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CARDIOVASCULAR RISK FACED BY SMOKERS AND BENEFITS OF CESSATION OF SMOKING

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Globally one of the major reason for mortality and morbidity is cardiovascular diseases (CVDs) and in the United States alone the expenditure for the health care services to cardiovascular disease patients as well as due to productivity loss and medication is annually about $200 billion[1,2]. The World Health Organization has determined smoking to account for development of 10 % of CVDs[3]. Worldwide the death rate due to tobacco smoking is about 6 million every year with 500,000 demises occurring in the United States due to smoking. It has been noted that smoking of cigarettes raises the myocardial infarction and coronary artery diseases incidence[4]. The risk of atherosclerotic diseases is also increased by 30% in passive smokers while in case of active smokers it is about 80%[5,6]. In the year 2014, study noted the risk of CVDs for active and passive smokers[6]. The study stated the following "there is sufficient evidence to derive a causal relationship between a smoke free policy and a reduction in coronary events in a population younger than 65 years of age". Several studies have been carried on CVD risk. In 2016, it was reported that there exists the perils of suffering extensive damage to health by young adults who smoke e-cigarettes and mentioned that the health of this population is to be protected on an urgent basis[7-11].

Several CVDs phenotype have been associated with tobacco smoking. Association has been noted between smoking and early atherosclerosis onset which begins as early as in adolescence and young adulthood. There is a rise in the risk of developing stroke, aortic aneurysm, acute myocardial infarction, and sudden demise[4-6,12,13]. Second hand smoking also may result in negative impact on the cardiovascular system due to inhalation of toxic substances present in the smoke like particulate matter and carbonyls[6]. Frey et al. noted that exposure to second hand smoking even for a small duration like 30 minutes causes deteriorating impact on function of endothelium and aggravates the acute coronary event risk[14]. A meta-analysis observed that passive smoking raises the risk of stroke by 20% to 30% and exhibit a dose-response relationship[15]. Smoking cigarette has been marked as an independent, strong factor of risk of CVD and early demise by the ACC/AHA (American College of Cardiology and American Heart Association) Prevention Guidelines in 2019[16,17]. A causal relationship between ASCVD (Atherosclerotic cardiovascular disease) and smoking has been reported in young adults by the National Health Interview Survey[18].

CVDs and smoking

Since the components of cigarette are over 7,000 chemical compounds from various classes which are free in the gas form or bind to the particles in the aerosol, it is difficult to explain the precise mechanism leading up to the development of CVDs. There are 72 carcinogenic chemicals found in cigarettes [19-21]. Fowles et al. found association between risk of cancer and 1, 3-butadiene, and cresol and cyanide arsenic have been linked to CVDs[22]. Other elements in cigarettes other than nicotine and carbonmonoxide include lead, ammonia, mercury and radioactive compounds. There are other harmful effects of smoking which include impotence but majority of population upto 60% are not aware of these detrimental outcomes of smoking[23-25]. Toxic metals like chromium, aluminium, lead, mercury, zinc, copper, and nickel may accumulate in the Nicotiana tanacum plant and therefore may be present in cigarette smoke. The homeostasis of metals may be altered by smoking cigarettes and lead to induction of chronic diseases[26].

Such metals in cigarettes have been noted to damage endothelium of blood vessels[27,28] and may act as catalysts in causing oxidative stress and inflammation. These changes may result in disease like aging, degenerative diseases, cancers, and cardiovascular diseases. Up regulation of gene for inflammation is also an outcome of smoking. Polycyclic aromatic hydrocarbons in cigarette binds to aryl hydrocarbon receptor. The 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is also another agonist for aryl hydrocarbon receptor and has been found to promote process of atherosclerosis in mice which were deficient in apolipoprotein E[29]. Cigarette smoking also aggravates cholesterol accumulation in macrophage in vitro. Here CXCR2 chemotactic receptor's role acts as a crucial factor for inflammatory disease like atherosclerosis[30].

The Flow Mediated Dilation (FMD) in brachial artery has been reported to be impaired as a result of chronic smoking[31] and similar decrease in endothelial dependent dilation in coronary artery has also been noted in previous study[32]. Cessation of smoking for a year has resulted in significant FMD reversal in a study by Johnson et al[33]. Another study observed that chronic cigarette smoking (even at a lowest dose) causes impairment of FMD[34]. FMD is also impacted negatively in those who are exposed to second hand smoking and such impact may be reversed when this exposure stops for a year[35]. A list of 6 pathophysiology of heart diseases resulting from smoking has been identified by the Surgeon General's report in 2004 which include inflammation, prothrombotic effect, endothelial damage, raised myocardial oxygen and blood demand, abnormal lipid metabolism and reduced myocardial oxygen and blood supply[36]. Nicotinic acetylcholine receptors (nAChRs) (found in the different organs of the body and the central nervous system) is stimulated by nicotine and these receptors are constituent of the parasympathetic nervous system. The rise in the risk of CVDs appears to be linked to the nicotine's adrenergic effects causing rise in heart rate, rise in resistance of coronary microvasculature and decrease in sensitivity to insulin[5]. Smoking, both active and passive, causes impairment of endothelium – dependent vasodilation, which requires nitric oxide[37,38]. The bioavailability of nitric oxide is reduced due to free radicals and superoxides in the gas phase of smoking[39]. The endothelial dysfunction is the initial stage leading up to atherosclerosis and the plaque formed due to smoking have a greater content of extracellular lipid and inflammatory cells. Smoking induced oxidative stress causes raised activity of matrix metalloproteinase, thus making these atheromatous plaques more vulnerable[40-43].

Smoking also increases platelet aggregation, raises prothrombotic factors, von Willebrand factor and causes impairment of fibrinolysis process[44-46]. Such changes may lead to acute myocardial infarction (MI) and sudden cardiac death due to coronary atheromatous plaque following acute coronary artery. The leading risk factor for acute coronary thrombosis is cigarette smoking[4]. Study done by Barua et al. found decrease in fibrin formation time and clot strength augmentation which may cause increase in thrombogenicity of atheromatous plaque formed due to smoking[47].

The lipid profile is also affected by smoking with increase in low density lipoprotein, very low density lipoprotein, total cholesterol, triglycerides and decrease in high density lipoprotein and apolipoprotein A1[48-50]. Oxidation of lipid in smoking causes modification of low density lipoprotein which is taken up by macrophage producing foam cell and therefore, plaque process formation[51-53]. Second hand smoking exposure in children with high predilection for developing early onset heart disease resulted in marked decrease in high density lipoprotein level[54]. A study done by Saladini et al. observed higher pulse pressure and central systolic blood pressure in smokers in comparison to non smokers[55].

The effect of quitting smoking was studied and it was observed that in case of heavy smokers who stopped smoking benefitted from decrease in CVD risk. Significant decrease in excess

risk of CVD occurred within 10 to 15 years of quitting in heavy smokers (≥20 pack-years) and also in smokers with<20 pack-years when compared to those who never smoked[56].

The risk of CVD in smokers depends on the number of pack years and smoking for longer duration with fewer cigarettes/day is more risky than smoking for shorter duration of more cigarettes/day[57]. Smoking aggravates pro-inflammatory state and inflammation promotes non-communicable disease. Complete abstinence from smoking is the proper approach to reduce CVD risk. Heart Association has defined ideal cardiovascular health as "The absence of clinically manifest CVD together with the presence of the 7 metrics that compose Life's Simple 7: not smoking, having a healthy diet pattern, adequate physical activity, healthy body weight, healthy blood pressure, cholesterol and blood glucose in the absence of pharmacological treatment"[57]. Good health habits need to be developed early and through out life to avoid CVDs and other non-communicable diseases.

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