Biomedical Letters ISSN 2410-955X DOI: https://doi.org/10.47262/BL/7.2.20210903

Review article
2021 | Volume 7 | issue 2 | Pages 199-208

ARTICLE INFO

Received
October 09, 2021
Revised
November 13, 2021
Accepted
December 29, 2021

***Corresponding Author**
Muhammad Saleem Khan

E-mail
samiikhan@uo.edu.pk

Keywords
Smoking
COVID-19
Seminal vesicle
SARS-CoV-2
Physiology

How to Cite
Mahmood GK, Wajid M, Waheed A, Aslam W, Khan T, Akmal H, Naz H, Sardar A, Shahid K, Akhtar MS, Khan MS. Relationship of smoking with COVID-19 and its adverse effects. Biomedical Letters 2021; 7(2): 199-208.

Scan QR code to see this publication on your mobile device.

Open Access

Relationship of smoking with COVID-19 and its adverse effects

Ghulam Khalid Mahmood[1], Muhammad Wajid[1], Ahmad Waheed[1], Waseem Aslam[1], Tehmina Khan[1], Hussnain Akmal[1], Hina Naz[1], Asma Sardar[1], Kaynat Shahid[1], Muhammad Shoaib Akhtar[2], Muhammad Saleem Khan[1*]

[1] Department of Zoology, Faculty of Life Sciences, University of Okara, Okara, Pakistan
[2]Department of Microbiology and Molecular Genetics, Faculty of Life Sciences, University of Okara, Okara, Pakistan

Abstract

There is a direct relationship between COVID-19 and smoking. This relationship has detrimental consequences for smoking and COVID-19 on body physiology. Smoking causes disc herniation, lungs diseases, heart illness, lipid profile changes, muscle protein synthesis declines, head, neck, and gastric cancers, cerebral inflammation, weight loss and obesity. The smoking habit of pregnant women leads to miscarriage, poor foetal growth, and low lipid and protein levels in breast milk. In males, it also reduces semen ejaculation and seminal vesicle volume. The treatment is based on quitting the smoking. Preventive measures such as a healthy diet and regular exercise can help to mitigate the negative consequences of smoking. In addition, smoking has been recognised as a major factor in COVID-19 transmission. Tobacco smokers are at increased risk of serious COVID-19 infection due to poor lung function, cross-infection, and vulnerable hygiene behaviors. People who have smoked in the past are thought to be more susceptible than non-smokers to have more severe COVID-19 illness symptoms. COVID-19 is more common among smokers than nonsmokers. Current smokers are five times more likely to have influenza infection than non-smokers. Smoking has been identified as one of the risk factors linked to infection and death.

Introduction

Smoking has a long history since the beginning of time. Tobacco and other poisonous substances were smoked in shamanistic ceremonies all over the Americas as early as 5000 BC [1]. Cigars and pipes were the most common use of tobacco. In the nineteenth century, cigarettes were first brought to the United States. The smoking of cigarettes is known by the time of Civil War [2].

The smoking alters the physiology of the body in the form of muscoskeletal disorder, arterial stiffness, cerebral aneurysm, lungs disease and cancer, cardiac diseases, change in lipid profile, the effect on the serum lipid and lipoprotein concentration, hypertension, depressing muscle protein synthesis, influenza and influenza like disease and inflammation of digestive track.

Muscoskeletal dysfunction was discovered in a Norwegian household survey and cough was observed as the major cause of disc herniation in smokers. Excessive smoking leads to increase the lipid profile through lowering high-density lipoprotein (HDL) levels. The amount of HDL in blood is inversely proportional to the level of smoke [3]. Smoking leads to weight loss and low Body Mass Index (BMI). The presence of nicotine increases the metabolic activity and decreases the appetite [4].

Smoking has a direct effect on the metabolism of muscle protein production. The muscle mass can deteriorate as get older and known as sarcopenia [5]. It can also lead to gut inflammation, which can develop to diseases like Bowls disease or gastric cancer [6] and alters the microbiota of the intestine [7]. Adhesion molecules, cytokines, and reactive oxygen species contribute to cerebral aneurysm inflammation [8].

Preterm delivery, poor foetal growth, and low levels of fat and protein in breast milk are all caused by maternal smoking [9]. Smoking also reduces the number of follicles in the ovary. Oxidative stress and enhanced cellular apoptosis are two symptoms of ovarian injury. There is a link between cigarette smoke and hair follicle loss. It affects the morphology and maturation of oocytes, resulting in aberrant follicle growth. Smoking has multigenerational influence on progeny ovarian function [10].

The COVID-19 virus has a similar effect on lungs as other respiratory illnesses. Serious patients of COVID-19 develop severe respiratory distress. Smoking can raise the risk of COVID-19, even induce exposure. COVID-19 enters the lungs through the nasal or oral routes, where it binds to cells and attaches to their surface structure through proteins. The lungs tissues are unable to digest oxygen effectively while sick [11].

Excessive oxygen in lungs broke down the tissues and the body become poisonous. This refers to the ability of blood to deliver oxygen to the lungs and other organs throughout the body. It causes organ failure or multi-organ failure. The repeated contact from hand-to-mouth during smoking increases the chance of viral infection and cigarette is considered as the major reason. The toxin in cigarettes results in lung infections. Smoking becomes a chain reaction across the body during a viral infection including COVID-19 that might decrease the capacity to fight respiratory sickness [12].

Muscoskeletal Disorganization

Smoking is linked to muscoskeletal disorders. Coughing may cause disc herniation due to smoking. It causes fatigue, tension, and headaches on regular basis. Smoking causes an autoimmune condition in which the immune system misidentifies, and targets own bodily tissues, causing inflammation in and around the joints. It also causes rheumatoid arthritis, in addition to inflammatory arthropathies. Muscoskeletal aches are aches of back, neck, upper and lower limbs.

Toxins in cigarette smoke are detrimental to the body in several ways. Nicotine, a psychostimulant that affects cortical and autonomic arousal, is one of them. Tobacco usage results in vasoconstriction, hypoxia, and fibrinolysis problems. Excessive smoking harmed personality traits such as neuroticism, extroversion, dependence, and a proclivity for somatization [13].

Inflammatory responses of lungs

Tobacco smoking promotes inflammatory reactions in the lungs due to respiratory contaminants and cause chronic obstructive pulmonary disease (COPD). Systematic inflammation, dietary irregularities and weight loss, skeletal muscle disinfection, and other possible systematic consequences are included in systematic impacts. Shortness of breath and coughing are also included in sputum production. The increased numbers of neutrophils, macrophages, and T-lymphocytes produce systemic inflammation. Smoking alters the

calorie intake, basal metabolic rate, intermediary metabolism, and body composition, resulting in weight loss and skeletal muscle mass loss. Dual-energy X-ray absorption or bioelectrical impedance measurements are used for identification. Skeletal muscle is made up of a net loss of muscle mass, intrinsic muscular phenomena, and residual muscle dysfunction [14].

Serum HDL level

Serum HDL level decreases with the increase in the number of smoked cigarettes. Smoking is directly linked with LDL and its levels in the blood. In comparison to cigarette smoke, bidi smoke contains three times the quantity of nicotine and carbon monoxide, as well as five times the amount of tar. These risk profiles might aid in the development of cardiovascular prevention measures for teenagers [15].

Pathophysiology and clinical implications

Pathophysiology and clinical effects have are associated with smoking [16]. frequent smoking caused Analgesia and nausea. It also harms other systems, causing osteoporosis, lumbar disc disease, and slowed bone recovery, to name a few. In both smokers and non-smokers, nicotine in nasal sprays and transdermal patches lowers pain sensitivity [17].

Hypertension

Smoking is the cause of hypertension. It causes arterial stiffness by activating the sympathetic nervous system. Arterial stiffness has significant impact on blood pressure. It causes atherosclerosis by causing malignant hypertension and renovascular hypertension. Variables that contribute to the atherothrombotic process include cardiovascular diseases, endothelial dysfunction, inflammation, lipid alteration, and changes in antithrombotic and prothrombotic factors [18].

Depressing muscle protein metabolism

Smoking can affect the physical function of the body and slows down muscle protein synthesis. It also raises the risk of sarcopenia (muscle wasting associated with advanced age) [19, 20]. It also slows down muscle renewal metabolism by inhibiting the muscle protein synthesis [21, 22]. Tobacco use can affect the physical function and musculoskeletal system. Tobacco smoking is linked to lower bone mineral density leads to osteoporotic fractures [23, 24]. Sarcopenia leads to the direct effects of smoking. Chronic smokers have lower blood flow in their skeletal muscles. The decrease of muscular mass or fat-free mass may be linked to cigarette smoking [19]. A single mechanism may be responsible for the suppression of muscle protein synthesis in smokers [25].

Inflammation of the digestive tract

Smoking causes inflammation to the digestive tract, small and large intestine, by altering the function and interaction of the intestinal epithelium, immune system, and microbiota [26]. Crohn's disease and ulcerative colitis are also linked to smoking [27-29]. Crohn's disease is more common as people get older. Ex-smokers and active smokers experience more relapses, have more severe pain, require more hospitalisation, have a worse response to treatment, and are more likely to require surgery [30-32].
Second-hand smoking is especially harmful to the health since it causes major cardiovascular and respiratory illness such as coronary artery disease and lung cancer [33]. Low birth weight and untimely deaths have an impact to pregnancy [34, 35].

The effect on the body physiology (The Breast Milk)

Smoking has a variety of physiological effects on the body. The milk of smoker mothers had reduced fats and protein however the density remained the same [36]. Smoking has a negative impact on breast alveolar cells, lowering the lipid and protein ratio as well as the lactation time [1]. In comparison to non-smokers, the newborns of smokers are ill and underweight [37].

Atherosclerosis

Environmental tobacco smoke (ETS) causes higher oxidative stress, arterial stiffness, inflammation, the plaque, heart rate variability, atherosclerosis, and poor blood flow in the cardiovascular system than active smokers [38]. Second-hand smoking stimulates blood platelets, causing thrombus formation, which destroys the artery lining to atherosclerosis. Smokers had more platelet activation than non-smokers.

Teenagers are more harmed by passive smoking and have greater fibrinogen levels [39]. Cigarette smoke induces the endothelium to release nitric oxide, which promotes vasodilation. Epinephrine stimulates the endothelium to secrete endothelin, which produces vasoconstriction. Endothelial injury causes the vessel dilatation to decrease and vascular contraction to rise [40].
The aortic stiffness in passive smokers and active smokers are similar [41]. Second-hand smoking is the leading cause of free radical emission, which results in oxidative stress and antioxidant depletion [42].

Microbiota in the intestine

Cigarette smoking had a direct or indirect effect on the gut microbiota. Smoking cessation changes the microbiota of the intestine by increasing the Phylum Firmicutes and Actinobacteria while decreasing the Bacteroidetes and Proteobacteria. The characteristics of observed microbial alterations affect the variations in body weight. It can also cause inflammatory Bowls disease (Crohn's disease and ulcerative colitis) [7].

Ovarian folliculogenesis

The effects of cigarette smoke on ovarian folliculogenesis are unfavourable. Increased oxidative stress, autophagy, DNA damage, and abnormalities in oocyte and granulosa cells are the symptoms of ovarian damage. It also affects the shape and maturation of oocytes. The number of follicles in the ovary is reduced. Cigarette smoking affects the main follicle pool in the offspring to be depleted during nursing. Toxicants in cigarettes, including nicotine, cotinine, and cadmium, have damage the ovarian follicle. The maternal smoking has an impact on the ovary [10].

Gut leakage

The gut microbiota and the host have a symbiotic and reciprocal interaction. However, with the passage of time, age, drug usage, food, alcohol, and smoking, it changes. Alcohol and smoking alter the stomach lining, resulting in H Pylori-related illnesses such as gastric cancer. Alcohol depletes microorganisms with anti-inflammatory activity in small intestine and colon, causing damage to the intestine known as leaky gut. Inflammatory smoking causes Bowls illness. Alcohol and smoking have a cause-and-effect connection that affects the micro biome of the gastrointestinal tract [43].

Cerebral aneurysm

Smoking causes the inflammatory reactions by causing chemicals, cytokines, reactive oxygen species (ROS), leukocytes, and vascular smooth muscle cells to stick together. A brain aneurysm can grow, progress, and rupture due to smoking [44]. The key determinant in the pathophysiology of cerebral aneurysms is vascular information. It establishes a relationship between cigarette smoking and aneurysm formation and rupture [44, 45].
The cigarette smoke carries a variety of toxins to bloodstream and cause inflammation. In the arteries, atherosclerotic lesions arise [46]. Endothelium changes morphological features through enhancing the procoagulant and vasoconstrictive properties, leukocyte adherence, and cytokine and growth factor production [47]. Cigarette smoke inactivates the nitric oxide output by increasing the production of ROS [48].
Cigarette smoke raises the volume and viscosity of blood vessel. An increase in shear stress causes endothelial dysfunction. Cigarette smoke affects vascular smooth muscle cells, lowering the amount of ROS and causing inflammation. A shift in atherosclerosis, a reduction in collagen production, and the creation of apoptosis in a cerebral conduit generates aneurysm, which is burst by cell death and thrombus formation [44].

Weight loss

Nicotine affects weight loss and obesity in smokers by increasing the energy expenditure and decreasing appetite [4]. In comparison to non-smokers, smokers have a lower BMI or body weight [49]. In smokers, it raises metabolic rate, lowers metabolic efficiency, and decreases the appetite. Female smoking is quite common in the United States. They were overweight and want to lose the weight [50]. The same reason guys have for smoking [51].
It has been demonstrated that the more cigarettes smoked, the lower the body weight. Heavy smokers may be at risk of obesity, according to cross-sectional research [52]. There is an increase in visceral fat and insulin resistance as a result of smoking lead to metabolic syndrome and type-2 diabetes [53]. Smokers have a larger waist-to-hip ratio than non-smokers [54].

Neonatal physiology

Maternal smoking has an impact on the physiology of babies. Smoking mothers have less stress reactivity [55]. It causes the hypothalamic-pituitary-adrenal axis to become dysregulated, resulting in obesity, diabetes, and reprogramming of the newborn modified blood pressure control system [56, 57]. Neonates have a limited ability to respond to life. Nicotine raises cortisol levels in the foetus [55].

Maternal smoking

Mother cigarette smoke while baby is still in the womb leads to develop chronic illnesses, cancer, and have poor cognitive function for the new-born. By causing mutations in nuclear and mitochondrial DNA, smoking has a direct influence. Smoking depletes the vitality through affecting the lungs. To compensate for energy and respiratory chain shortages, smoking alters the mitochondrial DNA by causing a change in the amount of copies [58]. During pregnancy, cigarette smoke has been linked to a childhood disease, chronic disease [59, 60], preterm delivery [61], asthma and infertility [62]. Preconception, in utero, and perinatal are the three sensitive phases during which a foetus might be harmed by changes in the environment [58].

Respiration

Cigarette smoking has become quite popular all around the world. However, it has a negative impact on pulmonary breathing. Second-hand smoking and direct exposure affect the adolescent reparative health, including asthma and lung illness [63]. Nicotine passes the placental membrane, affecting embryonic lung development by disrupting glucose metabolism, decreasing fibroblast growth, and changing cell signalling. In growing lungs, it reduces apoptosis. All of them are asthma and lung infection risk factors [64, 65].

COVID-19

In December 2019, a pneumonia pandemic of unknown origin was discovered in Wuhan, Hubei Province, China. Pneumonia cases were linked to the Huanan Seafood Open Market, according to epidemiologic studies. After inoculating respiratory components into human airway epithelial cells, a novel respiratory virus was discovered. The seventh human corona virus discovered in China. Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) was identified after a genomic investigation. Genetic research refutes the theory that SARS-CoV-2 is derived from the virus prior backbone [66]. COVID-19 binds to the angiotensin converting enzyme-2 (ACE2) receptor with high affinity. These receptors are found all across the body, causing organ damage. ACE2 receptors were found throughout the body and impair the cardiovascular, gastrointestinal, renal, hepatic, central nervous system, and ocular systems. [67]. The virus can spread through their lips or nose in little liquid particles when they cough, sneeze, talk, or breathe from an infected person. The number of lymphocytes and eosinophils in COVID-19 patients normally decreases.

A 14-days quarantine and ongoing monitoring by the local public health authorities are the main treatments [68]. Members of the household should reside in a separate room or compartment and keep at least 1 metre away from the quarantined individual [69].

Association of Smoking with COVID-19

Behavior of Smokers

The biological consequences and behaviors of smoking appear to increase the risk of COVID-19. Smoking damages the alveolar cells in the lungs, impairing lung function. It also impairs the pulmonary function [70]. The World Health Organization (WHO) has warned the public that smoking can raise the risk of COVID-19. Smokers' behavior includes touching their lips with their fingers and removing their protective face masks to smoke [71].

Despite the lack of statistical significance in smoking, alcohol consumption, BQ chewing, and COVID-19 patient severity, more studies have confirmed that these behaviors are harmful and risk factors for underlying diseases in population. Health Officials should develop regulations to raise awareness about the dangers of smoking, drinking, and chewing betel nut. They must encourage a healthy lifestyle [72].

Smoking and COVID-19

Tobacco smokers are at increased risk of serious COVID-19 infection due to poor lung function, cross-infection, and vulnerable hygiene behaviors. COVID-19 causes severe lung pneumonia and is spread by salivary droplets [73].

People who have smoked in the past are thought to be more susceptible than non-smokers to have more severe COVID-19 illness symptoms. COVID-19 is more common among smokers than nonsmokers [74]. Current smokers are five times more likely to have influenza infection than non-smokers, according to a major meta-analysis of nine studies (n = 40,685) [75]. Smoking has been identified as one of the risk factors linked to infection and death from the Middle East Respiratory Syndrome (MERS) [70, 76].

Entrance of the virus is blocked

Nicotine in cigarettes, according to some specialists, may protect the body from infection by the corona virus. Nicotine is known to interact with the Nicotinic Acetylcholine Receptor. Nicotine, on the other hand, may attach to the same receptor as the corona virus, according to the study. When a new corona virus approaches the same receptor, nicotine stops the corona virus from entering the cell by blocking the entry. [77].

Cytokine Storms

Studies are also being conducted to see if nicotine can prevent cytokine storms from forming in the body. The immune system overreacts, resulting in a cytokine storm. The majority of deaths caused by the corona virus are due to cytokine storage. It is a bodily process that happens when the immune system overreacts, resulting in organ failure. This experiment could be a game changer in the fight against COVID-19 if it proves to be successful.

Nicotine Patches

More experiments with two sets of health care personnel interacting with COVID-19 patients are being done to test this idea. Nicotine patches were administered to one group and fake patches to the other. The nicotine patch employees will next be evaluated to see if they are more resistant to the coronavirus than the Dummy patches. The patches have also been tested on patients in hospitals to determine whether they might aid with symptom relief [78].

Angiotensin Converting Enzyme-2 Receptors

People who smoke have a 25% increase in the number of ACE2 receptors. The increased expression of ACE2 receptors in smokers might increase the number of new coronal viral entry sites. The nicotinic acetylcholine receptor is binds at the binding positions of nicotine. Nicotine and smoking can affect ACE2 expression in the lungs and other important organs of the body, suggesting that smoking may enhance COVID-19 cellular entrance *via* nicotinic acetylcholine receptor (nAChR) signaling. In the lungs, kidneys, heart, brain, and other organs, nAChRs are located in cells that express ACE2 [79-81]. As a result, smoking has the potential to alter the etiology and prognosis of COVID-19 in a variety of organs. ACE2 expression is dramatically raised in 24 hours after SARS-CoV infection and stays high after 48 hours [82]. This suggests that ACE2 is involved in more than just viral susceptibility. Increased inflammatory responses were connected to elevated ACE2 expression, which might be associated with the signs of a cytokine storm [83].

Experts advise individuals not to smoke because of the dangers it poses to their health. Smoking has a harmful impact on the lungs, if a smoker becomes infected, he will have more severe symptoms. The corona virus can potentially be transmitted through the lungs. The upper respiratory airways are involved in mild symptoms, however the lower respiratory tract is involved in the more severe phases of illness [84, 85].

Hospitalized Patient

The patients neglect to notify hospital personnel of their smoking history or getting accurate medical histories under emergency settings is difficult. Hospital admissions staff may routinely underestimate the number of smokers among COVID-19 patients [86].

Smoking cessation is expected to minimize the chance of COVID-19. As a result, doctors should counsel their patients to quit smoking right away [87].

World Health Organization

However, the World Health Organization (WHO, 2020) claims that smokers have a greater chance of getting severe COVID-19 and dying from COVID-19. There is insufficient evidence to support any relationship between cigarette, nicotine, or alcohol usage and COVID-19 prevention or treatment. Smoker hand-to-mouth conduct and smoke-induced

lung illnesses may enhance their sensitivity to COVID-19 [88].

Conclusion

The use of tobacco has been linked to respiratory and cardiovascular problems. It also causes atherosclerosis, subarachnoid haemorrhage, and cerebral haemorrhage. Smoking has been found to have negative consequences on the physiology of the body. The lungs are affected in both instances; smoking has also been identified as a major contributor in COVID-19 transmission. According to the World Health Organization repeated hand-to-mouth contact with cigarettes can raise the risk of contracting the virus. Tobacco smokers are at increased risk of serious COVID-19 infection due to poor lung function, cross-infection, and vulnerable hygiene behaviors. COVID-19 causes severe lung pneumonia and is spread by salivary droplets. People who have smoked in the past are thought to be more susceptible than non-smokers to have more severe COVID-19 illness symptoms. COVID-19 is more common among smokers than nonsmokers.

Conflict of interest

The authors declare no conflict of interest.

References

[1] Agostoni C, Braegger C, Decsi T, Kolacek S, Koletzko B, Michaelsen KF, Mihatsch W, Moreno LA, Puntis J, Shamir RJJopg, nutrition. Breast-feeding: a commentary by the ESPGHAN Committee on Nutrition. 2009;49(1):112-125.

[2] CDC. 2000 Surgeon General's Report Highlights: Tobacco Timeline. Centres for Disease Control and Prevention; 2015 [cited 2021 5 July]; Available from: https://www.cdc.gov/tobacco/data_statistics/sgr/2000/highlights/historical/index.htm.

[3] Joshi N, Shah C, Mehta H, Gokhle PJIJMSPH. Comparative study of lipid profile on healthy smoker and non smokers. 2013;2(3):622-6.

[4] Chiolero A, Faeh D, Paccaud F, Cornuz JJTAjocn. Consequences of smoking for body weight, body fat distribution, and insulin resistance. 2008;87(4):801-809.

[5] Castillo EM, Goodman-Gruen D, Kritz-Silverstein D, Morton DJ, Wingard DL, Barrett-Connor EJAjopm. Sarcopenia in elderly men and women: the Rancho Bernardo study. 2003;25(3):226-231.

[6] Vedamurthy A, Ananthakrishnan ANJG, hepatology. Influence of environmental factors in the development and outcomes of inflammatory bowel disease. 2019;15(2):72.

[7] Biedermann L, Brülisauer K, Zeitz J, Frei P, Scharl M, Vavricka SR, Fried M, Loessner MJ, Rogler G, Schuppler MJIbd. Smoking cessation alters intestinal microbiota: insights from quantitative investigations on human fecal samples using FISH. 2014;20(9):1496-1501.

[8] Williamson DF, Madans J, Anda RF, Kleinman JC, Giovino GA, Byers TJNEJoM. Smoking cessation and severity of weight gain in a national cohort. 1991;324(11):739-745.

[9] Jauniaux E, Burton GJJEhd. Morphological and biological effects of maternal exposure to tobacco smoke on the feto-placental unit. 2007;83(11):699-706.

[10] Budani MC, Tiboni GMJRT. Ovotoxicity of cigarette smoke: A systematic review of the literature. 2017;72:164-181.

[11] Sa G. Smoking is associated with worse outcomes of COVID-19 particularly among younger adults: A systematic review and meta-analysis. 2020.

[12] WHO. WHO statement: Tobacco use and COVID-19. 2020 [cited 2021 Oct 27]; Available from: https://www.who.int/news/item/11-05-2020-who-statement-tobacco-use-and-covid-19.

[13] Holmen TL, Barrett-Connor E, Holmen J, Bjermer L. Health problems in teenage daily smokers versus nonsmokers, Norway, 1995–1997: the Nord-Trøndelag Health Study. American journal of epidemiology 2000;151(2):148-155.

[14] Agusti A, Noguera A, Sauleda J, Sala E, Pons J, Busquets X. Systemic effects of chronic obstructive pulmonary disease. European Respiratory Journal 2003;21(2):347-360.

[15] Joshi N, Shah C, Mehta H, Gokhle P. Comparative study of lipid profile on healthy smoker and non smokers. Int J Med Sci Public Health 2013;2(3):622-6.

[16] Shi Y, Weingarten TN, Mantilla CB, Hooten WM, Warner DO. Smoking and pain: pathophysiology and clinical implications. The Journal of the American Society of Anesthesiologists 2010;113(4):977-992.

[17] Girdler SS, Maixner W, Naftel HA, Stewart PW, Moretz RL, Light KC. Cigarette smoking, stress-induced analgesia and pain perception in men and women. Pain 2005;114(3):372-385.

[18] Virdis A, Giannarelli C, Fritsch Neves M, Taddei S, Ghiadoni L. Cigarette smoking and hypertension. Current pharmaceutical design 2010;16(23):2518-2525.

[19] Castillo EM, Goodman-Gruen D, Kritz-Silverstein D, Morton DJ, Wingard DL, Barrett-Connor E. Sarcopenia in elderly men and women: the Rancho Bernardo study. American journal of preventive medicine 2003;25(3):226-231.

[20] Szulc P, Duboeuf F, Marchand F, Delmas PD. Hormonal and lifestyle determinants of appendicular skeletal muscle mass in men: the MINOS study. The American journal of clinical nutrition 2004;80(2):496-503.

[21] Dorrens J, Rennie M. Effects of ageing and human whole body and muscle protein turnover. Scandinavian journal of medicine & science in sports 2003;13(1):26-33.

[22] Rennie MJ, Wackerhage H, Spangenburg EE, Booth FW. Control of the size of the human muscle mass. Annu Rev Physiol 2004;66:799-828.

[23] Lorentzon M, Mellstrom D, Haug E, Ohlsson C. Smoking in young men is associated with lower bone mineral density and reduced cortical thickness. J Clin Endocrinol Metab 2006;10:129416.
[24] Kanis JA, Johnell O, Odén A, Johansson H, De Laet C, Eisman JA, Fujiwara S, Kroger H, McCloskey EV, Mellstrom D. Smoking and fracture risk: a meta-analysis. Osteoporosis international 2005;16(2):155-162.
[25] Little HJ. Behavioral mechanisms underlying the link between smoking and drinking. Alcohol Research & Health 2000;24(4):215.
[26] Papoutsopoulou S, Satsangi J, Campbell BJ, Probert CS. impact of cigarette smoking on intestinal inflammation-direct and indirect mechanisms. Alimentary pharmacology & therapeutics 2020;51(12):1268-1285.
[27] Bastida G, Beltrán B. Ulcerative colitis in smokers, non-smokers and ex-smokers. World journal of gastroenterology: WJG 2011;17(22):2740.
[28] Burisch J, Ungaro R, Vind I, Prosberg MV, Bendtsen F, Colombel J-F, Vester-Andersen MK. Proximal disease extension in patients with limited ulcerative colitis: a Danish population-based inception cohort. Journal of Crohn's and Colitis 2017;11(10):1200-1204.
[29] Vedamurthy A, Ananthakrishnan AN. Influence of environmental factors in the development and outcomes of inflammatory bowel disease. Gastroenterology & hepatology 2019;15(2):72.
[30] Brant SR, Picco MF, Achkar J-P, Bayless TM, Kane SV, Brzezinski A, Nouvet FJ, Bonen D, Karban A, Dassopoulos T. Defining complex contributions of NOD2/CARD15 gene mutations, age at onset, and tobacco use on Crohn's disease phenotypes. Inflammatory bowel diseases 2003;9(5):281-289.
[31] Lunney P, Leong R. Ulcerative colitis, smoking and nicotine therapy. Alimentary pharmacology & therapeutics 2012;36(11-12):997-1008.
[32] Berkowitz L, Schultz BM, Salazar GA, Pardo-Roa C, Sebastián VP, Álvarez-Lobos MM, Bueno SM. Impact of cigarette smoking on the gastrointestinal tract inflammation: opposing effects in Crohn's disease and ulcerative colitis. Frontiers in immunology 2018;9:74.
[33] Hill CR, Blekkenhorst LC, Radavelli-Bagatini S, Sim M, Woodman RJ, Devine A, Shaw JE, Hodgson JM, Daly RM, Lewis JR. Fruit and vegetable knowledge and intake within an Australian population: The ausdiab study. Nutrients 2020;12(12):3628.
[34] Joya X, Manzano C, Álvarez A-T, Mercadal M, Torres F, Salat-Batlle J, Garcia-Algar O. Transgenerational exposure to environmental tobacco smoke. International Journal of Environmental Research and Public Health 2014;11(7):7261-7274.
[35] Forest S, Priest S. Intrauterine tobacco smoke exposure and congenital heart defects. The Journal of perinatal & neonatal nursing 2016;30(1):54-63.
[36] Bachour P, Yafawi R, Jaber F, Choueiri E, Abdel-Razzak Z. Effects of smoking, mother's age, body mass index, and parity number on lipid, protein, and secretory immunoglobulin A concentrations of human milk. Breastfeeding Medicine 2012;7(3):179-188.
[37] Dahlström A, Ebersjö C, Lundell B. Nicotine exposure in breastfed infants. Acta Paediatrica 2004;93(6):810-816.
[38] Barnoya J, Glantz SA. Cardiovascular effects of secondhand smoke: nearly as large as smoking. Circulation 2005;111(20):2684-2698.
[39] Stavroulakis GA, Makris TK, Hatzizacha-rias AN, Tsoukala C, Kyriakidis MK. Passive smoking adversely affects the haemostasis/fibrinolytic parameters in healthy non-smoker offspring of healthy smokers. Thrombosis and haemostasis 2000;84(11):923-924.
[40] Widlansky ME, Gokce N, Keaney JF, Vita JA. The clinical implications of endothelial dysfunction. Journal of the American College of Cardiology 2003;42(7):1149-1160.
[41] Mahmud A, Feely J. Effect of smoking on arterial stiffness and pulse pressure amplification. Hypertension 2003;41(1):183-187.
[42] Burke A, FitzGerald GA. Oxidative stress and smoking-induced vascular injury. Progress in cardiovascular diseases 2003;46(1):79-90.
[43] Capurso G, Lahner E. The interaction between smoking, alcohol and the gut microbiome. Best practice & research Clinical gastroenterology 2017;31(5):579-588.
[44] Chalouhi N, Ali MS, Starke RM, Jabbour PM, Tjoumakaris SI, Gonzalez LF, Rosenwasser RH, Koch WJ, Dumont AS. Cigarette smoke and inflammation: role in cerebral aneurysm formation and rupture. Mediators of inflammation 2012;2012.
[45] Mazzone P, Tierney W, Hossain M, Puvenna V, Janigro D, Cucullo L. Pathophysiological impact of cigarette smoke exposure on the cerebrovascular system with a focus on the blood-brain barrier: expanding the awareness of smoking toxicity in an underappreciated area. International journal of environmental research and public health 2010;7(12):4111-4126.
[46] Killer-Oberpfalzer M, Aichholzer M, Weis S, Richling B, Jones R, Virmani R, Cruise GM. Histological analysis of clipped human intracranial aneurysms and parent arteries with short-term follow-up. Cardiovascular Pathology 2012;21(4):299-306.
[47] Jamous MA, Nagahiro S, Kitazato KT, Satoh K, Satomi J. Vascular corrosion casts mirroring early morphological changes that lead to the formation of saccular cerebral aneurysm: an experimental study in rats. Journal of neurosurgery 2005;102(3):532-535.
[48] Cai H, Harrison DG. Endothelial dysfunction in cardiovascular diseases: the role of oxidant stress. Circulation research 2000;87(10):840-844.
[49] Huot I, Paradis G, Ledoux M. Factors associated with overweight and obesity in Quebec adults. International journal of obesity 2004;28(6):766-774.
[50] Cawley J, Markowitz S, Tauras J. Lighting up and slimming down: the effects of body weight and cigarette prices on adolescent smoking initiation. Journal of health economics 2004;23(2):293-311.
[51] Potter BK, Pederson LL, Chan SS, Aubut J-AL, Koval JJ. Does a relationship exist between body weight, concerns about weight, and smoking among adolescents? An integration of the literature with an emphasis on gender. Nicotine & Tobacco Research 2004;6(3):397-425.

[52] John U, Hanke M, Rumpf H-J, Thyrian JR. Smoking status, cigarettes per day, and their relationship to overweight and obesity among former and current smokers in a national adult general population sample. International journal of obesity 2005;29(10):1289-1294.
[53] Han TS, Sattar N, Lean M. Assessment of obesity and its clinical implications. Bmj 2006;333(7570):695-698.
[54] Jee SH, Lee SY, Nam CM, Kim SY, Kim MT. Effect of smoking on the paradox of high waist-to-hip ratio and low body mass index. Obesity research 2002;10(9):891-895.
[55] Haslinger C, Bamert H, Rauh M, Burkhardt T, Schäffer L. Effect of maternal smoking on stress physiology in healthy neonates. Journal of Perinatology 2018;38(2):132-136.
[56] Montgomery SM, Ekbom A. Smoking during pregnancy and diabetes mellitus in a British longitudinal birth cohort. Bmj 2002;324(7328):26-27.
[57] Cohen G, Jeffery H, Lagercrantz H, Katz-Salamon M. Long-term reprogramming of cardiovascular function in infants of active smokers. Hypertension 2010;55(3):722-728.
[58] Pirini F, Guida E, Lawson F, Mancinelli A, Guerrero-Preston R. Nuclear and mitochondrial DNA alterations in newborns with prenatal exposure to cigarette smoke. International journal of environmental research and public health 2015;12(2):1135-1155.
[59] Barker DJ, Eriksson JG, Forsén T, Osmond C. Fetal origins of adult disease: strength of effects and biological basis. International journal of epidemiology 2002;31(6):1235-1239.
[60] Doherty S, Grabowski J, Hoffman C, Ng S, Zelikoff J. Early life insult from cigarette smoke may be predictive of chronic diseases later in life. Biomarkers 2009;14(sup1):97-101.
[61] Kyrklund-Blomberg NB, Granath F, Cnattingius S. Maternal smoking and causes of very preterm birth. Acta obstetricia et gynecologica Scandinavica 2005;84(6):572-577.
[62] Alati R, Mamun AA, O'Callaghan M, Najman JM, Williams GM. In utero and postnatal maternal smoking and asthma in adolescence. Epidemiology 2006:138-144.
[63] Tager IB. The effects of second-hand and direct exposure to tobacco smoke on asthma and lung function in adolescence. Paediatric respiratory reviews 2008;9(1):29-38.
[64] Sekhon H, Proskocil B, Clark J, Spindel E. Prenatal nicotine exposure increases connective tissue expression in foetal monkey pulmonary vessels. European respiratory journal 2004;23(6):906-915.
[65] Maritz GS, Morley CJ, Harding R. Early developmental origins of impaired lung structure and function. Early human development 2005;81(9):763-771.
[66] Almazán F, Sola I, Zuñiga S, Marquez-Jurado S, Morales L, Becares M, Enjuanes L. Coronavirus reverse genetic systems: infectious clones and replicons. Virus research 2014;189:262-270.
[67] Renu K, Prasanna PL, Gopalakrishnan AV. Coronaviruses pathogenesis, comorbidities and multi-organ damage–A review. Life Sciences 2020;255:117839.
[68] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R. A novel coronavirus from patients with pneumonia in China, 2019. New England journal of medicine 2020.
[69] Organization WH. Home care for patients with COVID-19 presenting with mild symptoms and management of their contacts: interim guidance, 17 March 2020. World Health Organization, 2020.
[70] Arcavi L, Benowitz NL. Cigarette smoking and infection. Archives of internal medicine 2004;164(20):2206-2216.
[71] WHO. Corona Virus Disease Pandemic. 2020 [cited 2021 Nov 3]; Available from: https:/www.who.int/emergencies/diseases/novel-coronavirus-2019?gclid=Cj0KCQjw5oiMBhDtARIsAJi0qk3GjSBlS1IwGj114eMYrZqmC9Sznv5VdKIdsooc8umB2AqUwXWRZsaArlxEALw_wcB.
[72] Zhong R, Chen L, Zhang Q, Li B, Qiu Y, Wang W, Tan D, Zou Y. Which factors, smoking, drinking alcohol, betel quid chewing, or underlying diseases, are more likely to influence the severity of COVID-19? Frontiers in Physiology 2021;11:1836.
[73] Ahmed N, Maqsood A, Abduljabbar T, Vohra F. Tobacco smoking a potential risk factor in transmission of COVID-19 infection. Pakistan journal of medical sciences 2020;36(COVID19-S4):S104.
[74] Shastri MD, Shukla SD, Chong WC, Kc R, Dua K, Patel RP, Peterson GM, O'Toole RF. Smoking and COVID-19: What we know so far. Respiratory medicine 2020:106237.
[75] Lawrence H, Hunter A, Murray R, Lim W, McKeever T. Cigarette smoking and the occurrence of influenza–Systematic review. Journal of Infection 2019;79(5):401-406.
[76] Park J-E, Jung S, Kim A. MERS transmission and risk factors: a systematic review. BMC public health 2018;18(1):1-15.
[77] Print T. Nicotine patch test on Covid patients, healthcare workers to see if smokers are 'protected'. 2020 [cited 2021 November 3]; Available from: https://theprint.in/health/nicotine-patch-test-on-covid-patients-healthcare-workers-to-see-if-smokers-are-protected/413513/.
[78] Changeux J-P, Amoura Z, Rey FA, Miyara M. A nicotinic hypothesis for Covid-19 with preventive and therapeutic implications. Comptes Rendus Biologies 2020;343(1):33-39.
[79] Changeux J-P. Nicotine addiction and nicotinic receptors: lessons from genetically modified mice. Nature Reviews Neuroscience 2010;11(6):389-401.
[80] Tolu S, Eddine R, Marti F, David V, Graupner M, Pons S, Baudonnat M, Husson M, Besson M, Reperant C. Co-activation of VTA DA and GABA neurons mediates nicotine reinforcement. Molecular psychiatry 2013;18(3):382-393.
[81] Nordman JC, Muldoon P, Clark S, Damaj MI, Kabbani N. The α4 nicotinic receptor promotes CD4+ T-cell proliferation and a helper T-cell immune response. Molecular pharmacology 2014;85(1):50-61.
[82] Li G, He X, Zhang L, Ran Q, Wang J, Xiong A, Wu D, Chen F, Sun J, Chang C. Assessing ACE2 expression

patterns in lung tissues in the pathogenesis of COVID-19. Journal of autoimmunity 2020;112:102463.
[83] Sifat AE, Nozohouri S, Villalba H, Vaidya B, Abbruscato TJ. The Role of Smoking and Nicotine in the Transmission and Pathogenesis of COVID-19. Journal of Pharmacology and Experimental Therapeutics 2020;375(3):498-509.
[84] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. Jama 2020;323(13):1239-1242.
[85] Mason RJ. Pathogenesis of COVID-19 from a cell biology perspective. Eur Respiratory Soc; 2020.
[86] Cohen BN, Nichols AL, Grant S, Blumenfeld Z, Dougherty DA, Alvarez RM, Ritz B, Lester HA. Successful cessation programs that reduce comorbidity may explain surprisingly low smoking rates among hospitalized COVID-19 patients. 2020.
[87] Eisenberg S-L, Eisenberg MJ. Smoking cessation during the COVID-19 epidemic. Nicotine and Tobacco Research 2020;22(9):1664-1665.
[88] WHO. Tobacco use and COVID-19. 2020 [cited 2021 November 3]; Available from: : https://www.who.int/news-room/detail/11-05-2020.