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Research Paper

Impact of Smoking on the Mortality of Hospitalized Patients With COVID-19, Iran: A Cross-sectional Study

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ABSTRACT

Background: There are inconsistent data about the association of smoking with the prognosis of hospitalized patients with COVID-19. This inconsistency is so huge that some investigators have suggested some protective roles for smoking against COVID-19 disease.

Objective: This study was designed to investigate the association of smoking with mortality in hospitalized patients with COVID-19.

Methods: This cross-sectional study was conducted on 493 adult patients with COVID-19 disease. Other underlying diseases, clinical and laboratory findings, and mortality rates were compared between smoking and non-smoking patients using univariate and multivariate analyses.

Results: The prevalence of current smoking among hospitalized patients was 6.1%. Clinical complaints and disease severity at admission were similar between smokers and non-smokers. Leukocyte count and blood sugar were higher in smokers compared to non-smokers (P=0.003, P=0.018, respectively). The rate of ICU admission and days of hospitalization were comparable between smokers and non-smokers. However, smokers had a significantly higher mortality rate than non-smokers (36.7% vs 13.8%, respectively, P=0.001). After adjusting for significantly different variables in univariate analysis, smoking was associated with a 3.78 times higher mortality rate (OR=3.78, 95% CI: 1.48-9.67, P=0.005).

Conclusion: Smoking is an independent predictor of mortality in hospitalized patients with COVID-19.

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1. Introduction

Since the beginning of the COVID-19 pandemic, many studies have tried to determine the critical risk factors involved in this disease. In the first months of the pandemic, history of diabetes, hypertension, ischemic heart disease, smoking, and immunocompromised situations were introduced as the main risk factors for being infected with COVID-19 or developing severe forms of COVID-19 [1, 2].

Smoking is a risk factor for many diseases. Its causative role in chronic lung disease, hypertension, coronary disease, and some cancers is well-established [3]. Even passive smoking is accompanied by some pulmonary diseases such as asthma [4]. Smokers are susceptible to influenza and community-acquired pneumonia [5-7]. However, in all studies in hospitalized patients with COVID-19 disease, the percentages of current smokers were significantly lower than the reference general population [8-10]. Based on the low prevalence of smokers in hospitalized COVID-19 patients, some hypotheses have been suggested for the protective role of smoking against COVID-19 disease [11]. Despite this low prevalence of smokers among hospitalized patients, the role of smoking in the severity of COVID-19 has been shown in most meta-analyses [10, 12, 13]. Evidence of the impact of smoking on mortality is even more inconsistent. In some studies, higher mortality in smokers has been shown [14-16].

Nevertheless, in other studies, mortality was similar between smokers and non-smokers [12, 17]. However, there is enormous heterogeneity in evidence because of different definitions of severity, patients' race, the study time (in the times of peak or stability of disease), and types of care and treatment of patients. One interesting finding is the impact of the country of study on the reported association between smoking and poor prognosis in patients. In a systematic review and meta-analysis by Karanasos et al. [17], the association of smoking with the severity of COVID-19 was different between Chinese vs US studies. This association was significant only in the meta-analysis of Chinese studies.

Regarding the very high prevalent COVID19 disease in Iran [18], inconsistency of reported evidence on the role of smoking in the mortality of COVID-19 patients, and the possible impact of the country of study, this study was designed to investigate the association of smoking with mortality in hospitalized patients with COVID-19 in Qazvin City, Iran.

2. Materials and Methods

Study design and characteristics of the participants

The current cross-sectional study was conducted to investigate the association of smoking with mortality in 18≥ year old COVID-19 patients admitted to Velayat Hospital in Qazvin Province in Iran from September to November 2020. Polymerase Chain Reaction (PCR) was used to confirm COVID-19 disease in the participants. Current smoking was defined as patients who reported smoking ≥100 cigarettes in their lifetime and had been smoking at least until being symptomatic by COVID-19 disease. All information was collected through questionnaires designed before the patients were admitted, and the information was recorded daily. The questionnaire data included clinical symptoms, underlying diseases (hypertension, ischemic heart disease, diabetes, chronic respiratory, hepatic, and renal diseases), laboratory findings, admission to ICU, and mortality.

Statistical analysis

The Kolmogorov–Smirnov test was used to examine the distribution of quantitative variables. The comparison of quantitative data and categorical data between current smokers and non-smokers was conducted using the Mann-Whitney U test (all quantitative variables had non-normal distributions) and the Chi-square test, respectively. For investigating the independent role of smoking in mortality, a multivariate logistic regression test was performed using current smoking, age, and significantly different variables as independent and mortality as dependent variables between smokers and non-smokers in the Mann-Whitney U test (Table 1). The analyses were performed in SPSS software v. 22 (Chicago, IL, USA), and $P<0.05$ was considered significant.

3. Results

Among 493 patients, 30 patients (6.1%) were smokers. Clinical and laboratory data of smoker and non-smoker patients are presented in Table 1. The age distribution, patients' complaints, vital signs on admission, and capillary oxygen saturation without oxygen supply were not significantly different between smokers and non-smokers. Among medical comorbidities, only the rate of COPD (Chronic obstructive pulmonary disease) or asthma was higher in the smokers' group than in non-smokers (16.7% vs 4.1%, P=0.002). Regarding laboratory results at admission, leukocyte count, neutrophil percentage, and Blood Sugar (BS) were significantly higher

Table 1. Characteristics of patients categorized by smoking status

	Variables	Mean±SD/%			P
		Total (n=493)	Non-Smokers (n=463, 93.9%)	Smokers (n=30, 6.1%)	
	Age (y)	61.7±16.4	61.6±16.4	63.3±16.6	0.686
	Gender (Male%)	59	57.0	90.0	<0.001
Complaints (%)	Dyspnea	64.7	65.7	50.0	0.082
	Cough	60.6	60.9	50.0	0.645
	Chest pain	5.5	5.0	13.3	0.061
	Diarrhea	6.1	6.5	0	0.150
	Nausea/Vomiting	22.9	23.3	16.7	0.400
	Myalgia	26.2	25.9	30.0	0.622
Vital signs	T (°C)	36.8±0.7	36.8±0.8	36.6±0.7	0.206
	RR (per minute)	19.1±3.3	19.1±3.1	19.4±3.1	0.458
	PR (per minute)	90.2±16.1	90.3±16.0	88.6±17.9	0.957
	Systolic BP (mm Hg)	125.3±20.5	125.4±20.6	124.8±19.5	0.767
	Diastolic BP (mm Hg)	78.3±13.2	78.3±13.4	77.9±12.4	0.344
History	Hypertension	32.3	31.7%	40%	0.349
	Ischemic heart disease	16.4	15.8%	26.7%	0.118
	Diabetes	20.5	20.1%	26.7%	0.387
	Chronic obstructive pulmonary disease or asthma	4.9	4.1%	16.7%	0.002
	Chronic kidney disease	2.0	1.9	3.9	0.601
	Cirrhosis (%)	0	0	0	1
Laboratory findings	Capillary O_2 saturation without oxygen supply	86.3±5.1	86.3±5.0	86.2±4.4	0.793
	Leukocytes count (count/ml)	7500±4500	7300±4400	10200±5200	0.003
	Neutrophils	76.1±11.4	75.6±11.3	81.7±11.6	0.001
	Lymphocytes	19.5±11.5	19.9±11.6	14.4±10.0	0.001
	Blood glucose (mg/dl)	142.9±74.8	140.6±70.4	173.9±116.6	0.018
	Blood urea nitrogen (mg/dL)	23.5±23.9	23.2±24.1	27.9±20.3	0.425
	Creatinine (mg/dL)	1.4±1.2	1.3±1.1	1.7±1.7	0.347
	Sodium (mEq/L)	133.8±3.5	133.9±3.2	132.9±3.8	0.957
	Potassium (mEq/L)	4.0±0.6	4.0±0.5	4.2±0.6	0.397

All data are related to the first hours of admission.

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Quantitative data are presented as Mean±SD.

T: Temperature, RR: Respiratory rate, PR: Pulse Rate, BP: Blood Pressure.

Regarding its non-parametric nature, the Mann-Whitney U test was used to analyze quantitative data.

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Table 2. Clinical course of patients categorized by serum smoking status

Clinical Outcome	Mean±SD/%			P
	Total	Non-smokers	Smokers	
Intensive care unit admission	9.2%	9.1%	10%	0.864
Duration of hospitalization in survived patients (d)	6.1±6.6	6.0±6.1	7.7±6.8	0.261
Days to death in expired patients (d)	6.6±7.2	6.7±7.4	6.0±6.8	0.226
Expire rate	15.2%	13.8%	36.7%	0.001

Quantitative data are presented as Mean±SD.

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Regarding its non-parametric nature, the Mann-Whitney U test was used to analyze quantitative data.

in the smokers' group (P=0.003, P=0.001, and P=0.018, respectively) (Table 1).

Regarding the course of the disease, the rate of ICU admission and days of hospitalization were not different between smokers and non-smokers. However, smokers had a significantly higher mortality rate than non-smokers (36.7% vs 13.8%, respectively, P=0.001) (Table 2).

To investigate the independent role of smoking in mortality, a multivariate logistic regression test was performed by entering age and significantly different variables as independent covariates and mortality as dependent variables between smokers and non-smokers in the Mann-Whitney U test (Table 1). After adjusting, only age and smoking remained significant predictors of mortality. Smoking was independently associated with a 3.78 times higher mortality rate (95% CI: 1.48-9.67, P=0.005) (Table 3).

4. Discussion

The frequency of smokers in our study was low (6.1% of patients). At admission, in smokers, complaints and indexes of COVID-19 severity (as assessed by O2 saturation and respiratory rate) were the same as those in non-smokers. However, smoking was independently associated with about four times higher mortality.

There are many controversies about the impact of smoking on the rate of infection by COVID-19 and the prognosis of this disease. However, one issue is consistent in most of the studies: the low rate of smokers among hospitalized patients with COVID-19. The reported prevalence rates differ from 1.4% to 12.6% (6.5% in pooled analysis) [8]. There are some hypotheses for the cause of this finding. Some investigators believe that the main reason is incomplete data gathering due to the critical situation of patients. However, there is some evidence against this hypothesis. The prevalence of current smoking in Italy is reported as 25.7%. In the meta-analysis conducted by Reddy et al. [12], 26.9% of patients had a positive history of smoking (including past, current, and unspecified smokers). However, the overall prevalence of smoking in this meta-analysis reported is only 6.2%. The data on the rational prevalence of for-

Table 3. Predictive value of smoking for death in the multivariate analysis

Risk Factor	Adjusted OR (95%CI)
Age	1.04 (1.02-1.06)*
Gender (male)	1.04 (0.58-1.84)
Chronic obstructive pulmonary disease or asthma	1.57 (0.55-4.46)
Blood sugar	0.99 (0.99-1.00)
Leukocyte count	1.02(0.97-1.08)
Smoking	3.78(1.48-9.67)**

* P<0.0001; ** P=0.005

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mer smokers in hospitalized patients with COVID-19 are against the hypothesis of incorrect and incomplete history taking of ill patients. There are other hypotheses for the low prevalence of smoking in hospitalized patients with COVID-19. Fear of not receiving enough health care due to smoking habits may be another reason for low self-reporting of smoking in the pandemic. The last and most controversial hypothesis is related to the protective effect of nicotine in preventing infection with COVID-19 [19].

The association of smoking with patients' mortality of COVID-19 disease has been investigated in some studies. Results of systematic reviews and meta-analyses are very inconsistent. An early systematic review by Simons et al. was based on studies with more than 90% missing data about the smoking status [20]. In this meta-analysis, no association was found between smoking and COVID-19 mortality. In the meta-analysis by Karanasos et al. [17], five studies with 838 patients were included for evaluating the impact of smoking on inpatient mortality of COVID-19 disease. Similar to Simons' meta-analysis, this meta-analysis revealed no association between current smoking and mortality (OR=1.45, 95% CI: 0.78–2.72). In Alqahtani et al. meta-analysis of 15 studies and a total of 2473 patients, the mortality rate was 38% higher in current smokers compared to former or never smokers [21]. In one of the largest meta-analyses conducted on 32849 hospitalized patients, current smoking was associated with about 1.8 times higher risk of severe COVID-19 disease. However, despite higher disease severity in smokers, the authors did not find any significant difference between current smokers and non-smokers [12]. Interestingly in this study, patients with positive smoking history (including current or former smokers or e-cigarette users) had a 1.26 times higher risk of in-hospital mortality.

Reasons for such huge inconsistency in studies about the association between smoking and the prevalence or outcome of COVID-19 are not clear. In the meta-analysis by Karanasos et al. [17], some effective variables on heterogeneities were evaluated. Age and diabetes had negative effects on the association of smoking and COVID-19 severity. In populations with a lower prevalence (less than 15%) of diabetes, the impact of smoking on COVID-19 severity was significantly positive (OR=1.66, 95% CI: 1.26-2.18). Conversely, in populations with a higher prevalence of diabetes, the association between smoking and severity was non-significant, with a trend for negative impact (OR=0.7, 95% CI: 0.46-1.08. I2=0%). Apart from that, the impact of smoking on disease severity was more significant in younger patients. Countries of studies may influence the association of smoking with disease mortality, possibly due to patients' race, type of care, and treatment. In Karanasos' meta-analysis, there was a difference between Chinese and US studies. In Chinese studies (16 studies, 4423 patients), smoking was associated with 1.48 times (95% CI=1.17–1.87) higher risk of severe disease, whereas in US studies (2 studies with 1887 patients), there was no association and even a trend for the less severe disease existed in smokers (OR=0.65, 95% CI: 0.33-1.29, I2=0%).

There are some common physiological pathways between COVID-19 infection and smoking. COVID-19 virus uses Angiotensin-Converting Enzyme-2 (ACE-2) for entering the cell. Therefore, upregulation of this receptor may increase virus infectiousness. Paradoxically, upregulation of this receptor may cause protection from acute and severe lung injuries [22].

ACE-2 upregulation has been reported in current (but not former) smokers [23]. In addition, nicotine has some inhibitory effects on the secretion of inflammatory cytokines such as IL-6 and tumor necrosis factor, which have essential roles in cytokines storm in COVID-19 disease [24-26]. In animal studies, nicotine has been shown to prevent acute respiratory distress syndrome [27]. Based on the role mentioned above of ACE-2 in COVID-19 disease, higher prevalence and lower severity of COVID-19 disease among smokers are expected. However, epidemiological data are contrary to these physiological mechanisms, i.e., very low prevalence of smokers among hospitalized patients and more severe disease course in smokers in most studies. So more studies about the impact of smoking on mortality in different races and studies designed for investigating the pathophysiological role of smoking in COVID19 disease are strongly recommended.

5. Conclusion

In conclusion, our study revealed a strong association between smoking and in-hospital mortality of patients with COVID-19. This association was independent of other risk factors such as underlying diseases and biochemical abnormalities. Our studies have some limitations. In our questionnaire, only current smoking was asked about, and we do not have any information about former smokers. The second limitation is the relatively low sample size of our study. Thirdly, we did not compare the frequency of smokers in hospitalized patients with the normal general population.

Ethical Considerations

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Compliance with ethical guidelines

This study was approved by the Ethics Committee of Qazvin University of Medical Science (Code: IR.QUMS.REC.1399.467).

Conflict of interest

The authors declared no conflict of interest.

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Authors' contributions

Conceptualization and Supervision: Sima Hashemipour, Maryam Gheraati, and Milad Badri; Methodology:Sima Hashemipour, Maryam Gheraati, and Milad Badri; Investigation, Writing – original draft, and Writing – review & editing: All authors; Data collection: Sohrab Esmaielzade, Nafiseh Rastgoo, and Aref Shokri; Data analysis: Sima Hashemipour; All authors read the manuscript and participated in preparing the final version of the manuscript.

References

[1] CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019-United States, February 12-March 28, 2020. MMWR Morb Mortal Wkly Rep. 2020; 69(13):382-6. [DOI:10.15585/mmwr.mm6913e2] [PMID] [PMCID]

[2] Mohammadi F, Badri M, Safari S, Hemmat N. A case report of rhino-facial mucormycosis in a non-diabetic patient with COVID-19: A systematic review of literature and current update. BMC Infect Dis. 2021; 21(1):906. [DOI:10.1186/s12879-021-06625-3] [PMID] [PMCID]

[3] Allender S, Balakrishnan R, Scarborough P, Webster P, Rayner M. The burden of smoking-related ill health in the UK. Tob Control. 2009; 18(4):262-7. [DOI:10.1136/tc.2008.026294] [PMID]

[4] Zohal MA, Ehteshmi Afshar A, Zahmatkesh M, Lashkari M. Prevalence of exercise induced asthma among pupils and its relation with their parents'smoking habits. J Inflamm Dis. 2002; 5(4):79-83. [In Persian]. https://journal.qums.ac.ir/article-1-460-en.html

[5] Han L, Ran J, Mak YW, Suen LK, Lee PH, Peiris JSM, et al. Smoking and influenza-associated morbidity and mortality: A systematic review and meta-analysis. Epidemiology. 2019; 30(3):405-17. [DOI:10.1097/EDE.0000000000000984] [PMID]

[6] Baskaran V, Murray RL, Hunter A, Lim WS, McKeever TM. Effect of tobacco smoking on the risk of developing community acquired pneumonia: A systematic review and meta-analysis. PLos One. 2019; 14(7):e0220204. [DOI:10.1371/journal.pone.0220204] [PMID] [PMCID]

[7] Arcavi L, Benowitz NL. Cigarette smoking and infection. Arch Intern Med. 2004; 164(20):2206-16. [DOI:10.1001/archinte.164.20.2206] [PMID]

[8] Farsalinos K, Barbouni A, Niaura R. Systematic review of the prevalence of current smoking among hospitalized COVID-19 patients in China: Could nicotine be a therapeutic option? Intern Emerg Med. 2020; 15(5):845-52. [DOI:10.1007/s11739-020-02355-7] [PMID] [PMCID]

[9] Emami A, Javanmardi F, Pirbonyeh N, Akbari A. Prevalence of underlying diseases in hospitalized patients with COVID-19: A systematic review and meta-analysis. Arch Acad Emerg Med. 2020; 8(1):e35. [PMID] [PMCID]

[10] Gülsen A, Yigitbas BA, Uslu B, Drömann D, Kilinc O. The effect of smoking on COVID-19 symptom severity: Systematic review and meta-analysis. Pulm Med. 2020; 2020:7590207. [DOI:10.1155/2020/7590207] [PMID] [PMCID]

[11] Changeux JP, Amoura Z, Rey FA, Miyara M. A nicotinic hypothesis for Covid-19 with preventive and therapeutic implications. C R Biol. 2020; 343(1):33-9. [DOI:10.5802/crbiol.8] [PMID]

[12] Reddy RK, Charles WN, Sklavounos A, Dutt A, Seed PT, Khajuria A. The effect of smoking on COVID-19 severity: A systematic review and meta-analysis. J Med Virol. 2021; 93(2):1045-56. [DOI:10.1002/jmv.26389] [PMID] [PMCID]

[13] Umnuaypornlert A, Kanchanasurakit S, Lucero-Prisno DEI, Saokaew S. Smoking and risk of negative outcomes among COVID-19 patients: A systematic review and meta-analysis. Tob Induc Dis. 2021; 19:09. [DOI:10.18332/tid/132411] [PMID] [PMCID]

[14] Dai M, Tao L, Chen Z, Tian Z, Guo X, Allen-Gipson DS, et al. Influence of cigarettes and alcohol on the severity and death of COVID-19: A multicenter retrospective study in Wuhan, China. Front Physiol. 2020; 11:588553. [DOI:10.3389/fphys.2020.588553] [PMID] [PMCID]

[15] Liu W, Tao ZW, Wang L, Yuan ML, Liu K, Zhou L, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J (Engl). 2020; 133(9):1032-8. [DOI:10.1097/CM9.0000000000000775] [PMID] [PMCID]

[16] Vardavas CI, Nikitara K. COVID-19 and smoking: A systematic review of the evidence. Tob Induc Dis. 2020; 18:20. [DOI:10.18332/tid/119324] [PMID] [PMCID]

[17] Karanasos A, Aznaouridis K, Latsios G, Synetos A, Plitaria S, Tousoulis D, et al. Impact of smoking status on disease severity and mortality of hospitalized patients with COVID-19

infection: A systematic review and meta-analysis. Nicotine Tob Res. 2020; 22(9):1657-9. [DOI:10.1093/ntr/ntaa107] [PMID] [PMCID]

[18] Mohammadi F, Kouzehgari S. Predicting the prevalence of COVID-19 and its mortality rate in Iran using lyapunov exponent. J Inflamm Dis. 2020; 24(2):108-23. [In Persian]. [DOI:10.32598/JQUMS.24.2.2415.1]

[19] Wenzl T. Smoking and COVID-19: A review of studies suggesting a protective effect of smoking against COVID-19. Luxembourg: Publications Office of the European Union; 2020. [DOI:10.2760/564217]

[20] Simons D, Shahab L, Brown J, Perski O. The association of smoking status with SARS-CoV-2 infection, hospitalization and mortality from COVID-19: A living rapid evidence review with Bayesian meta-analyses (version 7). Addiction. 2021; 116(6):1319-68. [DOI:10.1111/add.15276] [PMID] [PMCID]

[21] Alqahtani JS, Oyelade T, Aldhahir AM, Alghamdi SM, Almehmadi M, Alqahtani AS, et al. Prevalence, severity and mortality associated with COPD and smoking in patients with COVID-19: A rapid systematic review and meta-analysis. PLos One. 2020; 15(5):e0233147. [DOI:10.1371/journal.pone.0233147] [PMID] [PMCID]

[22] Behl T, Kaur I, Bungau S, Kumar A, Uddin MS, Kumar C, et al. The dual impact of ACE2 in COVID-19 and ironical actions in geriatrics and pediatrics with possible therapeutic solutions. Life Sci. 2020; 257:118075. [DOI:10.1016/j.lfs.2020.118075] [PMID] [PMCID]

[23] Leung JM, Yang CX, Tam A, Shaipanich T, Hackett TL, Singhera GK, et al. ACE-2 expression in the small airway epithelia of smokers and COPD patients: Implications for COVID-19. Eur Respir J. 2020; 55(5):2000688. [DOI:10.1183/13993003.00688-2020] [PMID] [PMCID]

[24] Wittebole X, Hahm S, Coyle SM, Kumar A, Calvano SE, Lowry SF, et al. Nicotine exposure alters in vivo human responses to endotoxin. Clin Exp Immunol. 2007; 147(1):28-34. [DOI:10.1111/j.1365-2249.2006.03248.x] [PMID] [PMCID]

[25] Wang H, Yu M, Ochani M, Amella CA, Tanovic M, Susarla S, et al. Nicotinic acetylcholine receptor α7 subunit is an essential regulator of inflammation. Nature. 2003; 421(6921):384-8. [DOI:10.1038/nature01339] [PMID]

[26] Conti P, Ronconi G, Caraffa A, Gallenga C, Ross R, Frydas I, et al. Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): Anti-inflammatory strategies. J Biol Regul Homeost Agents. 2020; 34(2):327-31. [DOI:10.23812/CONTI-E] [PMID]

[27] Mabley J, Gordon S, Pacher P. Nicotine exerts an anti-inflammatory effect in a murine model of acute lung injury. Inflammation 2011; 34(4):231-7. [DOI:10.1007/s10753-010-9228-x] [PMID] [PMCID]

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