IMPACT OF SMOKING ON THE SEVERITY AND OUTCOMES OF CORONAVIRUS DISEASE: A RETROSPECTIVE ANALYSIS

Mahvesh Mahmud[1*], Muddasar Pervaiz[2], Shafaq Altaf[3], Anas Khan Channa[4], Mishaal Hafeez[5], Iqra Ibrar[6]

[1*]Associate Professor Nephrology Watim Medical College, Rawalpindi
[2]MBBS, MPH, Associate Professor in Community Medicine Department, Al-Nafees Medical College, Islamabad
[3]MBBS FCPS (Internal Medicine), Senior Registrar Watim Medical College, Rawalpindi
[4]MBB , MPH (Cont'd), Lecturer in Community Medicine Department, Al-Nafees Medical College, Islamabad
[5]MBBS, House Officer, Federal General Hospital, Islamabad
[6]MBBS, House Officer, Federal General Hospital, Islamabad

*Corresponding Author: Dr. Mahvesh Mahmud,
*Email: mahveshmahmud@gmail.com

ABSTRACT

Background: The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has led to global morbidity and mortality, with increasing recognition of risk factors that exacerbate disease severity. Smoking has been hypothesized to impact COVID-19 outcomes due to its known effects on the respiratory and immune systems, but evidence remains controversial.

Objective: This study aimed to investigate the association between smoking and the severity of COVID-19 outcomes. Specifically, we sought to compare the clinical characteristics, disease progression, and outcomes between smokers and non-smokers diagnosed with COVID-19.

Methodology: A retrospective analysis was conducted on 198 COVID-19 patients admitted to a private tertiary care hospital. Data were extracted from electronic medical records and included demographics, smoking status, comorbidities, clinical presentations, laboratory and radiological findings, disease severity, treatment modalities, and outcomes. Smokers were compared to non-smokers across various parameters. Statistical analyses were performed to determine significant differences between the two groups.

Results: Among the 198 patients, 38% were smokers. Smokers had a higher mean age (52 years vs. 49 years, p=0.042) and were more likely to have comorbidities such as hypertension, diabetes, and COPD. Clinically, smokers presented with more severe respiratory symptoms, higher inflammatory markers, and greater radiological lung involvement. Smokers were more likely to progress to severe COVID-19, requiring ICU admission (50.7% vs. 17.9%, p<0.001) and mechanical ventilation (46.7% vs. 13.8%, p<0.001), and had a higher mortality rate (40.0% vs. 14.6%, p<0.001).

Conclusion: Smoking significantly worsens COVID-19 outcomes, with smokers experiencing more severe disease progression, higher ICU admission rates, and increased mortality compared to non-smokers. The findings emphasize the need for targeted public health interventions to address smoking as a modifiable risk factor in COVID-19 management.

Keywords: COVID-19, smoking, disease severity, ICU admission, mortality, respiratory symptoms.

INTRODUCTION

Since the appearance of the Coronavirus outbreak in Hubei province, China, the world has been engulfed with the hysteria surrounding the pandemic. The global response to the pandemic has been unprecedented, with widespread lockdowns, travel restrictions, and the rapid development of vaccines and treatments. As of the time of this study, there have been nearly four hundred thousand mortalities worldwide due to COVID-19, with the numbers continuously rising. The pandemic has prompted a closer examination of various risk factors that contribute to the severity of COVID-19, including underlying comorbidities and smoking status.[1]

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has led to significant morbidity and mortality worldwide.[2] Several risk factors for severe COVID-19 outcomes, such as advanced age, obesity, hypertension, diabetes, and cardiovascular diseases, have been well established.[3] However, the impact of smoking on COVID-19 severity and outcomes remains a topic of ongoing debate.[4] Smoking is known to affect the respiratory and immune systems, potentially predisposing individuals to respiratory infections and complications.[5] Specifically, smoking can lead to increased expression of the angiotensin-converting enzyme 2 (ACE2) receptor, which is utilized by SARS-CoV-2 to enter host cells, thereby potentially increasing susceptibility to infection.[6] Additionally, smokers may have impaired lung function, chronic inflammation, and altered immune responses, all of which could contribute to more severe disease outcomes.[7]

Despite these potential mechanisms, the evidence regarding the association between smoking and COVID-19 severity is conflicting. Some studies suggest that smokers are at higher risk of severe outcomes, including hospitalization, intensive care unit (ICU) admission, and death.[8] Conversely, other research indicates that smokers might have a lower risk of severe COVID-19, possibly due to underreporting or the protective effects of nicotine.[9,10] Understanding the relationship between smoking and COVID-19 is crucial for developing targeted interventions and public health strategies.[11,12]

The rationale for this study is to clarify the conflicting evidence regarding the impact of smoking on COVID-19 severity and outcomes, thereby informing targeted public health strategies. Understanding this relationship is essential for developing effective interventions to mitigate the risk among smokers during the ongoing pandemic. While at present, there is evidence to indicate that smoking reportedly is of limited value to the occurrence of COVID-19 in an individual, it is however, concomitant to a greater probability of developing severe disease of COVID-19. There has been some evidence to indicate the link between patients diagnosed with COVID-19 and smoking, presenting a higher severity in such individuals of the disease as compared to never smokers. However, there seems to be no association between the incidence of COVID-19 and smoking behavior at present.

MATERIALS AND METHODS:

A retrospective analysis was performed on a cohort of COVID-19 patients admitted to a private tertiary care hospital between January 1, 2022, and June 30, 2022 in Nafees Hospital. Ethical approval for the study was obtained from the Institutional Review Board of the hospital, and the information collected was used strictly for research purposes. Data were stored in a password-protected computer, accessible only to the principal investigators, ensuring data security and confidentiality. The sample size of 195 patients was calculated based on a previous study, considering a 95% confidence level, 5% margin of error, and expected proportions of severe outcomes in smokers (30%) and non-smokers (15%), ensuring sufficient power to detect significant differences between the groups.[13]

Patients were categorized into two groups based on their smoking status: smokers and non-smokers. Smokers were further classified according to their smoking patterns, including the number of cigarettes smoked per day and the duration of smoking in years.

The study included all in-patients diagnosed with COVID-19 in the ICU setting, confirmed through COVID-19 RT-PCR or radiological findings such as high-resolution computed tomography (HRCT) showing bilateral ground-glass opacities in the lungs, which are highly suggestive of COVID-19. Eligible participants were between the ages of 20 to 80 years. The study included never smokers, current smokers (>5 pack/year smoking status), and patients diagnosed with chronic obstructive pulmonary disease (COPD). All patients with preexisting lung conditions other than COPD were excluded.

Data were collected from electronic medical records and included patient demographics, smoking status, comorbidities, clinical presentations, laboratory findings, radiological findings, disease severity (according to established criteria), treatment modalities, and outcomes, such as hospital length of stay, the need for mechanical ventilation, and mortality. A thorough assessment of the disease course and outcomes in ICU patients with diagnosed COVID-19 and their smoking status, including the pattern of smoking, was conducted through a structured proforma. This proforma captured relevant demographic information, smoking status (including frequency and duration of smoking), comorbidities, and prognostic markers, such as oxygen requirements, laboratory investigations, and periodic radiological assessments.

Laboratory investigations, in addition to radiological evaluation, included only those regularly monitored in the setting, such as complete blood count (CBC), renal function tests (RFTs), electrolytes, C-reactive protein (CRP), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), ferritin, and D-dimer levels—markers used to assess prognosis.

Data analysis was performed using SPSS version 26.0 (IBM). Statistical analysis was performed using appropriate tests, such as the chi-square test for categorical variables and the independent t-test or Mann-Whitney U test for continuous variables, to compare the clinical characteristics, disease severity, and outcomes between the two groups. Multivariate logistic regression was conducted to identify the independent impact of smoking on COVID-19 severity and outcomes while adjusting for potential confounders, such as age, gender, and comorbidities. A p-value of less than 0.05 was considered statistically significant.

RESULTS:

In this study, a total of 198 COVID-19 patients were included, with 38% identified as smokers. The mean age of smokers was slightly higher at 52 years, compared to 49 years for non-smokers (p=0.042). Smokers were more likely to have comorbidities, with significantly higher rates of hypertension (53.3% vs. 26.0%, p<0.001), diabetes (48.0% vs. 23.6%, p=0.001), and COPD (37.3% vs. 9.8%, p<0.001) compared to non-smokers, indicating that smokers had a higher burden of underlying health conditions as shown in table 1.

Table 1: Demographic and Clinical Characteristics of COVID-19 Patients

Characteristics	Total (n=198)	Smokers (n=75, 38%)	Non-Smokers (n=123, 62%)	p-value
Mean Age (years)	50.4 ± 12.3	52.0 ± 11.9	49.0 ± 12.5	0.042
Male (%)	110 (55.6%)	42 (56.0%)	68 (55.3%)	0.91
Hypertension (%)	72 (36.4%)	40 (53.3%)	32 (26.0%)	<0.001
Diabetes (%)	65 (32.8%)	36 (48.0%)	29 (23.6%)	0.001
COPD (%)	40 (20.2%)	28 (37.3%)	12 (9.8%)	<0.001

In table 2, Smokers in the study were more likely to present with severe respiratory symptoms and higher levels of inflammatory markers. Specifically, 66.7% of smokers exhibited severe respiratory symptoms compared to 30.9% of non-smokers (p<0.001). Additionally, smokers were found to have elevated C-reactive protein (CRP) levels and D-dimer levels, with 66.7% of smokers having elevated CRP compared to 34.1% of non-smokers (p<0.001), and 60.0% of smokers having elevated D-dimer compared to 26.8% of non-smokers (p<0.001). Radiological evidence also showed that lung involvement was significantly greater in smokers (69.3% vs. 27.6%, p<0.001).

Table 2: Clinical Presentation and Laboratory Findings

Clinical/Lab Findings	Total (n=198)	Smokers (n=75)	Non-Smokers (n=123)	p-value
Severe Respiratory Symptoms	88 (44.4%)	50 (66.7%)	38 (30.9%)	<0.001
Elevated CRP (>50 mg/L)	92 (46.5%)	50 (66.7%)	42 (34.1%)	<0.001
Elevated D-dimer (>500 ng/mL)	78 (39.4%)	45 (60.0%)	33 (26.8%)	<0.001
Lung Involvement (HRCT score ≥4)	86 (43.4%)	52 (69.3%)	34 (27.6%)	<0.001

In table 3, The study revealed that smokers had a higher likelihood of experiencing severe outcomes from COVID-19. ICU admission was required for 50.7% of smokers compared to 17.9% of non-smokers (p<0.001), and 46.7% of smokers needed mechanical ventilation compared to 13.8% of non-smokers (p<0.001). The mortality rate was also significantly higher among smokers, with 40.0% of smokers succumbing to the disease compared to 14.6% of non-smokers (p<0.001). Furthermore, the odds ratio for disease progression in smokers was 1.6 (95% CI 1.32-1.90), and for mortality, it was 1.18 (95% CI 1.03-1.40), demonstrating a significant association between smoking and adverse outcomes in COVID-19 patients.

Table 3: Disease Progression and Outcomes

Outcome	Total (n=198)	Smokers (n=75)	Non-Smokers (n=123)	p-value
ICU Admission (%)	60 (30.3%)	38 (50.7%)	22 (17.9%)	<0.001
Mechanical Ventilation (%)	52 (26.3%)	35 (46.7%)	17 (13.8%)	<0.001
Mortality (%)	48 (24.2%)	30 (40.0%)	18 (14.6%)	<0.001
Disease Progression (%)	56 (28.3%)	33.5%	21.9%	0.005
Odds Ratio for Disease Progression (95% CI)	-	1.6 (1.32-1.90)	-	-
Odds Ratio for Mortality (95% CI)	-	1.18 (1.03-1.40)	-	-

In table 4, The severity of COVID-19 outcomes was even more pronounced among heavy smokers. Heavy smokers were twice as likely to be admitted to the ICU and to require mechanical ventilation compared to moderate smokers (p=0.034 and p=0.046, respectively). The mortality rate was also higher among heavy smokers (51.4%) compared to moderate smokers (30.0%, p=0.022). The odds of hospitalization due to COVID-19 were significantly higher in heavy smokers, with an odds ratio of 2.0 (95% CI 1.5-2.7), indicating that heavy smoking was a major risk factor for severe COVID-19 outcomes.

Table 4: Smoking Intensity and COVID-19 Outcomes

Smoking Intensity	Total Smokers (n=75)	Moderate Smokers (n=40)	Heavy Smokers (n=35)	p-value
ICU Admission (%)	38 (50.7%)	16 (40.0%)	22 (62.9%)	0.034
Mechanical Ventilation (%)	35 (46.7%)	15 (37.5%)	20 (57.1%)	0.046
Mortality (%)	30 (40.0%)	12 (30.0%)	18 (51.4%)	0.022
Hospitalization Risk (OR, 95% CI)	-	-	2.0 (1.5-2.7)	-

DISCUSSION

Our study provides evidence suggesting a potential association between smoking and increased severity and adverse outcomes of COVID-19. Smokers with COVID-19 were more likely to have comorbidities and present with more severe respiratory symptoms compared to non-smokers.[14] Furthermore, smokers had a higher risk of progression to severe disease requiring ICU care and mechanical ventilation, ultimately resulting in higher mortality rates. These findings underscore the importance of smoking cessation interventions, especially in populations at high risk for COVID-19. Public health efforts should prioritize smoking cessation programs and awareness campaigns to mitigate the impact of smoking on COVID-19 outcomes.[15] Thorough assessment of disease course and outcome in in-patients with diagnosed COVID-19 and their smoking status including pattern of smoking was evaluated. Our study is comparable to other studies which report a direct relationship between smoking and the severity of COVID-19. A meta-analysis conducted in China revealed that smokers were 1.4 times more likely to have severe symptoms of COVID-19 and were 2.4 times more likely to be admitted to an intensive care unit (ICU), need medical ventilation, or die compared to non-smokers.[16]

Another meta-analysis which included papers from China, Korea and the United States showed that 29.8% disease progression was seen in smokers as compared to 17.6% of non-smokers. Hence, concluding that patients who are smokers were significantly more likely to experience disease progression and severe COVID-19 infection compared to nonsmokers (OR = 1.91; 95% CI: 1.42–2.59).[17] Another retrospective cohort study conducted in Kuwait examined 1096 patients, screened for risk factors that affected admission to ICUs, and also found a significant association between hospital admission and smoking (OR = 5.86; 95% CI: 1.40–24.47; $p = 0.015$).[18]

In contrast, there are other studies such as Lippi and Henry which demonstrated no significant association between active smoking and COVID-19 severity (OR 1.69 (95% CI 0.41 to 6.92); p=0.254).[19] Another retrospective study conducted in Jordan also indicated that smoking had no significant impact on the outcomes of COVID-19 patients.[20]

Conclusion: In conclusion, our study demonstrates a significant association between smoking and increased severity and adverse outcomes of COVID-19. Smokers with COVID-19 are at higher risk of developing severe disease and experiencing worse outcomes compared to non-smokers. These findings highlight the urgent need for targeted interventions aimed at reducing smoking prevalence and promoting smoking cessation, particularly in the context of the COVID-19 pandemic.

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