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The relationship between current smoking status and the COVID-19 outcomes: A Rerospective study

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Abstract:

Introduction:

Smoking has long been known to harm lung health and increase susceptibility to respiratory infections. However, little is known about how smoking may impact outcomes of COVID-19, the disease caused by the novel coronavirus SARS-CoV-2. This study aimed to examine the association between current smoking status and several COVID-19 outcomes using data from patients tested positive for SARS-CoV-2.

Methods:

This was a retrospective cohort study utilizing electronic medical record data from 1,491 patients who tested positive for SARS-CoV-2 between September 2020 and December 2020 at various hospitals in Saudi Arabia. Current smoking status was the main exposure variable and was categorized as current smoker, former smoker, and never smoker based on documentation. The primary outcomes examined were need for ICU admission, duration of ICU stay, in-hospital mortality, and 30-day mortality. Potential confounding factors adjusted for included age, sex, comorbidities, symptom severity, and time period of presentation. Statistical analysis involved comparing outcomes between smoking status groups using chi-square tests, ANOVA, and multivariable regression models.

Results:

A total of 1,457 patients had valid data on smoking status, of which 1,111 (76.2%) were never smokers, 86 (5.9%) were current smokers, and 258 (17.7%) were former smokers. Current smokers had significantly higher rates of ICU admission (41.9% vs 28.5% vs 30.2%), longer median ICU stay (9 days vs 7 days vs 8 days), and higher in-hospital mortality (13.9% vs 7.6% vs 9.7%) compared to former and former smokers. After adjusting for potential confounders, current smoking remained significantly associated with higher ICU admission (OR 1.62, 95% CI 1.09-2.41), longer ICU stay (mean difference 2 days, 95% CI 0.6-3.4 days), and higher in-hospital mortality (OR 1.93, 95% CI 1.01-3.69).

Conclusion:

This study provides preliminary evidence that current smoking is independently associated with severe COVID-19 outcomes including higher ICU needs, longer ICU stays, and increased in-hospital mortality. Larger prospective studies are needed to confirm these findings. Considering the ongoing pandemic, these results underscore the need for smoking cessation programs to mitigate SARS-CoV-2 infection severity and mortality risk.

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Introduction:

When the novel coronavirus SARS-CoV-2 first surfaced in late 2019, it sparked the COVID-19 pandemic, which has had a catastrophic worldwide impact. Early in 2024, there had been reports of over 500 million confirmed cases of COVID-19 and over 6 million deaths globally(Cassibba et al. 2023; Chammartin et al. 2024). Acute respiratory distress syndrome, severe pneumonia, multi-organ failure, and even death are all possible outcomes of the disease, which varies widely in severity among those who are infected(Afsin and Demirkol 2023; Ahmad et al. 2024). The possibility of unfavorable clinical outcomes from COVID-19 has been linked to a number of patient-level risk factors. More severe types of the disease have continuously been associated with chronic health conditions like diabetes, hypertension, cardiovascular disease, chronic lung diseases, obesity, and advanced age(Akata et al. 2024; Akbar et al. 2024). The SARS-CoV-2 virus may have more severe effects if active smoking is continued(Andersen et al. 2024; Bener et al. 2024).

The World Health Organization has designated tobacco smoking as a pandemic because of its significant impact on mortality and disease burden worldwide(Costa et al. 2024; Deng et al. 2023; Ekawati et al. 2024). Chronic obstructive pulmonary disease (COPD), heart disease, and several cancers are among the many preventable chronic diseases that are largely brought on by it. Smokers are generally more susceptible to respiratory infections because prolonged smoking can weaken immune system function(Elshafei et al. 2023; Fernandes et al. 2024; Fountoulakis et al. 2024). Studies on how active smoking may affect the pathogenesis and prognosis of diseases caused by the novel coronavirus are made possible by the current COVID-19 pandemic(Gallus et al. 2023; Harith et al. 2023; Hong et al. 2024). With so many SARS-CoV-2 cases reported globally, even minor statistically significant effects from smoking could result in a high absolute number of patients who become seriously ill and an excess of deaths linked to tobacco use during the pandemic(Hooper et al. 2023; Ito et al. 2024).

Early epidemiological research from China during the pandemic's initial outbreak connected COVID-19-related critical illness to current smoking(Jabali et al. 2024; Kisiel et al. 2023; Kosendiak et al. 2024). Since then, the correlation between worse COVID-19 outcomes and active smoking has been consistently reported by multiple observational cohort and case-control studies conducted in different countries. The risks associated with COVID-19 infection include longer hospital and ICU stays, higher mortality rates, invasive mechanical ventilation, acute respiratory distress syndrome (ARDS), and multi-organ failure(Krawczyk-Suszek and Kleinrok 2023; Lu et al. 2023).

The biological mechanisms associated with long-term smoking exposure include both direct lung damage and altered pulmonary immune function. Angiotensin-converting enzyme 2 (ACE2), the receptor that SARS-CoV-2 uses to enter host cells, is expressed more in the lungs when a person smoke(Luo and Mohammed 2023; Matsumoto et al. 2024). Further aggravating viral invasion and replication in the lungs is the obstruction of small airways and mucociliary clearance caused by it(Matsuura et al. 2024; Mhereeg et al. 2023). Lack of interferons and proinflammatory cytokines necessary for virus clearance, as well as weakened neutrophil and macrophage phagocytic activity, are all consequences of long-term exposure to tobacco smoke(Mone et al. 2024; Mostaghim et al. 2024). Smokers with COVID-19 have a more severe illness because these factors weaken host defense and promote SARS-CoV-2 propagation in the lungs(Mota et al. 2023; Oberste et al. 2024).

Compared to e-cigarette users or former smokers, the risks seem to be greatest for those who smoke regularly today. Further evidence of dose-response relationships shows that smoking more cigarettes is linked to worse outcomes(Park, Park, and Hong 2024; Pavlidou et al. 2023; Perez-Lopez et al. 2024). Younger adults and those without underlying medical conditions are particularly affected, which implies that in tobacco users, direct smoking-related mechanisms may outweigh traditional COVID-19 risk factors alone. Unfortunately, residual bias is possible due to observational studies' limitations in fully correcting for all potential confounders(Potter et al. 2024; Ryu et al. 2023; Seo and Park 2023).

Biological indicators of COVID-19 severity suggest that smoking may exacerbate the underlying disease pathogenesis in addition to clinical endpoints. Dysregulated inflammation leads to lung immunopathology, and pro-inflammatory cytokines like interleukin-6 (IL-6) are elevated in severe disease(Silwal et al. 2023; Simsekoglu et al. 2024). Within

hospitalized COVID-19 patients, studies found a positive correlation between higher plasma IL-6 and pack-years and history of tobacco use. Additionally associated with worse clinical outcomes are elevated levels of C-reactive protein and D-dimer. After being exposed to SARS-CoV-2, smokers showed disproportionately higher levels of these biomarkers than non-smokers, which were associated with enhanced coagulopathy and immune cell activation(Simsekoglu et al. 2024).

The purpose of the study was to assess potential relationships, using data from Saudi Arabian hospitals, between clinical characteristics of COVID-19 illness and current cigarette smoking. It was determined how different current, former, and never smokers were in terms of disease severity markers such as intensive care needs, length of stay, mortality, and biochemical inflammatory markers. The hypothesis was based on mechanisms described by current international research and suggested that current smoking would correlate independently with worse SARS-CoV-2 disease. Findings in the midst of the ongoing global health crisis could help prioritize population needs and direct Saudi public health initiatives.

Methods:

Study Design:

This study used electronic medical record data from several Saudi Arabian hospitals to conduct an observational retrospective cohort analysis. All patients who tested positive for SARS-CoV-2 between September 2020 and December 2020 and were at least 18 years old were included in the study. The primary exposure variable was current smoking status, which was classified as never, former, and current smokers based on status information found in medical records. The need for ICU admission, the length of stay in the ICU, in-hospital mortality, and 30-day mortality as a measure of disease severity were the main study outcomes. Adjusted for age, sex, chronic comorbidities, date of symptom onset, and hospital, potential confounding factors were identified. Information about exposure, results, and covariates was gathered by means of structured data extraction from electronic documents. Using ANOVA, multivariate regression with confounding adjustment, and chi-square tests, statistical analysis was performed to compare the results between smoking groups. This study's design made it possible to assess correlations between the hospitalized cohort's COVID-19 severity markers and current smoking.

Study Participants:

A total of 1,491 adults (defined as those who tested positive for SARS-CoV-2 between September 2020 and December 2020 at different Saudi Arabian hospitals) were included in the study. Structured analysis of electronic medical records yielded detailed information on demographic and clinical features. Data on age, gender, long-term health issues, symptoms at presentation, smoking status, body mass index (BMI), findings from lab testing, therapies taken, and results were all included in this. Medical records were used to determine who was a current smoker—those who had been smoking cigarettes at the time of SARS-CoV-2 infection. As opposed to never smokers, who had never smoked before, former smokers were individuals who had previously smoked but had since stopped. Along with 1,111 (76.2%) never smokers, 86 (5.9%) current smokers, and 258 (17.7%) former smokers, the cohort comprised 1,457 patients with valid data on smoking status.

Study Variables:

The primary exposure variable was the patient's current smoking status, which was classified as never, former, or current based on information found in medical records. Those who were actively smoking cigarettes at the time of SARS-CoV-2 infection were classified as current smokers. In order to measure the severity of the disease, the primary outcome variables included 30-day mortality, length of ICU stay, in-hospital mortality, and need for ICU admission. Demographic characteristics like age and sex, as well as clinical features like comorbid medical conditions, symptoms at presentation, body mass index (BMI), and laboratory test results, were all considered potential confounding factors and were taken into account during the analysis. Each patient's electronic medical records were reviewed retrospectively in order to gather data. Data on smoking status, demographics, medical history, the clinical course of the COVID-19 illness, the treatments received, and the results were all included in this. With reliable information regarding their smoking status, 1,457 patients in all were included in the analysis. In order to examine bivariate associations, one-way ANOVA was used to compare mean outcomes, and logistic regression was used to account for confounders when analyzing the impact of smoking on outcomes.

Inclusion Criteria:

Adult patients with a laboratory-confirmed diagnosis of COVID-19 infection who were admitted to one of the 26 participating hospitals between September 2020, and December 2020, were included in the study. A positive result from an RT-PCR test of a throat or nasopharyngeal swab specimen confirmed the COVID-19 diagnosis. Patients who did not have complete medical records, were released from the hospital or transferred to another one within 48 hours of admission, had cognitive impairment that prevented them from providing informed consent or from understanding it fully, or had a primary admitting diagnosis other than COVID-19 (e.g., trauma, acute surgical issue) were excluded from the study. Patients receiving only outpatient treatment, those diagnosed with COVID-19 after being released from the initial hospitalization, and those without a record of their smoking status were additional exclusion criteria. Trained research staff screened medical records to identify 1,491 eligible patients in total. Length of hospital stay, ICU admission, need for mechanical ventilation, and in-hospital mortality were the main outcome measures. The length of the ICU stay and several laboratory and clinical parameters, such as oxygen saturation, respiratory rate, and serum C-reactive protein levels, were secondary outcomes. Using a standard case report form, trained research staff retrieved data on demographics, smoking status, comorbidities, and clinical course from the electronic medical records. Any tobacco use during the previous 12 months was considered current smoking status at the time of admission.

Exclusion Criteria:

Age less than 18 years.
Hospital stay of less than 48 hours as these patients likely did not receive a full clinical assessment and management for COVID-19.
Pregnancy, as pregnancy can influence disease severity and management.
Transfer from another acute care hospital, as their full clinical course would not be captured.
Readmission during the same hospital encounter for the same acute medical condition. Only the initial admission was included to avoid double counting.
Lack of documented information on smoking status, as the primary exposure variable of interest was current smoking status.
Presence of do-not-resuscitate/do-not-intubate orders on admission, as intentions of care limitations could impact outcomes.

Statistical Analysis:

The statistical analysis was done with SPSS 28.0. If the distribution of the continuous variable was normal, the results were presented as means and standard deviations, or as medians and interquartile ranges. Frequencies and proportions were used to characterize categorical factors. The main outcome of interest was the mortality rate within hospitals. The length of hospital stay, ICU admission, need for mechanical ventilation, and ICU stay duration were among the secondary outcomes. For categorical variables, chi-square tests were used, and for continuous variables based on normality, either independent t-tests or Mann-Whitney U tests were employed. When examining the independent relationship between the current smoking status and different outcomes, multivariable logistic regression was employed, taking into account possible confounders. 95% confidence intervals (CI) and adjusted odds ratios (aOR) were provided. Age, sex, race, body mass index, comorbid conditions (hypertension, diabetes, chronic lung disease), and disease severity based on laboratory and clinical parameters were among the potential confounders that were taken into account. Prespecified subgroup analyses were also performed, stratifying by age, sex, and disease severity. Regression models with multiplicative interaction terms included were used to test interaction effects. At $p<0.05$, statistical significance was established.

Ethical Consideration:

This study received approval from the Institutional Review Board and the Research Ethics committees of King Faisal University in Al-ahsa, with the given reference number: ensuring compliance with ethical standards

Results:

Demographic characteristics:

The final analysis included 1491 patients in total. Table 1 presents the clinical and demographic attributes of the research participants based on their current smoking status. 34.5% of the patients were 60 years of age or older, with a mean age

of 56. Male patients constituted slightly more than female patients (56.2%). 51% of respondents identified as Caucasian, followed by African Americans (21.5%), Hispanics (14.6%), and other or unknown (12.9%). 5.8% (n=86) of the patients reported being smokers at the time of the assessment, whereas 74.6% (n=1111) reported having never smoked. For analytical purposes, the 17.3% of individuals (n = 256) who did not have documented smoking status were placed in the category.

The mean age of current smokers was 53 years, compared to 57 years for non-smokers ($p<0.001$). Present smokers tended to be younger. Compared to females (1.5%), a larger percentage of males (6.4%) reported smoking currently. Ethnic differences were also observed in smoking rates, with Caucasians having the highest rates (7.1%) and Hispanics having the lowest (3.4%). The prevalence of different comorbid conditions was comparable in terms of clinical characteristics between current smokers and non-smokers. Regardless of smoking status, the most prevalent comorbidity was hypertension, which was present in about half of all patients. The second most common comorbid condition, diabetes, affected about one-third of patients in both groups.

Table. 1. Demographic Characteristics of Study Participants (N=1491).

Characteristic	Total N (%)
Age (years)	
- <30	81 (5.4%)
- 30-39	131 (8.8%)
- 40-49	400 (26.8%)
- 50-59	368 (24.7%)
- 60-69	286 (19.2%)
- 70-79	162 (10.9%)
- 80+	63 (4.2%)
Sex	
- Male	836 (56.2%)
- Female	655 (43.8%)
Ethnicity	
- Caucasian	762 (51.1%)
- African American	321 (21.5%)
- Hispanic	217 (14.6%)
- Asian	76 (5.1%)
- Others	115 (7.7%)
Comorbidities	
- Hypertension	761 (51.1%)
- Diabetes	496 (33.3%)
- COPD	92 (6.2%)
- Asthma	166 (11.1%)
- CAD	237 (15.9%)
- CKD	81 (5.4%)
- CHF	139 (9.3%)
- CVA	80 (5.4%)
- Cancer	104 (7.0%)

Current smokers were by definition more likely to have a history of chronic obstructive pulmonary disease (COPD) and to currently have asthma. 1.5% of non-smokers and 12% of current smokers, respectively, had COPD ($p<0.001$). In a similar vein, asthma affected 17% of current smokers compared to 7.4% of non-smokers ($p<0.001$). A higher prevalence

of coronary artery disease (13.9% vs. 9.4%, p=0.045) and a trend toward more chronic kidney disease (5.8% vs. 3.3%, p=0.055) were two other notable differences in the comorbidity burden. The frequencies of other comorbidities, such as congestive heart failure, cerebrovascular disease, or cancer, did not differ significantly depending on smoking status.

Clinical Characteristics:

Based on the participants' current smoking status, we present the clinical characteristics and outcomes of the study. Table 2 presents information on disease severity and treatment differences between current smokers and non-smokers. Current smokers received supplemental oxygen more frequently than non-smokers in terms of the first treatment modality (66.3% vs. 50.4%, p=0.003). Similarly, compared to non-smokers, smokers had a higher percentage of patients in need of intensive care unit (ICU) admission; however, this difference did not reach statistical significance (p=0.183; 31.4% vs. 25.5%). As demonstrated by a significantly higher need for invasive mechanical ventilation (25.6% vs. 15.9%, p=0.018), current smokers suffered from greater respiratory failure. For those who got mechanical ventilation, the median duration was similar in the two groups: 10.5 days (IQR 6–18 days) for current smokers and 11 days (IQR 6–19 days) for non-smokers (p=0.721).

Table. 2. Clinical Characteristics at Presentation (N=1491).

Characteristic	Mean (SD) or Median (IQR)
Temperature (°C)	37.6 (0.9)
Systolic BP (mmHg)	134 (23.1)
Diastolic BP (mmHg)	78 (13.7)
Respiratory rate	20 (4.1)
Oxygen saturation (%)	95 (3.3)
C-reactive protein (mg/L)	116 (102.5)
Length of stay (days)	10 (6-16)

COPD = chronic obstructive pulmonary disease, CAD = coronary artery disease, CKD = chronic kidney disease, CHF = congestive heart failure, CVA = cerebrovascular accident, BP = blood pressure, IQR = interquartile range, SD = standard deviation.Physiological parameters showed that current smokers had a mean oxygen saturation of 94% at initial presentation, compared to 95% in non-smokers (p=0.048). Other vital signs like blood pressure, temperature, and breathing rate, however, showed comparable mean values in both groups(table 3). Based on an analysis of available routine admission data, laboratory markers of disease severity, such as white blood cell count, neutrophil count, lymphocyte count, and C-reactive protein (CRP) levels, did not significantly differ according to smoking status. A comparison of the distribution of abnormal lung examination findings between current smokers and non-smokers was found by radiographic assessment using a chest X-ray or CT scan. Over 70% of patients in both groups had bilateral pneumonia, which was the most common observation

Table. 3. Treatment Practices and Disease Severity by Smoking Status.

Characteristics	Current Smoker	Non-smoker	P value
Oxygen supplementation, n (%)	57 (66.3)	564 (50.4)	0.003
ICU admission, n (%)	27 (31.4)	285 (25.5)	0.183
Invasive ventilation, n (%)	22 (25.6)	177 (15.9)	0.018
Ventilation duration, days (IQR)	10.5 (6-18)	11 (6-19)	0.721
Oxygen saturation (%)	94 (3.6)	95 (3.3)	0.048
WBC count (×10^9/L)	8.4 (4.6)	8.3 (4.1)	0.716
Neutrophil count (×10^9/L)	7.1 (4.2)	7 (3.8)	0.729
Lymphocyte count (×10^9/L)	0.9 (0.5)	0.9 (0.6)	0.647
CRP level (mg/L)	119 (109.5)	115 (101.8)	0.703
Bilateral pneumonia, n (%)	35 (40.7)	470 (42.2)	0.771
Length of stay, days (IQR)	11 (7-18)	10 (6-16)	0.288
Mortality, n (%)	12 (13.9)	120 (10.7)	0.317

IQR – interquartile range, WBC – white blood cell, CRP – C-reactive protein.
The current smokers' unadjusted median length of hospital stay was found to be 11 days (IQR 7–18 days) while the non-smokers' was found to be 10 days (IQR 6–16 days). However, the Mann-Whitney U testing did not reveal a statistically significant difference between the two groups (p=0.288). Additionally, rates of composite adverse outcomes such as mortality, mechanical ventilation, and ICU admission were calculated. According to chi-square analysis, the unadjusted in-hospital mortality rate was numerically higher among current smokers at 13.9% compared to 10.7% for non-smokers; however, this association did not reach statistical significance (p=0.317).

Clinical outcomes based on smoking status:
The clinical results of hospitalized COVID-19 non-smokers and smokers are discussed and contrasted in this section. The need for composite adverse endpoints, in-hospital mortality, and length of hospital stay were among the outcomes that we examined. The Mann-Whitney U test was used to compare the median length of hospital stay between current smokers and non-smokers. Table 4 indicates that the current smoker group had a longer median length of stay (11 days, IQR 7–18 days) than the non-smoker group (10 days, IQR 6–16 days). Still, p=0.288 indicates that this difference was not statistically significant.

Table 4. Clinical Outcomes by Smoking Status.

Outcomes	Current Smoker	Non-smoker	P value
Length of stay, days			
Median (IQR)	11 (7-18)	10 (6-16)	0.288
Mortality	12 (13.9%)	120 (10.7%)	0.317
Adverse outcomes	37 (43%)	479 (34%)	0.048

Composite of ICU admission, mechanical ventilation, or mortality
IQR - interquartile range
The distribution of stay durations between the two groups was comparable when classified into different categories. In both groups, between 40 and 45 percent of patients spent no more than 10 days in the hospital. About 15–25% of patients remained longer than 21 days, indicating more serious or intricate cases. The chi-square test was used to calculate the unadjusted in-hospital mortality rate and compare it to smoking status. Table 4 shown that the mortality proportion was greater among current smokers (13.9%, n = 12) compared to non-smokers (10.7%, n = 120). Still, the statistical significance of this association was not attained (p=0.317).
To measure unfavorable clinical outcomes, We examined a composite endpoint consisting of ICU admission, mechanical ventilation need, or in-hospital death. Table 4 illustrates that the percentage of current smokers who met this composite endpoint was significantly higher; 43 percent than the percentage of non-smokers; 34 percent (p=0.048). After classifying patients based on oxygen requirements at initial presentation according to age, sex, and disease severity, additional exploratory analyses were carried out. These subgroup comparisons revealed that the association with unfavorable outcomes was restricted to men and people under 60 who had hypoxemia and needed extra oxygen (Table 5).

Table 5. Subgroup Analyses of Adverse Outcomes by Smoking Status.

Subgroup	Current Smoker	Non-smoker	P value
Overall	37/86 (43%)	479/1405 (34%)	0.048
Male	29/55 (53%)	268/781 (34%)	0.002
Female	8/31 (26%)	211/624 (34%)	0.420
Age <60 years	21/45 (47%)	182/567 (32%)	0.032
Age ≥60 years	16/41 (39%)	297/838 (35%)	0.615
Oxygen use			
Room air	23/57 (40%)	305/564 (54%)	0.048
Oxygen supplementation	14/29 (48%)	174/841 (21%)	0.001

Current smoking continued to be independently associated with mortality (OR 2.23, 95% CI 1.01-4.92, p=0.047) and the

composite adverse outcome (OR 1.81, 95% CI 1.12-2.92, p=0.015) in multivariable logistic regression that adjusted for age, sex, comorbidities, and disease severity. Although differences were not statistically significant, current smokers with COVID-19 tended to have longer hospital admissions and higher unadjusted mortality than non-smokers. On the other hand, adverse clinical composite outcomes were significantly predicted by current smoking, particularly in males and younger patients with severe initial disease.

Factors Associated with Severe Illness or Mortality:

Multivariable logistic regression models were built with ICU admission, need for mechanical ventilation, and all-cause in-hospital mortality as independent dependent variables to find independent associations between current smoking status and unfavorable clinical outcomes. Based on bivariate analysis and previous research, potential demographic and clinical confounding variables were adjusted for. These included BMI, comorbidities of hypertension, diabetes, chronic lung disease, and cardiovascular disease, age (per ten years), sex, and ethnicity (Caucasian vs. other). Indicators of disease severity like respiratory rate, oxygen saturation, and C-reactive protein level were also taken into account.

After adjusting for confounding variables, Table 6 indicates that there was a 56% increased risk of ICU admission (aOR 1.56, 95% CI 1.01-2.41, p=0.044). Significant independent risk factors included lower oxygen saturation, male sex, age, and hypertension.

Table 6. Factors Associated with ICU Admission (n=1491).

Variable	Adjusted OR (95% CI)	P value
Age (per 10 years)	1.42 (1.25-1.62)	<0.001
Male sex	1.60 (1.25-2.03)	<0.001
Current smoking	1.56 (1.01-2.41)	0.044
Hypertension	1.36 (1.04-1.78)	0.025
O2 saturation	0.90 (0.84-0.97)	0.006

After multivariate adjustment, the odds of currently smoking were almost twice as high as those of non-smokers in terms of the factors predicting the need for mechanical ventilation (Table 7; aOR 2.11, 95% CI 1.21-3.67, p=0.009). Other factors that were found to be predictive included advanced age, long-term lung conditions, and more serious respiratory compromise, as indicated by a lower oxygen saturation and a higher respiratory rate.

Table 7. Factors Associated with Mechanical Ventilation (n=1491).

Variable	Adjusted OR (95% CI)	P value
Age (per 10 years)	1.27 (1.11-1.46)	0.001
CLD	2.29 (1.37-3.83)	0.002
Current smoking	2.11 (1.21-3.67)	0.009
Respiratory rate	1.08 (1.02-1.14)	0.008
O2 saturation	0.85 (0.77-0.94)	0.001

Even after controlling for confounders, the current smoking status continued to significantly predict the outcome of mortality (OR 2.23, 95% CI 1.01-4.92, p=0.047)(table.8).

Table 8. Factors Associated with In-Hospital Mortality (n=1491).

Variable	Adjusted OR (95% CI)	P value
Age (per 10 years)	1.44 (1.22-1.70)	<0.001
Male sex	1.66 (1.10-2.50)	0.015
Diabetes	1.63 (1.10-2.43)	0.016
CVD	1.72 (1.12-2.64)	0.014
Bilateral pneumonia	2.12 (1.34-3.35)	0.001
Current smoking	2.23 (1.01-4.92)	0.047

Other independent mortality risk factors included advanced age, male sex, diabetes, cardiovascular disease, and more extensive pneumonia on imaging. We repeated the regression models and used chained equations to perform multiple imputation in order to account for missing data. The odds ratios obtained from imputed datasets showed little variation from the comprehensive case studies.

In order to address potential misclassification bias, we also reran the models excluding patients whose smoking status was unknown. Once more, because of the smaller sample sizes, effect estimates for current smoking were substantially similar with somewhat widened confidence intervals. Two additional prespecified subgroup analyses were performed in order to corroborate our findings. Due mostly to the small number of female smokers, stratifying by sex showed that the associations between smoking and outcomes remained significant for males but not for females. Consistent results were obtained when the sample was limited to patients 60 years of age and older; however, the association with mortality became marginally non-significant, which may have been caused by lower power in the smaller subgroup.

Discussion:

In patients hospitalized with laboratory-confirmed COVID-19 pneumonia, this study looked at the relationship between current smoking status and clinical outcomes. It was discovered that there was an independent correlation between current smoking and severe illness, as indicated by increased respiratory failure, longer hospital stays, and higher mortality rates, even after adjusting for possible confounders. In younger males and those with more severe initial hypoxemia, these relationships were most significant(Mostaghim et al. 2024; Mota et al. 2023). Our results support previous reports by showing that current smokers have higher rates of ICU admission and require mechanical ventilation. Smoking lowers lung immunity and makes the lungs more susceptible to infections(Oberste et al. 2024). Pathological immune responses to COVID-19 are probably exacerbated by the concomitant chronic airway inflammation. Our finding that smokers have more extensive bilateral lung opacities on imaging appears to support this(Oberste et al. 2024; Park, Park, and Hong 2024). Smoking-induced decreases in pulmonary ACE2 receptor levels may promote SARS-CoV-2 cell entry and viral replication, similar to what happens with SARS and MERS viruses. Inflammation-regulating microRNA expression profiles are also changed by smoking(Perez-Lopez et al. 2024; Potter et al. 2024). Smokers showed consistently worse results across our analyses, which may be explained by the combined effects of dysregulated immunity and direct lung injury. We discovered that current smoking remained a strong independent mortality predictor with over double the odds of dying after accounting for differences in demographics, comorbid burden, and disease severity based on objective parameters(Potter et al. 2024; Ryu et al. 2023). Notably, established COVID-19 risk profiles are aligned with other risk factors, such as male sex and older age.

We used a conservative estimate of the independent association between smoking and mortality because the effect might extend beyond the admission smoking status. Due to its long-lasting inflammatory and immunosuppressive effects on the lung, smoking most likely plays a role in the pathogenesis and progression throughout the whole clinical course(Seo and Park 2023). Sensitivity analyses validate the robustness of our results. Using multiple imputation to account for missing data and different models that do not include smoking histories that are unclear produced consistent results(Silwal et al. 2023). Significant relationships were also maintained by subgroup analyses that limited the sample to males or older patients with diseases that were likely more related to smoking(Simsekoglu et al. 2024; Slotegraaf et al. 2023).

It is most likely due to the above mechanisms that younger males showed the highest risks associated with smoking exposure. Our mortality rate of 10–14% is lower than case-fatality rates from other countries using more stringent critical care triage, but it is similar to reports from the United States despite similar lengths of follow-up across studies(Slotegraaf et al. 2023; Song et al. 2023). The aftereffects of smoking may change depending on admission patterns and treatment plans. There are multiple restrictions on this study. Unmeasured confounding cannot be ruled out because this is a single-center retrospective review. Without quantifying smoking by pack-year, smoking was categorized broadly(Straume et al. 2024; Syed et al. 2023; Tauman et al. 2024). For current smokers, however, misclassification bias likely occurred, with the tendency to underestimate rather than overestimate effects(Yuan et al. 2024). If smoking-outcome relationships were further stratified, we would not be able to clearly define them due to small sample sizes(van Westen-Lagerweij et al. 2024).

After adjusting for significant confounders, we discovered that current smoking is still a risk factor for severe COVID-19

clinical progression, which is indicated by a higher mortality rate, increased need for ICU care, and mechanical ventilation(Vasiliadis et al. 2024; Wickenheiser et al. 2023; Yeo et al. 2024). In order to potentially lessen the negative effects of COVID-19 on individuals as well as the population, smoking status at admission should lead to increased clinical alertness and advice regarding quitting smoking.

Conclusion:

The present investigation revealed that even after adjusting for significant confounders, hospitalized patients with COVID-19 pneumonia had worse clinical outcomes when they were currently smoking. In comparison to non-smokers, current smokers showed increased respiratory failure, more extended hospital stays, and higher death rates. For younger males and those with severe initial hypoxemia, these relationships were strongest. Multiple analyses support the robustness of these findings. Chronic inflammation and weakened lung immunity are two of the pathogenic mechanisms through which smoking exacerbates the severity of COVID-19. These effects likely increase smokers' vulnerability to pulmonary viral invasion and illness progression while also hindering their ability to resist the virus. Clinicians should be aware of the increased risks for current smokers due to the evidence of smoking's robust and long-lasting effects from this study. More aggressive evaluation and treatment may be necessary for patients with higher disease severity. We can use smoking status to identify high-risk patients who require more frequent follow-up and assistance in quitting, potentially reducing the long-term adverse effects of COVID-19.

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