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# Tobacco and COVID-19

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**Abstract:**

Tobacco and its products are the well-known causes of premature deaths associated with cancer, cardiovascular disease, and chronic obstructive pulmonary disease, as well as they constitute a significant risk factor that increases the tendency to respiratory system infection and other systemic infections. Active tobacco use and passive smoking increase the risk of infection. Both increase peribronchial and alveolar inflammation and fibrosis and mucosal permeability, cause inadequate mucociliary cleaning, damage to the respiratory tract epithelium resulting in fibrosis, and they adversely affect cellular and humoral immunity. Smoking has been known to increase the risk for viral infections and influenza. Similar data have been approved found for coronavirus disease-2019 (COVID-19) pandemic. Smoking is reported to be associated with the frequency of the disease and its severity of the clinical course. Severe acute respiratory syndrome-coronavirus-2 penetrates the cell using the angiotensin-converting enzyme 2 receptors. Such receptor proteins had been shown to increase in smoker individuals. Also, smoking facilitates penetration of the virus into the cell. The frequency of smoking and the rates of admission to intensive care, mechanical ventilation, and mortality have been also found to be higher was higher in severe cases. The risk for disease progression was found to be 14-fold higher in smokers. Further, the World Health Organization emphasized similar negative effects of hookah and new tobacco products such as electronic cigarettes and heated tobacco products. It is vital to underline the adverse effects of tobacco and tobacco products and to raise awareness among the public and to make efforts to smoking on every opportunity during the COVID-19 pandemic. Public awareness campaigns during the pandemic must always accompanied by the methods and strategies to avoid active and passive smoking.

**Keywords:**

COVID-19, SARS-CoV-2, smoking, tobacco use

## Tobacco and Infection

Use of tobacco and tobacco products is a well-known cause of premature deaths associated with cancer, cardiovascular disease and chronic obstructive pulmonary disease (COPD)<sup>[1]</sup> Active tobacco use and exposure to smoke passively a significant risk factor that increases tendency to the respiratory tract and other systemic infections.<sup>[1]</sup> There are multifactorial causes that create tendency to infection

in smokers. Such causes can be classified under two groups, namely structural and immunologic changes. Structural causes are peribronchial and alveolar inflammation, increased mucosal permeability, insufficient mucociliary cleaning, and damage to respiratory epithelium resulting in fibrosis.<sup>[2]</sup> Immunologic changes are impaired cellular and humoral immunity in smoker individuals.<sup>[3-5]</sup> Invasive pneumococcal and influenza infections have been reported to be more frequent and more severe in smokers.<sup>[1]</sup> Increased frequency of otitis media and meningococcus infections have been reported in children who are

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passive smokers.<sup>[6,7]</sup> Exposure to tobacco smoke and active tuberculosis and tuberculosis related mortality is associated.<sup>[8,9]</sup>

There are extensive epidemiological studies that were conducted on smoking and its contribution to infection development. In a study, the frequency of upper respiratory infection was reported as 22.7% and 16% in the smokers and nonsmokers, respectively, among the 1230 US soldiers with a relative risk of 1.5.<sup>[10]</sup> Another study conducted by Cohen *et al.*, with 400 volunteers, demonstrated that the development of infection was 2,23-fold in smokers following the application of intranasal low dose respiratory virus in.<sup>[11]</sup>

### Cigarette and COVID-19

Coronavirus disease-2019 (COVID-19) is mainly a respiratory system disease and characterized by severe acute respiratory failure syndrome. The causative agent is a severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). Main route of the entrance of the virus to the body is mucosal tissues, such as nose, mouth, upper respiratory tract, and less frequently conjunctival mucosa. Smoking tobacco or exposure to tobacco smoke cause an inflammatory response and process in the lungs; they increase mucosal inflammation and the expression of cytokines and tumor necrosis factor-alpha as well as increasing the permeability of epithelial cells, and excess mucus decreases or damages mucociliary cleaning.<sup>[12]</sup> Detection of controllable factors in a potential patient (host-human) and appropriate treatment may decrease viral contamination, and disease severity and smoking are one of those factors.

There are current discussions in the reports published on COVID-19 about which factors may cause the variability of the viral infection and change the clinical course of the patients. Gender and smoking status have been reported to be associated with the frequency of the disease and severity of the clinical condition, and this might be proportionate with the elevated expression of angiotensin-converting enzyme 2 (ACE2), also named as SARS-CoV-2 receptor. Expression of ACE2 was reported to be increased in Asian males, and this explains the higher frequency of the disease in this group when compared with females and individuals with a different ethnic origin in a report prepared for publication.<sup>[13]</sup> Although the effect of gender on the disease frequency is reported to be controversial in China, it is noted that the incidence is just a little higher in men and men have a tendency to have the disease (58%-67%).<sup>[14-16]</sup>

The ACE2 receptor is the human body part to which the S protein of SARS-CoV and SARS-CoV-2 binds.

ACE2 protein expression is upregulated in the airway epithelium of smokers (increased number of functional receptors during the postsynaptic regulation in the control of neurotransmitter release in the autonomic nervous system). Cai *et al.* compared the airway samples of smokers and nonsmokers and found increased ACE2 gene expression in smokers.<sup>[17]</sup> Zhao *et al.* also observed increased viral reproduction and transmission with increased expression of the ACE2 gene. These results have demonstrated that smokers are more sensitive to SARS-CoV-2.<sup>[13]</sup>

A recent new study has demonstrated that the modified S protein of SARS-CoV-2 binds to the ACE2 receptor with a 10–20-fold higher affinity compared to the first defined SARS-CoV.<sup>[18]</sup> This affinity also explains why it is so easy for human-to-human transmission of the virus. ACE2 protein is expressed on the surface of type 2 pneumocytes. This area is the focal point for the development of therapeutic agents

Brake *et al.* demonstrated increased expression of ACE2 gene expression in the resected lung tissue of smoker COPD patients. They found the expression of ACE2 on type 2 pneumocytes and small airway epithelium to be normal in healthy nonsmokers.<sup>[18]</sup> The overexpressed ACE2 receptors also wait readily as potential attachment regions for SARS-CoV-2. Attachment of the virus to the ACE2 receptors on the cell surface may not be revealed in surveillance studies. Virus may lodge in the host for an extended period of time in which case the individual may be a carrier and might mediate the spread of the virus. Virus proliferates in the cellular system of the host and simultaneously mutates and may inactivate the host immune mechanisms.

Among men, rate of smoking was found to be 50% in rural parts of China and 44.8% in all around the country. Increased incidence of COVID-19 infection and the worst course of the disease in men in China may associate with a higher rate of smoking in between men. ACE2 expression was reported to be similar in Asians and non-Asians, males and females, and in different age groups; however, it was reported to be significantly higher in smoker Asian males as compared to nonsmokers. ACE2 expression was detected to be similar among smokers and nonsmoker white race in the same publication.<sup>[17,19]</sup> These data explain the basics of the association of COVID-19 and smoking. Current data reported from the field also support this information.

A study conducted in China, a study evaluated the comorbidities and smoking status of 1590 patients with COVID-19, and the smoking rate was reported to be higher in cases with comorbidities compared to cases with no comorbidities. The prognosis was

1.79-fold worse in cases with at least one comorbidity compared to the cases with no comorbidity. The disease prognosis was 2.59-fold worse in cases with two or more comorbidities.<sup>[20]</sup>

Association between the status of smoking and clinical severity of the disease is observed in patients with COVID-19.<sup>[21,22]</sup> In a review, 5 studies, 4 from Wuhan and one from mainland China were evaluated from this perspective.<sup>[22]</sup> The ratio of active smokers and people who quit smoking was reported to be 3.4% and 6.9%, respectively, by Zhang *et al.*, in 58 seriously ill patients in a series including 140 patients. The ratio of active smokers and people who quit smoking was 0% and 3.7%, respectively, among the remaining 82 patients who were not seriously ill.<sup>[14]</sup> In the largest series including 1099 cases in the same review, Guan *et al.* evaluated cases with COVID-19 in the mainland China and found that 16,9% and 5,2% among 173 seriously ill patients were active smokers and people who quit smoking respectively, and 11.8% and 1.3% among 926 nonseriously ill patients were active smokers and people who quit smoking, respectively. Requirement of intensive care unit (ICU) admission and mechanical ventilation (MV) and mortality was observed in 25.5% and 7.6% among active smokers and people who quit smoking, respectively. On the other hand, only 11.8% of the patients with a non-progressive course were active smokers and 1.6% among them were the people who quit smoking.<sup>[16]</sup> A study conducted by Liu *et al.* consisting of 78 cases was evaluated and a history of smoking was found to be 27.3% among the group with a poor course of the disease and 3.0% in the group with a stable course, and this difference was found to be statistically significant.<sup>[23]</sup> Zhou *et al.* evaluated 191 cases infected with COVID-19 and reported that 54 out of 191 died while remaining 137 survived; 9% of the cases with a fatal course and 4% of the survivors were active smokers.<sup>[24]</sup> In the above mentioned review, as a conclusion for the association of smoking and COVID-19, the risk of developing severe COVID-19 symptoms was found to be 1.4 fold in cases with smoking, and the requirement for ICU and MV and probability of death was almost 2.4 fold in smokers as compared to nonsmokers.<sup>[22]</sup>

While the negative correlation of transmission and mortality of COVID-19 infection and smoking is becoming apparent, World Health Organization has emphasized the effect of new tobacco products such as electronic cigarettes, hookah and heated tobacco products on COVID-19 will also be similar and adverse. Therefore, patients should always be asked whether they are using tobacco and tobacco products and if they did quit smoking, the time should be determined and recorded in the medical records of the patient. In

addition, society based studies are noted to search for answers of the following questions:

- Will COPD and other smoking-related diseases cause fatal COVID-19 cases?
- Is SARS-CoV-2 transmission more frequent among smokers?
- Are the high smoking rates point to a worse course of disease for COVID-19 outbreak?

In addition, does the repetitive mouth-lip contact increase the transmission through viral contamination of mucosal surfaces? Also, some comorbidities such as diabetes, cardiovascular diseases, hypertension and cancer that might be a risk factor for COVID-19 are found in an increased rate among smokers. Direct or indirect effects of this should be differentiated in larger series.

Social isolation methods, awareness for staying home or lockdowns will increase tobacco and tobacco products consumption by the addicted individuals as well as the exposure tobacco smoke will effect the household as passive exposure. Children and youngsters will possibly have the chance to observe and witness their parents more frequently while they are using tobacco products.

In conclusion, smoking quitting methods and strategies should be added to the public awareness campaigns during the COVID-19 pandemic, during which it is very important to emphasize the negative effects of tobacco and tobacco products, raise public awareness and appreciate efforts of quitting smoking. Efforts of quit smoking and using tobacco and tobacco products such as electronic cigarettes, hookah should be added to the ongoing public health campaigns that aim to raise awareness of the community during the pandemic.

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### Conflicts of interest

There are no conflicts of interest.

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