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Impact of COVID-19 Infection and Its Association With Previous Vaccination in Patients With Myasthenia Gravis in Korea: A Multicenter Retrospective Study

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ABSTRACT

Background: During the coronavirus disease 2019 (COVID-19) pandemic, patients with myasthenia gravis (MG) were more susceptible to poor outcomes owing to respiratory muscle weakness and immunotherapy. Several studies conducted in the early stages of the COVID-19 pandemic reported higher mortality in patients with MG compared to the general population. This study aimed to investigate the clinical course and prognosis of COVID-19 in patients with MG and to compare these parameters between vaccinated and unvaccinated patients in South Korea.
Methods: This multicenter, retrospective study, which was conducted at 14 tertiary hospitals in South Korea, reviewed the medical records and identified MG patients who

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Disclosure

The authors have no potential conflicts of interest to disclose.

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contracted COVID-19 between February 2022 and April 2022. The demographic and clinical characteristics associated with MG and vaccination status were collected. The clinical outcomes of COVID-19 infection and MG were investigated and compared between the vaccinated and unvaccinated patients.

Results: Ninety-two patients with MG contracted COVID-19 during the study. Nine (9.8%) patients required hospitalization, 4 (4.3%) of whom were admitted to the intensive care unit. Seventy-five of 92 patients were vaccinated before contracting COVID-19 infection, and 17 were not. During the COVID-19 infection, 6 of 17 (35.3%) unvaccinated patients were hospitalized, whereas 3 of 75 (4.0%) vaccinated patients were hospitalized ($P < 0.001$). The frequencies of ICU admission and mechanical ventilation were significantly lower in the vaccinated patients than in the unvaccinated patients ($P = 0.019$ and $P = 0.032$, respectively). The rate of MG deterioration was significantly lower in the vaccinated patients than in the unvaccinated patients ($P = 0.041$). Logistic regression after weighting revealed that the risk of hospitalization and MG deterioration after COVID-19 infection was significantly lower in the vaccinated patients than in the unvaccinated patients.

Conclusion: This study suggests that the clinical course and prognosis of patients with MG who contracted COVID-19 during the dominance of the omicron variant of COVID-19 may be milder than those at the early phase of the COVID-19 pandemic when vaccination was unavailable. Vaccination may reduce the morbidity of COVID-19 in patients with MG and effectively prevent MG deterioration induced by COVID-19 infection.

Keywords: Myasthenia Gravis; COVID-19 Infection; Vaccination; Outcomes; Worsening

INTRODUCTION

Myasthenia gravis (MG) is an autoantibody-mediated autoimmune disorder that affects the neuromuscular junction, and is characterized by fatigable muscle weakness.[1] MG may lead to bulbar and respiratory muscle weakness and can be exacerbated by infections.[2] Immunotherapy, one of the mainstays of MG therapy, may lead to an immunocompromised state in patients with MG. Therefore, patients with MG face a higher risk of infection than healthy people, and infection often adversely affects the progress of MG, and vice versa.[3,4]

The outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in November 2019.[5] During the COVID-19 pandemic, patients with MG faced a greater risk of poor outcomes than the general population.[6] According to the World Health Organization, a cumulative total of approximately 25 million COVID-19 cases and 800,000 deaths with a mortality rate of approximately 3% had been reported globally between the beginning of the pandemic and August 2020.[7] Studies conducted around the same time reported that the mortality rate was 11–27% in patients with MG who contracted COVID-19.[8-10] A systematic review showed that the mortality rate was 11.8% in patients with MG, and 42.4% required invasive ventilation treatment.[11] Thus, the mortality rate was extremely high in the MG population when compared to the general population. However, most previous studies that investigated the effects of COVID-19 infection on MG were performed in the early stages of the pandemic, when COVID-19 vaccination was not available.[8-10] The situation in South Korea, where most COVID-19 infections occurred after February 2022, was different from that in other countries in the early days of COVID-19. Almost all COVID-19 infections in South Korea were caused by the omicron variant of SARS-CoV-2, whose disease severity is milder than that caused by

Han HJ. Methodology: Shin HY. Supervision: Shin HY. Writing - original draft: Shin HY, Han HJ. Writing - review and editing: Kim H, So J, Lee EJ, Lim YM, Lee JH, Lee MA, Kim BJ, Beak SH, Lee HS, Sohn E, Kim S, Park JS, Kang M, Park HJ, Yoon BA, Kim JK, Seok HY, Kim S, Min JH, Chung YH, Cho JH, Kim JE, Oh S, Kim SW, Han HJ.

the alpha and delta predecessor variants.[12] In April 2022, the full vaccination rate was about 86% of the population and more than 63% of the population received the booster dose.[13] Therefore, it can be assumed that a substantial number of patients with MG were vaccinated against COVID-19. This unique situation is amenable to investigate the effect of COVID-19 vaccination on patients with MG who contracted COVID-19.

To the best of our knowledge, data on the effect of COVID-19 vaccination on MG patients who contracted COVID-19 are limited. One previous study investigated the effect of vaccination by comparing 13 patients with MG who contracted COVID-19 in the period between March 2020 and May 2021, when COVID-19 vaccination was not available, and 14 patients with MG who contracted COVID-19 after the availability of vaccination in April 2021.[14] That study concluded that vaccination has a protective effect in patients with MG. However, the study was not free from selection bias. Owing to the difference in the timing of COVID-19 infection, the vaccinated and unvaccinated patients were probably infected with different variants of SARS-CoV-2.

We aimed to investigate the clinical course and prognosis of patients with MG who contracted COVID-19 during the period of SARS-CoV-2 omicron dominance and the effect of COVID-19 vaccination in patients MG with who contracted COVID-19.

METHODS

Patient enrollment

This multicenter, retrospective study was conducted at 14 tertiary hospitals in South Korea (Yonsei University Severance Hospital, Yonsei University Gangnam Severance Hospital, The Catholic University of Korea Seoul St. Mary's Hospital, Keimyung University Dongsan Medical Center, Korea University Ansan Hospital, Korea University Anam Hospital, National Health Insurance Service Ilsan Hospital, Dong-A University Hospital, Samsung Medical Center, Asan Medical Center, Ewha Woman's University Seoul Hospital, Inje University Busan Paik Hospital, Chungnam National University Hospital, and Kyungpook National University Chilgok Hospital). We identified patients with MG who first contracted COVID-19 between February 2022 and April 2022 by perusing the electronic medical records, when the omicron variant of SARS-CoV-2 was dominant in South Korea.

Data collection and definition

The demographic and clinical characteristics associated with MG (including the age of onset, presence of autoantibodies, subtype, Myasthenia Gravis Foundation of America [MGFA] clinical classification, Myasthenia Gravis Activities of Daily Living [MG-ADL] score, and MG treatment at the time of COVID-19 infection) and COVID-19 vaccination status were extracted from the patients' electronic medical records. During the study period, conservative management was the standard of care for mild COVID-19 infection in healthy adults in South Korea. COVID-19-specific antiviral agents were prescribed restrictively to patients with mild to moderate infection with risk factors for progression to severe disease, such as chronic illness, ongoing immunosuppressive therapies, and old age. Moreover, the clinical course and prognosis of COVID-19 infection and MG deterioration within one month after the diagnosis of COVID-19 infection were investigated. MG deterioration was defined as clinically significant worsening of the signs or symptoms related to MG, resulting in elevation of the MG-ADL score by ≥ 2 points, or respiration insufficiency that is severe enough to necessitate mechanical ventilation. When a patient with MG was quarantined and could not

be evaluated by a neurologist during MG exacerbation, deterioration in MG was determined by a neurologist based on the patient's report. Patients with MG who were vaccinated against COVID-19 at least once were defined as the vaccinated group and the remaining patients were allocated to the unvaccinated group. During the study period, BNT162b2, mRNA-1273, and AZD1222 were available for vaccination in Korea.

Statistical analysis

Data were presented as the median (Q1–Q3) for continuous variables and as numbers (percentages) for categorical variables. The patients were stratified into vaccinated and unvaccinated groups to assess the difference in the prognosis of COVID-19. The difference in the clinical factors between the vaccinated and unvaccinated groups was evaluated using the χ^2 test or Fisher's exact test, depending on the expected frequencies. Variables with P values < 0.05 were considered statistically significant. Univariate logistic regression analysis with inverse probability of treatment weighting for sex, age at COVID-19 infection, and MG severity before COVID-19 infection was employed to assess the effect of vaccination on MG deterioration after COVID-19. MG severity before COVID-19 infection was dichotomized into moderate to severe disease (MGFA clinical classification class ≥ III) and mild disease (MGFA clinical classification class ≤ II).

Ethics statement

This study was reviewed and approved by the Severance Hospital Institutional Review Board (approval No. 4-2022-0431), which waived the requirement for informed consent owing to its retrospective design. All other participating centers individually obtained approval from their ethical committees.

RESULTS

Patient recruitment and clinical characteristics

During the study period, a total of 92 patients with MG from 14 tertiary hospitals reported their experience of COVID-19 infection. All patients had no previous COVID-19 infection. The participants' mean age was 49.4 ± 15.0 years and 61 (66.3%) of 92 patients were women (**Table 1**). Most patients had generalized MG (n = 74, 80.4%), and 70 (76.1%) and 2 (2.2%) patients tested positive for the anti-acetylcholine receptor binding antibody and anti-muscle-specific kinase antibody, respectively. Forty-six patients (50%) underwent thymectomy (**Table 2**). On their last visit before contracting COVID-19, 10 (10.9%) patients were asymptomatic for MG, 29 patients (31.5%) patients had only ocular muscle weakness (MGFA clinical class I), 49 (53.3%) patients had mild generalized weakness (MGFA clinical class II), and 4 (4.4%) patients had moderate to severe generalized weakness (MGFA clinical class III or IV). The baseline MG-ADL score was measured 52.9 ± 46.8 days before COVID-19 infection, and the mean baseline MG-ADL score was 3.3 ± 3.7. Sixty-six (71.7%) patients were receiving oral corticosteroids, and 56 (60.9%) patients were receiving oral immunosuppressive agents, including azathioprine, cyclosporine, mycophenolate mofetil, and tacrolimus. There were no patients who received rituximab within 12 months before COVID-19 infection. Seventy-five (80.5%) of 92 patients were vaccinated before contracting COVID-19, and 17 (18.5%) patients were not vaccinated. Based on the first dose, 52 of 75 patients received BNT162b2, 4 received mRNA-1273, and 16 received AZD1222. Regarding the second dose, 54 patients received BNT62b2, 6 received mRNA-1273, and 12 received AZD1222. The type of vaccines was not known in three patients.

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Table 1. Basic characteristics of patients with myasthenia gravis who contracted COVID-19

Clinical characteristics	Total (n = 92)
Age at COVID-19 infection, yr	49.4 ± 15.0
Onset age, yr	39.2 ± 16.4
Disease duration, yr	9.8 ± 9.7
Body mass index, kg/m^2	25.1 ± 5.5
Sex (female)	61 (66.3)
Antibody	
AChR	70 (76.1)
MuSK	2 (2.2)
Subtype (generalized)	74 (80.4)
MGFA clinical class (at nadir)	
I	18 (19.6)
II	34 (37.0)
III	24 (26.1)
IV	4 (4.3)
V	12 (13.0)
MGFA clinical class (before COVID-19)	
No symptoms	10 (10.9)
I	29 (31.5)
II	49 (53.3)
III	3 (3.3)
IV	1 (1.1)
MM or better (before COVID-19)	50 (54.3)
MG-ADL score (before COVID-19)	3.3 ± 3.7
Thymectomy	46 (50.0)
Thymoma	36 (39.1)
Treatment	
Pyridostigmine	63 (68.5)
Prednisolone	66 (71.7)
Prednisolone dose (before COVID-19 infection), mg	11.5 ± 8.4
Oral immunosuppressant	56 (60.9)
IVIg (within 3 mon)	11 (12.0)
Plasmapheresis (within 3 mon)	0 (0.0)
Rituximab (within 12 mon)	0 (0.0)
Vaccination against COVID-19	75 (80.5)

Values are presented as mean ± standard deviation or number (%).
COVID-19 = coronavirus disease 2019, AChR = acetylcholine receptor, MuSK = muscle-specific kinase, MGFA = Myasthenia Gravis Foundation of America, MM = minimal manifestation, MG-ADL = Myasthenia Gravis MG Activities of Daily Living, IVIg = intravenous immunoglobulin.

Table 2. Clinical course of COVID-19 infection

Outcomes	Total (n = 92)
Symptoms of COVID-19	
Upper respiratory infection symptoms	58 (63.0)
Fever	35 (38.0)
COVID-19-specific antiviral agents	54 (58.7)
Hospitalization	9 (9.8)
ICU admission	4 (4.3)
Mechanical ventilation	2 (2.2)
Death	1 (1.1)

Values are presented as number of patients (%).
COVID-19 = coronavirus disease 2019, ICU = intensive care unit.

Clinical course of COVID-19 infection in MG patients

During COVID-19 infection, 58 (63.0%) and 35 (38.0%) patients experienced respiratory symptoms and fever, respectively (**Table 2**). Eighteen (19.6%) patients were asymptomatic, while 9 (9.8%) patients required hospitalization, and 54 (58.7%) patients received COVID-19-specific antiviral agents. Four (4.3%) hospitalized patients were admitted to the intensive

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care unit (ICU), 2 (2.2%) of whom required mechanical ventilation. One (1.1%) patient succumbed to COVID-19 infection.

Comparison between vaccinated and unvaccinated patients

We conducted a comparative analysis of the 75 vaccinated patients and 17 unvaccinated patients. **Table 3** depicts the comparison of the baseline characteristics between the vaccinated and unvaccinated patients. The proportion of women was significantly lower in the unvaccinated group (7/17, 41.2%) than in the vaccinated group (54/75, 72%, $P = 0.015$). The frequency of generalized MG was significantly higher in the unvaccinated group (17/17, 100.0%) than in the vaccinated group (57/75, 76.0%, $P = 0.024$). The frequency of minimal manifestation was significantly lower in the unvaccinated patients (5/17, 29.4%) than in the vaccinated patients (45/75, 60.8%, $P = 0.024$). The MG-ADL score was significantly higher in the unvaccinated patients (5.4 ± 4.1) than in the vaccinated patients (2.8 ± 3.5, $P = 0.007$).

Table 4 summarizes the comparison of the clinical course of COVID-19 infection between the vaccinated and unvaccinated groups. Ten (71.4%) unvaccinated patients had developed fever, while 25 (41.0%) vaccinated patients developed fever ($P = 0.039$). Six (35.5%) of the 17 unvaccinated patients were hospitalized, whereas 3 (4.0%) of the 75 vaccinated patients were hospitalized ($P < 0.001$). Among the 4 patients requiring ICU admission for

Table 3. Comparison between vaccinated and unvaccinated patients: baseline characteristics

Clinical characteristics	Vaccinated (n = 75)	Unvaccinated (n = 17)	*P*
Age at COVID-19 infection, yr	50.8 ± 14.6	43.2 ± 15.6	0.080
Onset age, yr	40.4 ± 16.1	33.6 ± 16.9	0.142
Disease duration, days	124.1 ± 112.7	113.8 ± 129.0	0.766
Body mass index, kg/m^2	25.2 ± 5.6	25.0 ± 5.3	0.942
Sex (female)	54 (72.0)	7 (41.2)	0.015
Antibody			0.773
AChR	57 (76.0)	13 (81.3)	
MuSK	2 (2.7)	0	
Subtype (generalized)	57 (76.0)	17 (100.0)	0.024
Thymectomy	34 (45.3)	12 (70.6)	0.060
MGFA clinical class (at nadir)			0.072
I	18 (24.0)	0	
II	28 (37.3)	6 (35.3)	
III	19 (25.3)	5 (29.4)	
IV	3 (4.0)	1 (5.9)	
V	7 (9.3)	5 (29.4)	
MGFA clinical class (before COVID-19)			0.048
No symptoms	10 (13.3)	0	
I	26 (34.7)	3 (17.6)	
II	37 (49.3)	12 (70.6)	
III	1 (1.3)	2 (11.8)	
IV	1 (1.3)	0	
MM before COVID-19	45 (60.8)	5 (29.4)	0.019
MG-ADL score (before COVID-19)	2.8 ± 3.5	5.4 ± 4.1	0.007
Treatment			
Pyridostigmine	50 (66.7)	13 (76.5)	0.432
Prednisolone	50 (66.7)	16 (94.1)	0.023
Prednisolone dose (before COVID-19), mg	10.4 ± 9.1	15.6 ± 11.1	0.064
Oral immunosuppressant	43 (57.3)	13 (76.5)	0.144
IVIg (within 3 mon)	7 (9.3)	4 (23.5)	0.103

Values are presented as mean ± standard deviation or number (%).
COVID-19 = coronavirus disease 2019, AChR = acetylcholine receptor, MuSK = muscle-specific kinase, MGFA = Myasthenia Gravis Foundation of America, MM = minimal manifestation, MG-ADL = Myasthenia Gravis MG Activities of Daily Living, IVIg = intravenous immunoglobulin.

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Table 4. Comparison between vaccinated and unvaccinated patients: clinical course of COVID-19 and myasthenia gravis

Outcomes	Vaccinated (n = 75)	Unvaccinated (n = 17)	*P*
Symptoms of COVID-19			
Upper respiratory infection symptoms	44 (71.0)	14 (93.3)	0.071
Fever	25 (41.0)	10 (71.4)	0.039
Antiviral agent	45 (72.6)	9 (69.2)	0.807
Hospitalization	3 (4.0)	6 (35.3)	< 0.001
ICU admission	1 (1.3)	3 (17.6)	0.019
Mechanical ventilation	0 (0.0)	2 (11.8)	0.032
MG deterioration	17 (22.7)	8 (47.1)	0.041
Rescue therapy	5 (6.7)	4 (23.5)	0.287
MG-ADL score (after COVID-19)	2.8 ± 4.3	6.8 ± 6.1	0.021
Δ MG-ADL (after to before)	0.1 ± 3.3	1.35 ± 5.8	0.225

Values are presented as mean ± standard deviation or number (%).
COVID-19 = coronavirus disease 2019, MG-ADL = Myasthenia Gravis Activities of Daily Living.

COVID-19 infection, 3 (17.6%) were unvaccinated, and 1 (1.3%) was vaccinated ($P = 0.019$). Both patients requiring mechanical ventilation were unvaccinated ($P = 0.032$). A total of 25 patients experienced MG deterioration after COVID-19 infection. The frequency of MG deterioration was significantly lower in the vaccinated patients (17/75, 22.7%) than in the unvaccinated patients (8/17, 47.1%, $P = 0.041$). The MG-ADL score after COVID-19 infection, which was measured in 91 patients 28.6 ± 16.5 days after COVID-19 infection, was higher in the unvaccinated patients (unvaccinated: 6.8 ± 6.1) than in the vaccinated patients (2.8 ± 4.3, $P = 0.021$). However, the change in the MG-ADL score (Δ MG-ADL = MG-ADL score after COVID-19 infection – MG-ADL score before COVID-19 infection) did not differ significantly between the two groups ($P = 0.225$).

After the inverse probability of treatment weighting for sex, age, and MG severity, the vaccinated and unvaccinated groups were balanced for these covariates (**Supplementary Table 1**). The odds ratio (OR) and 95% confidence interval (CI) between the weighted vaccinated and unvaccinated patients was calculated using univariate logistic regression (**Table 5**), which revealed that the risk of MG deterioration after COVID-19 infection was significantly lower in the former than in the latter (OR, 0.335; 95% CI, 0.178–0.633; $P = 0.001$). Moreover, the risk of developing upper respiratory tract symptoms (OR, 0.124; 95% CI, 0.040–0.386; $P < 0.001$) or fever (OR, 0.276; 95% CI, 0.142–0.536; $P < 0.001$) due to COVID-19 infection was significantly lower in the weighted vaccinated patients. The risk of hospitalization for COVID-19 infection was also lower in the weighted vaccinated patients (OR, 0.071; 95% CI, 0.022–0.223; $P < 0.001$).

Table 5. OR of COVID-19 and myasthenia gravis outcomes in the vaccinated patients over the unvaccinated patients after the inverse probability of treatment weighting

Outcomes	OR	95% CI	*P*
Symptoms of COVID-19			
URI symptoms	0.124	0.040–0.386	< 0.001
Fever	0.276	0.142–0.536	< 0.001
Antiviral agents	1.381	0.687–2.775	0.365
Hospitalization	0.071	0.022–0.223	< 0.001
ICU admission	0.707	0.050–10.039	0.798
Mechanical ventilation	-	-	1.000
MG deterioration	0.335	0.178–0.633	0.001

OR = odds ratio, COVID-19 = coronavirus disease 2019, ICU = intensive care unit, CI = confidence interval, MG = myasthenia gravis.

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DISCUSSION

The present study analyzed 92 patients who contracted COVID-19 between February 2022 and April 2022, when the omicron variant of SARS-CoV-2 was dominant in South Korea. The symptoms of COVID-19 were mild in most patients, except for 9 (9.8%) patients who required hospitalization for COVID-19 infection. The vaccinated patients had significantly milder symptoms and more favorable outcomes compared to the unvaccinated patients. The frequency of hospitalization was significantly lower in the vaccinated patients than in the unvaccinated patients. The frequency of ICU admission and the need for mechanical ventilation were also lower in the vaccinated patients than in the unvaccinated patients. MG deterioration after COVID-19 infection occurred in 25 of 92 patients. MG deterioration was also significantly less frequent in the vaccinated patients than in the unvaccinated patients.

Previous studies on COVID-19 infections in patients with MG were mainly conducted during the early stages of the pandemic when the alpha and delta variants were predominant and COVID-19 vaccination was not available.[11,15-17] In South Korea, however, the incidence of COVID-19 was very low during that period, and most COVID-19 infections occurred since February 2022, coinciding with the predominance of the omicron variant. According to data from the Ministry of Health and Welfare of the Republic of Korea, by March 2022, merely a month after the emergence of omicron dominance, 93.8% of all COVID-19 cases in South Korea are attributed to this variant.[18,19] COVID-19 vaccination became available from February 2021 and by April 2022, the full vaccination rate was about 86% of the population.[20] This situation in South Korea in 2022, which is the subject of the present study, stood in stark contrast to that of previous studies about COVID-19 infection in patients with MG. Previous studies reported the mortality rate for COVID-19 infection in patients with MG ranged from 11 to 27%.[8-10] However, in the present study, the mortality rate for COVID-19 infection was 1.1%. A retrospective study conducted in the United States reported that 53.8% of MG patients who contracted COVID-19 were hospitalized, and 17.9% needed mechanical ventilation.[21] Similarly, a cohort study conducted in Canada reported that the hospitalization rate for COVID-19 was 30.5% in patients with MG.[6] A study conducted in Brazil reported that 87% and 73% of hospitalized MG patients for COVID-19 needed ICU care and mechanical ventilation, respectively.[22] In the present study, 9.8% of MG patients who contracted COVID-19 were hospitalized for COVID-19, and 4.3% were admitted to the ICU. Among the 9 hospitalized patients with MG, 44% and 22% needed ICU care and mechanical ventilation, respectively. Although direct comparison between individual observational studies is not feasible, the prognosis of COVID-19 in the participants of the present study seems to be better than that reported by previous studies. The difference in the prognosis of COVID-19 may be attributed to the culprit variant of SARS-CoV-2 and vaccination status. Previous observational studies have suggested that the severity of the omicron variant is probably milder than that of earlier variants of SARS-CoV-2.[23-28] Meta-analyses have indicated that COVID-19 vaccines are effective in decreasing hospitalization and mortality as well as preventing COVID-19 infections.[29,30]

In the present study, the grade of MGFA clinical classification, MG-ADL score, the proportion of patients who experienced myasthenic crisis, and the rate of treatment with prednisolone were significantly higher in the unvaccinated group compared to the vaccinated group. These differences between the vaccinated and unvaccinated patients with MG have also been observed in previous studies investigating their intention to receive COVID-19 vaccination. In a previous study, patients with a severe form of MG exhibited reluctance toward

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vaccination.[31] The principal reasons for vaccine hesitancy were fears of the adverse effects of vaccination, worries about interactions between MG medications and COVID-19 vaccination, and doubts that the patients' own medical condition is not suitable for vaccination. These reasons may be related to the difference in the MG characteristics between vaccinated and unvaccinated patients in the present study. The rates of hospitalization, ICU care, and mechanical ventilation were significantly lower in the vaccinated patients than in the unvaccinated patients. This is consistent with the results of previous studies investigating the efficacy of COVID-19 vaccination in the general population, which demonstrated that the frequency of severe COVID-19 outcomes is lower in vaccinated individuals than in their unvaccinated counterparts.[32,33] COVID-19 vaccination may reduce morbidity in the MG and general populations.[6] The frequency of MG deterioration after COVID-19 was also significantly lower in the vaccinated patients than in the unvaccinated patients. After balancing the confounding covariates, sex, age, and MG severity before COVID-19 infection, vaccinated patients had a significantly lower risk of MG deterioration after COVID-19 infection. Therefore, COVID-19 vaccination may be effective in preventing MG exacerbation by reducing the morbidity of COVID-19 infection because MG can be exacerbated by infections and the severity of infection may influence the disease activity of MG.[34] However, this tendency should be interpreted with caution because the basic demographic characteristics and baseline MG status before COVID-19 infection differed between the vaccinated and unvaccinated groups. Although we employed the inverse probability of treatment weighting method to reduce the differences in baseline characteristics between the vaccinated and unvaccinated groups, differences in various factors might have influenced the outcomes of COVID-19 infection and the disease activity of MG.

This study has some limitations. First, this study entailed a by retrospective review of the patients' medical records. Some biases are inherent in the retrospective study design. Most importantly, this study could only investigate patients who visited hospitals. Patients who did not visit the hospital after COVID-19 infection, such as those who died succumbed to COVID, would not have been included in the present study and therefore this study cannot be free from selection bias. Further large-scale studies are needed to minimize bias caused by various confounding factors. Second, the treating physicians determined MG deterioration based on the patients' self-reported worsening and recovery of MG symptoms during the mandatory quarantine period, when the patients were not able to see their physicians. Third, only tertiary hospitals participated in the present study. Although MG is a rare disease and most patients are treated in tertiary hospitals, 30–40% of patients are treated at general hospitals and clinics in South Korea.[35] Therefore, the present study may have included patients with MG with relatively severe disease activity. To overcome this selection bias, we endeavor to conduct a study using big data from the National Health Insurance Service, which covers almost all South Koreans.

In conclusion, the results of the present study suggest that the clinical course and prognosis of patients with MG who contracted COVID-19 after the availability of COVID-19 vaccination and during dominance of the omicron variant of SARS-CoV-2 may be milder than those in the early days of COVID-19 pandemic when vaccination was unavailable. COVID-19 vaccination may reduce the morbidity of COVID-19 in the MG and general populations. COVID-19 vaccination may also be effective in preventing MG exacerbation by reducing the morbidity of COVID-19 infection.

SUPPLEMENTARY MATERIAL

Supplementary Table 1

Inverse probability of treatment weighting to assess the effect of COVID-19 vaccination on myasthenia gravis

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