

**Research Article** 

# Association between Chronic Obstructive Pulmonary Disease and Severity of COVID-19 in a Tertiary Care Centre of Pune City, Maharashtra

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## INFO

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# ABSTRACT

*Background:* COVID-19 is a global pandemic caused by SARS-CoV2, spreading across every continent in world. The risk of developing severe COVID-19 with underlying disorder like COPD might be higher as compared to patients with no comorbidity. This study was undertaken to assess the association between COPD and severity of COVID-19.

*Material & Methods:* This was a hospital-based cohort study conducted between July to December, 2020. Study subjects were confirmed COVID-19 patients admitted to this tertiary care centre and all patients were followed up to final outcome as discharge or death. Depending upon the history of COPD total 113 COVID-19 patients with COPD (exposed) and 339 COVID-19 patients without history of COPD (unexposed) were included in analysis. Statistical analysis was done using logistic regression analysis, and adjusted odd's ratio with 95% CI were calculated.

*Results:* Age >60 years (OR = 1.38, 95% CI 1.12–3.30) and breathlessness (OR = 2.42, 95% CI 1.21–4.85) were independent risk factors for mortality in COVID-19 patients. In addition to this, other co-morbidities were associated with mechanical ventilation. On multivariable analyses, COPD was not significantly associated with mortality in COVID-19 (OR 0.93; 95% CI 0.15–1.58).

*Conclusion:* Underlying COPD was not an independent risk factor for poor outcome in COVID-19 patients.

**Keywords:** COVID-19, COPD, Mechanical Ventilation, Severity of COVID-19

## Introduction

COVID-19 is a global pandemic caused by SARS-CoV2 (severe acute respiratory syndrome Corona Virus-2), spreading

across all the continents in the world.<sup>1,2</sup> The infection of SARS-CoV2 can spread through aerosol particles of cough, sneeze or while talking from a person infected with SARS-

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CoV2.<sup>3,4</sup> The clinical manifestations of COVID-19 range from asymptomatic or mild symptoms like cough, runny nose to a serious lung involvement like pneumonia, acute respiratory distress syndrome and multiple organ dysfunction syndrome (MODS) and can even lead to fatality.<sup>5</sup> India reported its first case on 20th Jan, 2020 in Thrissur district of Kerala with a history of travel to Wuhan city, China.<sup>6</sup> Later, on 9th Mar, 2020, the state of Maharashtra reported its first confirmed case of COVID-19 in the Pune city which is one of the worst hit city in the country amid this pandemic.<sup>4,10</sup> Currently, India reports 2nd highest number of total COVID-19 cases in the world with around 33.8 million confirmed cases and 0.449 million deaths due to COVID-19 pandemic at the end of 1st October, 2021.<sup>1</sup> Maharashtra reported the highest number of COVID-19 positive cases in India with 6.56 million confirmed cases and 0.139 million deaths with the fatality rate of 4.5% till 1st October, 2021.8 Pune, being the 2nd most populous city in Maharashtra, also witnessed highest number of cases in the state since the beginning of the pandemic.<sup>9</sup> The course of COVID-19 disease is severe with higher mortality in patients with underlying medical conditions like diabetes, hypertension, chronic obstructive pulmonary disease (COPD), etc.<sup>5</sup>

COPD is a chronic disease of lungs with restraint airflow that is irreversible and presents with breathlessness, wheeze, and cough with expectoration.<sup>11</sup> It includes both emphysema and chronic bronchitis.<sup>11</sup> History of smoking and environmental or occupational exposure are the major risk factors to cause COPD.<sup>11</sup> The risk of developing severe COVID-19 with underlying disorder like COPD might be higher as compared to patients without any comorbidity.<sup>5</sup> A study has shown higher mortality among patients with pre-existing COPD in COVID-19 patients.<sup>13</sup> The course and progression of COVID-19 in the admitted patients is critical, especially with those having comorbidities like COPD. As the presence of COPD has a rapid and severe progression in COVID-19 patients and the city of Pune reported higher mortality due to COVID-19 as compared to other districts of Maharashtra, the assessment of impact of COPD on the severity of COVID-19 will be quite helpful for further prevention of deaths occurring due to COVID-19 in cases of COPD. Hence, this study was planned with an objective to assess the association of COPD with the severity of COVID-19.

## **Materials and Methods**

The current study was a hospital-based cohort study conducted in Sassoon General Hospital. This was a tertiary care hospital in Pune and was a dedicated COVID hospital (DCH) for isolation and management of suspected and confirmed cases of COVID-19 with moderate to severe in condition during the pandemic.<sup>12</sup> The study was conducted for a period of 6 months from July to December, 2020.

## **Conduct of the Study**

All sociodemographic characteristics like age, sex, education, occupation, socio-economic status, duration of hospital stay, history of contact with COVID-19 positive patient, history of symptoms due to COVID-19, the duration of onset of symptoms to hospital admission, history of known case of COPD, history of other co-morbidities and history of mechanical ventilation was taken personally from the patients or patients' relatives with informed consent in a predesigned proforma.

## Patient Recruitment and Follow-up

The study subjects were enrolled from the ward/ICU depending on the history of COPD and were classified as exposed or unexposed. All these subjects were followed up daily and severity was noted as requirement of ICU admission, mechanical ventilation and the final outcome was noted as discharged or death.

## **Inclusion Criteria**

All admitted laboratory confirmed cases of COVID-19 through RTPCR/Antigen test diagnosed from the month of July to December, 2020, above 18 years of age, and willing to participate were included in the study.

## Sample Size

In the study, with the confidence level of 95%, power of 80%, the sample size was calculated to be 113 as exposed and 339 as unexposed in the ratio of 1:3 with the total sample size as 452, with an error of 12%, considering the proportion of severe outcome in COPD patients as 58.33%.<sup>13</sup>

As the COVID-19 patients with history of COPD were comparatively less, in this study for each COVID-19 positive COPD patient three COVID-19 positive non-COPD patients were included (1:3, total 113 vs 339, respectively).

## **Ethical Consideration**

Permission of Institute Ethical Committee (IEC) was taken. Full confidentiality of patient's information was maintained and information was used only for the research purpose.

## Operational Definitions COPD

Patient will be labelled as exposed as COPD when he/ she was diagnosed case of COPD for a duration of two or more than 2 years with the history of acute exacerbation of productive cough, shortness of breath, wheezing for one or multiple times in a year using the diagnostic tools like spirometry, pulmonary function tests, chest x-ray, and follow-up for the monitoring of the disease progression.<sup>10</sup>

## **COVID-19** Positive

A COVID-19 positive patient is defined as a patient with

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symptomatic influenza-like illness who test positive for rapid antigen test and or real-time RT-PCR.<sup>14</sup>

#### **Outcome of COVID-19 Positive Patient**

In this severity of the infection was assessed by means of requirement of mechanical ventilation and the mortality (death).

#### **Data Analysis**

Data entry was done in Microsoft Excel. The data was tabulated and analyzed using SPSS version 23. Chi-square test was used to find out the association. The outcome variables were mechanical ventilation and death. Logistic regression analysis and adjusted odd's ratio with 95% CI was also calculated to find out the association of COPD and severity of COVID-19. A p-value less than 0.05 was considered as significant.

#### Results

In this study, total 452 laboratory confirmed positive COVID-19 patients were interviewed among which 113 patients, who had a known history of COPD, were considered as exposed group while 339 patients, who had no history of COPD, were considered as non-exposed.

The comparison of presenting symptoms of COVID-19 in COPD and non-COPD group was shown in Figure 1. Breathlessness was the chief complaint (75.2%) of COVID-19 in COPD group while fever was the chief complaint (55.7%) of COVID-19 in non-COPD group.

The baseline demographics of the study population are shown in Table 1. The COPD group had significantly greater proportions of older (>60 years old) (77.9% vs. 28.9%, p < 0.0001) patients than the non-COPD group. No significant association was observed between gender, religion, address, socioeconomic status, and COPD. It was observed that the majority of the patients among both the groups were admitted within 3 days to the hospital and the difference was not significant (p=0.84). Breathlessness was the presenting symptom for 85 (75.2%) of the patients among COPD group, and the difference was statistically significant (p < 0.0001). The mean hospital stay in days was significantly more with COPD group than non-COPD (12.7+ 6.7 Vs 11.1+6.0, p<0.01). Smokers were significantly more in COPD group (30.1 vs 3.8, p < 0.0001). The severity of COVID-19 was more among COPD group as assessed by the proportions of patients who require mechanical ventilation (61.1%vs. 33.9%, p < 0.0001) were higher in the COPD group than non-COPD group. In addition to this, mortality was also higher in COPD group (44.2% vs. 22.7%, p < 0.0001).

#### Risk Factors for Mechanical Ventilation and Mortality among COVID-19 Patients

Table 2 shows logistic regression analyses of risk factors for mechanical ventilation and mortality in COVID-19 patients. An age of more than 60 years (OR = 6.73, 95% CI 3.49–12.96), presenting symptom of breathlessness (OR = 2.35, 95% CI 1.50–3.71), and presence of other comorbidities (OR = 2.99, 95% CI 1.91-4.68) were independent risk factors for mechanical ventilation. Underlying COPD was not a contributing factor for mechanical ventilation in COVID-19 patients (OR = 1.19, 95% CI 0.67-2.13). Moreover, age more than 60 years (OR = 1.38, 95% CI 1.12-3.30 and presenting symptom of breathlessness (OR = 2.42, 95% CI 1.21–4.85) were all independent risk factors for mortality in COVID-19 patients. After adjusting for confounding factors in multivariable analyses, underlying COPD was not found associated with mortality among COVID-19 patients (OR 0.93; 95% CI 0.15-1.58).

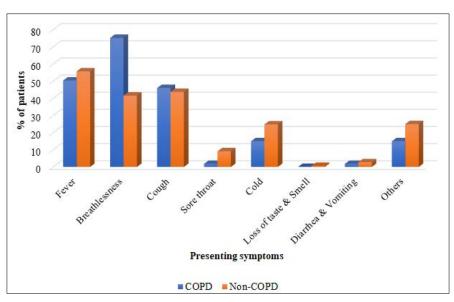


Figure 1.Presenting Symptoms of COVID-19 in COPD & Non-COPD patients

| Parameters  |                     | Non-COPD (n=339) COPD (n=113) |            | Chi-square  | p Value |
|---|---------------------|-------------------------------|------------|-------------|---------|
|   | Upto 40             | 107 (31.6)                    | 1 (0.9)    |             | <0.0001 |
| Age (Years)                                       | 41-60               | 134 (39.5)                    | 24 (21.2)  | 90.8        |         |
|   | >60                 | 98 (28.9)                     | 88 (77.9)  |             |         |
| Gender –  | Male                | 165 (48.7)                    | 58 (51.3)  | 0.00        | 0.62    |
|   | Female              | 174 (51.3)                    | 55 (48.7)  | 0.23        |         |
| Address —   | Urban               | 310 (91.4)                    | 105 (92.9) | 0.24        | 0.62    |
|   | Rural               | 29 (8.6)                      | 8 (7.1)    | 0.24        |         |
| Religion  | Hindu               | 272 (80.2)                    | 96 (85.0)  |             | 0.30    |
|   | Muslim              | 64 (18.9)                     | 15 (13.3)  | 2.35        |         |
|   | Other               | 3 (0.9)                       | 2 (1.8)    |             |         |
| Socioeconomic Status                              | Upper and<br>middle | 122 (36.0)                    | 34 (30.1)  | 1.30        | 0.12    |
|   | Lower               | 217 (64.0)                    | 79 (69.9)  |             |         |
| Gap between Onset<br>of Symptoms and<br>Admission | Same day            | 41 (12.1)                     | 13 (11.5)  |             | 0.84    |
|   | 1-3 days            | 234 (69.0)                    | 79 (69.9)  | 0.82        |         |
|   | 4-7 days            | 49 (14.5)                     | 14 (12.4)  | 0.83        |         |
|   | >7 days             | 15 (4.4)                      | 7 (6.2)    |             |         |
| Breathlessness -                                  | Yes                 | 141 (41.6)                    | 85 (75.2)  | 38.3        | <0.0001 |
|   | No                  | 196 (58.4)                    | 28 (24.8)  | 58.5        |         |
| Hospital Stay                                     | Mean <u>+</u> SD    | 11.1 (6.0)                    | 12.7 (6.7) | 5.7(t test) | <0.01   |
| Smoking -   | Yes                 | 13 (3.8)                      | 34 (30.1)  | 62.6        | <0.0001 |
|   | No                  | 326 (96.2)                    | 79 (69.9)  | 02.0        |         |
| Other Co-morbidities                              | Yes                 | 117 (34.5)                    | 49 (43.4)  | 2.0         | 0.09    |
|   | No                  | 222 (65.5)                    | 64 (56.6)  | 2.9         |         |
| Mechanical<br>Ventilation                         | Yes                 | 115 (33.9)                    | 69 (61.1)  | 25.86       | <0.0001 |
|   | No                  | 224 (66.1)                    | 44 (38.9)  | 23.00       |         |
| Outcome -   | Survived            | 262 (77.3)                    | 63 (55.8)  | 19.4        | <0.0001 |
|   | Death               | 77 (22.7)                     | 50 (44.2)  | 19.4        |         |

### Table I.Characteristics of COVID-19 Patients Associated with the Underlying COPD

 
 Table 2.Multivariate Analyses of Risk Factors Associated with Mechanical Ventilation and Mortality in COVID-19 Patients

| Variables            | Mechanical  | Ventilation | Mortality (Death) |           |  |
|----------------------|-------------|-------------|-------------------|-----------|--|
| Variables            | Adjusted OR | 95%CI       | Adjusted OR       | 95% CI    |  |
| Age 41-60 years      | 1.93        | 0.98-3.80   | 0.94              | 0.28-3.13 |  |
| Age >60 years        | 6.73        | 3.49-12.96  | 1.38              | 1.12-3.30 |  |
| Smoking              | 1.06        | 0.50-2.22   | 2.80              | 0.90-8.70 |  |
| Breathlessness       | 2.35        | 1.50-3.71   | 2.42              | 1.21-4.85 |  |
| COPD                 | 1.19        | 0.67-2.13   | 1.01              | 0.46-2.22 |  |
| Other co-morbidities | 2.99        | 1.91-4.68   | 0.93              | 0.15-1.58 |  |

## Discussion

This cohort study examined the relationship between the underlying COPD as comorbidty and the severity of COVID-19. Total 452 COVID-19 patients were enrolled, out of which 113 patients were of COPD. When the association between age was studied, it was observed that among COPD group, more older patients were there and had more comorbidities compared to the non-COPD group. The mortality was 44.2% among COPD group and was significantly higher than that of the patients who didn't have a history of COPD. Breathlessness was the presenting symptom for 75.2% of the patients among COPD group, and the difference was statistically significant. The mean hospital stay in days was significantly more with COPD. Smokers were significantly more in COPD group. The severity of COVID-19 was more among COPD group as the proportions of patients who required mechanical ventilation was higher in the COPD group as compared to non-COPD group. In addition, mortality was higher in the COPD group than in the non-COPD group (44.2% vs. 22.7%, P < 0.0001). An age of older than 60 years, presenting symptom of breathlessness and presence of other comorbidity were independent risk factors for mechanical ventilation while underlying COPD was not a contributing factor for mechanical ventilation in COVID-19 patients. Moreover, age more than 60 years and presenting symptom of breathlessness were all independent risk factors for mortality in COVID-19 patients. In the multivariate analyses, the association of COPD with severity of COVID-19 was not seen. This means that there was no association of underlying COPD disease with outcomes of COVID-19. Therefore, underlying COPD does not have adverse effect in the prognosis of COVID-19.

This means that we should not worry much about the uncertain fear of COPD associated with COVID-19 infection. These were very important results that solve the controversy surrounding the effect of underlying COPD disease and COVID-19 severity. Other studies also noted the proportion of patients with progression to severe COVID-19 among COPD patients between 20% to 50%.<sup>15-17</sup> This proportion is comparable to the findings reported in our study. This result was also in line with a previous meta-analysis.<sup>18</sup>

In this study, the severity of COVID-19 was associated with old age, other comorbidities, and presenting symptom of breathlessness rather than COPD itself. Breathlessness is one of the hallmark symptom of COVID-19 severity. COPD is a disease which usually occurs in later part of life and was commonly associated with multiple comorbidities. Multivariate analyses of confounding factors clarified that COPD was not a factor associated with COVID- 19 severity patients. COPD disease itself might lead to increased risk for worse clinical outcomes due to poor lung function and immune modulation of the airways. However, COPD is a heterogeneous disease having variations in disease severity and comorbidities. Among COVID-19 patients, relatively greater proportions of patients with COPD received mechanical ventilation and intensive critical care. COPD is an independent risk factor for all-cause mortality in COVID-19 patients.<sup>19</sup> In a Korean nationwide cohort, neither asthma nor COPD were associated with COVID-19, but severe COPD was associated with the severity and mortality of COVID-19.<sup>20</sup>

There were several limitations in this study. First, we cannot analyse the effects of the severity of COPD in COVID-19 in this study. Second, this study had been conducted in a dedicated COVID hospital where moderate-to-severe grade COVID-19 patients were admitted so was unable to find out effect of COPD among mild COVID-19 patients. Third, there were limitations in obtaining various types of information regarding treatment; only few variables were adjusted in logistic regression analyses. For example, further detailed information about inhalers used and the amount of corticosteroids were not analyzed with regard to their effects on the risk for and progression of COVID-19. Further studies are recommended to determine which features increase the likelihood for poor outcomes in COPD with COVID-19 infection.

#### Conclusion

Underlying COPD was not an independent risk factor associated with severity of COVID-19 patients. Higher age, other comorbidities, and presenting symptom of breathlessness associated with severity of COVID-19.

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## Conflicts of Interest: None

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