuzumab, is believed to alter lymphocytes' proliferation and function, increasing the risk of infections. Recent studies did not provide a conclusive evidence to implicate a severe COVID-19 infection in patients receiving such therapies (Bsteh et al., 2021; Willis and Robertson, 2020; De Angelis et al., 2020; Seferoglu et al., 2021; Luna et al., 2020; Carandini et al., 2020; Naghavi et al., 2021). The risk factors for severe COVID-19 in MS patients were not different from the general population (Louapre et al., 2020; Ghadiri et al., 2022). The benign COVID-19 course in our group could be the consequence of modifying the timing of high efficacy infusion therapy during the pandemic's peak, but could also be related to the fact that DMTs did not have an effect on COVID-19 outcomes in MS patients. In the face of earlier recommendations of discontinuing DMTs in MS patients during the pandemic, it is less likely that DMTs interrupt the immune response during COVID-19 infection (Baker et al., 2020).

Our study had a few limitations. Despite the adequate sample size in this study, our retrospective study design lacked a study protocol that could control the participants' follow ups. Such a design may influence the true estimation of the effect of the pandemic on disease activities. Also, the unequal follow up period before and during the pandemic (3 years vs 19 months, respectively) could influence the comparison of the disease activity between the two periods. A prospective cohort study would minimize these flaws, although it will be inconceivable in 2017 to prospectively follow MS patients, in order to assess the effect of the pandemic on MS activities. The COVID-19 restrictions and policies, on the other hand, may abate the prevalence of MS disease activities during the pandemic, as discussed earlier. Also, underestimating the number of COVID-19 cases is undoubtfully a worldwide concern raised by most epidemiological studies tackling the incidence or prevalence of COVID-19 infection, because of policies guiding testing for COVID-19 and its availabilities (Saudi Centre for Disease Control SA 2021). Mild or asymptomatic COVID-19 cases may not ever get tested, and patients'

preference of not getting tested can contribute to a lower prevalence of COVID-19 cases in MS population. A community mass screening in Saudi Arabia indicated 6.6% positive COVID-19 PCR in asymptomatic subjects (Khan et al., 2021). To estimate the effect of COVID-19 infection on MS relapses or MRI changes, we only reported 30 cases of COVID-19 in our patients, a number that was not enough to adequately draw conclusions on the effect of COVID-19 on MS disease activities. The number of infected MS patients in our group could be influenced by our screening policies.

5. Conclusions

COVID-19 pandemic did not appear to be associated with an increase in MS disease activities. The apparent decrease in MS disease activities is probably due to under reporting and not a real decrease in disease activities because of the pandemic. Evidence suggests that the disease activities of MS were determined largely by the compliance to DMTs and MS itself, before and during the pandemic. Finally, most of the infected MS patients with COVID-19 reported mild symptoms, with no increased risk of a severe infection compared to the general population. Standard precautions, when applicable, to reduce the risk of COVID-19 transmission should be applied accordingly.

CRediT authorship contribution statement

Fawzi Babtain: Conceptualization, Methodology, Formal analysis, Writing – review & editing. **Abdulaziz Bajafar:** Data curation. **Ohoud Nazmi:** Data curation, Software. **Manal Badawi:** Resources. **Ahmed Basndwah:** Resources. **Areej Bushnag:** Resources. **Edward Cupler:** Resources. **Ahmed Hassan:** Resources.

Declaration of Competing Interest

All authors reported no conflict of interest related to this work or its production.

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