C - Reactive Protein Levels among COVID-19 Positive And Negative Patients With Chronic Obstructive Pulmonary Disease And Asthma: An Observational Study

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Abstract

Introduction: Evidence suggests there is an increased risk of severe pneumonia and poor outcomes when patients with COPD develop COVID-19. This increased risk has been postulated to the insufficient underlying lung reserves or increased expression of ACE-2 receptors in small airways. With this background, we conducted a study to understand the association of CRP levels among COPD patients with and without COVID-19 infection.

Materials and methods: A retrospective observational study was conducted among the patients with COPD admitted under the department of medicine of Dr. Punjabrao Memorial Medical College, Amravati. The data records of COPD patients admitted for six months [March 2021 to August 2021] were reviewed. We included all the COPD and bronchial asthma patients in the present study. Those patients with a history of cardiac failure were excluded from the present study. We took verbal consent from the individuals included in the study. Age, sex, co-morbidities, clinical symptoms, vital signs and laboratory indices, routine blood tests, liver, and kidney function tests, and C-reactive protein were retrospectively reviewed and documented.

Results: The mean age of the cases was 52.34 ± 9.23 years with male preponderance (69.77%). Fever (83.72%) and dry cough (63.95%) were the most common symptoms reported in the present study. The median levels among COVID-19 positive patients was 86.75 [28.33 to 124.20] and among the COVID-19 negative had median levels were 32.45 [10.34 to 62.34] and this difference was statistically significant.

Conclusions: We found 5th decade was the most common age group in our present study. Diabetes and hypertension were the most common associated comorbidities. The average CRP levels among the patients with RT-PCR positive were higher when compared to COVID-19 negative patients.

Keywords: COVID-19; COPD, C-reactive protein

Introduction

In December 2019, the world witnessed a pandemic of unknown viral pneumonia, with Wuhan city in China as the epicenter. [1] The aetiological agent of this disease was initially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, in February 2020 World Health Organization (WHO) renamed it Coronavirus Disease 2019 (COVID-19). [2,3] COVID-19 infections are transmitted mainly through the respiratory tract with a high transmission speed and infectivity. [4] Therefore, it is imperative that the impact of COVID-19 illness among patients with any other pulmonary insult would be devastating. Hence, it is natural to fear that patients with underlying chronic obstructive pulmonary disease (COPD) would have excess risk and can manifest into more severe manifestations of COVID-19 infection.[5]

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Furthermore, there is an increased risk of severe pneumonia and poor outcomes when patients with COPD develop COVID-19. This increased risk has been postulated to the insufficient underlying lung reserves or increased expression of ACE-2 receptors in small airways. [5] C-reactive proteins are an acute-phase reactant that has been regarded as a marker for diagnosis and prognosis in COVID-19 infection. Also, poor outcomes among COPD patients are associated with higher CRP levels in the literature studied. [6,7] However, CRP levels among COVID-19 disease and COPD have been less reported. Hence, we conducted this study to understand the association of CRP levels among COPD patients with and without COVID-19 infection.

Materials and methods:

A retrospective observational study was conducted among the patients with COPD admitted under the department of medicine of Dr. Punjabrao Memorial Medical College, Amravati. The data records of COPD patients admitted for six months [March 2021 to August 2021] were reviewed. We included all the COPD and bronchial asthma patients in the present study. Those patients with a history of cardiac failure were excluded from the present study. We took verbal consent from the individuals included in the study. Written consent was waived due to the existing infectiousness of the disease. We took the necessary permissions from the records in-charge of the institution to collect the data and ethical clearance before starting the study. We conducted a pilot study in which the difference in the CRP levels among COVID-19 positive and negative COPD patients was 20 mg/dl. Considering this with a 95% confidence interval and 80% power, we found the minimum sample size to be 40 in each group. So we have considered a total of 80 cases in the present study. We included 86 patients in the present study for our convenience.

Definitions:

Definitions for the categorization of COVID 19 were adapted using WHO guidelines. [8] Critical COVID 19 was defined by the presence of acute respiratory distress syndrome, sepsis, septic shock, or other conditions that would generally require the provision of life-sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor treatment. Severe COVID 19 infection was defined by the presence of oxygen saturation < 90% on room air, respiratory rate > 30 breaths/min in adults, signs of severe respiratory distress (accessory muscle use, inability to complete whole sentences, etc.). Non-severe COVID-19 infected patients were those patients who were not categorized into severe and critical COVID 19 infection.

Research methods:

Age, sex, co-morbidities, clinical symptoms, vital signs and laboratory indices, routine blood tests, liver, and kidney function tests, and C-reactive protein were retrospectively reviewed and documented.

Statistical analysis

The data was collected, compiled, and analyzed using EPI info (version 7.2). We used sample size based on the correlation coefficient formula using the online calculator by the clinical and translational science institute for sample size calculation. The qualitative variables were expressed in terms of percentages. The normality of the data was tested using the Kolmogorov Smirnov test. We defined the quantitative variables in terms of mean and standard deviations for average data and duration of the median and inter-quartile range (IQR) in non-normal data. The difference between medians of more than two groups was tested using the Wilcoxon rank-sum test. The difference between the two proportions was analyzed using the chi-square or Fisher exact test. To test the difference medians of the two groups, Mann Whitney U test was used. Pearson's correlation coefficient was used to find the correlation between the quantitative variables. All the analysis was two-tailed, and the significance value was set at 0.05.

Results:

We have included 86 cases in the present study.

Table 1: Demographics of the sample

Demographic particulars	Frequency	Percentage
Age group		
<40	12	13.95
40 to 50	27	31.40
50 to 60	28	32.46
60 to 70	21	24.42
>70	12	13.95
Gender		
Female	26	30.23
Male	60	69.77
Associated diseases		
Diabetes	22	25.58
Hypertension	34	39.53
Ischemic heart disease	6	6.98
HIV/AIDS	3	3.49
Cerebrovascular accidents	3	3.49

The mean age of the cases was 52.34 ± 9.23 years with male preponderance (69.77%). Diabetes (25.58%) and hypertension (39.53%) were the most common associated diseases in the present study.

Table 2: Distribution of the COPD cases based on RT-PCR swab

RT-PCR swab	Frequency	Percentage
Positive	43	50.00
Negative	43	50.00
Total	100	100.00

Of the 86 cases studied, 50.00% were positive for RT-PCR.

Table 3: Distribution of the cases base on the chief complaints (n=86)

Chief complaints	Frequency	Percentage
Cough with expectoration	26	30.23
Fever	72	83.72
Fatigue	29	33.72
Dry cough	55	63.95
Breathlessness	65	75.58
Headache	11	12.79

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Diarrhoea	4	4.65

Fever (83.72%) and dry cough (63.95%) were the most common symptoms reported in the present study.

Table 4: Distribution of the CRP levels of patients with COPD

CRP levels	COVID-19 positive		COVID-19 negative		P value
	Median	**IQR**	**Median**	**IQR**	
	86.75	28.33 to 124.20	32.45	10.34 to 63.34	<0.001

The median levels among COVID-19 positive patients was 86.75 [28.33 to 124.20] and among the COVID-19 negative had median levels were 32.45 [10.34 to 62.34] and this difference was statistically significant.

Chart 4: Distribution of the CRP levels of patients with COPD
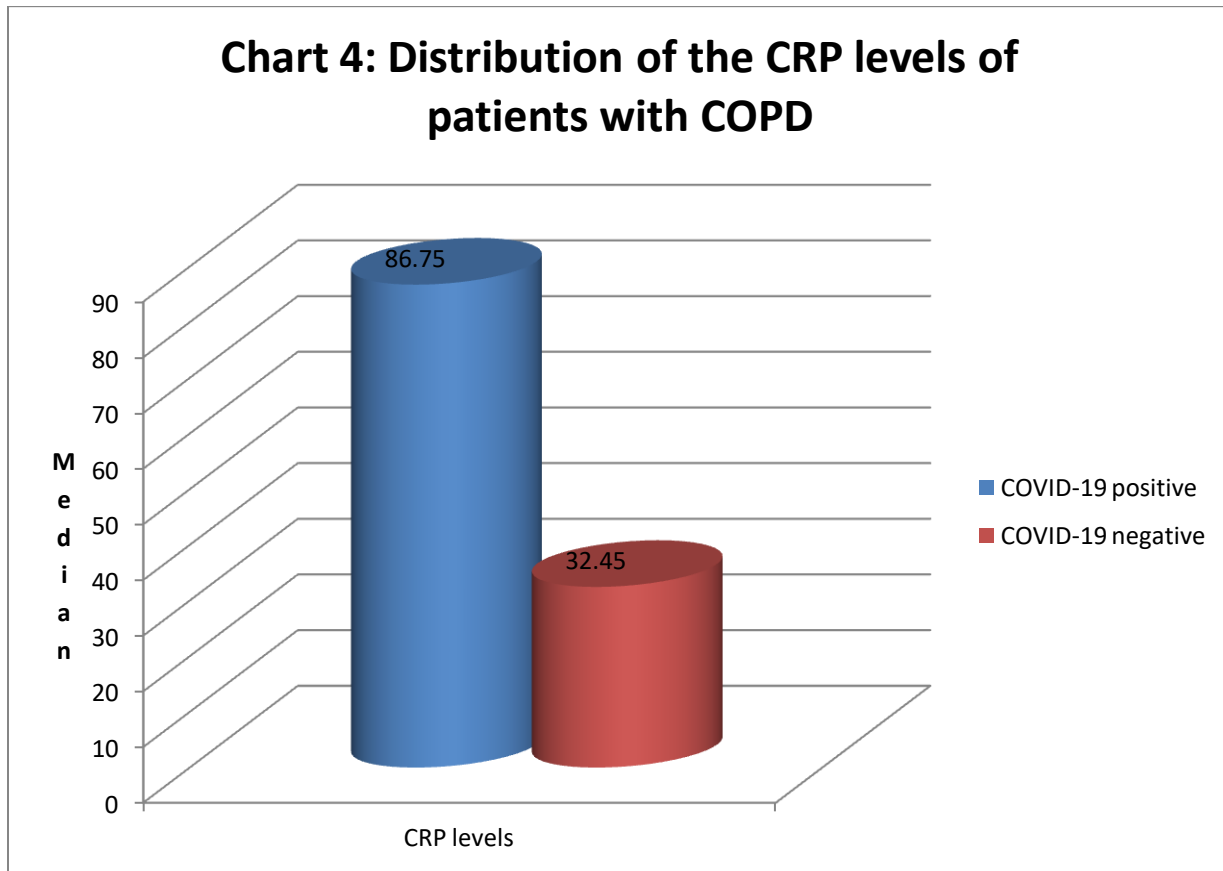
Discussion:

The present prospective study is, for our information, one of its kind to test the hypothesis of CRP levels among COPD patients with COVID-19 infection. Many studies have inferred that there are raised CRP levels among the patients with COVID-19 disease as tested by RT-PCR.[6,7] Two essential things to be noted in a specific cohort of COPD: they are more prone to infection due to the obstructive nature of the disease, and two, the risk of recurrence of the condition will be more when compared to the patients without

COPD.[9] As we all know, COPD is a progressive enhanced chronic inflammatory response in the airways. It is a multi-factorial disease composed of non-modifiable and modifiable risk factors.[10,11]

C-reactive protein (CRP) is a β-globulin, increased in production in acute illness, contributing to the activation of the complement system; it is termed C because it causes precipitation of fraction C of extract of pneumococci, such as erythrocyte sedimentation rate (ESR), CRP increased in many inflammatory and infectious problem, and it is nonspecific but a

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sensitive test for acute illness; moreover, the fluctuation of CRP level is more rapidly changeable with the change of clinical status as compared to the slow change in ESR; consequently, monitoring the activity of disease process will be more valuable. Trivial increase in CRP can be detected by techniques that determine high-sensitivity CRP test (hsCRP); the emergence of these techniques has led to the rise in the use of hs-CRP in many acute and acute chronic illnesses, including inflammatory, infectious, degenerative, endocrine, metabolic, and even neuropsychiatric problems. There are various studies on the importance of hs-CRP in assessing the severity and outcome of illnesses such as acute myocardial infarction and dementia. [12,13] There are continued and considerable concerns for applying hs-CRP assessment in asthma, and multiple studies focused on the relation of asthma severity as assessed by symptoms questionnaire and spirometric values with the levels of hs-CRP in adult and pediatric age groups.

For the past four decades, asthma has been considered a chronic inflammatory condition associated with acute exacerbation. Several underlying conditions have been associated with severe acute respiratory syndrome coronavirus two illness, but it remains unclear whether underlying asthma is associated with worse coronavirus disease 2019 (COVID-19) outcomes.[14,15] The Centres for Disease Control and Prevention and the American Academy of Allergy, Asthma & Immunology consider asthma a risk factor for severe COVID-19. [16] Coronavirus is among the top 5 isolated viruses during acute asthma exacerbations, with a higher prevalence in adults. However, the previous severe acute respiratory syndrome coronavirus outbreak of 2003 was not associated with increased asthma exacerbations. A handful of early studies from China reported underlying respiratory diseases as comorbidity among hospitalized patients with COVID-19, with a few explicitly mentioning an underrepresentation of asthma in hospitalized patients. In the United States, where asthma prevalence is twice that of China, several reports have documented wide ranges of asthma prevalence associated with COVID-19, ranging from 9% to 25% of hospitalized patients. [15,17]

The present study focused on the CRP levels among COPD patients with or without RT-PCR positive status and found that CRP levels were significantly higher among the patients who had COVID-19 infection. Similar inferences have been drawn by studies conducted by Smilowitz NR et al[18], Mestri NB et al[19], Wang L et al[20],and Zavereh MSH et al [21]. But, the main difference between our study with these studies is that cohort was heterogeneous in the latter. These studies also reported a cumulative increase in the CRP levels as the stage of COVID-19 infection increases. Nonetheless, one of the pioneer studies inferred that there are raised CRP levels among COVID-19 and COPD patients. However, the study had some limitations. It was a cross-sectional study with and small sample size. Longitudinal studies with a multicentric approach would help generate and test the hypothesis in a better way.

Conclusions:

We found 5th decade was the most common age group in our present study. Diabetes and hypertension were the most common associated comorbidities. The average CRP levels among the patients with RT-PCR positive were higher when compared to COVID-19 negative patients.

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