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Impact of the COVID-19 Pandemic on Hospital Admission Rate, Length of Stay, and Mortality Rate for Patients with Chronic Obstructive Pulmonary Disease Exacerbation: A Retrospective Study

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Abstract

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a common cause of hospital admissions. Coronavirus disease 2019 (COVID-19) has large impact on patients with pulmonary diseases. The purpose of the study is to evaluate the impact of COVID-19 on patients with AECOPD.

Method: Retrospective study with two cohorts, the first period included patients with AECOPD before COVID-19 pandemic; the second period included patients with AECOPD since the beginning of COVID-19 pandemic. The length of stay (LOS), number of patients requiring mechanical ventilation, and all-cause mortality were calculated.

Results: There was a total of 55 (44.72%) patients in the pre-COVID period compared to 68 (55.28%) patients in the COVID period. In the pre-COVID period: 14 (19.44%) had hypertension, 26(36.11%) had diabetes, 27(37.50%) had ischemic heart disease, 3(4.17%) had myocardial infarction; in the COVID period: 20 (29.41%) had hypertension, 24(35.29%) had diabetes, 27(39.71%) had ischemic heart disease, 1(1.47) had myocardial infarction. The LOS was shorter in pre-COVID period compared to COVID period, 6.51(SD 5.02) days vs 8.91(SD7.88) days with P-value of 0.042 respectively. The total number of patients needing mechanical ventilation in pre-COVID period was similar to the COVID period with P-value of 0.555. All-cause mortality number was 2 (3.64%) in the pre- COVID period compared to 6 (8.82%) in COVID period with P-value of 0.217.

Conclusion: Study results revealed significant difference in length of stay for patients with AECOPD, patient in COVID period had increased LOS compared to pre-COVID period. There was no significant difference in the other parameters.

Keywords: Chronic obstructive pulmonary disease (COPD), Coronavirus disease 2019 (COVID-19), Length of stay (LOS)

1. Introduction

Coronavirus disease 2019 (COVID-19) is a highly heterogeneous disease with symptoms vary from asymptomatic infection, to mild disease, severe disease, or a critical illness that can progress to death in 1–2 % of patients.^{1,2} COVID-19 was declared by the World Health Organization (WHO) as a pandemic on March 11, 2020 and since that time there have been more than 6 million deaths worldwide. People with underlying respiratory diseases such as chronic obstructive pulmonary disease (COPD) or asthma were considered to be at significant risk for developing severe COVID-19 disease

with an arduous recovery.^{3,4} The discovery of the SARS-CoV-2 virus' ability to bind to angiotensin converting enzyme 2 (ACE2) receptors present in the lungs, heart, kidneys, brain, intestine, liver, pharynx and other tissues, depicted not only how adversely the virus can affect every system of the body, but the profound comorbidities can have on disease severity, progression, and outcome.⁵⁻⁹

Chronic obstructive pulmonary disease is a heterogeneous lung disease that results from inhalational exposure to oxidative irritants, whereby prolonged exposure leads to significant lung injury.^{10,11} Diagnosis of COPD requires the presence of incomplete reversible airway obstruction as

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assessed by pulmonary function test.^{12,13} According to the Global Burden of Disease Study, there was a prevalence of 251 million cases of COPD in 2016 with an estimated 3.2 million deaths in 2019.^{14,15} COPD exacerbation is defined by change or worsening in respiratory symptoms,^{16–18} and is usually associated with worsening airflow obstruction. A severe exacerbation is associated with increases in both short-term and long-term all-cause mortality.¹⁹

The aim of our study is to evaluate the impact of COVID-19 infection on rate of COPD exacerbation in patient who required hospital admission before and during the COVID-19 pandemic. The primary end point is to evaluate the effect of COVID-19 pandemic on COPD exacerbation admission rate. The secondary end points are: The length of stay (LOS), risk for intensive care unit admission, need for mechanical ventilation, and mortality rate.

2. Methods

This is a single-center, non-interventional, retrospective observational study using data gathered from the electronic medical record of patients admitted for treatment of acute COPD exacerbation. This retrospective study has two cohorts. The first cohort includes patients admitted to the hospital with the diagnosis of acute exacerbation of COPD (AECOPD) before the COVID-19 pandemic (January 1st, 2019 to December 30th, 2019) and the second cohort includes patients admitted with the diagnosis of acute exacerbation of COPD during the COVID-19 pandemic (April 1st, 2020 to March 31st, 2021). Both the pre- COVID-19 and COVID-19 pandemic periods were twelve months each.

Data was obtained by retrieval of admission records from the hospital's Electronic Medical Record (EMR). Principal diagnosis with ICD-10 codes of J44 and J12.81 were used to search within the EMR.

Demographic data (including age and sex) and clinical data (including date of admission, length of hospital stay and use of invasive mechanical ventilation) were collected. Additionally, data on other comorbidities including hypertension, diabetes, ischemic heart disease, and myocardial infarction were also retrieved. Finally, all-cause hospital mortality was calculated, and these findings were then compared between the two-groups based on age, sex, and comorbidities.

Inclusion criteria: 1) Age 45 or older, 2) Diagnosis of COPD based on previous spirometry, 3) Hospitalization with AECOPD, 4) COVID-19 test positive by PCR (for the second cohort). Exclusion criteria: 1) Age less than 45, 2) Known diagnosis of COPD admitted for causes of dyspnea other than AECOPD

like pneumonia, 3) Patients with coexisting pulmonary diseases including asthma-COPD overlap syndrome, bronchiectasis, lung volume reduction surgery, bronchial stenting, lung transplant or any other operative procedure.

3. Statistical methods and considerations

3.1. Descriptive analysis of the index of COPD admissions

This includes analysis of the proportion of patients admitted and discharged on a weekday, patients admitted and discharged on weekend, the proportion of patients admitted for less than one day, and a description of the LOS. Weekday was defined as Monday to Friday, and weekend as Saturday or Sunday.

3.2. Analysis of patients who died during the admission

A comparison was made of the age, sex, and deprivation scores of patients admitted with COPD before and during the COVID-19 pandemic. The differences between the groups were analyzed using the Chi-square test and the independent samples t-test.

The COPD admission rate, LOS and the mortality rate within one year before and one year during COVID-19 pandemic were evaluated.

3.3. Determinants of COPD admission rates, LOS and mortality

To determine the influence of COVID-19 on the admission rate, LOS and mortality, a two tailed partial correlation between the two groups was used. We used multiple logistic regression models to control for patient sex, age, and comorbidity.

4. Data collection, retention and monitoring

Data was collected in a HIPPA compliant manner, within secure servers. Data was de-identified per protocol. Data was collected for a retrospective review, from 01/01/2019 to 12/30/2019 and from 4/1/2020 to 3/31/2021. Our study did not require ongoing contact with subjects. Data and information were anonymized (but uniquely identified) before it was stored. The study was compliant with legal and regulatory requirements and research practices. Since the study posed minimal risk to the patient, it was granted a consent waiver.

5. Results

From January 2019 to December 2019, a total of 55 patients were admitted for COPD exacerbation (a twelve-month pre-COVID period), while from April 2020 to March 2021 a total number of 68 patients were admitted to hospital for COPD exacerbation (a twelve-month COVID period).

We observed that the number of patients younger than 60 (45–59) and above 59 were more in the COVID period (n = 39, 70.91 %) and (n = 48, 55.17) when compared to the pre-COVID period (n = 16, 29.09 %) and (n = 39, 44.83 %) with a p value of 0.618 and 0.391 respectively (Table 1). The percentages listed are based on percentages in one pre-COVID/ COVID group compared to the other. A binomial test was utilized to compare the distributions and yielded a ratio of 0.5.

There was no major difference based on sex demographics; in the pre-COVID period, the number of male patients was 29 (53.73 %) while the number of female patients was 26 (46.27 %) with p value of 0.788 respectively; the number of male and female patients admitted during the COVID period were 29 patients (42.65 %) and 39 patients (53.35 %) with p value of 0.275 respectively. The percentages listed are based on percentages in one pre-COVID/ COVID group compared to the other (Fig. 1).

When comparing comorbidities in the pre-COVID and COVID period: Hypertension was found in 14 (19.44 %) of patients in the pre-COVID period compared to 20 patients (29.41 %) in the COVID period, with a p value of 0.187; diabetes mellitus was seen in 26 patients (36.11 %) compared to 24 patients (35.29 %) with a p value of 0.382; ischemic heart disease was present in 27 patients (37.50 %) pre-COVID similarly to 27 patients COVID (39.71 %)

with a p value of 0.516; and myocardial infarction was present in 3 patients (4.17 %) compared to 1 patient (1.47 %) with a p value of 0.299 (Table 1, Fig. 2). Percentages listed are based on patients in a group with conditions compared to the total number of patients in the same group. A chi-square test was utilized.

The number of patients admitted with AECOPD during the pre-COVID period compared to the COVID period was 55 (44.72 %) and 68 (55.28 %) respectively with a p value of 0.241. The length of stay for the pre-COVID period compared to the COVID period was 6.51 days (SD 5.02) and 8.91 days (SD 7.88) respectively with a p value of 0.042 (Fig. 3). The number of patients who needed mechanical ventilation for the pre-COVID period compared to the COVID period was 3 (5.45 %) and 3 (4.41 %) respectively with a p value of 0.555. A dependent sample t-test was utilized (Table 1).

The number of patients admitted on weekdays compared to weekend days was 87 (70.73 %) and 36 (29.27 %) respectively with a p value of 0.466. The number of patients discharged on a weekday compared to weekend day was 105 (85.37 %) and 18 (14.63 %) respectively with a p value < 0.001 (Table 1). A binomial test to compare distributions was utilized. Because the ratio of weekdays to weekend days is 5:2, a proportion of 0.7143 was used.

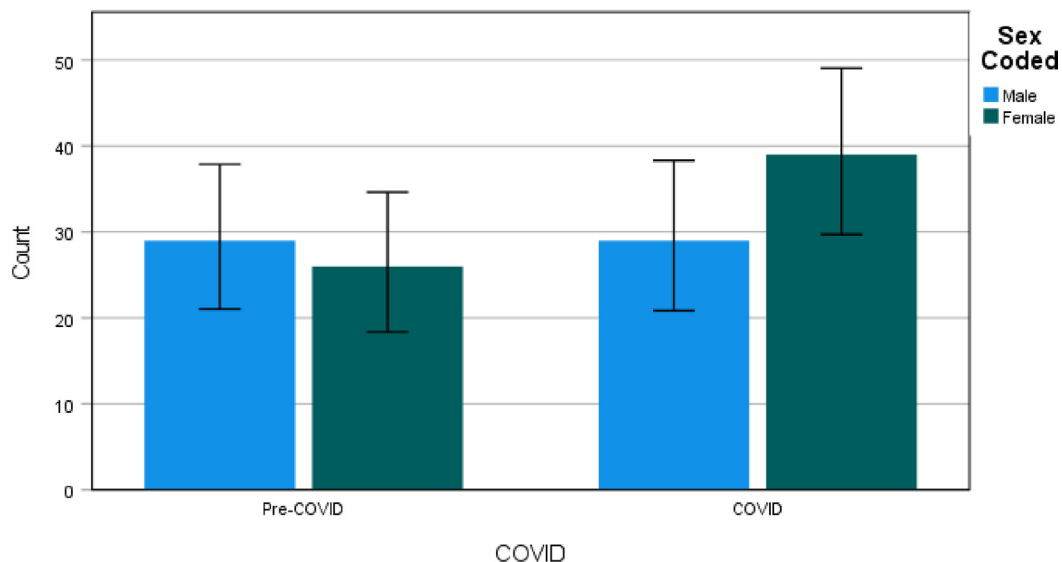
6. Discussion

COVID-19 pandemic had a significant impact on patients with underlying systemic disease and specifically those with underlying lung disease. Patients with COPD were considered at significant risk for developing severe disease.^{3,4} This hypothesis was

Table 1. Comparing various characteristics, age, comorbidities, outcomes, length of stay, need for mechanical ventilation and all-cause mortality in the pre-COVID and COVID period.

Characteristics	Characteristics pre- COVID COPD (n = 55)	Characteristics COVID COPD (n = 68)	P-value
Age (years)			
45–59	16 (29.09 %)	39 (70.91 %)	0.618
60 and above	39 (44.83 %)	48 (55.17 %)	0.391
Number of patients	55 (44.72 %)	68 (55.28 %)	0.241
Hypertension	14 (19.44 %)	20 (29.41 %)	0.187
Diabetes	26 (36.11 %)	24 (35.29 %)	0.382
Ischemic heart disease	27 (37.50 %)	27 (39.71 %)	0.516
Myocardial infarction	3 (4.17 %)	1 (1.47 %)	0.299
Length of stay	6.51 days (SD 5.02)	8.91 days (SD 7.88)	0.042
Patients needing mechanical ventilation	3 (5.45 %)	3 (4.41 %)	0.555
All - cause mortality	2 (3.64 %)	6 (8.82 %)	0.217
Variable	Week day	Weekend day	P-value
Admission	87 (70.73 %)	36 (29.27 %)	0.466
Discharge	105 (85.37 %)	18 (14.63 %)	<0.001

COVID cases by Gender



Error Bars: 95% CI

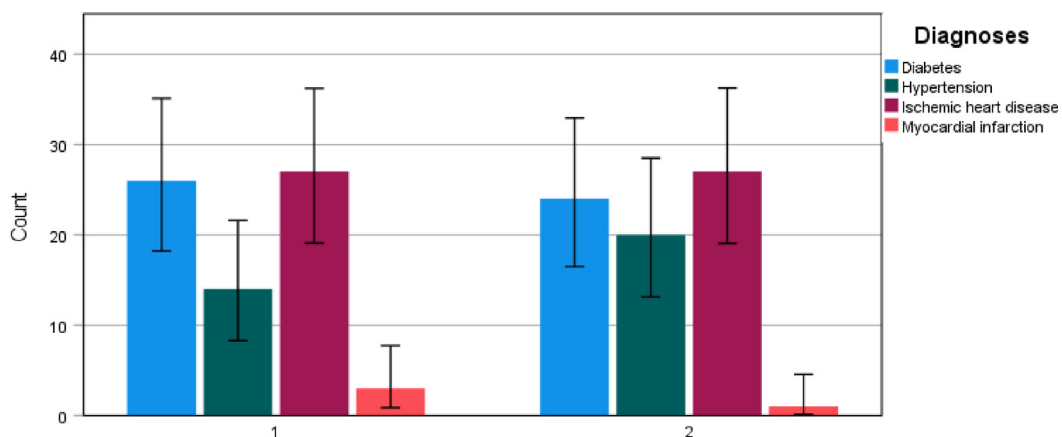
Fig. 1. Cases by sex demographics, pre-COVID compared with COVID period.

based on the understanding that respiratory viruses are a primary cause of COPD exacerbations; patients with COPD have weaker immune response to viral infections, an important factor in the disease process.^{3,20} Multiple studies of patients with different comorbidities admitted to the hospital with COVID-19 have revealed variable results regarding

morbidity, LOS and mortality. Comorbidities have been common among patients hospitalized with COVID-19 and there was significant correlation with outcome.⁵⁻⁸

Our analysis revealed that the rate of hospital admission for COPD exacerbation prior to the COVID-19 pandemic has not changed with the

Diagnoses



Error Bars: 95% CI

Error Bars: 95% CI

Fig. 2. Comparing comorbidities in the pre-COVID and COVID period.

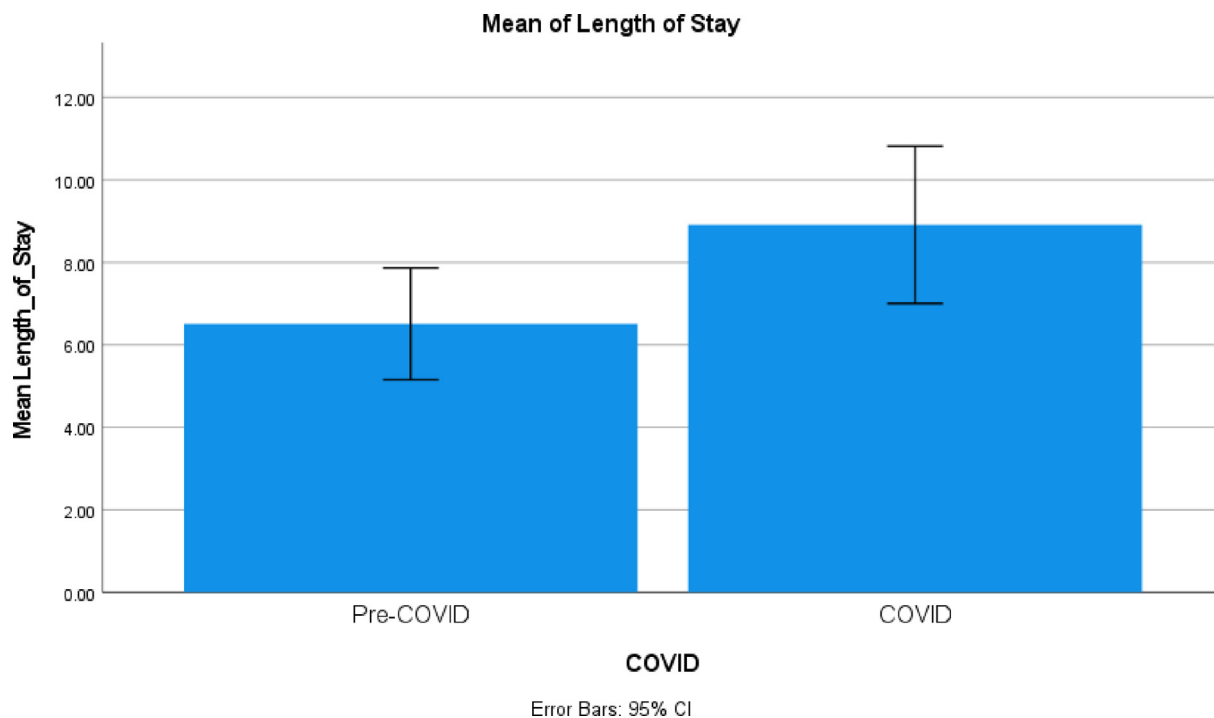


Fig. 3. Length of stay for the pre-COVID period compared to the COVID period.

pandemic itself. However, we did find a higher percentage of younger patients (age 45 to 59) admitted for exacerbation during the pandemic compared to pre-pandemic period (Table 1).

Jain and Yuan found that the male sex was predictive for ICU admission but not severe disease, suggesting that hospitalized patients with COVID-19 who are male and have severe disease may be at an increased risk of clinical deterioration and poor outcome(s).²¹ Our study showed a higher incidence of male patients admitted for COPD exacerbation during the pre-COVID-19 pandemic period while, in contrast, a higher incidence of female patients admitted during the COVID-19 pandemic period (Fig. 1).

Comorbidities may have a negative impact on outcomes for COPD patients infected with COVID-19. Most recent studies suggested that 3-month mortality in hospitalized COPD patients was correlated to a higher Charlson Comorbidities Index. Therefore, the presence of more underlying comorbidities may result in worse outcomes in COPD patients with COVID-19.^{22,23}

Surprisingly, many studies revealed that COPD was underrepresented among the comorbidities of COVID-19 patients when compared with other comorbidities or with the global burden of the disease.^{24,25} Moreover, COPD patients with COVID-19

pneumonia had more severe disease than non-COPD patients.²⁶

A meta-analysis by Jain and Yuan also found that COPD patients with cardiovascular disease and hypertension were at higher risk for severe illness and ICU admission.²¹

In June 2020, WHO stated that smoking could be a risk for the poor prognosis of COVID-19 infection.²⁷

When it comes to comorbidities, we found that during the pre-COVID-19 period, 14 (19.44 %) patients had hypertension, 26 (36.11 %) patients had diabetes, 27 (37.50 %) patients had ischemic heart disease and 3 (4.17 %) patients had myocardial infarction. However, during the COVID-19 pandemic there were 20 (29.41 %) patients that had hypertension, 24 (35.29 %) with diabetes, 27 (39.71 %) with ischemic heart disease and 1 (1.47 %) patient with myocardial infarction (Table 1).

Overall, we did not find a major difference in the distribution of comorbidities between the two groups. COVID-19 pandemic did not cause a higher rate of COPD exacerbations or increase the rate of hospital admissions. Jaber and colleagues conducted a study during the early period of pandemic and found a 50 % reduction in admission rate for COPD exacerbations compared to the pre-pandemic times, which might be explained by COVID-19 restrictions that resulted in a reduction of spread of respiratory

viral infections and in turn less triggers for acute exacerbation.²⁸

Multiple studies have found an apparent reduction in the rate of COPD exacerbation during the COVID-19 pandemic. However, the exact relationship between COVID-19 preventative measures and COPD exacerbation reduction, specifically hospital admissions for severe exacerbation, is yet to be identified.²⁹⁻³¹ Most of the studies addressing the rate of hospital admission for AECOPD were conducted during the early stages of the pandemic.

We found more patients admitted with COPD exacerbations during the COVID-19 pandemic than the pre-COVID-19 times; however, it did not reach statistical significance.

One of the most notable findings in our study was the difference in the length of stay. Patients with COPD exacerbation secondary to COVID-19 stayed longer in the hospital than those with COPD exacerbation in the pre-COVID period. The average LOS for patients admitted during the pandemic was 8.91 days (SD 7.88) compared to the average LOS of 6.51 days (SD 5.02) pre-pandemic, with a p value of 0.042 (Table 1, Fig. 3).

There was no significant difference between the number of patients needing mechanical ventilation when comparing the two groups. A recent study of the COPD impact on the mortality of patients hospitalized with COVID-19 infection revealed

conflicting results.⁶ Studies have shown that mortality rates among patients infected with COVID-19 with underlying chronic pulmonary disease is higher than patients without any underlying respiratory conditions.³² In another study, Guan et al. reported worse outcomes in COPD patients with COVID-19, which was consistent with our reported results despite the smaller sample size.⁵ Riou et al. evaluated the impact of chronic lung disease on mortality in patients with COVID-19 pneumonia and found a tendency for higher mortality.³³

A meta-analysis of 15 studies revealed that COVID-19 was associated with substantial increase in mortality rates in COPD patients.³⁴ Other studies have shown similar results with increased mortality among patients infected with COVID-19 and having underlying COPD.^{35,36} Our study found a higher mortality rate (all-cause mortality) during the COVID-19 pandemic duration compared to pre-COVID-19; however, it did not reach statistical significance likely because of the small sample size (Table 1, Fig. 4).

There are several limitations to our study. First, it was a single-center retrospective study. Furthermore, the sample size was small and not sufficient to illustrate a statistical significance on multiple variables. Moreover, the study had potentially unmeasured confounding factors, despite the inclusion of the age, sex, and systemic comorbidities. We did not

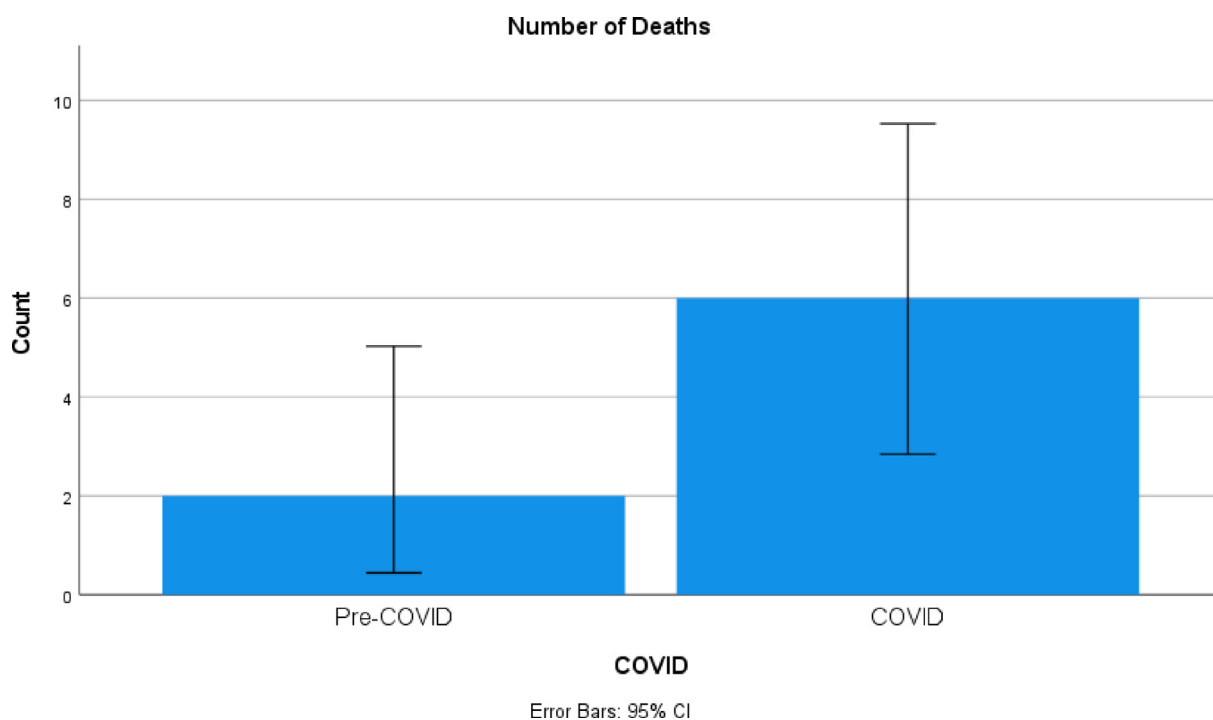


Fig. 4. Mortality for the pre-COVID period compared to the COVID period.

have cause-specific mortality. Lastly, COPD is underdiagnosed in the general population, and many patients that were admitted to the hospital may have undiagnosed COPD and thus likely were not effectively included within our sample size.

7. Conclusion

To our knowledge, this is the first study to evaluate the impact of the COVID-19 infection on COPD exacerbation length of stay. Our data concludes that patients admitted with COPD exacerbations have a longer duration of hospital stay than those admitted with COPD exacerbations prior to the COVID-19 pandemic. Other variables in this study also showed a difference in mortality rate and ICU admissions; however, it did not reach statistical significance. This could be partially explained by a small sample size. Further studies evaluating the impact of COVID-19 on COPD admission rate, LOS, need for mechanical ventilation, and mortality are needed, preferably with a larger sample size.

Conflict of interest

The authors declare no conflict of interest.

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