MMSL Military Medical Science Letters Since 1925

Mil. Med. Sci. Lett. (Voj. Zdrav. Listy) 2022, 91(2), 98-104
ISSN 0372-7025 (Print)
ISSN 2571-113X (Online)
DOI: 10.31482/mmsl.2021.044

ORIGINAL ARTICLE

THE IMPACT OF SMOKING ON SEVERITY AND OUTCOME IN PATIENTS WITH COVID-19 INFECTION IN MOSUL CITY

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Received 24th October 2021.
Accepted 7th December 2021.
Published 3rd June 2022.

Summary

Introduction: The novel corona virus (SARS-CoV-19) is mainly accountable for the disease outbreak infection, which began in Wuhan, China, in 2019. Numerous modest research has been carried so far to ascertain the risks of smoking on the magnitude, consequence, and morbidity of patients with COVID-19, but the findings have been incomplete.

Aims: This study assesses the effects of current smokers on the magnitude and consequence in patients with COVID-19 infectious disease in Mosul, Iraq.

Materials and Methods: A total of 160 patients (80 active smokers and 80 non-smokers) who were confirmed with COVID-19 infection using polymerase chain reaction (PCR) test were enrolled in this study. A detailed history was obtained from of the subjects, as well as a thorough clinical evaluation and laboratory tests. The intensity of illness, biomarkers, D-dimer, liver enzymes (LFT), oxygen consumption, hospitalization, and outcome were all documented and analyzed between a two groups.

Results and conclusion: The symptoms of COVID-19, measured laboratory markers were significantly higher in the sample of smokers compared to non-smokers. There has been no significant difference in the use of oxygen, hospitalization, ICU admission, death, or post-recovery problems. Serious clinical COVID-19 infection was much more prevalent in current smokers, and inflammatory markers such as D-dimer and LFT appeared greater in non - smokers than in smokers. There was no statistically significant difference in O2 usage, hospitalization, ICU admittance, death, or persistent morbidity.

Key words: COVID-19; smoking; severity of symptoms; inflammatory markers

Introduction

Coronavirus disease 2019 (COVID-19) was diagnosed in December 2019 when the first case was identified in Wuhan city/China, since then it has been spread all over the world and has been declared a pandemic by the WHO on March 2020 (1,2). The disease is caused by severe acute respiratory syndrome corona-virus 2 (SARS- CoV-2), the clinical presentations vary from person to person, it can be asymptomatic or causing upper respiratory tract symptoms, but since the primary target of the virus is the epithelial cells of the lungs, it can lead to viral pneumonia, acute respiratory distress syndrome (ARDS), respiratory failure and even death (3).

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Smoking is well known risk factor for many respiratory diseases like chronic obstructive airway diseases, viral and bacterial infections of the lungs and malignancy, smokers are usually not only more prone to respiratory infections, but also the severity of these infections is higher (4). In the previous MERS-COV outbreak, smokers had a higher mortality rate than non-smokers according to the studies (5).

Since the discovery of COVID-19, there has been an interest in the association of tobacco smoking with the symptoms, severity and outcome of patients with COVID-19 infection, but the data were conflicting regarding this issue and there was a gap in the evidence (6). Smoking is sometimes associated with paradoxical favourable outcome in certain diseases which may have immunological bases like ulcerative colitis (7), extrinsic allergic alveolitis (8) and sarcoidosis (9), based on this hypothesis of a protective effect of current smoking on certain diseases, many studies have to be done to establish the effect of smoking on COVID-19 infection (10).

In this context, the links between smoking and Covid-19 should be further investigated and whether such associations may be a manifestation of the effects of nicotine or smoking. It should also be established that lower rates of infection among smokers can indicate protection from infection or an improvement in asymptomatic or mild types, which could affect overall immunity because higher rates of asymptomatic patients will increase spread of the virus. The purpose of this research is to determine the effect of current smokers on the incidence and prognosis of COVID-19 infection in people in Mosul, Iraq.

Patients and methods

Study design

A prospective cohort study was conducted on 160 patients who were polymerase chain reaction (PCR)-positive for COVID-19 infection.

Sample collection

The sample was conducted at Ibn-Sina teaching hospital in Mosul city, Iraq from May 2020 until December 2020. Detailed history was taken from the patients, full clinical examination, and blood tests were done.

The patients were divided into 2 groups: 80 patients were active smokers (69 males, 11 females) and 80 patients were non-smokers (67 males, 13 females). For each group, the following parameters were documented: severity of symptoms, SpO_2 concentration throughout the illness, inflammatory markers (CRP, Ferritin, LDH, ESR) at presentation, D-dimer, liver and renal function tests , the percentage of ground glass appearance on CT scan of the lungs, the need for oxygen use (at hospital or at home) , the need for hospital admission, the need for ICU admission, if the patient needed CPAP or mechanical ventilation, which treatment has been given to the patient and the outcome of the illness (3 months after recovery).

The severity of symptoms was classified into mild symptoms which include (low grade fever, nasal congestion, anosmia, ageusia or dysgeusia, headache and myalgia) and severe symptoms which include (severe cough, dyspnea, high fever, severe GIT symptoms). Although there is no clear cut point for the classification of The severity of inflammatory markers but one study was done to determine the role inflammatory markers in severe COVID-19 infection (11), so the inflammatory markers were classified the into mild elevation (CRP < 10 mg/l, ferritin < 500 ng/l, D-dimer < 1000 ng/ml, LDH < 500 IU/L) and severe elevation (CRP > 10 mg/l, ferritin > 500 ng/l, D-D-dimer > 1000 ng/ml, LDH >500IU/L).

The treatment was divided into supportive (vitamins, analgesics and antipyritics) which was given for mild cases and critical (steroids, anticoagulants, Remdesevir and antibiotics) for severe cases. The outcome of the illness was followed for 3 months after recovery and it was judged by CT scan and residual symptoms. The two groups (smokers and non-smokers) were compared according to the mentioned parameters. The exclusion criteria from the study were: obese patients (BMI >30 [Normal range 18.5 to 24.9]), patients with chronic obstructive pulmonary disease (COPD) and asthma, patients with ischaemic heart disease (IHD) and failure, pre-existing lung fibrosis, patients with malignancy, uncontrolled diabetes, and ex-smokers.

Statistical analysis

The data were recorded, organized, and coded by using Microsoft Excel 2007. The statistical package of social science SPSS 20 was conducted to perform the mean, standard deviation, and percentages. Chi-square test for the nominal data was used, and the p-value less than 0.05 was considered significant. Spearman correlation was used to find the correlation between the pack per year and some variables, 0.9-1.0 considered as strong; 0.7-.09 high; 0.5-0.7 moderate; 0.3-0.5 low.

Results

The study sample consists of 160 patients equally divided into two groups according to the smoking status, 24 (15.0%) were females and 136 (85.0%) were males, with mean age 50.3 ± 8.094; minimum 34 and maximum 65 years old. The distribution of sample study according to demographic and clinical variables is shown in table 1, reveals the insignificant difference between smokers and non-smokers regarding the age groups with (p=0.077).

Regarding the severity of symptoms, in the smoker's group 40 patients (25 %) presented with mild symptoms and 40 patients (25 %) presented with severe symptoms, while in the non-smoker's group 25 patients (15.6 %) presented with mild symptoms and 55 patients (34.4%) presented with severe symptoms, indicates more severe symptoms in the non-smoker group and it was statistically significant (p-value= 0.016).

Comparing SpO_2 between the 2 groups, SpO_2 was ≤ 70% in about 4.4% of smokers and 10% of non-smokers, about 8.1 % of smokers and 5.0% of non-smoker had SpO_2 ranging from 71-80%, 23.1% of smokers and 20.6% of non-smokers had SpO_2 of 81-90%, while 14.4% of both groups have SpO_2 >90%, the overall differences were statistically insignificant (p-value=0.176).

Table 1. Smoking status with demographic and clinical variables.

Demographic and Clinical Variables		Smoking Status		p-value
		Smoker	Non Smoker	
Age groups	30-40	10 (6.2%)	18 (11.2%)	0.077
	41-50	31 (19.4%)	31 (19.4%)	
	51-60	28 (17.5%)	28 (17.5%)	
	61-70	11 (6.9%)	3 (1.9%)	
Gender	Male	80 (50.0%)	56 (35.0%)	0.000
	Female	11 (6.87%)	13 (8.13%)	
Severity of Symptoms	mild	40 (25.0%)	25 (15.6%)	0.016
	severe	40 (25.0%)	55 (34.4%)	
SpO_2 %	≤ 70%	7 (4.4%)	16 (10.0%)	0.176
	71-80%	13 (8.1%)	8 (5.0%)	
	81-90%	37 (23.1%)	33 (20.6%)	
	>90%	23 (14.4%)	23 (14.4%)	

The comparison between smokers group and non-smokers group according to the investigations done to the patients is shown in table 2, the inflammatory markers (ESR, LDH, CRP and ferritin) were normal in about 13 (8.1%) of smokers and 8 (5.0%) of non-smokers, mild elevation was detected in about 35 (21.9%) of smokers and 21 (13.1%) of non-smokers, while severely elevated inflammatory markers were present in 32 (20.0%) of smokers and in 51(31.9%) of non-smokers and it was statistically significant (p-value= 0.011). the D-dimer level was normal in 45 (28.1%) of smokers and 23 (14.4%) of non-smokers, D-dimer was ≥ 2000 in 1 (0.6%) of smokers and in 11 (6.9%) of non-smokers, indicates higher D-dimer level in the non-smokers group (p-value=0.01), the other D-dimer values are shown in table 2.

The ground glass opacity (GGO) on CT scan was represented by percentages of involvement and revealed the followings: the CT was normal in 14 (8.8%) of smokers and 10 (6.2%) of non-smokers, the GGO on CT was >70% in about 5 (3.1%) of smokers and in 16 (10 %) of non-smokers, other values are also shown in table 2, although there was a significant difference in CT involvement between smokers and non-smokers, there was no statistical significance (p-value =0.067). regarding the liver function tests (LFT), it was high in 6 (3.8%) of smokers and in about 18 (11.2) of non-smokers and it was statistically significant (p-value = 0.008).

The patients need for oxygen use, admission to the hospital, admission to the ICU and the use of CPAP was compared between the smokers and non-smokers group as shown in table 3. The oxygen use was nearly the same in the two groups, about 57 (35.6%) of smokers and 56 (35.0%) of non-smokers required oxygen supplementation (p-value = 0.862), about 24 (15.0%) of smokers required hospital admission and 56 (35.0%) treated at home, while in the non-smokers group, 33 (20.6%) of patients required hospitalization and 47 (29.4%) treated at home (p-value= 0.137). regarding the ICU admission and CPAP use, there was also no statistical significance between the 2 groups (p-value = 0.096).

Table 2. The comparison of investigation results and smoking status.

Investigation Results		Smoking Status		p-value
		Smoker No. (%)	Non Smoker No. (%)	
Inflammatory markers	Normal	13 (8.1%)	8 (5.0%)	0.011
	Mild	35 (21.9%)	21 (13.1%)	
	Severe	32 (20.0%)	51 (31.9%)	
D-Dimer (500ng/ml)	Normal	45 (28.1%)	23 (14.4%)	0.01
	≤1000	15 (9.4%)	20 (12.5%)	
	-1500	15 (9.4%)	18 (11.2%)	
	-2000	4 (2.5%)	8 (5.0%)	
	>2000	1 (0.6%)	11 (6.9%)	
CT scan	Normal	14 (8.8%)	10 (6.2%)	0.067
	10%	11 (6.9%)	10 (6.2%)	
	20%	20 (12.5%)	8 (5.0%)	
	30%	10 (6.2%)	8 (5.0%)	
	40%	10 (6.2%)	13 (8.1%)	
	50%	6 (3.8%)	9 (5.6%)	
	60%	4 (2.5%)	6 (3.8%)	
	≥70%	5 (3.1%)	16 (10.0%)	
LFT	Normal	74 (46.2%)	62 (38.8%)	0.008
	High	6 (3.8%)	18 (11.2)	

Table 3. Patients need for O_2, hospital admission, ICUand CPAP.

Patients' needs		Smoking Status		p-value
		Smoker No. (%)	Non Smoker No. (%)	
Oxygen	No	23 (14.4%)	24 (15.0%)	0.862
	Yes	57 (35.6%)	56 (35.0%)	
CPAP	No	70 (43.8%)	68 (38.8%)	0.096
	Yes	10 (6.2%)	12 (11.2%)	
Hospital	No	56 (35.0%)	47 (29.4%)	0.137
	Yes	24 (15.0%)	33 (20.6%)	
ICU	No	70 (43.8%)	68 (38.8%)	0.096
	Yes	10 (6.2%)	12 (11.2%)	

Regarding the treatment options among the 2 groups, supportive treatments have been used in 26 smoker patients (16.3%) and in 25 non-smoker patients (15.6%), while critical treatment with (steroids, anticoagulants, Remdesevir and antibiotics) were used in 54 (33.6%) smoker patients and in 55 non-smoker patients (34.4%), difference was statistically insignificant (p=0.865) as shown in table 4.

Table 4. Treatment options among smokers and non-smokers.

Treatment Options	Among Smokers	Among Non-Smokers	p-value
Supportive	26 (16.3%)	25 (15.6%)	0.865
Critical	54 (33.6%)	55 (34.4%)	

Table 5 displays the difference in outcome between smokers and non-smokers and it shows that death due to COVID-19 and its complications was documented in 3 smoker's patients (3.8%) and in 5 non-smokers patients (6.3%), although the number of deaths is a little bit more in the non-smoker group, but there was no statistical difference (p-value = 0.719). residual symptoms and morbidity like persistent dyspnea, lung fibrosis documented by CT scan, fatigue and myalgia was documented 3 months after the initial infection in about 27 patients (33.7%) for each group with a p-value of 1.000. Full recovery was documented in 50 (62.5%) and 48 (60.0%) of smokers and non-smokers respectively but there was no statistical significance (p-value = 0.746).

Table . Difference in outcome between smokers and non-smokers with COVID-19.

Outcomes	Among Smokers	Among Non-Smokers
Death	3 (3.8%)	5 (6.3%)
Full recovery	50 (62.5%)	48 (60.0%)
Residual symptoms	27 (33.7%)	27 (33.7%)

Discussion

The effect of smoking on COVID-19 severity and outcome was assessed in many studies recently and there was a big concern whether smoking can have protective effects on COVID-19 patients or not, but the data were conflicting. Theoretically, smoking may have potential protective effects on COVID-19 patients by several mechanisms: (I) smoking may cause upregulation of ACE2 receptor, which is the main target for SARS cov19 in the lung tissues, smoking may cause decrease expression of ACE2 will lead to decrease the viral attachment and replications (12); (II) nicotine may have anti-inflammatory effects by inhibiting the production of certain pro-inflammatory markers like IL-1, IL-6 and TNF (13,14), and by this mechanism it may decrease the incidence of cytokine storm that is responsible for the severe cases of COVID-19 (15); (III) smoking induce production of nitric oxide, which has been shown to decrease SARS CoV2 replication and entry into the cells (16).

In this study, the symptoms of COVID-19 were more severe in the non-smoker group compared to the smokers, and this is comparable to study done by Miyara et al. which also has shown that current smoking was associated with a very low probability of developing severe symptomatic infection (17). Furthermore, the inflammatory markers (CRP, ferritin, LDH and ESR), D-dimer and the LFT were all higher in the non-smoker group when compared to the actively smokers group, and this is may be explained by the previously mentioned theory that the smoking may be protective against cytokine storm by inducing modulation of the immune system (18, 19). This assumption was also highlighted in other article by Garufi et al (20), in addition Lippi and Henry conducted a meta-analysis on Chinese patients and they have found that active smoking does not seem to be associated with severe COVID-19 infection (21). On the other hand, some studies contradict this (protective theory of smoking in COVID-19), a meta-analysis done by Gülsen and colleagues found that active smoking has been associated with increased COVID-19 symptoms severity (22, 23). Similarly, another study suggested that active smoking is associated with severe COVID-19 infection (24, 25).

In our study, oxygen use , ICU admission and the need for assisted ventilation was nearly the same between the smokers and non-smokers, hospital admission was slightly higher in the non-smoker group without statistical significance , furthermore no statistical difference was found regarding death rate and long term complications between the 2 groups although the number of deaths was slightly higher in the non-smokers, another study by Karanasos *et al*. suggested more adverse impact on severity and mortality in hospitalized patients with COVID-19 (26).

Even if there is hypothetical protective effect of smoking on the severity of COVID-19, we have to keep in mind other harmful effects of active smoking on the cardiovascular, respiratory and cerebrovascular system. The limitation of the current study is the small sample size, therefore, the impact of smoking on severity and mortality of patients with COVID-19 is yet to be assessed in larger multi-centre studies because the data is still conflicting and questionable, future prospective studies should focus on the amount of smoking, the effect of passive smoking vs active smoking, genetic factors, the long term effect of smoking on COVID-19 patients and comorbidities.

Conclusion

This study revealed that severe symptomatic COVID-19 infection was more common in the non-smokers when compared to the smoker groups, furthermore, COVID-19 infection in the non-smokers was associated with higher inflammatory markers, higher D-dimer level and higher LFTs than active smokers. There was no statistical difference regarding oxygen use, hospitalization, death rate, ICU admission, or post recovery complications between the 2 groups.

Acknowledgments

The authors are very grateful to the University of Mosul/College of Pharmacy and the Ibn Sina Teaching hospital, Ninevah Health Directorate for their provided facilities, which helped to improve the quality of this work.

Adherence to Ethical Standards

The authors declare that the study is registered and conducted in adherence to ethical standards. The study registered in College of Medicine, University of Mosul and approved by ethical committee in the university.

Conflict of Interest

The authors have no conflicts of interest regarding the publication of this article.

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