



THE EFFECT OF SMOKING STATUS ON DISEASE SEVERITY IN HOSPITALIZED PATIENTS FOLLOWED-UP FOR COVID-19 PNEUMONIA

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ABSTRACT

Introduction: Severe acute respiratory syndrome (SARS-CoV-2) virus, which has emerged since December 2019, still affects the world with all its violence. The disease presents with different clinical pictures ranging from an asymptomatic case to severe respiratory failure resulting in death. Our aim in this study, is to investigate the relation of smoking with symptoms, clinical course and disease severity in patients hospitalized for COVID-19 pneumonia.

Method: 107 patients who were hospitalized with the diagnosis of COVID-19 pneumonia and received treatment, between February 1st, 2021 and March 15th, 2021, were analyzed retrospectively. In particular, their smoking history, symptoms at hospital admission, comorbidities, non-invasive mechanical ventilation (NIMV) and intensive care unit (ICU) requirements needed during hospitalization, mortality and the relationship between smoking status and disease severity were examined.

Results: 107 patients (68 males and 39 females) with a mean age of 49 years, were included in the study. 42% of the patients were smokers, 22.4% quitters, and 35.5% of them had never smoked. Cough, sputum, and shortness of breath were found to be higher in smokers. Muscle and joint pain was statistically significantly higher in the smoking group. The symptoms and length of hospital stay were not related with smoking status. **Conclusion:** As a result of our study; we found that symptoms, comorbidities, need for NIMV and mortality were higher in the smoking group and smoking was higher in the severe disease group. Although these differences were not statistically significant, they were determined as numerical deflections.

KEYWORDS : Smoking, SARSCoV-2, COVID-19, Pneumonia, NIMV, Mortality

INTRODUCTION

The new coronavirus (COVID-19) epidemic caused by SARS-CoV-2 started in Wuhan, China in December 2019 and spread all over the world. Many studies have been conducted so far, including demographic, clinical, immunological, hematological, biochemical and radiographic findings predicting the clinical course and results of COVID-19. While advanced age, additional diseases such as diabetes and hypertension, low oxygen value, widespread lung involvement, various laboratory test abnormalities are associated with increased disease severity and/or mortality, smoking, which is an ongoing epidemic all over the world, is likely to play a role in the clinical course of the COVID-19 disease in patients alone or along with these factors. The negative effects of smoking on general health are well known. Tobacco and tobacco products make the lung vulnerable to infections by suppressing its immune system functions and may increase the severity of lung infections (1,2). Although there are studies showing that hospitalization and hospital mortality in COVID-19 patients who smoke are high, there are also studies showing the opposite (3). While smoking delays the healing of inflammation with its immunosuppressive effect in community-acquired pneumonias, in COVID-19 pneumonia patients, smoking can prevent intense inflammations such as cytokine storm and macrophage activation syndrome which cause death, with its immune system weakening effect (4,5,6). On the contrary, it is known that free radicals in cigarette smoke can weaken the antioxidant defense mechanism by increasing oxidative damage. In order to solve this dilemma, we planned to examine the smoking status of COVID-19 pneumonia patients we followed in our clinic and the effect of smoking status on the severity of the disease.

METHOD

107 patients who were hospitalized with the diagnosis of COVID-19 pneumonia between February 1st, 2021 and March 15th, 2021, were analyzed using the retrospective analysis method. Smoking histories, symptoms during hospital admission, comorbidities, noninvasive mechanical ventilation (NIMV), invasive mechanical ventilation (IMV) and

intensive care needs during hospitalization were recorded. The relation of smoking status with disease severity and survival was examined.

Statistical Analysis

Descriptive statistics were expressed by means of mean, standard deviation, minimum and maximum values for continuous variables of interest, and by means of numbers and percentages for categorical variables. One-way analysis of variance was performed to compare group means regarding the continuous variables. Pearson correlation coefficients were calculated to determine the relationship between these variables. Chi-square test was used to determine the relationship between groups and categorical variables. The statistical significance level was taken as 5% in the calculations and the SPSS statistical package program was used for the calculations.

RESULTS

A total of 107 patients, 68 male and 39 female, with a mean age of 48.9 ± 17 years, were included in the study. Although all categorical and quantitative variables are shown in Table 1, when the prominent results were evaluated, 42% of the patients were smokers, 22.4% were the ones who had quit smoking, and 35.5% were the ones who had never smoked. Cough, sputum, and dyspnea were higher in smokers but not statistically significant. Muscle and joint pain was statistically significantly higher in the smoking group ($p: 0.021$). Smoking status was not related with the duration of symptoms and the length of hospital stay ($p > 0.005$). No relationship was found between additional lung diseases (asthma, COPD) and smoking. Hypertension, diabetes mellitus, presence of cancer, kidney failure were proportionally higher in the smoking group. The relationship between comorbidities and mortality could not be evaluated due to the low number of deaths. The need for NIMV and the mortality rate were higher in the smoking group, but they were not statistically significant ($p > 0.005$). When we divided the patients into three groups as mild, moderate and severe, in line with the COVID-19 guidelines, the ratio of smokers was higher than the ratio of the non-smokers and ex-smokers in the severe disease group as well as in the total of patients (Table 2), but the differences

were not statistically significant ($p > 0.005$). Although not statistically significant, it was seen that symptoms, comorbidities, need for NIMV and mortality were higher in the smoking group, and smoking was higher in the severe disease group.

Table 1. Distribution of demographic characteristics of patients regarding their smoking status.

Smoking status	Non-smoker	Quitted	Smoking	Total	p value
Number of patients	38 (%35.5)	24 (%22.4)	45 (%42.0)	107	
Average age	47.26 ± 1.67 ^c	47.92 ± 1.53 ^c	50.84 ± 19.32 ^c	48.92 ± 17.29 ^c	0.615
Gender (M/F)	25/13	16/8	27/18	68/39	0.807
Symptom duration (days)	4.70 ± 4.01 ^c	5.21 ± 4.13 ^c	4.57 ± 4.3 ^c	4.76 ± 4.13 ^c	0.828
Symptoms					
Cough	20 (%37.7)	9 (%17.0)	24 (%45.3)	53 (%49.5)	0.407
Sputum	18 (%35.3)	13 (%25.5)	20 (%39.2)	51 (%47.7)	0.743
Shortness of breath	33 (%36.7)	19 (%21.1)	38 (%42.2)	90 (%84.1)	0.721
Muscle joint pain	6 (%28.6)	1 (%4.8)	14 (%66.7)	21 (%19.6)	0.021
Hospitalization	9.74 ± 5.17	8.75 ± 3.17	9.64 ± 4.34	9.48 ± 4.41	0.659
Comorbidities					
Hypertension	13 (%32.5)	11 (%27.5)	16 (%40.0)	40 (%37.4)	0.619
Diabetes Mellitus	7 (%33.3)	3 (%14.3)	11 (%52.4)	21 (%19.6)	0.480
COPD/Asthma ^a	12 (%35.3)	10 (%29.4)	12 (%35.3)	34 (%31.8)	0.444
Heart failure	18 (%37.5)	12 (%25.0)	18 (%37.5)	48 (%44.9)	0.676
Cancer	3 (%37.5)	1 (%12.5)	4 (%50.0)	8 (%7.50)	0.771
Kidney failure	2 (%28.6)	2 (%28.6)	3 (%42.9)	7 (%6.50)	0.892
NIMV need ^b	2 (%33.3)	0 (%0.0)	4 (%66.7)	6 (%5.60)	0.309
Intensive care follow-up	7 (%46.7)	1 (%6.7)	7 (%46.7)	15 (%14.0)	0.268
Mortality	0 (%0.0)	0 (%0.0)	2 (%100)	2 (%100)	0.261

^aCOPD: Chronic obstructive pulmonary disease, ^bNIMV: Non-invasive mechanical ventilation, ^c ± SD: Standard deviation.

Table 2. The relationship between disease severity and smoking status

Smoking Status	Does not smoke	Quitted	Smoking	Total	p value
Light	76.3%	79.2%	60.0%	70.1%	0.116
Intermittent	5.3%	16.7%	13.3%	11.2%	
Heavy	18.4%	4.2%	26.7%	18.7%	
Total	35.5%	22.4%	42.1%	100.0%	

DISCUSSION

The negative effects of smoking on general health are well known. Tobacco and tobacco products suppress the immune system-related functions of the lung, making it vulnerable to infections, and may increase the severity of lung infections (1,2). COVID-19 infection is a major epidemic and there is no known cure yet. In all treatment options created; the effectiveness of immunosuppressive drugs used in severe patient groups as well as antiviral treatments cannot be ignored (7). It is indisputable that a factor such as smoking, which seriously impairs the lung immune system and makes it open to infections, will increase the risk of catching COVID-19 infection. However, it is being discussed whether the immunosuppressive effect of smoking may provide an advantage in the disease stage, especially in patients who are likely to have a severe COVID-19 infection (4).

Although some studies show that hospitalization and

mortality rates are increased in COVID-19 patients who smoke, some studies also argue the opposite (8,9). Although the number of our patients was low, when our data were evaluated, no statistically significant difference was found between smokers and non-smokers in conditions such as severity of the disease, symptom duration, NIMV/IMV, and need for intensive care. But a numerical difference was found. We think that a statistical significance may be determined if the number of patients will be much higher. Because smoking is a bigger epidemic than the COVID-19 epidemic and the known proven harms are known.

It is known that angiotensin converting enzyme 2 (ACE-2) receptors are decreased in smokers (8,9). COVID-19 virus enters the cell via ACE-2 receptors. Although this situation seems like an advantage for smokers, it is a fact that regardless of the number of ACE-2 receptors, exposure to a certain number of viruses is sufficient to get sick. Another suggested mechanism is related with high CD 8 lymphocyte levels and low NK cells in smokers (6). Similar rates were encountered in bronchoalveolar lavage (BAL) examinations in COVID-19 patients (10,11). This situation has led to the interpretation that the cells targeted by the COVID-19 infection are the same as the cells targeted by cigarettes, and therefore the virus cannot find an environment to settle in. But these mechanisms are not clear. Data of comprehensive studies should be evaluated to comment on the clinical course of the disease in smokers. In the meta-analysis completed by Lippi et al., five studies in China were evaluated and no relationship was found between smoking status and disease severity (5). Only one of these studies found a relationship between disease severity and smoking (12). No correlation was found by Guan et al. (13), which included the highest number of cases (n:1046). On the other hand, the patient numbers of other studies were similar with the numbers in our center. In a meta-analysis by Roen et al., where they have analyzed 19 studies, 18.3% of the total 11590 COVID-19 patients deteriorated, and 6.3% of them were smokers (4). 29.8% of smokers and 17.6% of non-smokers got worse. According to the data of this meta-analysis, a relationship was found between smoking and disease severity. In this study, the rate of exacerbation of the disease was found to be 1.91 times higher in smokers. According to the results of early meta-analyses, this was an opposite result (9). However, the number of patients in this analysis was much higher and more accurate results were obtained. It is not surprising that pulmonary immune function (acquired) is impaired due to the effect of smoking, and it will not be surprising that these patients gets worse (1,2). Although there are studies reporting a low prevalence of smoking in COVID-19 patients (14,15), it may be misleading to present this as the protective effect of smoking. In any case, the rate of disease progression and additional infections will increase in smokers. Although the studies were performed on patients diagnosed with COVID-19, sufficient data has not yet been created to comment on the entire population. In a study conducted in Turkey, 114 patients were evaluated and no relationship was found between smoking and disease severity (3). Although the number of patients was low as in our study, the lack of a statistical relationship between the severity of the disease and smoking supported our study. In our study, it was remarkable that muscle pain was more common in the smokers group. It is known that smoking impairs oxygen transfer with the formation of carboxyhemoglobin, and initiates an inflammatory and degenerative process in the musculoskeletal system via causing vasoconstriction (16). With smoking, an increase in proinflammatory cytokines occurs, stimulating the central nervous system and an increase in the perception of pain can be observed. This may be the reason for the increased muscle pain in COVID-19 patients who smoke.

Conditions such as pulmonary comorbidities, hypertension, diabetes, age, gender, heart failure, and kidney failure may be associated with the severity of the disease (17). In our study,

there were 3 groups as smokers, quitters and non-smokers, and the numbers of these groups were not at a level to make a statistical difference with the possibility that these conditions might be a confounding factor. However, due to the relatively low number of deaths, we could not perform the survival analysis which is required to see the effects of these factors on survival. This situation can be considered among the limitations of our study.

Limitation

Our work is limited by the fact that it is a single center study and the analysis was carried out using the retrospective analysis method, we found it appropriate to present our data as it will contribute to future meta-analyses.

CONCLUSION

Smoking causes the death of 8 million people worldwide every year due to the health problems it causes. More than 3 million people have died in the COVID-19 pandemic so far. Although we couldn't find a statistically significant relationship between smoking and the severity of COVID-19 disease, we observed a tendency of increasing in disease severity in COVID-19 patients who smoke. When compared with the COVID-19 epidemic, regarding the mortalities, smoking appears to be a much bigger health problem. There is a need for clear studies that will illuminate the smoking- COVID-19 relationship. In order to reach statistically significant results, studies with larger patient numbers are needed for determining the relationship between smoking and COVID-19 and its effect on the disease.

Author contributions

All authors contributed to the conception and design of the study, analysis and interpretation of the data, and critical revision of the manuscript

Conflict of interest

The author(s) declare that there is no conflict of interest.

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Ethical approval

This study was approved by the Yuzuncu Yil University School of Medicine non-interventional clinical research ethics committee:2021/09-05.

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