Impact of COVID-19 Infection Among Myasthenia Gravis Patients- a Cerner Real-world Data™ Study

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Research Article

Keywords: COVID-19, Myasthenia gravis (MG), Cerner Real-World, infection

Posted Date: March 11th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-289348/v1

Version of Record: A version of this preprint was published at BMC Neurology on January 27th, 2022. See the published version at https://doi.org/10.1186/s12883-022-02564-x.

Abstract

Background:

Myasthenia gravis (MG) is an auto-immune disease, and the mainstay of therapy is immunomodulation. Such patients are at high risk of acquiring any infections. Hence, we sought to determine the impact of the current global pandemic COVID-19 infection in MG patients.

Methods:

For our study, we used Cerner Real-World Data^{TM} that was provided through Cerner's HealtheDataLab research tool. We ran a database query from January 2019 to July 2020 in our study. To extract these patients' data, we used ICD 9-CM, ICD-10, and SNOMED-CT codes. We report data using means, range, and prevalence rates. The p-values were calculated using the two-sample t-test and Pearson's chi-squared test.

Results:

In the COVID-19 data set, a total of twenty-seven myasthenia patients were identified with a positive COVID-19 infection, and four diagnosed with an exacerbation. Male to female ratio was equal and one unknown gender (3.7%) with a mean (± SD) age of 64.33 ± 18.42 years. This study group was compared with a non-COVID-19 data set in which a total of sixty-four myasthenia patients were identified, and twenty-three had an exacerbation. Among the hospitalized patients in the two groups, the mean length of hospitalization for all the myasthenia patients in the COVID-19 data set was 8.28 days (n=7), and the non-COVID-19 set was 4.33 days (n=6), and it was statistically significant (p-value= 0.007).

Conclusion:

The mean length of hospital stay is prolonged in Myasthenia patients who tested positive for COVID-19.

Background

Myasthenia Gravis is an auto-immune disease characterized by fluctuating weakness in the voluntary muscles caused by antibodies towards the neuromuscular junction. When severe weakness develops in the respiratory muscles, it leads to a significant life-threatening complication called a myasthenic crisis, resulting in respiratory failure. [1] Around 15 to 20% of myasthenic patients develop exacerbation that requires intubation resulting in hospitalization once in a lifetime. [2, 3] The current global pandemic caused by the COVID-19 predominantly presents with fever, tachypnea, and dyspnea, causing hypoxemic respiratory failure in severe cases. [4] Myasthenia patients who are on immunosuppressive drugs are at increased risk of COVID-19 infection and COVID-19 complications. [5] Hence we sought to determine the impact of COVID-19 infection in these patients.

Materials And Methods

This is a retrospective, observational study utilizing real-world data. For our study, we used Cerner Real-World Data™ that was provided through Cerner's HealtheDataLab research tool.[6] The COVID-19 dataset in HealtheDataLab contained de-identified patient data of one hundred and seventeen thousand (117K) patients from 62 contributing health systems after a database refresh in July 2020. The dataset contained all patients tested for COVID-19 at some point during their visits to one of the 62 health centers. The database contained tables with names like *condition, demographics, COVID-19 labs, encounters*, and *medication* that contained information for each of the de-identified patients. Note that the database undergoes a frequent refresh to keep the patients' data up to date.

To begin with, all patients that had Myasthenia Gravis were identified from the *condition* table using the ICD-9-CM codes (i.e., 358.0 and 358.01), ICD-10-CM codes (i.e., G70.00 and G70.01), and SNOMED-CT codes (i.e., 91637004, 230686005, 193207007, 230685009, 77461000119109, 77471000119109, 31839002, 55051001, 80976008) irrespective of their COVID-19 test result. We chose an exhaustive list of codes to avoid missing any Myasthenia Gravis patients in the database. The database only yielded G70.00 and G70.01, and in total, 91 patients had Myasthenia Gravis. A SQL join was done on the *condition* and *COVID labs* table to extract Myasthenia Gravis patients (with or without exacerbation) that had received a COVID-19 test done along with the test date. The patients were then divided into two sets: one with a positive COVID-19 test and the other set that contained patients that always tested negative for COVID-19. There were a total of 27 hospitalized Myasthenia Gravis patients (from November 2019 to July 2020) that tested positive for COVID-19. To find patients who always tested negative for COVID-19, we computed the set difference between all patients with Myasthenia Gravis (91) and those patients who had this condition and tested positive for the COVID-19 (27), and then manually verified the result. This set of non-COVID-19 patients contained 64 patients. For each patient in both the sets, we extracted information such as race, ethnicity, and gender from the *demographics* table. We extracted information on patient complications, comorbidities, and first-reported-date-of-condition from the *condition* table. We also extracted start date and end date of medications that were prescribed after the COVID-19 test result from the *medication* table. Finally, we extracted the discharge disposition and length of stay after the COVID-19 test result from *encounter* table. The number of deceased patients were obtained from the *demographics* table and were then verified using the latest discharge disposition from the *encounter* table. We report the data using means, range, prevalence rates in these two sets of patients. The p-values were calculated using the two-sample t-test and Pearson’s chi-squared test. The p-values are also reported for statistical significance (< 0.05).

Results

Twenty-seven myasthenia patients were identified with a positive COVID-19 infection with a mean (± SD) age of 64.33 ± 18.42 years, and four of them were diagnosed with an exacerbation.[7] In the non-COVID myasthenia study group, sixty-four patients were identified, with a mean (± SD) age of 63.23 ± 18.60

years, and twenty three had an exacerbation. The male-to-female ratio, mean age, race, and medications are described in Table 1, and the comorbidities and complications and their p-values in Table 2.

Table 1
Mean age, gender, race, and myasthenia drug distribution in the two groups.

	COVID Patients with Myasthenia (n = 27)		Non-COVID Patients with Myasthenia (n = 64)	
Mean age (± SD)	64.33 ± 18.42 (n = 27)		63.23 ± 18.60 (n = 64)	
Mean age (± SD) for patients with exacerbation	51.5 ± 14.93 (n = 4)		64.13 ± 17.95 (n = 23)	
Female	13	48.15%	36	56.25%
Male	13	48.15%	27	42.19%
Unknown	1	3.70%	1	1.56%
Caucasian	16	59.26%	46	71.88%
African American	4	14.81%	8	12.50%
Other racial group	7	25.93%	10	15.62%
Immune globulin intravenous	7	25.93%	13	20.31%
Methylprednisolone	9	33.33%	21	32.81%
Prednisone	18	66.67%	37	57.81%
Mycophenolate Mofetil	6	22.22%	3	4.69%
Pyridostigmine	16	59.26%	33	51.56%

Table 2
Comorbidities and complications in COVID-19 positive and non-COVID patients with Myasthenia.

Co-morbidities	COVID Patients with Myasthenia (n = 27)		Non-COVID Patients with Myasthenia (n = 64)		P-value
Hypertension	1	3.70%	4	6.25%	0.986
Diabetes mellitus	5	18.52%	6	9.38%	0.384
Obstructive Sleep apnea	5	18.52%	12	18.75%	0.979
Hyperlipidemia	9	33.33%	32	50.00%	0.144
Atrial fibrillation	3	11.11%	13	20.31%	0.452
Obesity	0	0.00%	1	1.56%	0.654
COPD	4	3.70%	13	4.69%	0.538
Complications	**COVID Patients with Myasthenia (n = 27)**		**Non-COVID Patients with Myasthenia (n = 64)**		**P-value**
Pneumonia	13	48.15%	28	43.75%	0.7
Septic shock	9	33.33%	13	20.31%	0.185
Acute Respiratory failure	10	37.04%	22	34.38%	0.808
Chronic Respiratory failure	1	3.70%	3	4.69%	0.725

Abbreviation: COPD, Chronic Obstructive Pulmonary Disease.

Among the COVID-19 positive myasthenia patients, thirteen developed pneumonia, nine patients developed septic shock, and ten patients developed acute respiratory failure. Out of four patients diagnosed with exacerbation, two expired, one got discharged home, and the other was discharged to skilled nursing facility. Among the hospitalized patients in the two groups, the mean length of hospitalization for all the myasthenia patients with COVID-19 was 8.28 days (n = 7), and that for the non-COVID-19 patients was 4.33 days (n = 6). The p-value was 0.007.

Discussion

Two case reports, a single case series, and one retrospective study on Myasthenia patients with COVID-19 infection reported till today. One case describes the myasthenic crisis secondary to COVID-19 infection. [8] Another case reported is a myasthenia patient with positive COVID-19 infection with a successful outcome. [9] In a case series, five myasthenia patients with positive COVID-19 were reported. [10] A retrospective study in Brazil was recently published describing the characteristics and outcomes of the COVID-19 positive Myasthenia patients. [11] The patients' outcomes reported in the aforementioned cases and studies are highly variable.

Comorbidities like hypertension, diabetes mellitus, cardiovascular disease, and respiratory diseases may pose a significant risk in developing complications in patients with COVID-19 infection. [12, 13] Diabetes and hypertension are the most common comorbidities in previous case series and studies. [10, 11] In our study, we found hypertension in only one patient among the COVID-19 positive group. Also, the most common comorbidity observed in our study in both groups is hyperlipidemia. The complications observed in our study are pneumonia, septic shock, acute, and chronic respiratory failure. There is *no statistical difference* among the distribution of the comorbidities and complications in both COVID-19 and non-COVID-19 groups of our study.

Infections are the most common triggering factors of exacerbation in myasthenia patients. [14, 15] A single case of myasthenic crisis secondary to COVID-19 infection was reported. [8] The combined use of Hydroxychloroquine and Azithromycin might have precipitated the crisis in that patient. [8] In our study, four patients with COVID-19 infection developed exacerbation, and the precipitating factor is likely to be the COVID-19 infection.

Our study observed *a statistically significant* higher mean length of hospitalization of 8.28 days in the COVID-19 group among the hospitalized patients compared to 4.33 days in the non-COVID-19 group. Infections are the most common etiology of Myasthenia exacerbation cases resulting in hospitalization. [16, 17] In an observational study, the average length of hospitalization from the myasthenia exacerbation was reported as 6.5 days. [15] In a large national registry study in Finland, the hospital's median length of stay with an exacerbation reported was around six days secondary to infection. [17] The mean length of hospital stay is prolonged in Myasthenia patients who tested positive for COVID-19.

Abbreviations

COVID-19: Corona virus; COPD: Chronic obstructive pulmonary disease; ICD: International Classification of Diseases.

Declarations

Ethics approval and consent to participate:

Not applicable. This study did not require any ethics committee approval, as only the de-identified patient data was utilized.

Consent for publication:

Not applicable.

Availability of data and materials:

The data that support the findings of this study are available from a third party [CERNER], but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

Competing interests:

The authors declare that they have no competing interests.

Funding:

No target funding reported.

Author Contributions:

SP is responsible for the data collection. LD, PR, AQ, and RG are responsible for the data interpretation and drafting of the manuscript. PR, AQ and RG are responsible for the revision of the manuscript.

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