Original Article

ISSN: 1735-0344 *Tanaffos 2024; 23(1): 83-89*

TANAFFOS

The Association of Smoking and SARS-CoV-2 Infection

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Received: 13 June 2023
Accepted: 5 December 2023

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Background: SARS-CoV-2 is a member of the coronavirus family that has caused infections in humans. Iran, as one of the countries in West Asia, is facing a high prevalence of this virus. In this study, we aimed to investigate the association between smoking and COVID-19 outcomes during the pandemic and sociodemographic characteristics.

Materials and Methods: This cross-sectional survey was done to assess the frequency of tobacco smoking in COVID-19 patients hospitalized at Masih Daneshvari Hospital, Tehran, Iran. All patients' basic and clinical characteristics, smoking status, and outcomes (ICU admission) were recorded.

Results: A total of 254 participants, of whom 206 (81.10%) provided complete data on variables included in the present analyses. In the present study, 137 (66.5%) of all patients were men and 69 (33.5%) were women. Also, 63 (30.4%) of the study population had a family member with a current disease or history of COVID-19. Fourteen patients (6.79%) were ex-smokers and 34 (16.50%) were current smokers. We found significant relationships between Ex-smoking and ICU admission in COVID-19 patients.

Conclusion: Ex-smoker inpatients with COVID-19 require special attention since they are a vulnerable population with a much higher morbidity rate.

Keywords: COVID-19; Smoking; Intensive Care Unit

INTRODUCTION

Since December 2019, at the same time as the first report of a novel coronavirus from Wuhan, China, human societies have been facing an extensive challenge (1-3). SARS-CoV-2 also known as Covid-19 is a member of the coronavirus family that has caused mild to severe infections in humans over the past 20 years (4). According to a report released by the World Health Organization (WHO), nearly 70 million people worldwide have been infected with the infection so far, and the mortality rate is estimated at more than 1.6 million (5). According to statistics published by WHO, nearly 180 countries around the world are facing the spread of the virus. However, some countries, such as the United States, India, Brazil, Russia, and Spain, have the highest number of cases (6). This type of disease distribution indicates that the prevalence of the virus worldwide does not follow a specific pattern or is not related to a particular race (7). Iran, as one of the countries in the region of West Asia

(Middle East), is facing a high prevalence of this virus, so up to 15/10/2020, 513219 cases of definitive infection with SARS-COV-2 have been reported (8).

The infection of SARS-CoV-2 is associated with mild complications in many patients, but in some cases, can lead to severe respiratory distress syndrome (9, 10). The manifestations of these symptoms and the severity of the disease seem to be associated with underlying causes such as a history of cancer, organ transplantation, or the use of immunosuppressive drugs (11). Thus, since there is no known treatment for this disease so far, controlling and preventing clinical deterioration could be the most appropriate approach. Therefore, understanding the current condition of the patient and evaluating his records seems to be very important in classifying patients based on the level of the disease, adopting therapeutic interventions, and identifying risk factors.

One of the main factors affecting infections of the respiratory system is tobacco smoking (12). Smoking is also one of the most well-known causes of mortality and morbidity in different diseases such as COPD, cancer, and cardiovascular disease (13).

Unfortunately, among the various risk factors that contribute to SARS-COV-2 disease, the role of smoking is still unclear. Data on the rate of smokers infected with coronavirus range from 1.4% to 18.5%. Some studies have suggested a direct association between smoking and the severity of SARS-CoV-2 disease (14).

Also, studies have shown that the expression of SARS-COV-2 specific receptor (ACE2) in the lower airways of smokers is higher than in other patients (15). Some cytokines released due to lung inflammation caused by smoking can cause this receptor to be upregulated (16).

Sustained inflammation (known as cytokine storm) has been observed in the majority of severe COVID-19 cases (17). High concentrations of cytokines such as IL-2, IL-7, IL-10, G- SCF, IP10, MCP1, MIP1A, and TNF-α were recorded in the plasma of critically ill patients infected with SARS-CoV-2, indicating that the cytokine storm could be associated with disease severity (18). It is said that tobacco smokers are at high risk of severe COVID-19 infection due to compromised lung function, cross-infection, and susceptible hygiene habits (19); although, these data have not been confirmed yet.

Given the differences and uncertainties in the results of previous evidence, in this study, we were to evaluate the association between smoking and COVID-19 outcomes including the severity of the disease by measuring the need for intensive care unit (ICU) hospitalization in patients referred to Masih Daneshvari Hospital in Tehran, Iran.

MATERIALS AND METHODS

Study design, participants

The study was done through a cross-sectional design to assess the frequency of tobacco smoking amongst COVID-19 patients in Masih Daneshvari Hospital, Tehran, Iran. We used data from all patients who were hospitalized between March and July 2020.

As pointed out before, according to census-based measures, sampling was census tracts, including approximately more than 200 inpatients. A total of 254 participants responded to the survey, of whom 206 (81.10%) provided complete data on variables included in the present analyses. The targeted population was all diagnosed with COVID-19 inpatients who were hospitalized for at least 2 days in Masih Daneshvari Hospital, at the time of the study.

Definition

COVID-19: The diagnosis of Covid-19 was based on the detection of SARS-CoV-2 utilizing a polymerase-chain-reaction (PCR) assay (20). PCR testing of nasopharyngeal swabs was used.

Smoking status: Smoking status was categorized as never smoker, ex-smoker, or current smoker.

Outcome measures

All patient's clinical conditions were collected. This study was performed based on a checklist in which the basic and clinical information of patients was recorded. Checklists were filled out by interviewers. Age, sex, marital status, employment, duration of hospitalization,

patients' outcome, ICU admission, underlying diseases, comorbidities, and laboratory parameters were the items to assess. The checklist was developed using a preexisting validated questionnaire that had already been used in multinational studies (9,16,20).

Smoking status

Refers to the active smoking of one or more manufactured or hand-rolled tobacco cigarettes (or parts thereof) per day. Patients who reported currently smoking tobacco of any kind were considered current smokers. Those who reported having stopped smoking more than a year ago were considered ex-smokers. All others were considered never smokers. Never smokers were used as the reference category when calculating odds ratios (ORs).

Statistical Analysis

The present study used SPSS (version 21; SPSS Inc., Chicago, Ill., USA) to gather and analyze the data. In all analyses, the significance level was considered less than 0.05. Multiple logistic regression was used to assess the association between smoking status and ICU admission.

RESULTS

Out of 206 patients enrolled in the study, 137 (66.5%) were men and 69 (33.5%) were women. More than 63% of hospitalized patients had 45 years or more and the median was 50 years. 63 (30.4%) patients of the study population had a family member with a current disease or history of COVID-19. The main demographic characteristics of study populations are shown below (Table 1).

Patients' education also showed that the number of patients without academic education was approximately 2.5 times the number of patients who completed their academic education. The ratio of married patients compared to single patients was 4 to 1. Also, according to the results presented in Table 1, fifty-nine (28.67%) patients were hospitalized for 4-7 days, and 17(8.39%) of the total hospitalizations were admitted to the intensive care unit. Sample characteristics of smoking status are shown in Table 1. More than 20% of hospitalized patients had been smoking tobacco for at least 15 years. 14 (6.7%) were ex-smokers and 34 (16.5%) were current smokers.

Among all patients, 108 (52.4%) patients had a history of the underlying disease (Figure 1), of which diabetic patients and patients with cardiovascular disease had the highest share. Also, 15(44.1%) of smokers reported consuming less than 10 cigarettes a day, and 3 (9.3%) of patients consuming more than 30 cigarettes per day (Figure 2).

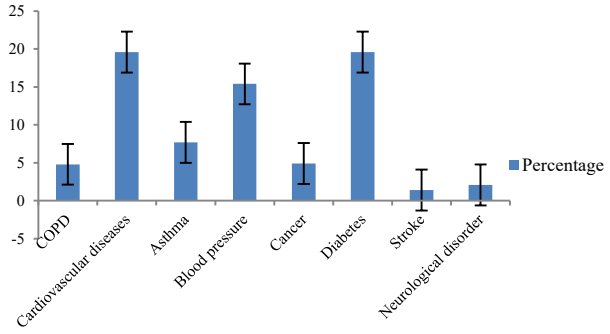

Figure 1. Comparative diagram of the history of various diseases in patients with SARS-COV-2

Table 1. Descriptive characteristics of subjects

			Current smokers	Ex-smokers	Never smokers	Total (n=206)	P-value
Sex (Male), n (%)			27 (19.7)	12 (8.75)	98 (71.55)	137 (66.5%)	0.077
Age (Year), n (%)	15-30		8 (4.44)	0 (0.00)	10 (55.55)	18 (8.7%)	0.188
	30-45		10 (16.66)	2 (3.33)	48 (80.00)	60 (30%)	0.093
	45-60		12 (17.91)	5 (7.46)	50 (74.62)	67 (32.5%)	0.102
	60<		4 (6.45)	7 (11.29)	51 (82.25)	62 (31%)	0.076
Education, n (%)	Academic		9 (15.25)	5 (8.47)	45 (76.27)	59 (28.6%)	0.092
	Non-academic		25 (17.00)	9 (6.12)	113 (76.87)	147 (71.3%)	0.146
Marital status, n (%)	Single		13 (28.88)	2 (4.44)	30 (66.67)	45 (21.8%)	0.092
	Married		21 (11.58)	12 (7.59)	149 (81.86)	182 (88.3%)	0.061
Hospitalization, n (%)	Hospital ward	0-3	8 (50.00)	4 (25.00)	4 (25.00)	16 (7.69%)	0.102
		4-7	20 (33.89)	7 (11.86)	32 (54.23)	59 (28.67%)	0.084
		8<	6 (16.66)	3 (8.33)	27 (75.00)	36 (17.48%)	0.90
	ICU		8 (47.05)	4 (23.52)	5 (29.41)	17 (8.39%)	0.195

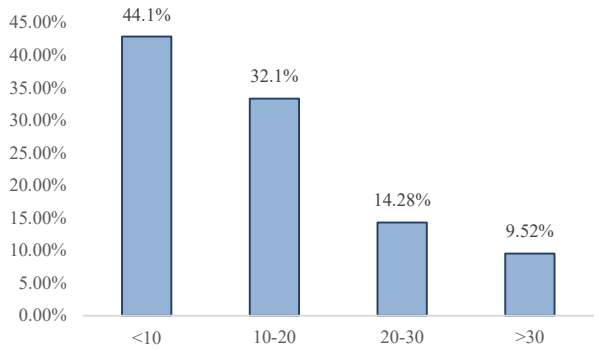

Figure 2. Patients' smoking history based on the number of cigarette butts used per day

Out of 206 patients in this study, 44 (21.3%) had a history of consuming any type of tobacco, including cigarettes, e-cigarettes, or hookah, while 7 (3.4%) had opium use. Smokers with 21 to 30 cigarettes per day had the longest duration of hospitalization (Figure 3).

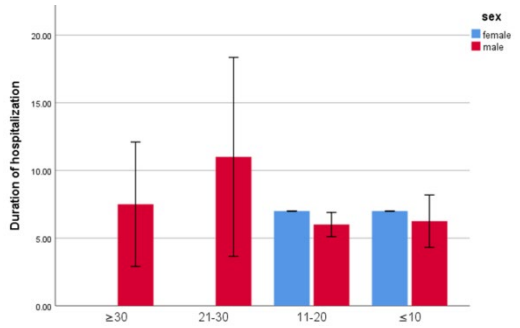

Figure 3. Duration of hospitalization based on daily cigarette use

Differences in socio-demographic factors are presented in Table 2. It was observed that the highest number of contaminated patients with SARS-COV-2 belonged to housewives and retired groups, accounting for 49 (23.7%) of the cases.

Table 2. Employment levels of patients with SARS-COV-2 understudy

Occupational status	N	(%)
Employee	35	16.9 %
Freelance	43	20.8 %
Retired	49	23.7 %
Student	9	4.3 %
Unemployed	6	2.9 %
Housewife	49	23.7%
Other	15	7.2 %

Logistic regression analysis (Table 3), showed significant relationships between ex-smoking and ICU admission in covid-19 patients. Ex-smokers were 3 times more likely [OR = 1.20, 95% CI: 1.03–10.74] to have been in ICU. Current smokers had protective odds of becoming seriously ill from COVID-19 (Table 4).

Table 3. Logistic Regression analysis for sex, age, and Ex-smoke

Variable	B	SE	OR	95%CI (OR)	P value
sex	1.03	.619	2.81	(0.83,9.46)	0.096
age	.03	.018	1.02	(0.99, 1.06)	0.122
Ex-smoke	1.20	.599	3.32	(1.03,10.74)	0.045
Constant	-4.34	1.149			

Table 4. Logistic Regression analysis for sex, age, and current-smoking

Variable	B	SE	OR	95%CI (OR)	P value
sex	-0.009	0.532	0.99	(0.35, 2.81)	0.986
age	0.02	0.016	1.02	(0.99, 1.05)	0.230
Current-smoke	-1.44	0.529	0.24	(0.08, 0.67)	0.007
Constant	-2.01	.871			

DISCUSSION

To the best of our knowledge, the date of this study was among the first studies to develop an understanding of the tobacco smoking pattern and severity of inpatients diagnosed with COVID-19 in Iran. We provided a precise report about smoking prevalence in hospitalized inpatients. Our main outcomes showed that the overall prevalence of tobacco smoking in COVID-19 inpatients was higher than this figure in the general population and that the probability of severity was higher in ex-smokers, which indicates ex-smokers with confirmed COVID-19 are at a greater risk of severe complications. On the other hand, current smoking was linked with decreased odds of severity in COVID-19 inpatients.

A growing debate about increasing the susceptibility to COVID-19 by tobacco smoking has been developing (21). According to this hypothesis, a meta-analysis of 19 studies from different countries reported that tobacco smoking was a risk factor for the progression of COVID-19 (22). On the contrary, a systematic review from China (23) found a

lower smoking prevalence among inpatients hospitalized with COVID-19 and hypothesized that nicotine might protect against COVID-19. Data from several countries reported lower smoking prevalence among inpatients with COVID-19 than would be expected based on population smoking prevalence (24-26). In Iran, the prevalence of current smoking was estimated to be 10.6% overall, 20.9% in males, and 2.2% among females respectively (26). We reported a lower smoking prevalence in men, but higher rates in women and overall, among inpatient COVID-19. Similarly, in many studies smoking prevalence among hospitalized COVID-19 patients was substantially below smoking prevalence in the corresponding populations. In 10 Chinese studies, smoking prevalence in hospitalized COVID-19 patients ranged from 3.8% to 14.6% while in the general population, it is 27.7% (52.1% for men and 2.7% for women) (27). Low smoking prevalence among hospitalized patients was observed also in German and US patients (23). It seems that the lower prevalence of smokers among COVID-19 hospitalized patients could be biased by confounding identifying smokers among patients with COVID-19.

However, there could be other underlying reasons behind this prevalence such as different study designs, regions, and outcomes. Some studies were done in the context of an emerging epidemic; consequently, the collection of smoking habits was not given priority. In addition, smokers with severe symptoms of COVID-19 may have quit smoking before hospitalization and therefore may not have been recorded as current smokers. These may have led to an underestimation of the prevalence of smoking tobacco.

We found that 3.9% (8 out of 34) of current smokers and 5.5% (8 out of 46) of ex-smokers had severe complications and admitted to ICU, and ex-smokers were 3 times more likely [OR=1.20, 95% CI:1.03–10.74] to have been in ICU. Guan et al. (28) showed that 32% of patients with a history of smoking (smokers and/or ex-smokers) at the time of hospitalization had a severe form of COVID-19, compared to 15% of never-smokers. In addition, 16% of smokers required hospitalization in intensive care units or died, compared to 5% of non-smokers. Another systematic review showed that there was greater disease severity in ever compared with non-smokers (RR=1.43, 95% CI: 1.15-1.77, p=0.002) (24). Also, Williamson et al. (29) who conducted the largest cohort studies to date from the UK reported an increased risk for in-hospital COVID-19 death in ex-smokers compared to never-smokers (HR 1·8 [95% CI 1·7–1·9]) when adjusted for age and sex. A meta-analysis by Alqahtani et al. based on 15 studies on COVID-19 patients with COPD showed that 22% of current smokers and 46% of ex-smokers had severe complications (30).

On the other side, in a systematic review of the role of smoking on the severity of COVID-19, Lippi et al. reported that active smoking was not found to be a significant predictor of COVID-19 severity (31).

It seems that the quality of the recorded data on smoking habits is not well documented in the majority of articles. Moreover, due to the emergency situation, articles were carried out in the context of an emerging epidemic; therefore, the collection of smoking habits was not considered a priority. This may have led to an underestimation of the prevalence of smokers and former smokers may have been conflated with never smokers.

CONCLUSION

Ex-smoker inpatients with COVID-19 require special attention since they are a vulnerable population with a higher admission in the intensive care unit (ICU) rate than the general population.

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