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ORIGINAL COMMUNICATION

BNT162b2 mRNA COVID-19 vaccine three-dose safety and risk of COVID-19 in patients with myasthenia gravis during the alpha, delta, and omicron waves

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Abstract

COVID-19 affects the respiratory parenchyma and may potentially contribute to the tendency of myasthenia gravis (MG) patients to develop respiratory failure. It is, therefore, important to study the safety of vaccines against SARS-CoV-2 and to assess the risk of COVID-19 in MG patients. The safety of the three-dose BNT162b2 mRNA vaccine and outcomes of COVID-19 during the alpha, delta, and omicron waves were studied in MG patients as well as the rate of exacerbations and safety for a period of up to 6 weeks from each vaccine dose and patient morbidity and mortality during COVID-19 compared to the general population. 430 vaccine doses were administered across 150 patients. Thirteen patients (8.7%) complained of exacerbation within 6 weeks of each vaccine dose. Both MG onset rate and exacerbation rate were similar to previous years. MG exacerbation rate among fifteen patients who had COVID-19 was significantly higher (40%) compared to the rate following vaccination. During the alpha and delta waves, COVID-19 mortality and severe disease were significantly higher (26.7%) compared to the general population (0.96%). All of them were unvaccinated and had generalized MG. During the omicron wave, all the MG patients who contracted COVID-19 were vaccinated and had mild disease. We concluded that COVID-19 is hazardous for generalized MG patients, while the vaccination did not raise the risk for either exacerbation or new onset of MG and was associated with a reduced risk for severe COVID-19. Hence, it is recommended for generalized MG patients to get vaccinated.

Keywords Myasthenia gravis · COVID-19 · Vaccine · Safety · SARS-CoV-2 variants

Introduction

As part of dealing with the Coronavirus Disease 2019 (COVID-19) pandemic, the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), efforts have been made to vaccinate the population worldwide. In Israel, health authorities have made these efforts from the first days that the BNT162b2 mRNA vaccine was available, starting on December 20th, 2020 [1]. A third vaccine dose was introduced to the population in July 2021. As of December 23rd, 2021, nearly 6.5 million people in Israel (more than 73.3% of the population) had received one dose of the BNT162b2 mRNA COVID-19 vaccine, and more than 5.8 million people (66.2%) had received two doses of the vaccine, and more than 4 million people (47.2%) had received three doses of the vaccine. The safety profile of vaccines in the general population was reported as safe with very low rates of severe adverse events [2]. Nevertheless, it is important to examine the vaccine's safety in specific medical conditions, especially in autoimmune diseases, where there is a concern that activation of the immune response by vaccination may lead to disease exacerbation. A multi-center study focusing on immune-mediated disease flares 28-days from vaccinations has shown that flares are relatively rare in people receiving the COVID-19 vaccine, and while most of

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them were moderate in severity, some severe flares occurred [3].

The Omicron variant arrived in Israel in late December 2021, peaking at mid-January, and is continuing currently, albeit in a lower incidence [4]. While initially considered a variant of great concern due to great infectivity, the disease associated with the Omicron variant appears to be milder with greatly diminished morbidity and mortality compared to the alpha and delta variants [5, 6].

Myasthenia gravis (MG) is a classic autoimmune disease mediated by autoantibodies against post-synaptic neuromuscular junction epitopes [7–10].

Several case reports and studies with a small number of MG patients have reported the effect of different types of vaccines against SARS-CoV-2 [3, 11–19] and raise the possibility that MG may be aggravated following vaccination against COVID-19, with uncommon exacerbations according to a recent review [20]. The question regarding the ability of vaccines to aggravate MG pertains to various vaccines, such as vaccines against hepatitis B or papillomavirus. This raises the discussion about the safety of COVID-19 vaccines in MG patients [21]. A small-scale, questionnaire-based study was conducted to assess the early safety of these vaccines, and although reassuring, has not included boosters [22]. As far as we are aware, only one study has examined the safety of "booster" vaccinations, albeit with a small sample [23] and without addressing new-onset cases. To the best of our knowledge, no study has been conducted regarding the effect of the Omicron wave on this susceptible population.

On the other hand, MG may be triggered or worsened by infections in general [24]. Small-scale studies have been conducted regarding COVID-19 specifically, showing increased exacerbation rate, need for increased dosage, and prolonged hospital stay following infection [25, 26]. A case report has shown a myasthenic crisis as a complication of COVID-19 [27]. Moreover, most generalized MG patients are treated with immunosuppressive agents [7] which predispose them to infectious disorders [28]. Since the most severe exacerbation of MG is a myasthenic crisis, a respiratory insufficiency due to weakness of the respiratory muscles, and COVID-19 affects the respiratory parenchyma as well, it seems that infection with SARS-CoV-2 may be dangerous for MG patients. We previously reported about the poor compliance of MG patients to receive vaccines and the hesitation of their physicians to recommend it to those patients [29]. The reports about the association between the vaccine and disease activity and the fear of getting vaccinated among MG patients may lead MG patients to be less protected against COVID-19 even though they may be at increased risk for severe illness of COVID-19. Therefore, we conducted a cross-sectional study to examine the safety and risk for exacerbation following the BNT162b2 mRNA COVID-19 vaccine in patients with MG and evaluated the morbidity and mortality of MG patients who developed COVID-19 compared to the general population.

Methods

Study design and participants

This retrospective study was conducted at the Neuroimmunology Unit of Tel Aviv Sourasky Medical Center, a tertiary academic hospital in Israel. We have searched electronic medical records (Chameleon, version 5.12.2.43395, Elad Health) for patients diagnosed with MG as documented in their files until December 23rd, 2021. Myasthenia gravis diagnosis was defined by the typical clinical manifestation supported by a positive serology test for the anti-acetylcholine receptor (AChR) or anti-muscle specific kinase (MuSK) and/or supportive neurophysiological studies of single-fiber electromyography. Two hundred and fifteen MG patients were found to be eligible for the study. The study included two components. First was a cross-sectional study that examined the safety of the COVID-19 vaccine in MG patients. In this study, we included all the patients ($n=160$) that agreed to be interviewed about their COVID-19 vaccine dates and responses and whether they were infected and found to be positive in the PCR SARS-CoV-2 test (Fig. 1). Then, we examined the effect of COVID-19 disease on MG patients and included all diagnosed patients with MG ($n=215$), and compared disease outcomes to the general population.

We collected the demographic, clinical manifestations, current treatments, co-morbidity, and vaccination parameters from patient files and confirmed this information during the interview. In the case of patients who were reported deceased in their files, the reason for death was recorded. The study protocol was approved by the institution's ethics committee (Helsinki No. 0060-21) and all participants consented to participate in the study before the interview.

Patients were asked using a closed-form questionnaire in late December 2021 whether they had experienced an exacerbation of their myasthenic symptoms, the duration of the exacerbation, and whether they required a change in treatment or hospitalization following vaccination. Patients were also asked whether they experienced common adverse effects after administration of the vaccine and to clarify any other side effects they had experienced. Parallelly, we reviewed medical records for patients with confirmed exacerbation by a neurologist from our clinic and the nature of the medical treatment (if treated) was documented.

When patients reported an exacerbation, it was considered by the MG-ADL scale [30]. Exacerbation was confirmed if there was an increase of at least two points in the MG-ADL scale.

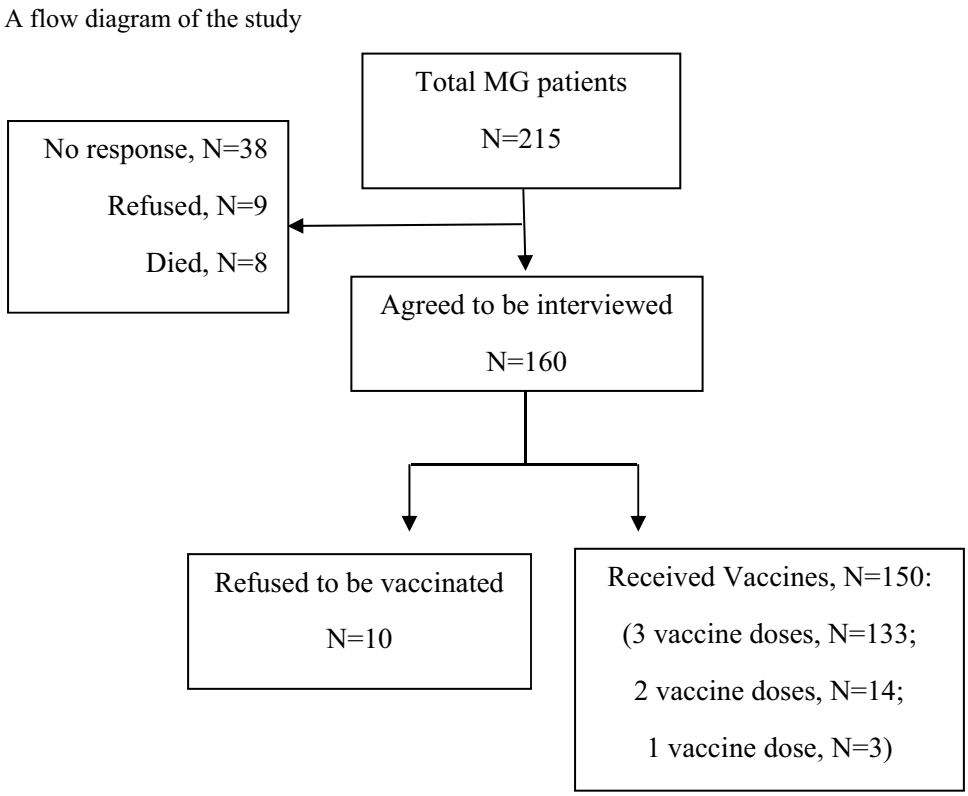

Fig. 1 A flow diagram of the study

Patients with documentation of SARS-CoV-2 infection were also asked whether they had exacerbations of MG during COVID-19, corroborated by data from patient files. Patients who did not receive full vaccination according to national guidelines were asked to explain the reason why.

The risk period for adverse effects and exacerbations following vaccination was defined as 6 weeks after each vaccine dose. The rationalization behind this definition is the period considered a vaccine-related effect in other studies in the context of Guillain–Barre syndrome [31] and H1N1 vaccination and MS exacerbations [29].

Cross-sectional study

Alpha and delta waves

To examine whether the rate of exacerbations has increased during the vaccination period, we defined the period between the day of the first vaccine and 6 weeks (42 days) after administration of the last vaccine dose for each participant as the risk period. Then, we compared exacerbation rates in the risk period to the corresponding period in 2019–2020. We selected this period to negate the possible effect of seasonality on MG exacerbations. Per definition, for this comparison, we required patients diagnosed before December 20th, 2019, exactly one year before the first vaccine dose in Israel.

To assess the outcomes of COVID-19 among MG patients, we compared the rates of morbidity and mortality due to COVID-19 in these patients to those of the general population according to official reports by the Israeli Ministry of Health (https://datadashboard.health.gov.il/COVID-19/general).

Omicron wave

Due to the resurgence of the Omicron variant in late December 2021 which peaked in mid-January 2022 and is continuing, we reached out to the patients who answered our questionnaire to evaluate the effect of the Omicron wave, using a separate questionnaire, distributed during mid-April 2022. Patients were asked whether they had contracted COVID-19 during the Omicron wave and its effects on their function, similarly to the previous questionnaire.

Statistical analysis

Categorical variables for a dependent variable were compared using McNemar's test and for independent variables by Chi-squared test, both with Yate's correction. In cases of values less than 5 in any of the cells of a contingency table, the Fisher's Exact Test was used. Odds ratio (OR) and 95% confidence interval (CI) were calculated. Continuous parametric variables were compared using the

unpaired student's *t*-test. A *p*-value of under 0.05 was considered statistically significant.

Table 1 Demographic and clinical characteristics of the patients

	Total	Male	Female	Age at onset (Years) Mean ± SD
Ocular MG	64	41	23	60.5 ± 16.8
Generalized MG	96	48	48	55 ± 18.6
Early-onset MG (Age ≤ 50 years)	47	15	32	34.1 ± 9.8
Late-onset MG (Age > 50 years)	113	74	39	66.8 ± 10.3
Seropositive for anti-AchR[a]	129	79	50	58.1 ± 18.1
Seropositive for anti-MuSK[a]	2	0	2	56.9 ± 6.3
Double seronegative (anti-AchR and anti-MuSK)[a]	28	9	19	52.7 ± 18.4
Thymectomy	36	15	21	43.1 ± 17.1
Total MG patients	160	89	71	57.2 ± 18

[a]One patient had no serology available

Results

Alpha and delta waves

By December 23rd, 2021, a search of medical records revealed 215 patients diagnosed with MG who have been followed up in our clinic from at least January 1st, 2020. Of them, 160 (74.4%) agreed to participate in the study while 9 patients refused, 38 did not respond and 8 died, 3 of them due to COVID-19 (Fig. 1). The demographic and clinical characteristics of these participants are described in Table 1 and the frequency of comorbidities as well as treatment types for MG are described in the Supplementary Table 1.

Overall, 150 patients with MG received 430 vaccine doses. All given vaccines were of the Pfizer BioNTech BNT162b2 mRNA COVID-19 vaccine (Fig. 1).

Exacerbation of MG following vaccines against SARS-CoV-2

Thirteen of the 150 patients (8.7%) reported worsening myasthenia symptoms within the postulated risk period of 6 weeks from each vaccine administration. Exacerbation was confirmed by neurological examination in 8 patients (5.3%). Among these thirteen patients, 9 were previously diagnosed with MG (patients no. 1–9 in Table 2), and 4 had new-onset MG (patients no. 10–13 in Table 2). Two

Table 2 MG patients who reported exacerbations within 6 weeks of vaccine administration

	Sex	Onset age	DD (Years)	MG type	Anti AChR	Days from vaccine	Vaccine number	Symptoms	Objective findings
1	F	70	2.5	G	SP	0.5	Third	Limb weakness	No
2	M	60	2.6	G	SP	0.5	Third	Head drop Limb weakness	No
3	F	33	10.7	G	SN	1	Second Third	Limb weakness Limb weakness	Yes Yes
4	F	49	5.6	G	SN	1	Second	Ptosis	No
						1	Third	Dysphagia	No
5	M	65	5.6	G	SN	1	Third	Limb weakness	No
6	M	24	6.8	O	SP	3	First	Limb weakness	No
7	F	50	1.5	G	SP	4	Second	Dysphagia	Yes
8	M	19	13.3	G	SP	30	Second	Limb weakness and ptosis	Yes
9	M	75	0.4	G	SP	10	Third	Ptosis, diplopia, head drop	Yes
10	F	70	0	G	SP	1	First	Dyspnea, dysphagia Limb weakness	Yes
11	M	71	0	G	SP	10	Second	Ptosis, dysarthria, dyspnea, neck weakness	Yes
12	M	81	0	O[a]	SP	10	Second	Diplopia	Yes
13	F	36	0	G	SP	24	Second	Ptosis, dysarthria, limb weakness	Yes

F female, *M* male, *G* generalized, *O* ocular, *SP* seropositive for anti-AChR, *SN* seronegative for anti-AChR and anti-MuSK

[a]Ocular MG presentation at onset

of the thirteen patients reported twice exacerbations after 2 different vaccine doses. Patients no. 6 and no. 10 who reported exacerbation after the first dose had received 2 more doses of vaccines without similar myasthenic complaints. Patients no. 7, 8, 11, and 12, who reported exacerbation after the second vaccine, received the third vaccine dose without further MG-related complaints. Patients no.8 and no. 13 had not received the third dose; the first has not disclosed the reason why and the second was afraid of further exacerbation. None of these exacerbations required hospitalization. Among those already diagnosed with MG who exacerbated, 3 patients were advised to increase prednisone dosage.

The duration of these exacerbations lasted for less than 21 days in 6/13 of these patients, over 3 months in 6/13 and one had an undeterminable exacerbation duration.

To assess the significance of the rate of exacerbations reported following the vaccine, we compared the number of exacerbations reported in the risk period for each patient to the number of exacerbations in the parallel period in the year before vaccination. A total of 125 patients, diagnosed before December 20th, 2019, and who were vaccinated at least once, were included in this comparison. Among these 125 patients that were vaccinated at least once and had disease duration for at least 2 years, 7 patients (5.6%) reported an exacerbation in the vaccination period in 2021 compared to 6 patients (4.8%,) in the control period in 2020 ($p=0.880$, OR = 1.176, 95% CI = 0.384–3.605).

Beyond exacerbations in previously diagnosed patients with MG, 4 cases were the first manifestation of MG within 6 weeks of one of the vaccines (patients no. 10–13, Table 2). This raises the question of whether the vaccine may trigger MG onset. To address this issue, we examined whether there was an increase in new MG diagnoses in the year in which the vaccines were given in Israel, which began on December 20th, 2020, and was practical during the whole year of 2021. Assuming that there was no meaningful change in the population that received services from the Neuroimmunology Unit at Tel Aviv Sourasky Medical Center between the years 2018–2021, the number of newly diagnosed MG patients was 14 cases in 2021, 19 cases in 2020, 27 cases in 2019 and 15 cases in 2018. This data does not support the notion of increased MG incidence in association with the mass vaccination by the studied vaccine against SARS-CoV-2.

We did not find significant differences between patients who reported to have an exacerbation of their myasthenia symptoms within 6 weeks after vaccination according to their sex ($p=0.876$, OR = 1.081, 95% CI = 0.3465–3.3742), MG age of onset (EOMG vs. LOMG, $p=0.285$, OR = 2.216, 95% CI = 0.703–6.988), MG type (ocular vs. generalized, $p=0.077$, OR = 0.249, 95% CI = 0.053–1.164) or the serology test (SP vs. SN, $p=0.703$, OR = 1.428, 95% CI = 0.366–5.565).

Adverse events of the SARS-CoV-2 vaccine

Vaccine-related adverse events were reported in 18 patients (12.0%) after the first vaccine, 28 patients (19.0%) after the second vaccine, and 31 patients (23.3%) following the third vaccine (Supplementary Table 2). Most reported side effects lasted less than 72 h and consisted mainly of flu-like symptoms (40.3%), local pain (26.0%), and isolated fatigue (14.3%). None of the patients who have suffered adverse effects, without exacerbation of MG, have chosen not to have an additional vaccine.

Vaccine hesitancy among MG patients

Ten out of 160 patients (6.3%) had not received a single vaccination and agreed to disclose their reasoning behind their decision. Four patients were afraid of allergies and general adverse reactions to the vaccine. Two refused to get the vaccine due to concerns regarding exacerbations of MG. Two refused because of prior COVID-19 infection (despite being eligible for another dose). One patient had refused to get vaccinated due to positive serology for antibodies against SARS-CoV2. The remaining patient refused to get the vaccine since his disease emerged shortly after getting a vaccination against hepatitis B.

The morbidity and mortality rate of COVID-19 among patients with MG

MG patients' COVID-19 outcome is reported in Table 3. Among 215 patients with MG, 15 patients (6.9%) developed COVID-19 after MG was already diagnosed. Of them, 6 patients (40%) had a confirmed exacerbation of MG during the illness of COVID-19. This exacerbation rate was significantly higher than the 6 weeks following vaccine administration (8.7%, $p=0.001$, OR = 7.026, 95% CI = 2.161–22.847).

Overall, 12 patients recovered and 3 died of COVID-19. Among the recovered patients, ten did not require hospitalization, and 2 were hospitalized in the intensive care unit (ICU). Of these two, one was intubated for artificial respiration. The rate of death from COVID-19 among these patients with MG was 20%, which is significantly higher than the rate of death from COVID-19 in the general population in Israel. On December 22nd, 2021, COVID-19 related deaths accounted for 8,239 out of 1,350,137 closed cases (recovered/discharged or deaths) of COVID-19 (0.6%, $p<0.0001$, OR = 118.166, 95 CI% 33.327–418.972). To objectively evaluate the rate of severe disease we compared the combined rate of death and patients who needed artificial respirator assistance due to COVID-19, 4 out of 15 (26.7%) among

Table 3 MG patients who contracted COVID-19 during alpha and delta waves

	Sex	Age at infection	MG type	Vaccinated Previously	COVID-19 Severity	MG Exacerbations
1	F	75	G	Yes (2)	Asymptomatic	No
2	F	52	G	Yes (1)	Mild	No
3	M	53	G	No	Asymptomatic	No
4	M	71	G	Yes (3)	Asymptomatic	No
5	F	35	G	Yes (2)	Mild	No
6	M	66	G	No	Severe (ICU)	Yes
7	F	49	O	No	Asymptomatic	No
8	F	58	O	No	Asymptomatic	No
9	M	76	O	Yes (2)	Asymptomatic	No
10	F	38	G	No	Severe (ICU)	Yes (Crisis)
11	F	20	G	Yes (1)	Asymptomatic	No
12	F	84	G	No	Death	Yes
13	M	49	G	No	Death	Yes
14	F	38	G	No	Mild	Yes
15	M	65	G	No	Death	Yes

F female, *M* male, *G* generalized, *O* ocular

patients with MG, to 13,005 out of 1,350,137 in the general population (0.96%, $p < 0.0001$, OR = 37.388, 95% CI = 11.903–117.433). As the median and most frequent age group for COVID-19 mortality in the general population was 80–90 years old, death or severity in the aforementioned MG patients could not be attributed to age alone (median age 65, 95% CI = 38.53–82.27). To negate for comorbidities, we compared MG patients who had comorbidities and patients who did not in terms of disease outcome: 3/11 of MG patients who had comorbidities had severe illness compared to 1/4 of patients who did not (OR = 1.09, 95% CI = 0.1548–7.6873, $p = 0.9$). To further negate immunosuppressive (IS) therapy, we examined whether disease course was affected by concurrent treatment with these agents. 4/11 of patients who were treated with IS had severe disease compared to 0/4 who were not (OR = 3.75, 95% CI = 0.2448–57.4513, $p = 0.3425$). Within the limits of this small sample size, no association is seen between the presence of IS treatment, the presence of comorbidities, or age on COVID-19 severity. To note, none of the patients who contracted COVID-19 had received treatment with rituximab at the time of infection.

Among these 15 MG patients who had COVID-19, 9 patients have not received any vaccine dose, 2 patients received 1 vaccine dose, 3 patients received 2 vaccine doses and 1 patient received 3 doses. Among the 9 MG patients that were infected with SARS-CoV-2 and who did not receive any vaccine dose, 5 died or needed ICU hospitalization (all of them with generalized MG) as compared to none of the 6 MG patients that were infected with SARS-CoV-2 and received at least one vaccine dose (OR = 15.8889, 95% CI = 0.691–365.156, $p = 0.0838$).

Omicron wave

Of the 160 patients who were interviewed originally, 130 had answered the second questionnaire regarding the omicron variant. Fifty-seven were female and 73 were male. Thirty-nine had early-onset MG and 91 had late-onset MG. Eighty-one had generalized MG and 49 had ocular MG. One hundred and six were seropositive for anti-acetylcholine receptor antibodies, two were positive for anti-MuSK antibodies and twenty-two were double seronegative. Twenty-nine underwent thymectomy.

Twenty-seven patients contracted COVID-19 during the omicron wave. The mean age at infection was 57.7 years (95% CI = 50.5–64. 9 years). Sixteen were male and eleven were female. Nineteen had generalized MG and 8 had ocular MG. Twenty-two were seropositive for anti-acetylcholine receptor antibodies and 5 were double seronegative. Eight of them underwent thymectomy.

Four patients were completely asymptomatic and the other twenty-three patients had mild to moderate disease without the need for hospitalization.

Eight patients (29.6%) reported an exacerbation of their symptoms, confirmed by a change in the MG-ADL scale. Six of them had generalized MG and two had ocular MG. Six complained of limb muscle weakness, 3 complained of dysphagia, 2 complained of dyspnea, one complained of dysarthria, and one complained of diplopia. Three patients required a transient change in treatment for worsening myasthenic symptoms. To note, all patients were vaccinated at least once (one four times, 5 three times, one patient two times, and one patient who was infected previously and vaccinated once). There were no significant differences between

the rate of exacerbation during the alpha and delta waves as compared to the rate during the omicron wave ($p=0.733$).

Revisiting mortality rates after the omicron wave

To further evaluate the effect of COVID-19 infection on patient mortality, we added up the mortality from COVID-19 in all waves and compared it to the general population.

42 patients with MG were infected with COVID-19, the youngest aged 26 years old. Of them 3 died (7.14%) at age 49, 65 and 84, while in the general population over the age of 30 years 1,930,911 contracted COVID-19 and 10,976 died (0.57%, $p=0.002$, OR = 13.455, 95% CI = 4.158–43.547).

Since most of the study population of our study had LOMG, we also conducted a stricter comparison of mortality rates due to COVID-19 in MG patients to the general population over the age of 50. It was found that 806,634 contracted COVID-19 and 10,685 died (1.32%, $p=0.018$, OR = 5.730, 95% CI = 1.771–18.545).

Discussion

The results of our study show that the rate of MG exacerbations during the period of exposure to vaccines does not exceed the rate in previous years without exposure to the vaccine, including the booster vaccine dose. This was also true even when we included the patient-reported exacerbations without corroborating data. If post-vaccination exacerbations occurred, they were mild and did not require hospitalization. As the patient population treated by our tertiary center did not change significantly over the years and we did not find an increase in the number of MG onsets in the year of exposure to vaccines compared to previous years, our data do not support the association between the introduction of either initial BNT162b2 doses or booster shots with increased MG onset rate.

The profile of the vaccine-related side effects in MG patients was generally mild, similar to previously described side effects in the general population [32, 33].

Conversely, the risk of mortality and severe illness due to COVID-19 in generalized MG patients was significantly increased. The data we presented suggest that vaccination has a protective effect in MG patients against severe illness and mortality. Among patients with MG, patients with COVID-19 were more likely to suffer an MG exacerbation than those who were vaccinated.

Nevertheless, our study has several limitations. One such limitation is recollection or recalls bias, inherent in all questionnaire-based studies which we tried to negate by parallelly inquiring into patient files and documentation of exacerbations, as well as performing analyses with and without relying solely on patient reports. Another is that in the comparison between SARS-CoV-2 positive patients and the general population we could not exclude them from the general population, but with their numbers being so few ($n=15$) one could assume no major effect was imposed on a population of millions. A different limitation of our study derives from the fact that there is no defined referral zone that our tertiary center presides over, therefore new-onset rates assumed that the patient population had not changed substantially over the years. This was supported by the fact that no new hospitals or MG centers have arisen in the study period. Another limitation is that the frequencies of ocular MG (40%) and EOMG (29.4%) in our studied group are not the typical distribution of these MG subtypes.

Furthermore, one is unable to determine the exact weight of each of the factors involved in ICU admission including the nature of the individual's disease, multiple infections (i.e., concurrent viral and bacterial infections), and medications, but when one considers the overall result, we have shown that risk was greatly increased among SARS-CoV-2 infected MG patients.

The Omicron wave appears to have affected our patients similarly to the general population [6], as all MG patients who contracted the Omicron variant suffered mild to moderate symptoms. None of the patients who reported an MG exacerbation required hospitalization, and less than half required a transient change in medical treatment. Revisiting mortality rates after the Omicron wave still demonstrated that MG patients are at higher risk for mortality compared to the general population regardless of age.

Given the reports of fear of vaccination in MG patients and physician's hesitation to recommend immunization [21], the results of our study demonstrate that it is important to strongly recommend vaccine against SARS-CoV-2 for MG patients, especially those with generalized disease, due to their significantly increased risk of mortality and severe disease, all in light of the safety profile of the vaccine among MG patients. To date recommendations regarding MG patients were reliant on extrapolations from other illnesses, mainly rheumatologic [3, 21] and other vaccines[34]. We provide real-world data on the effect of the vaccine on MG patients, and specifically, add knowledge regarding the third BNT162b2-mRNA vaccine dose and the Omicron wave, which was not examined in this patient population to date. As the world is in the stage of further immunizations against SARS-CoV-2, new concerns are rising [35, 36]. Our study supports the repeat vaccination of patients with MG. Future prospective studies are needed to corroborate the effect of further booster shots on MG patients.

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Declarations

Conflicts of interest All the authors have no competing interests to declare that are relevant to the content of this article.

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