



Toxicological effects of tobacco dust and smoke on human health

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Abstract

This classic review aims to assess and describe the adverse effects of tobacco on people who either work at tobacco field or factories or use them in any form for chewing, smoking etc. These mainly occur due to the presence of various toxic chemicals in it, which enter the human body either through cutaneous or oral route. During the study, previous literature from research and review articles pertaining the harmful effects of tobacco were concerned and the cumulative effects being described. The possible mechanisms by which chemicals in tobacco cause illnesses have been analyzed and the overall negative influences of tobacco on human health have been discussed. Consumption of tobacco lead to various health hazards including hormonal dysfunction, cancer, lungs disorders, genotoxicity, tuberculosis, cardiovascular disorders and several others. Tobacco being a cash crop on one hand has negatively impacted human's health on the other hand resulting in severe disorders. And keeping in mind the WHO estimates of mortality rate by 2030, public awareness programs should be commenced to tackle this sweltering concern across the globe.

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Introduction

Nicotiana tabacum is a plant which is widely grown and cultivated in different countries all over the world. Its yellow-brown leaves are collected from it, dried and a commercial product is obtained which is called tobacco. According to data report collected by World Health Organization, about 2.4 billion peoples all over the world have consumed tobacco for the purpose of smoking, chewing, snuffing or dipping (WHO, 2009). They also estimate that in 2015, about 6.4 million people died due to tobacco use, and in 2030 about 8.3 million peoples will die and about one billion deaths occurred during the 21st century. A study conducted by Harvard University School of Public Health implies that tobacco use increase the mortality and morbidity rate threefold globally in 20 to 25 years (Murray and Lopez, 1997). In 1950s, Sir Richard Doll, the Center head of Oxford University was among the first researchers who linked cigarette smoking with lung cancer. He also predicted that tobacco users associated with several health problems like cancer, heart problem and respiratory disorder (Doll, 1996; Doll, 1996 (repeated because these are two different publications by Doll in 1996). In 2004, the center for Disease Control and Prevention report argue that in the United States, nearly 2600 people die every day due to cardiovascular disease. So it indicates that one out of every 33 deaths is due to cardiac disease. Besides this, tobacco use increases the cardiac disease fourfold (CDC, 2008).

Leaf of tobacco plant is non-edible; these leaves are dried and used to produce cigarettes, cigar, chewing tobacco, and snuff. Universally it is known that tobacco use bring hazard related to health. Use of tobacco may lead to chronic diseases and health problems including cancer, cardiovascular diseases, tuberculosis etc. The 50% known carcinogens that are present in tobacco product cause mutation by disrupting the cell cycle, so this may increase risk of cancer (Pasupathi *et al.*, 2009). Tobacco dust can also cause trouble in breathe, dyspnea and rhinitis (Uitti *et al.*, 1998). Nausea, dizziness and retching may also be caused by tobacco use (Poonam *et al.*, 2010). Tobacco uses and cigarette smoking also lead to the

alteration of the lipoprotein levels. Many studies are performed on tobacco which proved that it has toxic effects on many organ systems that is respiratory and cardiovascular systems. It contain 6000 chemical substances, it have pharmacological, mutagenic, carcinogenic, toxic and inflammatory effects (Gaur *et al.*, 2012). Nicotine and carcinogens are toxic substances which are present in tobacco plant. Nicotine is a chemical that is plant-based known as alkaloids found in leaves and is released during the manufacturing process in the tobacco factory. Tissues like skin, respiratory epithelium and mucous membrane of the mouth can absorb it. Bacterial spores, fungal spores, mites, pollen, insects and inorganic particulates such as quartz and insecticides or pesticides remainders are also present in tobacco dust. In tobacco industry, the concentration of microorganism including bacteria, moulds and endotoxins has been assessed (Manoj *et al.*, 1995). The neurotransmitter are increase in those areas of body where nicotine are absorbed because the inhaled or absorbed nicotine attached to nicotinic acetylcholine receptors. These receptors are present in the central nervous system at neuro-muscular junction of skeletal muscles, which prevent the retake of acetylcholine. Due to this activity, heart rate increases, alertness and reaction time is quicker (Parkin *et al.*, 1998).

While work in factory to process tobacco to manufacture products, the dust and volatile compounds are inhaled. Other tobacco parts are also absorbed by the workers via the cutaneous route (Bagwe and Bhisey, 1993). Many workers do not use protection for skin or respiration during exposure to tobacco. Most of the workers in tobacco industries are smokers, while the workers who are non-smokers in tobacco industries at their work places are also exposed to passive smoking and absorption is commonly through inhalation of contaminated air caused by tobacco dust and smoke. The inhalation of dust also cause deterioration of lung functions. Among the tobacco workers, oxidative stress is induced by exposure to tobacco dust that cause damage of lung functions. The increased cotinine (a

metabolite of nicotine) level in urine, urine mutagenicity and increase in micro nuclei frequency in buccal epithelial cells are also due to exposure to tobacco dust (Kumar and Bharathi, 2010). Exposure to tobacco component having cumulative effect on genetic material (Davies *et al.*, 2006).

Methodology

In an effort to write a classic review on ill-effects of tobacco smoking and its usage on human health, and interaction of numerous chemicals contained in it while working in tobacco fields or industries, almost 100 papers were downloaded from Google Scholar which consisted of research studies, review articles, survey reports from organizations including WHO, CDC from several countries illustrating the harmful effects of tobacco chemicals and smoking on human health. These articles were published in NCBI, PUBMED database and other peer-reviewed journals. Firstly, they were screened to find relevant articles for concerned objectives and the rest of them were excluded. A total of 60 articles were selected and their abstracts, introduction and results were rigorously studied by the authors in order to get the desired information to design a review article describing various negative impacts of tobacco. All the articles used to get the required information have been properly referenced in each section of the manuscript and listed in the bibliography section.

Results and discussion

Among the myriad number of complications that has been noticed in smokers and tobacco factory workers, effects on hormonal, cardiovascular, respiratory and reproductive system are noteworthy resulting in genotoxicity, diabetes, tuberculosis, infertility, cancer and heart disorders which are described below.

Tobacco and human health

Effect of nicotine on insulin action: People who smoke and are diabetic are more likely to have impaired insulin action as compared to non-smokers. Abdominal fat can also be increased by taking nicotine and hence it can affect the level and effectiveness of insulin. Excess of glucose in the blood

is removed via insulin hormone. High glucose level in blood is majorly caused by impaired insulin action. Blood glucose is controlled through insulin resistance which allows the body to make more insulin, and if the body cannot generate the required level of insulin than blood glucose ultimately increases and hence it can lead to prediabetes followed by diabetes (Brown, 2007).

Different research and clinical reports studies describe prominent association between cigarette smoking, diabetes development, glycemic control and other complications related to diabetes. Nicotine or cigarette component are sometimes debated as social factors however prenatal or postnatal exposure to nicotine can induce metabolic control imbalance. Insulin action is affected through nicotine which is studied in humans in addition to animal models. Results show that nicotine exposure reduces the release of insulin in the body. Oxidative stress and mitochondrial dysfunction are involved in mechanism of nicotine-induced beta cells. Hence these evidences show us that insulin and pancreatic cell function is affected via cigarette smoking. Thus, getting rid of smoking is important in limiting of several diabetic complications and glycemic control (Jesse *et al.*, 2012).

Research is needed to unravel changes in the endocrine system through nicotine and cigarette with respect to clinical relevance of changes in hormones, as current literature lacks it. In addition, passive smoking and rest of forms of nicotine need to be checked with respect to endocrine system. Future studies should focus on smoking-associated metabolic and endocrine diseases and get rid of smoking that is smoking cessation (Sepaniak *et al.*, 2006).

Genotoxicity: Variety of toxic constituents like nicotine, formaldehyde, nitrosamines, polycyclic aromatic hydrocarbons and hydrogen etc. are well known during the process of *bidis*. These are released into the ambient air. Skin, mucous membrane of the mouth and respiratory epithelium absorb nicotine released from tobacco leaves. The carcinogenic

perspective of tobacco is most familiar (Manoj *et al.*, 1995; Umadevi *et al.*, 2003). Umadevi *et al.*, evaluated the cytogenetic effects of contact to tobacco dust in male workers at tobacco factory. In peripheral blood lymphocytes, chromosomal aberrations (CA) was evaluated by age and sex-matched controls (Haber *et al.*, 2004). In non-smoking and smoking individuals, statistically major increase in frequency of chromosomal aberration was observed compared to their respective control. Prolonged the service duration in the exposed group, the more frequent the CA was noticed in them. Occupational asthma is also caused by tobacco dust (Bhisey *et al.*, 1999; Utti *et al.*, 1998). Diseases of respiratory tract such as wheezing, rhinitis, and dyspnea have also been reported (Bhisey and Govekar, 1991; Poonam *et al.*, 2010). Nausea, dizziness, and vomiting may also occur because of tobacco dust. Thus, bidi rollers (which are mostly in females) are exposed to tobacco components through cutaneous route or an inhalation of tobacco dust (Khanna *et al.*, 2014). On an average, every roller makes 500-1000 bidis and handles 225450g of tobacco in a day (Milic *et al.*, 2008), so they are exposed to enough tobacco dust. This may have cumulative effect on their genomic content as with year's long exposure.

Genotoxic studies in bidi workers of tobacco region have not been done, although it is a major center for bidi making. Thus, the present investigation was undertaken to study the genotoxic effects of bidi rolling in workers as an occupational risk with the objectives to study the chromosomal and deoxyribonucleic acid (DNA) damage caused in them (Zhu *et al.*, 1999; Asha *et al.*, 2014). The study shows that genome damage was induced in people associated with this occupation upon exposure to tobacco dust. In women, developed risk was observed. In monitoring chronically exposed subject, the micronucleus rate and sister chromatid exchange tests shows more reliable indication of genome damage compared to chromosomal aberrations (Shona *et al.*, 2010). The human tissues such as skin, respiratory epithelium, mucous membrane of nose, mouth and intestines freely absorbed nitrosamines

mostly contained in tobacco dust.

Tobacco effect on cardiovascular system: Cardiovascular diseases are the main cause of death worldwide. Some environmental factors are involved to cause cardiovascular diseases. Cigarette smoking has very bad effect in the human health and also give rise to cardiovascular diseases (Bahattin *et al.*, 1999). Statistical ratio shows that cigarette smoking have main role in the development of cardiovascular disease. Tobacco smoke contain approximately 4000 chemicals. Nicotine is the main components of tobacco which major impact on cardiovascular system. Some experiment shows that the oral inhalation of nicotine increase the level of total cholesterol in plasma, high density lipoprotein-cholesterol(HDL-c) and low density lipoprotein-cholesterol (LDL-c). Research studies show that the frequency of risk factors in cardiovascular disease in woman who work in the tobacco company is similar to the exposure of the cigarette smoke. And also show that nicotine is one of the risk factors of atherosclerosis. The research is very important because it aware the people to stop smoking and stop nicotine chewing. People working in the tobacco factory continuously inhaled the harmful chemicals of which tobacco dust is composed. Some research show that nicotine and tobacco dust also effect the serum level of lipid and also have adverse effect on lipoprotein and apo-lipo protein in the worker (Sinczuk-Walczak *et al.*, 2001). Due to lack of exercise, high blood pressure and diabetes smoking, poor diet, high cholesterol level in the blood and also alcohol consumption cardiovascular diseases arise. One result shows that 13% cardiovascular death occur due to high blood pressure, 9% due to tobacco smoking, 6% due to diabetes, 6% due to lack of exercise and 5% due to obesity. It is estimated that prevention of 90% of cardiac diseases is possible. Hygienic food, more exercise, curb smoking and limit alcohol consumption are better to prevent of atherosclerosis (Umadevi *et al.*, 2003).

Infertility: Maternal smoking has many effects in gestation period, such as pregnancy complications,

retarded growth of the fetus, premature delivery, neonatal deaths and potential effects on lactation as well as child survival. Further, women fertility is decreased as a result of tobacco use because the irregularities in menstrual cycle increases and the age of spontaneous menopause is decreased (Xie *et al.*, 2009; Jesse *et al.*, 2012). It has also been suggested that tobacco use have adverse effects on every system in males, involving the reproductive system. The fertilizing capacity of spermatozoa have reduced in smokers and implantation rate of embryos is lower (Sepaniak *et al.*, 2006; Soares and Melo, 2008).

Cancer: Cigarette smoking has highly recognized role in lung cancer. Other chronic diseases, including chronic bronchitis and pulmonary emphysema has been also implicated. Since the mid-1980s, a decline in death due to lung cancer was seen in men by the reduction in smoking at United States. However, when breast cancer is continue to increase the rate of lungs cancer has risen (Soares *et al.*, 2007; Ramlau Hansen *et al.*, 2008). Women have higher susceptibility to tobacco carcinogens (Hoffman and Hoffman, 1997). All lung cancers, 80% to 90% are linked with active smoking. In women, tobacco uses cause breast cancer. However, present studies urge that breast cancer is also caused by both active and passive smoking. One example in a study show that prior to 12 years of age, when women are expose to passive smoking, chances of breast cancer is 4.5 and for active smoking it is 7.5 (US DOH, 2008). Cancer in the head and neck region also occur in human of both genders. And this is due to use of more smokeless tobacco product (Patel, 2005).

Some studies which are about toxicities showed that the tobacco which is heated is comparatively less toxic than standard cigarettes (Henschke *et al.*, 2006). Lee determined in 2001 that the risk of lung cancer in smoking filtered cigarettes is 36% lower than those who smoke unfiltered cigarettes, and using low-tar cigarettes, the risk of cancer is reduced 23% than of using high-tar cigarettes. In hand-rolled cigarette smokers, the risk of cancer is increased by 42% and in black tobacco user, the risk is increased by 75% (Lash

and Aschengrau, 1999).

One attractive study related to lung cancer shows different locations of the type of lung tumors in smokers. In the early primary tumor has been found among the smoker which was centrally situated in squamous cell carcinomas of the airways. Now the predominant of lung tumor in smoker are due to adenocarcinomas and other non-small-cell lung cancers. In previous 30 years, the composition of cigarette and its effect on tobacco user are changed (Pershagen *et al.*, 1994; Ramlau Hansen *et al.*, 2008).

In molecular biology, advanced techniques are used for the detection of tobacco related cancer in the general population. They take blood sample from the patient and use polymerase chain reaction, a molecular assay for the confirmation of different immune and enzymatic function of the body. Polymerase chain reactions are more used for the practical study of gene and gene environmental interaction. In recent year one area has received large awareness attention that polymerase chain reaction (PCR) have worthy role for the detection of major disease. Now it is clear that genetic changes occur in the body, so the chances of cancer are increased.

The ratio of defected allele of proto-oncogenes, tumor suppressor genes and xenobiotic bio-transformation genes much significantly among different populations and impact substantially on their susceptibility to cancer. Now those entire enzymes are found which have role in the carcinogenic metabolic pathway in the different structures. And some enzyme are absent in the individuals, therefore the influencing ratio is increased to cause a disease (Foy *et al.*, 2004).

Tuberculosis: At the beginning of 20th century, cigarette smoking was just in the beginning among men. In United States, tuberculosis was a primary cause of death at that time. Although rates of both smoking and TB continued to drop in the US, the two epidemics are expanding globally. About 1.3 billion folks use tobacco across the world (Lee, 2000). Each year, nearly 9 million people are diagnosed with TB

and 1.3 million die because of this disease (Hoffman *et al.*, 1996). TB is at risk of active disease because an estimate indicates that *Mycobacterium tuberculosis* (*M. tuberculosis*) infect approximately one-third of the global population. In China and India, more than 30% of TB patients are identified with the disease every year. Further, above 40% of the global smokers account for these two countries (Sibu *et al.*, 2007).

A possible risk factor for TB mortality is smoking (WHO, 2010), but recently group studies and large case-control shown that smoking attributes extremely high rates of TB mortality (Mathers and Loncar, 2006).

A number of systematic reviews assume that there is a link between smoking and TB (WHO, 2008). According to each review, tobacco use can result in doubling the chances for TB infection, for having clinical proof of TB disease, and for TB death rate. Worldwide TB prevalence program determined that among 80% of the worldwide TB burden from 22 countries, 23% cases belongs to tobacco use (Doll and Hill, 1956). In China and India, the smoking related problems of TB changes with the epidemiologic property of the population, with the high ascribable risks for smoking is found, while in sub-Saharan Africa the major risk for TB is HIV (Jha *et al.*, 2008; Lonnroth *et al.*, 2010).

Conclusion

Tobacco plant is grown for commercial purposes widely. Although it contributes much to the economy of a country but at the same time have been deteriorating the health of people which in turn cause both short time and long term losses to a country. Research work should be performed to improve the diagnosis of tobacco related disorders. In this regard, government should also play a key role in alleviating such ailments from the society and developing the interests of farmers in growing other alternative crops. Moreover, public awareness programs should be started across the country to inform the compatriots about ill effects of tobacco consumption.

This way we can mitigate the issue up to a major extent.

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Author statements

Ethical approval

During the study, data from publicly available secondary sources was used, which do not need any ethical approval.

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Competing interest

We declare no conflict of interest with anyone.

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