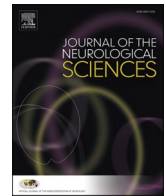




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Letter to the Editor



## Electronic health record derived-impact of COVID-19 on myasthenia gravis

## ARTICLE INFO

## Keywords

Myasthenia gravis  
 COVID-19  
 Outcomes  
 Hospitalization  
 Vaccination

## Dear Editor,

As effective vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerge, it is important to have timely real-world data that guides immunization prioritization for our patients and especially possibly more vulnerable neuromuscular populations [1]. Recent data have shown that patients with chronic autoimmune neuromuscular disorders who are on immunosuppression were more likely to require hospitalization with Coronavirus Disease 2019 (COVID-19) [2]. Similarly, recent preliminary data published from the COVID-19 Associated Risks and Effects in Myasthenia Gravis (CARE-MG) registry, demonstrated a mortality of 24% and MG relapse rate of 40% among 91 patients [3]. In order to further assess risk of infection and outcomes in myasthenia gravis (MG) we conducted an electronic health record (EHR) based study to address key data gaps.

De-identified patient information was extracted on December 22, 2020 using the TriNetX COVID-19 Research Network platform ([www.trinetx.com](http://www.trinetx.com)), one of the largest global COVID-19 datasets. Details of study approval, methods and data extraction are available in the supplementary appendix [2].

A total of 40,392 patients with MG were identified of which 380 had COVID-19 (Table 1). Mean age of patients with MG who developed COVID-19 was  $63.2 \pm 16.4$  years. Of the COVID-19 MG patients, 102 (26.8%) required hospitalization, 20 (5.6%) experienced MG exacerbation/crisis, and 26 (6.8%) died. Having MG was associated with a significantly increased risk of hospitalization (odds ratio, 3; CI, 2.4–3.8) and death (odds ratio, 4.3; CI, 2.9–6.4) when compared against the entire COVID-19 patient cohort in the TriNetX database, and remained significant when compared against an age and gender matched sub-cohort (Table 1).

While hospitalization, MG exacerbation, and death rates were lower than previously reported from the CARE-MG registry interim analysis, our current data continue to suggest high risk from COVID-19 in patients

with MG [3]. As a physician-reported registry the CARE-MG data may be partially skewed toward reporting more severe cases or other selection bias, we do acknowledge that physician-reported data would likely be more accurate as compared to an EHR database. As there are a multitude of limitations based on the nature of our study, we must be careful to avoid making more than basic or descriptive conclusions [2]. However, these results add to the small knowledge base of the impact of COVID-19 in MG patients and can aid in public health decision-making practices and recommendations. Our study demonstrates that while the rate of SARS-CoV-2 infection was comparable to the general population, the risk of hospitalization and death was greater.

Despite not having data from COVID-19 vaccines in MG currently, multiple studies suggest that the influenza vaccine is safe in MG patients for instance [4,5]. Additionally, both work by triggering immune response regardless of preparation differences, and would be expected to have similar safety in MG patients as in the general population. Considering present data available, patients with MG should be prioritized for SARS-CoV-2 vaccination with additional consideration of best practice standards.

## Disclosures

Dr. Roy reports no conflicts directly related to this work. Dr. Roy has served as a consultant for Alexion Pharmaceuticals. Drs. Kovvuru, Nalleballe, and Onteddu have no conflicts of interest to report. Dr. Nowak reports no conflicts directly related to this work. Dr. Nowak has received research support from the National Institutes of Health (NIH), Genentech, Alexion Pharmaceuticals, argenx, Annexon Biosciences, Ra Pharmaceuticals, Myasthenia Gravis Foundation of America, Momenta, Immunovant, and Grifols. He has served as consultant/advisor for Alexion Pharmaceuticals, argenx, CSL Behring, Grifols, Ra Pharmaceuticals, Immunovant, Momenta and Viela Bio.

<https://doi.org/10.1016/j.jns.2021.117362>

Received 15 February 2021; Accepted 17 February 2021

Available online 20 February 2021

0022-510X/© 2021 Published by Elsevier B.V.

**Table 1**  
Demographics and Outcomes of COVID-19 Patients with Myasthenia Gravis.

| Cohort characteristics                                      |  |  |
|---|--|--|
| No. of MG patients with COVID-19                            | 380 (out of 40,460) <sup>a</sup>   |  |
| Demographics  |  |  |
| Age, mean (SD), years                                       | 63.2 ± 16.4  |  |
| Women, n (%)  | 185 (48.7%)  |  |
| Men, n (%)  | 195 (51.3%)  |  |
| Race  |  |  |
| White Caucasian   | 241 (63%)  |  |
| African American  | 62 (16%)   |  |
| Unknown race  | 68 (18%)   |  |
| Ethnicity   |  |  |
| Not Hispanic or Latino                                      | 243 (64%)  |  |
| Hispanic or Latino  | 36 (9%)  |  |
| Unknown Ethnicity   | 101 (27%)  |  |
| Outcome   |  |  |
| Hospitalization   | 102 (26.8%)  |  |
| ICU requirement   | 38 (10%)   |  |
| Intubation  | 20 (5.3%)  |  |
| Death   | 26 (6.8%)  |  |
| MG Crisis/Exacerbation <sup>b</sup>                         | 20 (5.3%)  |  |
| Odds ratio (95% CI) of clinical outcome in MG with COVID-19 |  |  |
|   | Compared to entire COVID-19 cohort without MG (n = 370,009) <sup>c</sup> | Compared to age/gender matched COVID-19 cohort without MG (n = 380) <sup>d</sup> |
| Hospitalization   | 3 (2.4–3.8)  | 1.7 (1.2–2.5)  |
| ICU requirement   | 5.2 (3.7–7.3)  | 2.9 (1.5–5.5)  |
| Intubation  | 4.6 (2.9–7.3)  | 1.7 (0.8–3.5)  |
| Death   | 4.3 (2.9–6.4)  | 2 (1.1–3.9)  |

Myasthenia Gravis (MG); Intensive Care Unit (ICU); Confidence Interval (CI).

<sup>a</sup> Infection rate of 0.93% in the MG cohort.

<sup>b</sup> MG crisis/exacerbation was captured based on ICD code (see appendix for details).

<sup>c</sup> A total of 370,009 non-MG COVID-19 patients were identified in the database (out of 61,344,077).

<sup>d</sup> An age and gender matched non-MG cohort was identified by propensity score matching as a comparison group.

## Funding

None.

## Acknowledgement

We are thankful for the active support from the data scientist at the Arkansas Clinical Data Repository (AR-CDR) for this study. Direct guidance was obtained from TriNetX to ensure data accuracy for which we are extremely thankful and would like to acknowledge.

## Appendix A. Supplementary data

Supplementary material to this article can be found online at <https://doi.org/10.1016/j.jns.2021.117362>.

## References

- [1] COVID-19 Vaccines, 2021. <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines>.
- [2] S. Kovvuru, K. Nalleballe, S.R. Onteddu, et al., Immunosuppression in chronic autoimmune neurological disorders during the COVID-19 pandemic, *J. Neurol. Sci.* (2020) 117230.
- [3] S. Muppidi, J.T. Guptill, S. Jacob, et al., COVID-19-associated risks and effects in myasthenia gravis (CARE-MG), *Lancet Neurol.* 19 (12) (2020) 970–971.
- [4] E. Strijbos, M.R. Tannemaat, I. Alleman, et al., A prospective, double-blind, randomized, placebo-controlled study on the efficacy and safety of influenza vaccination in myasthenia gravis, *Vaccine.* 37 (7) (2019) 919–925.
- [5] L. Zinman, J. Thoma, J.C. Kwong, A. Kopp, T.A. Stukel, D.N. Juurlink, Safety of influenza vaccination in patients with myasthenia gravis: a population-based study, *Muscle Nerve* 40 (6) (2009) 947–951.

Bhaskar Roy<sup>a,\*1</sup>, Sukanthi Kovvuru<sup>b,1</sup>, Krishna Nalleballe<sup>b</sup>, Sanjeeva Reddy Onteddu<sup>b</sup>, Richard J. Nowak<sup>a,\*</sup>

<sup>a</sup> Yale University School of Medicine, New Haven, CT, USA

<sup>b</sup> University of Arkansas for Medical Sciences, Little Rock, AR, USA

\* Corresponding authors at: Department of Neurology, Yale University School of Medicine, P.O. Box 208018, New Haven, CT 06520, USA. E-mail addresses: [bhaskar.roy@yale.edu](mailto:bhaskar.roy@yale.edu) (B. Roy), [richard.nowak@yale.edu](mailto:richard.nowak@yale.edu) (R.J. Nowak).

<sup>1</sup> These authors contributed equally