



# Severity of COVID-19 Disease Among Unvaccinated Users and Non-users of Tobacco Products

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## Abstract

**Background** Previous studies have identified several risk factors associated with the severity of COVID-19, the disease caused by the SARS-CoV-2 virus. However, studies on the effects of tobacco use on COVID-19 severity have shown contradictory results. This study was aimed at investigating the relationship between COVID-19 and tobacco use.

**Methods** A cross-sectional study was conducted among patients previously hospitalized because of COVID-19, none of whom had received any COVID-19 vaccinations. Subjective data, such as medical history of chronic diseases, hospital length of stay (LOS), intensive care unit (ICU) admission, requirement for mechanical ventilation, and tobacco use history, were gathered through telephone interviews through a pre-designed questionnaire.

**Results** Fifty-eight patients with COVID-19 used tobacco products, whereas 114 patients were non-users (tobacco use prevalence of 34%). The most common methods of tobacco use were smoking cigarettes (69%), smoking shisha (50%), using electronic cigarettes (10%), and chewing tobacco (3%). Although most patients developed COVID-19 symptoms, most of the reported symptoms were more frequent among the non-tobacco users. The associations of tobacco use with COVID-19 symptoms, mean LOS, ICU admission, and the need for mechanical ventilation were not significant ( $P > 0.05$ ).

**Conclusions** Although no significant association was found between COVID-19 severity and tobacco use, continued comprehensive tobacco cessation strategies remain important to mitigate the overall health consequences associated with tobacco consumption.

**Keywords** SARS-CoV-2 viral infection · Tobacco consumption · Smoking · Hospitalization · Signs and symptoms

## Abbreviations

|          |                          |
|----------|--------------------------|
| CI       | Confidence interval      |
| COVID-19 | Coronavirus disease 2019 |
| ICU      | Intensive care unit      |

|     |                |
|-----|----------------|
| LOS | Length of stay |
| OR  | Odds ratio     |

## 1 Introduction

Tobacco consumption is among the most common causes of illness and is responsible for millions of deaths each year globally. Tobacco users are at high risk of organ-related disorders, including acute respiratory distress syndrome, cardiovascular complications, hepatic disease, and kidney disease [13, 19]. In addition, the use of tobacco products alters immunologic host defenses, thereby increasing susceptibility to viral, bacterial, and fungal infections [21].

Previous studies have identified several risk factors associated with the severity of COVID-19 caused by the SARS-CoV-2 virus; these factors include including old age, male sex, and underlying comorbidities. Three studies conducted early in the COVID-19 pandemic have reported

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an association between tobacco smoking and lower risk of COVID-19 mortality [11, 17, 40], whereas other studies have shown contradictory results [7, 23, 28, 30, 36, 39].

Therefore, this study aimed to investigate the relationship between COVID-19 and tobacco use.

## 2 Materials and Methods

### 2.1 Study Design, Study Participants, and Sample Size

A cross-sectional study was conducted during the first wave of the COVID-19 pandemic in Saudi Arabia (March to September 2020). The study included patients previously hospitalized because of COVID-19, none of whom had received any COVID-19 vaccination, because no vaccines were approved and available for use at that time. According to the recommendations of the Saudi Centers for Disease Prevention and Control, during the initial wave of COVID-19, individuals with mild cases of COVID-19 and no risk factors for severe outcomes could be isolated in designated facilities. Asymptomatic patients were advised to undergo retesting every 3 days after confirmation of COVID-19, to enable timely discontinuation of isolation precautions in the designated facility [32].

A multistage sampling technique was used to select participants. The first stage involved simple random sampling to select one hospital from each health cluster in Saudi Arabia [20]. The second stage involved simple random sampling to select eligible patients discharged from the selected hospitals during the study period.

### 2.2 Data Collection and Analysis

The patients' contact details were obtained from the medical records available at the Saudi Ministry of Health. The medical details were collected subjectively through a pre-designed questionnaire via telephone calls. The questionnaire was designed by the authors, and revised and reviewed by experts for validation and reliability of each item. The following items were included: (1) background variables; (2) history of chronic diseases; (3) history of COVID-19 (length of stay [LOS]), intensive care unit (ICU) admission, and need for mechanical ventilation); and (4) tobacco use history (duration of use and type of tobacco products).

Because the data were not normally distributed, Mann–Whitney *U* test and Chi-square test were performed in Statistical Package for the Social Sciences software version 25 for analysis of the results. The data were reviewed, cleaned, and tested for homogeneity with the Shapiro–Walk test. The results were considered significant when the *P*-value was < 0.05.

## 2.3 Ethical Considerations

The study was approved by the Institutional Review Board Committee of the Saudi Ministry of Health (No: 23-3 M). Verbal consent by telephone was obtained from each participant after the reason for data collection was explained. Patients who refused to participate in the study were excluded.

## 3 Results

A total of 172 hospitalized patients with COVID-19 consented to participate in the study. The mean LOS was  $12.01 \pm 8.54$  days, and the mean age was  $45.16 \pm 14.17$  years. Approximately 34% of the included patients had used tobacco products for a mean duration of  $13.5 \pm 10.79$  years (Table 1). Cigarettes (69%), shisha (50%), electronic cigarettes (10%), and chewing tobacco (3%) were the most common methods of tobacco product use.

Table 2 presents symptoms and severity of COVID-19 according to tobacco use status among the studied patients. Most patients reported developing COVID-19 symptoms; however, these symptoms were more frequent among non-tobacco users, except for sore throat, diarrhea, and headache. The associations of tobacco use with COVID-19 symptoms, mean LOS, ICU admission, and the need for mechanical ventilation were not significant ( $P > 0.05$ ).

No significant difference was observed in relation to the duration of tobacco use between patients who had smoked for  $\geq 10$  or  $< 10$  years (odds ratio [OR] 2.11, confidence interval [CI] 0.33–13.72,  $P = 0.43$ ; Table 3). In contrast, the risk of ICU admission was approximately four times higher among individuals who had used tobacco products for  $\geq 10$  years, although the statistical analysis did not reveal a significant difference between groups (OR 4.31, CI 0.84–22.13,  $P = 0.08$ ). Among individuals who had used tobacco products for  $\geq 10$  years, 15% required mechanical ventilation during COVID-19 treatment. In contrast, no individuals who had used tobacco products for  $< 10$  years required mechanical ventilation ( $P = 0.04$ ).

**Table 1** Baseline characteristics of the studied patients ( $N = 172$ )

| Baseline characteristics     | <i>N</i> (%) / (mean $\pm$ SD) |
|------------------------------|--------------------------------|
| Age (years)                  | $45.16 \pm 14.17$              |
| Males                        | 123 (72%)                      |
| Saudi nationality            | 95 (55%)                       |
| Hospital stay (days)         | $12.01 \pm 8.54$               |
| Tobacco use duration (years) | $13.5 \pm 10.79$               |
| Tobacco users                | 58 (34%)                       |

**Table 2** Symptoms and severity of COVID-19 relative to smoking status among the studied patients

| COVID-19 symptoms reported | Tobacco use status    |      |                    |      | Total N=172 |       | $\chi^2$            | P     |
|----------------------------|-----------------------|------|--------------------|------|-------------|-------|---------------------|-------|
|                            | Tobacco users<br>N=58 |      | Non-users<br>N=114 |      | N/mean      | % /SD |                     |       |
|                            | N/mean                | %/SD | N/mean             | %/SD |             |       |                     |       |
| Any symptoms               | 53                    | 91   | 108                | 95   | 161         | 94    | 0.7239              | 0.395 |
| Fever                      | 40                    | 69   | 85                 | 75   | 125         | 73    | 0.6062              | 0.436 |
| Dry cough                  | 30                    | 52   | 75                 | 66   | 105         | 61    | 3.1981              | 0.073 |
| Sore throat                | 28                    | 48   | 39                 | 34   | 67          | 39    | 3.1981              | 0.073 |
| Muscle pain                | 33                    | 57   | 59                 | 52   | 92          | 53    | 0.4086              | 0.523 |
| Difficulty in breathing    | 13                    | 22   | 40                 | 35   | 53          | 31    | 2.8964              | 0.089 |
| Diarrhea                   | 19                    | 33   | 33                 | 29   | 52          | 30    | 0.2647              | 0.607 |
| Headache                   | 31                    | 53   | 50                 | 44   | 81          | 47    | 1.4186              | 0.234 |
| Loss of smell/taste        | 28                    | 48   | 63                 | 55   | 91          | 53    | 0.7533              | 0.385 |
| Any chronic disease        | 27                    | 47   | 59                 | 52   | 86          | 50    |                     | 0.52  |
| LOS                        | 10.84                 | 6.94 | 12.59              | 9.20 | 12.01       | 8.54  | 1.2751 <sup>a</sup> | 0.204 |
| ICU admission              | 11                    | 9    | 19                 | 17   | 30          | 17    | 0.14 <sup>b</sup>   | 0.707 |
| Mechanical ventilation     | 5                     | 19   | 14                 | 12   | 19          | 11    | 0.524 <sup>b</sup>  | 0.469 |

ICU intensive care unit, LOS length of hospital stay

<sup>a</sup>Mann–Whitney test

<sup>b</sup>Chi-square test

**Table 3** Symptoms and severity of COVID-19 relative to the duration of tobacco use

| COVID-19 symptoms reported | Tobacco use status                    |      |                                  |      | Total N=58 |      | OR (CI)           | P    |
|----------------------------|---------------------------------------|------|----------------------------------|------|------------|------|-------------------|------|
|                            | Tobacco users $\geq$ 10 years<br>N=33 |      | Tobacco users < 10 years<br>N=25 |      | N          | %    |                   |      |
|                            | N                                     | %    | N                                | %    |            |      |                   |      |
| Any symptoms               | 31                                    | 94   | 22                               | 88   | 53         | 92   | 2.11 (0.33–13.72) | 0.43 |
| LOS mean (SD)              | 11.56                                 | 6.39 | 9.92                             | 7.62 | 10.84      | 6.94 | 0.89 <sup>a</sup> | 0.38 |
| ICU admission              | 9                                     | 27   | 2                                | 8    | 11         | 19   | 4.31 (0.84–22.13) | 0.08 |
| Mechanical ventilation     | 5                                     | 15   | 0                                | 0    | 5          | 9    | 0 <sup>b</sup>    | 0.04 |

ICU intensive care unit, LOS length of hospital stay

<sup>a</sup>Mann-Whitney test

<sup>b</sup>Fisher’s exact test

The association between the duration of tobacco use and the mean LOS was statistically insignificant ( $P=0.38$ ).

### 4 Discussion

This study investigated the frequency of tobacco use among patients with COVID-19 and assessed associations between tobacco use and disease severity, in terms of LOS, ICU admission, and the need for mechanical ventilation. In this study, 34% of the included patients were tobacco users. This percentage is notably higher than the national smoking prevalence of 19.8% estimated by the Saudi Ministry of Health [33]. Importantly, we did not

find significant associations between the status and duration of tobacco product use and the severity of COVID-19 ( $P > 0.05$ ).

In previous studies, Ismail et al. [19] and Gonzalez-Rubio et al. [14] have reported that the prevalence of tobacco smoking is lower among hospitalized patients with COVID-19 than the among the national population. Farsalinos et al. [9] have estimated the prevalence of current tobacco smokers among hospitalized patients with COVID-19 is unexpectedly low. Moreover, Ismail et al. [19] and Mohsin et al. [26] have revealed that people using tobacco for longer durations are at higher risk of having poor health condition during SARS-CoV-2 infection, such as severe lung, renal, and hepatic disorders.

Our study indicated no significant associations of tobacco use with COVID-19 symptoms, LOS, ICU admission, or the need for mechanical ventilation.

Similarly, Farsalinos et al. [9], in a study using a random-effect model, have found no significant associations of tobacco smoking with COVID-19 morbidity and mortality (OR 1.40, 95% CI 0.98–1.98 and OR 1.86, 95% CI 0.88–3.94, respectively).

In agreement with these findings, Hoballah et al. [18] and Prinelli et al. [29] have reported no significant association between the severity of COVID-19 and factors such as smoking status or the type of tobacco product used, and no dose–response relationships were observed.

In contrast, Vallarta-Robledo et al. [34] have reported that, after adjustment for comorbidities, and socioeconomic and demographic variables, tobacco smoking is a protective factor against COVID-19 and is negatively associated with the incidence of SARS-CoV-2 infection (OR 0.44, 95% CI 0.35–0.77). The findings in the current study, along with those of previous studies indicating a low prevalence of tobacco use among patients with COVID-19 and a lack of significant association with disease severity, may be attributable to challenges in accurately detecting tobacco users and objectively assessing their tobacco use [4]. Furthermore, age is a predisposing factor for COVID-19 hospitalization, and hospitalization is more likely in older people regardless of tobacco use status [12].

#### 4.1 Risks of Using Tobacco Products

Whereas nicotine, one of many chemicals present in tobacco products, has shown some potential benefits for individuals with ulcerative colitis and in mitigating adverse events associated with antipsychotic medications, the overall risks associated with tobacco products, which contain various toxic compounds, importantly outweigh the potential benefits of nicotine [8, 25].

Tobacco use has been associated with poor health consequences, particularly on the cardiovascular and respiratory systems [5, 37]. People with cardiac and respiratory illnesses are at high risk of developing severe COVID-19 symptoms [15]. Furthermore, tobacco products contain several toxins that have no immunomodulatory or antiviral properties against COVID-19 [38].

The present study showed that the most prevalent tobacco products used among participants were regular cigarettes (69%) followed by shisha (50%). Although all types of tobacco are harmful to the body, shisha smoking also is associated with a risk of spreading COVID-19 [24]. Similarly, Hoballah et al. [18] have found that water pipe smoking is associated with severe SARS-CoV-2 infection (OR 2.64, 95% CI 1.32–5.27).

Clift et al. [6] have established that current smokers, compared with non-smokers, have greater risks of SARS-CoV-2 infection (OR 1.45, 95% CI 1.10–1.91) and hospitalization (OR 1.60, 95% CI 1.13–2.27). Moreover, the risk of hospital mortality increases with the number of cigarettes smoked per day (1–9 cigarettes per day: OR 2.14, 95% CI 0.87–5.24; 10–19 cigarettes per day: OR 5.91, 95% CI 3.66–9.54;  $\geq 20$  cigarettes per day: OR 6.11, 95% CI 3.59–10.42).

In addition, Reddy et al. [31] have found that current tobacco users have a risk of severe COVID-19 approximately two fold greater than that of non-users (relative risk 1.80, 95% CI 1.14–2.85;  $P=0.012$ ), and that a history of previous tobacco use is a significant risk factor for severe COVID-19 (relative risk = 1.31; 95% CI 1.12–1.54;  $P=0.001$ ). Similarly, a positive association between tobacco use and adverse outcomes among hospitalized patients with COVID-19 has been documented in several studies [3, 10, 16, 27, 35]. Other studies have revealed that tobacco smoking is an independent risk factor for COVID-19 progression, including critical illness and mortality [1, 28]. Theoretically, tobacco users have multiple risk factors that might lead to severe COVID-19, including underlying chronic diseases [19]. In addition, Liu et al. [22] have stated that greater severity of COVID-19 is associated with underlying comorbidities caused by tobacco smoking, and with an increased risk of disease progression and occurrence of COVID-19 pneumonia.

#### 4.2 Limitations

The main limitations of this study were its cross-sectional design, self-reported symptoms, and small sample size. Furthermore, former tobacco users were not distinguished, and the frequency of tobacco use per day was not assessed, thus potentially reflecting the insignificant association found in this study.

In addition, because the percentage of female patients with COVID-19 undergoing hospital isolation and quarantine was low, this study included mostly male patients (72%). Finally, the prevalence of female smoking in Saudi Arabia is low (4.2%), and women may avoid revealing their tobacco use status [2, 33].

### 5 Conclusion

Although this study revealed no significant association between the severity of COVID-19 and the tobacco use, comprehensive strategies for tobacco cessation should continue to be pursued to decrease the overall poor health consequences.

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**Data Availability** The study's supporting data are obtained from the corresponding authors upon reasonable request.

## Declarations

**Conflict of interest** The authors declare no conflicts of interest.

**Ethical Approval** Approval for the study was provided by the Institutional Review Board Committee of the Saudi Ministry of Health (No: 23-3 M). Verbal consent was obtained from the participants by telephone after explanation of the reason for data collection. Patients who refused to participate in the study were excluded.

**Consent for Publication** Not applicable.

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