

Review Article

Effects of Tobacco on the respiratory system with reference to COVID-19: A Review

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ABSTRACT

The novel coronavirus (COVID-19) is a lower respiratory tract disease that has negatively affected the health and well-being of millions globally. World Health Organization (WHO) has since declared COVID-19 a pandemic. The highly contagious virus spreads via respiratory droplets and aerosol particles when people cough, sneeze or talk close to others. The effects on the lungs include inflammation, fluid accumulation, reduced gaseous exchange, hypoxemia, and tissue necrosis. As the virus affects the respiratory system of humans, there are many assumptions as to whether or not smoking increases the threat of COVID-19. Tobacco use kills up to half of its all-time users, with current predictions estimating that more than 1 billion people could die from tobacco use in the 21st century. This study aims to unpack the pathological effects of tobacco smoking on the respiratory system and explore the potential impact of COVID-19 on the lungs of smokers. This is a review article that is based on secondary information collected from various sources such as published and unpublished Journal Articles, Newspapers, Books, and Reports from various Government Organizations, Non-Governmental Organizations, and Commissions.

Keywords COVID-19, Tobacco, Smoking, Lungs, Airway diseases



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1. Introduction

The World Health Organization (WHO) had declared the novel coronavirus, also referred to as COVID-19, a public health emergency of international concern on 30 January 2020. Owing to the alarming increase in infection rate across many countries, on 11 March 2020, WHO announced COVID-19 as a global pandemic [1]. The first case of the novel coronavirus was reported in China in December 2019. COVID-19 severely impacts the health of individuals by specifically targeting the lower respiratory tract. The highly contagious virus spreads via respiratory droplets and aerosol particles when people cough, sneeze or talk close to others. The symptoms of COVID-19 include, but are not limited to, fever, cough, headache, sore throat, fatigue, and difficulty breathing. The majority of people infected with COVID-19 show mild symptoms, and most of the time people regard this as mild flu. The causative agent, SARS-CoV-2, attacks the type 2 alveolar pneumocytes in the lungs [2]. WHO and various other local, national, and international organizations continuously update measures and standard operating procedures used to tackle and contain the spread of the deadly virus. COVID-19 continues to have disastrous effects on families and loved ones. It has also impacted the social, political, and economical landscapes across the globe [3].

As COVID-19 is a respiratory disease, there are many assumptions as to whether smoking tobacco increases the threat of COVID-19 or not [4]. The impact of tobacco and other substances are well known to many, but whether or not smoking enhances the impact of COVID-19 is yet to be fully explored. Studies reveal that smokers are most vulnerable to acquiring infection when they share cigarettes as the virus can spread through droplets of saliva [5]. In effect, sharing cigarettes with the infected person can increase the risk of transmission of COVID-19. One of the greatest public health threats today is the tobacco epidemic, being the leading cause of preventable death, illness, and impoverishment. More than 1 billion people worldwide use tobacco, with approximately 80% from low- and middle-income countries [6]. Globally, tobacco kills more than 8 million people, 7 million deaths of which result from direct tobacco use and 1.2 million deaths being the result of passive smoking i.e. non-smokers being exposed to second-hand smoke. It is believed that 80% to 90% of adult smokers began smoking during adolescence, and two-thirds have become regular, daily smokers before reaching 19 years of age. Some have argued tobacco to be viewed as a paediatric disease [7]. Tobacco use kills up to half of its all-time users. 100 million people died from tobacco use in the 20th century. If current trends continue, then 1 billion people could die from tobacco use in the 21st century [8]. In adult men, tobacco accounts for 20% of deaths, whilst in adult women, 5% of deaths are attributed to women. Analysis of five studies that have investigated and examined large populations of men and women who have begun smoking at an early age and never quit reveal a twofold to threefold increase in mortality rate and a reduction in lifespan of at least a decade.

All forms of tobacco are harmful and there is no safe level of exposure to tobacco. Deaths related to tobacco smoking account for more deaths each year than the following causes combined: HIV/AIDS, illegal drug use, alcohol use, motor vehicle injuries, and firearm-related incidents [9]. Studies reveal that smoking increases the risk of coronary heart disease and stroke two-fold to four-fold, whereas the risk of lung cancer increases by 25 times. Furthermore, smoking leads to diminished overall health, increased absenteeism from work and school, and increased healthcare utilization and costs. Smoking causes significant damage to the lung airways and small air sacs (alveoli) within the lungs, leading to conditions such as chronic obstructive pulmonary disease (COPD), emphysema, and chronic bronchitis. Asthmatic patients who smoke tobacco suffer from more severe and frequent attacks. Smokers who have COPD are 12 to 13 times more likely to die [10].

The WHO reports that tobacco smoking causes enormous health and non-health-related costs to society. Globally, smoking causes an estimated US\$500 billion in economic damage each year [4]. Tobacco's cost to governments, employers, and the environment, in general, expand across social, welfare, and healthcare expenditure, loss of foreign exchange in importing cigarettes, loss of land that grow food, costs of fires, and damage to buildings caused by careless and irresponsible smoking, environmental costs from deforestation, absenteeism, decreased productivity, higher numbers of accidents, and higher insurance premiums. Tobacco Industries often aim to persuade governments and the media that smoking benefits the economy. It claims that if tobacco control measures are instituted, tax revenues will fall, jobs will be lost and there will be a great hardship to the economy. But these industries tend to exaggerate economic losses and often remain silent about the non-economic costs that tobacco inflicts upon every country [11]. Passive smoking, also known as second-hand smoking, is the result of either intentional or non-intentional inhalation of tobacco. Several health authorities such as the WHO and CDC have confirmed that second-hand smoke is counted among the causes of lung cancer in humans. Exposure of tobacco smoke to people with respiratory conditions such as bronchitis or asthma can trigger or worsen symptoms. Non-smokers who reside in households with smokers become exposed to tobacco and its damaging effects. Passive smoking causes the blood to become more 'sticky' and likely to clot, thereby leading to increased risks of health conditions such as heart attacks and stroke [12]. Evidence increasingly suggests that long-term exposure to second-hand smoke may lead to atherosclerosis (narrowing of the arteries) and lower levels of antioxidant vitamins in the blood. The regulation of blood flow in blood vessels is affected by just 30 minutes of exposure to second-

hand smoke. Passive smokers have a 20 to 30 percent chance of developing lung cancer. Children who are exposed to second-hand smoke experience frequent asthma exacerbations which affect their ability to lead a healthy and productive life. One in five smokers will get chronic bronchitis, causing a chronic cough, COPD, or emphysema [13]. Subsequently, patients become breathless and are heavily dependent on inhalers.

2. What are the compounds in Tobacco?

The American Lung Association reveals that cigarettes contain more than 600 ingredients and when burned, more than 7000 chemicals are created. Of these, at least 70 chemicals are carcinogenic i.e. cancer-causing agents [14]. Substances found in tobacco include nicotine, tar, hydrogen cyanide, formaldehyde, lead, radioactive elements (e.g. uranium), polycyclic aromatic hydrocarbons, methanol, carbon monoxide, and many more.

3. What are the pathophysiological effects of smoking on the lungs?

The lining of the respiratory tract tissue is by pseudostratified ciliated columnar epithelium. The respiratory tract lining contains cilia on the luminal surface which propels various particles out of the bronchioles. These tiny hair-like structures, cilia, beat upwards and carry particles up the bronchi for coughing out [15]. In smokers, there is abnormal functioning of cilia. Smoking inhibits mucociliary clearance. The sequence of events that occur is from short-term to long-term. The harmful effect of tobacco smoke on the lungs is primarily due to the tar present. Upon inhalation of tobacco smoke, tar enters and accumulates in the bronchioles i.e. lower respiratory tract. The presence of tar obstructs the cilia thereby impeding the ability of cilia to remove mucus from the respiratory tract [16]. Consequently, goblet cells are activated which leads to increased mucus production. This causes obstruction and inactivation of cilia.

The airways become narrower due to the build-up of tar. The gas exchange becomes less efficient. Pathogens release toxins to surrounding areas and attract phagocytes. Phagocytes arrive and break down tissues around them to access the pathogens. During this process, phagocytes release digestive enzymes such as elastase. Elastase digests tissues in the bronchioles and damages the lung tissue [17]. In effect, the surface area of alveoli is significantly reduced, thereby reducing gaseous exchange. Tobacco smoking eventually leads to chronic bronchitis due to irritation of the tracheobronchial tract. Tobacco smoke causes inflammation by stimulating the release of inflammatory mediators through the production of the enzyme elastase [18]. Alveoli lose their elasticity and are unable to recoil. The lumen of the airways becomes narrower and causes the alveoli to burst. The long-term condition is referred to as emphysema. Patients with emphysema show symptoms such as short-term coughing due to build-up of mucus, increased lung infections, difficulty breathing, and shallow breaths, thereby reducing oxygen in the body and blood [19]. This leads to less oxygen delivery to the heart thereby depriving tissues of oxygen leading to fatigue and tissue necrosis. Accumulation of mucus also leads to the accumulation of pathogens as pathogens are trapped in mucus. Since pathogens are still present in the bronchiole lining, the risk of acquiring infection is increased. Cells become inflamed leading to bronchitis [20].

As the gaseous exchange is reduced due to tobacco smoking, carbon monoxide builds up in the body. Toxic levels of carbon monoxide in the body inhibit the oxygen's binding capacity to red blood cells. Red blood cells contain hemoglobin which carries oxygen throughout the body. These oxygen molecules combine reversibly with red blood cells, specifically the hemoglobin component. However, the high concentration of carbon monoxide in the blood occupies the hemoglobin binding site, thereby preventing oxygen molecules from binding to red blood cells. Carbon monoxide impairs oxygen transport and utilization, causing hypoxia. Tar is a carcinogen that induces mutations in DNA. Cell division and cell growth are affected by mutations in genes, leading to cancer of the lungs in the long term. Studies reveal that 90% of lung cancer cases are due to cigarette smoking. 15% of people who smoke develop lung cancer [21]. Tobacco contains nicotine. Nicotine is responsible for the addictive effect of smoking thereby making habitual smokers finding it difficult to quit smoking tobacco. Nicotine binds to nicotinic acetylcholine receptors and stimulates the release of catecholamine to increase the following: heart rate, blood pressure, cardiac muscle contractility, and cardiac output [22]. Tobacco smoke combined with the use of alcohol increases the risk of laryngeal carcinoma.

4. The link between Tobacco smoke and COVID-19

Countries such as Italy, China, and South Korea have shown to have an increase in COVID-19 incidence of infection in males and incidentally, an increase in the smoking rate in males compared to females. Studies reveal that in severe smokers who have acquired COVID-19, there is an increase in hospital stay, increased need for mechanical ventilation, and higher mortality rates [23]. During nationwide lockdowns, countries such as South Africa and India have banned the sale and purchase of tobacco products. Though the relationship between COVID-19 and smoking is yet to be uncovered, various studies show smoking directly or indirectly having an impact in humans with COVID-19 [24]. A study done in Korea showed an increased risk of 2.55% on the morbidity profile of individuals who smoke. The threat of COVID-19 also increases if individuals have a weak immune system and smoking contributes to weakening the immune system of individuals. The European Center for Disease Prevention and Control (ECDC) also pointed out that chewing tobacco or smoking can increase the threat of COVID-19 in people [25]. Most smokers suffer from various cardiovascular diseases, cancer, chronic obstructive pulmonary disease (COPD), and diabetes. In effect, the immunity of these individuals is

compromised, and this may further increase the vulnerability and threat of COVID-19 on them. According to a University College London (UCL) study, smokers are 1.45 times more likely to have severe complications compared with non-smokers and those who quit smoking [26].

A study done in China stated that smoking kills “cilia” which is the preventative shield of dust particles and foreign material in the lung airway and with the absence of cilia, there is an increased chance of severe symptoms of COVID-19 [27]. There are biologically plausible pathways through which nicotine may impact SARS-CoV-2, but the clinical significance of these is entirely unclear [28]. Tobacco use poses a substantial risk by hastening the spread of COVID-19 because the virus spreads primarily through droplets of saliva or discharge from the nose. When an infected person coughs or sneezes, there are chances that the virus can be transmitted to other people. Chewing tobacco products (Khaini, Gutkha, Paan, and Zarda) increases the impulse to spit [29]. Spitting (the act of discharging saliva from the mouth) in public places increases health risks, especially the spreading of infectious and contagious diseases like COVID-19, tuberculosis, swine flu, encephalitis, etc. Health experts also warn against the use of smoking hookah (waterpipes), which mostly involves the sharing of mouthpieces and hoses. The act of sharing these mouthpieces may serve as a transmission route for COVID-19 in local communities. The Angiotensin-Converting Enzyme type 2 receptor (ACE2) serves as the entry point on human cells for which the viral pathogen, SARS-CoV-2, binds to cause infection. SARS-CoV-2 invades human host cells’ lung tissue [30]. In humans, the heart, kidney tissues, and vascular tissue have many ACE Type 2 receptors.

A study was conducted by a group of experts whereby the lung tissue which was infected with SARS-CoV-2 was stained using a dye to highlight the density of ACE2 receptors. The study found that there was an increased ACE2 amount in alveolar epithelium, type 2 pneumocytes, and airway macrophages [31]. A study that investigated normal lung tissue with damaged lung tissue due to smokers with COPD showed clear evidence that smokers with COPD had a significantly higher number of ACE2 receptors. Smokers have an upregulation of ACE2 receptors, thereby increasing the propensity of SARS-CoV-2 invasion into the host cell, causing infection and subsequently low oxygen levels in blood [32]. Additionally, type 2 alveolar pneumocytes that ordinarily produce surfactants to prevent the alveoli from collapsing can no longer produce the phospholipid protein thereby increasing the surface tension in the lung alveoli [33].

5. Smoking cessation

Tobacco withdrawal symptoms make it difficult for many people to quit. These symptoms are unpleasant and show a high degree of variability among people. Symptoms include, but are not limited to anxiety, restlessness, irritability, difficulty concentrating, hunger, impatience, insomnia, headaches, hunger, tremor, sweating, and depression. Within two weeks of quitting smoking, there is improved lung function and in 10 years, the chances of getting lung cancer are reduced by half [33]. Nicotine dependence is viewed as a chronic, relapsing disease owing to its addictive nature. This coupled with the severe and unpleasant withdrawal symptoms experienced when people try to quit smoking makes quitting almost impossible. All people who smoke tobacco can quit. When smokers are aware and realize the harmful effects of smoking, they become more inclined to quit. General health education is needed for smokers [34]. These include methods to enhance the quality of life, motivation, and developing a plan of action to quit smoking. Behavioral modifications are needed to maintain quitting. Nicotine patches/gum/inhalers are also available to assist with smoking cessation. Certain medications such as Bupropion are also used [35].

6. Conclusion

Smoking tobacco damages the lungs in several ways, thereby increasing the risk of inflammation and exacerbating disease outcomes. Smoking impairs the human body’s natural immune response to foreign invaders, such as viruses. Therefore, once COVID-19 infection has been acquired by a patient who is a smoker, the likelihood of disease progression and severity remain high. Tobacco smoke induces epigenetic changes to the bronchial epithelium of the lung, increasing the propensity of the patient acquiring cancer of the mucous cells i.e. mucous (goblet) cell metaplasia. Given that goblet cells constitute a large reservoir of ACE2 receptors in the lung, the risk of severe disease with COVID-19 in smokers is a plausible deduction. Conversely, goblet cells also provide the first line barrier protection to the body as they produce mucous to ward off foreign pathogens, thus fighting off infection. To delineate the effect of COVID-19 on the human lung of tobacco smokers and whether or not disease progression is greater in smokers, more investigations and more thorough analyses are to be conducted.

Conflict of Interest

The authors declare that there is no conflict of interest.

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