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**Research Paper**

# Lifestyles and Non-Communicable Diseases Smoking: PART II Cancer, Diabetes Mellitus, Kidney Diseases, Alzheimer's Disease, Arthritis

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***ABSTRACT***
*Tobacco smoking is responsible for significant global morbidity and mortality. It also has adverse effects on non-smokers exposed to second-hand and third-hand smoke. E-cigarettes are also harmful to human health. Smokeless tobacco also contains many toxic substances. Nicotine is the common addicting substance in all tobacco concoctions. Several well-done studies confirm that no amount of tobacco exposure is safe. The first part of this two-part series discussed smoking and its effects on cardiovascular and respiratory diseases, obesity, depression, and liver ailments. This second part discusses the deleterious effects of smoking on five non-communicable diseases, viz., cancer, diabetes mellitus, chronic kidney disease, Alzheimer's disease, and arthritis.*

***KEYWORDS****: smoking, non-communicable diseases, cancer, diabetes mellitus, chronic kidney disease, Alzheimer's disease, arthritis*

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## I. INTRODUCTION

It is estimated that over a billion people smoke globally [1]. First-hand smoke is the smoke that enters the smoker's mouth directly and is also known as mainstream smoke [2]. Side-stream cigarette smoke emanates from the burning ends of a cigarette. Environmental tobacco smoke or second-hand smoke is a combination of side-stream smoke (85%) and the exhaled main-stream smoke (15%) [3]. Third-hand smoke is the gas and particulate residue from tobacco products, including smoking cigarettes, that cling to surfaces such as skin, hair, clothing, and furniture [4]. These pollutants adhere strongly to these surfaces and may persist for minutes to months.

Smoked tobacco includes products like cigarettes, e-cigarettes, and water pipes [5]. Smokeless tobacco products include loosely chewed tobacco leaves, tobacco paste, and several other tobacco-based concoctions [6]. Cigarette smoke has thousands of gaseous and particulate substances, with many being toxic and cancer provoking [7]. Water pipe smoking is immensely popular in the Middle East but has now become fashionable globally. Water pipe (also known as hookah, narghile, argileh, goza, and sheesha in different countries) smoking contains many of the same toxicants as cigarette smoking [8]. Water pipe smoking may result in the inhalation of 50–100 times the smoke volume during a single smoking session when compared to that inhaled from a single cigarette [9]. Electronic cigarettes (e-cigarettes) are battery-powered devices providing aerosol vapors for inhalation [10]. These vapors are usually produced by heating a liquid that has propylene glycol and/or vegetable glycerin, nicotine, and flavoring. Though they are significantly lower in carcinogens and toxins, they still cause harm [11]. Smokeless tobacco provides nicotine like cigarettes, with a slower absorption and still has more than 20 carcinogens [12].

Of all the known constituents, nicotine is the addictive substance in tobacco, smoked or taken in otherwise [13]. Toxic compounds in tobacco-derived smoke are nitrosamines and polycyclic aromatic hydrocarbons [14,15]. Other toxic materials found in both tobacco cigarette/waterpipe smoke and e-cigarette vapor are volatile organic compounds and inorganic compounds such as metals and carbon monoxide. Carbon monoxide is toxic to humans, even at low concentrations [16]. E-cigarette liquid usually contains, propylene glycol, and glycerin in addition to nicotine. The inhaled e-cigarette vapor contains toxic compounds derived from these three ingredients [17]. Smokeless tobacco also contains harmful substances like nitrosamines, polycyclic aromatic hydrocarbons, and aldehydes [18]. In general, no tobacco product is safe.

The estimated economic cost associated with smoking is 1.8% of the global gross domestic product. In 2012, the world's total medical expenditure for smoking-attributable diseases reached 467 billion US dollars and accounted for 5.7% of the global health expenditure. Meanwhile, the total economic cost of smoking (including medical expenditures and productivity losses) in 2012 was 1852 billion US dollars, accounting for 1.8% of the global gross domestic product. Almost 40% of the economic cost occurs in low-income or middle-income countries.

## II. DISCUSSION

Noncommunicable diseases (NCDs) are the leading cause of mortality, killing more than 36 million people each year, globally [19]. They are responsible for 63% of all annual deaths. Developing countries bear the main brunt of this enormous mortality, with almost 80% of NCD deaths occurring in low and middle-income countries [20]. Modifiable behavioral health risk factors such as smoking tobacco, inadequate vegetable and fruit consumption, high alcohol consumption, physical inactivity, and obesity increase the risk of NCD morbidity and mortality [21]. Tobacco smoking is a major player in this deleterious association. NCD diseases discussed in this manuscript include cancer, diabetes, chronic kidney diseases, Alzheimer's disease, and arthritis.

Cancer prevalence is rising and commonly involves the bladder, breast, colon, rectum, lung, cervix, and head and neck [22]. In 2018, GLOBOCAN estimated that 18.1 million people had been diagnosed with cancer, with 9.6 million people dying from it, worldwide [23]. Type 2 diabetes invariably leads to the development of several microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (coronary artery disease, stroke, peripheral artery disease) complications [24]. Deaths from diabetes mellitus (DM) have increased by more than 60% since 2000 and now rank in the top 10 causes of death [25]. Chronic kidney disease (CKD) affects over 10% of the population worldwide. It was ranked 16th among the leading causes of death in 2016 and is expected to become the 5th leading cause of death by 2040 [26]. Diabetic kidney disease is the leading cause of CKD [27]. Alzheimer's disease (AD) and other dementias afflict nearly 44 million people worldwide [28]. The annual healthcare expenditure for AD patients was $277B in 2018 and is expected to go up to $1100B annually by 2050. Arthritis is of over 100 types, the most common being rheumatoid arthritis, osteoarthritis, psoriatic arthritis, and inflammatory arthritis [29]. These diseases result in considerable functional disability in the sufferers, especially with increasing age.

All these diseases are not only non-communicable but usually chronic. The Centers for Disease Control and Prevention of USA [30] defines chronic diseases as "conditions that last 1 year or more and require ongoing medical attention or limit activities of daily living or both." NCDs are gradually replacing infectious diseases as the major health burden in developing countries. Deaths from NCDs are also on the rise, globally. As discussed in the previous part of this two-part manuscript, smoking is one lifestyle that plays an important adverse role in the genesis and progression of these diseases.

### 2.1 Cancer

Cancer was the second leading cause of death (after cardiovascular diseases (CVDs)) in 2017, accounting for 17% of all global deaths [31]. Cancer-related mortality exceeds that caused by communicable diseases such as human immunodeficiency virus/acquired immunodeficiency syndrome, tuberculosis, and malaria, combined [31].

Smoking is strongly associated with cancer, accounting for 19% of all cancer cases [32]. Tobacco smoke is full of carcinogens [33]. Active smoking has been associated with cancer of almost every organ of the human body. It is estimated that smoking accounts for 81.7% of lung cancers, 73.8% of larynx cancers, 50% of esophageal cancers, 46.9% of bladder cancers and is responsible for 28.8% of all cancer deaths [32]. Other methods of smoking tobacco, such as water pipe smoking [34]. Electronic Nicotine Delivery System (ENDS) smoking [35], and Heat-not-Burn (HNB) smoking [36] have also been implicated in increasing the cancer risk. Second-hand smoke also increases the risk of cancer [37]. Smokeless tobacco also poses a risk, causing cancers of the oral cavity, esophagus, and pancreas [38]. Smoking after the diagnosis of cancer is associated with a poor treatment response and higher treatment-related toxic effects [39]. Recurrences [40] and a primary second cancer development is more common in these individuals [41], compared to non-smokers. They suffer from an increased mortality [42]. However, the mortality risk is reduced by 30% to 40% with smoking cessation [43]. Overall, smoking cessation after cancer diagnosis has benefits that equal or exceed those achieved by cancer treatments [44]. Smoking cessation continues to be difficult, with almost 80% of smokers relapsing within the first month of abstinence, and only about 5% achieve long-term abstinence.

### 2.2 Diabetes Mellitus

DM is increasing in prevalence, both in developed and developing countries [45,46]. According to the International Diabetes Federation, there were 451 million adults live with diabetes worldwide in 2017 and this

number is projected to increase to 693 million by 2045 [47]. Type 2 diabetes (T2D) accounts for 90–95% of all diabetes cases and is caused by insulin resistance and progressive loss of pancreatic β cell mass and function. Diabetes is associated with an increase in mortality from several co-morbid conditions, such as CVDs, CKD, cancer, and liver diseases [48]. It also increases the risk of contracting several infections with adverse outcomes. Diabetes is solely responsible for 1.5 million deaths worldwide. It also contributes to an additional 17.5 million deaths each year [49].

Any kind of tobacco smoke exposure increases the risk of T2D [50]. It is estimated that 11.7% of diabetes cases among men and 2.4% of diabetes cases among women relate to active smoking [51]. This association appears to be dose-response related. In 2014, the Surgeon General reported that active smoking in individuals increases their risk of T2D by 30–40% compared to non-smokers [52]. In a meta-analysis of 88 prospective studies of almost 6 million participants, Pan and the group found that passive smoking was also associated with a 22% increased risk of incident type 2 diabetes in never smokers compared to never smokers not exposed to passive smoke [51]. Alternate tobacco smoking methods and smokeless tobacco products also appear to increase the risk of diabetes [53]. Smoking during pregnancy increases the risk of gestational diabetes mellitus [54] and may also increase the risk of future diabetes in the offspring [55]. Infants exposed to secondhand cigarette smoke also experience an increased risk for T2D development.

Active smoking has been associated with reduced appetite and weight loss. On the other hand, smoking cessation is often associated with weight gain. Several studies reported that diabetes risk was increased in individuals who had recently quit smoking, raising a concern about elevated diabetes risk with smoking cessation [56]. This phenomenon occurs more frequently during the first 3 years post-cessation and appears to be related to an increase in body weight upon withdrawal of nicotine [56].

Smoking appears to acutely worsen glucose tolerance, alter peripheral insulin signally and impair beta-cell function [57].

**2.3 Chronic Kidney Disease**

The worldwide prevalence of CKD is estimated to be 8–16% [58]. CKD is associated with a reduction in the glomerular filtration rate (eGFR) <60 ml/min/1.73 $m^2$ [59]. Untreated CKD usually progresses to end-stage renal disease (ESRD) (GFR<15 ml/min), requiring dialysis or kidney transplantation. CKD increases the risk of developing cardiovascular diseases, mineral and bone disorders, and anemia. Worldwide, a 31.7% increase in CKD mortality has occurred over the past decade [60]. Lifestyle factors, including smoking, alcohol, obesity, and physical inactivity have been implicated in this increase in CKD.

In an analysis of 15 prospective cohort studies involving 65,064 incident CKD cases, Xia et al. found an increased risk of CKD in smokers vs nonsmoker [61]. Smoking also enhances its progression [62]. It is associated with a higher incidence of death from ESRD in both males and females [63]. Smoking cessation reduces the risk of incident CKD [64].

Nicotine causes tubule-interstitial injury and plays a central role in smoking-mediated renal dysfunction [65].

**2.4 Alzheimer's Disease**

Cognition is involved in attention, memory, language, orientation, performance, judgment, and problem-solving skills. A gradual decline occurs with age and is considered normal. Mild cognitive impairment is a pre-dementia stage. AD, however, is a much more serious and progressive disease. It accounts for 50–70% of dementia cases [66]. According to the WHO, 44 million individuals had AD globally, in 2016. This number is on the increase and is projected to reach 82 million by 2030 and 152 million by 2050 [67].

Smoking has been linked to an increased cognitive decline. Several studies reported that smokers are 1.9–4.3 times more likely to develop AD than non-smokers [68]. Nicotine has short-term cognitive-enhancing effects, and this may help explain the high rate of smoking in individuals with psychiatric disorders and the difficulty in quitting in this population [69]. However, in the long run, smoking decreases cognitive function and may lead to the development of neurodegenerative disorders including AD [70]. Second-hand smoke is also harmful, with an increase in cognitive impairment of 24% noted in older adults with such an exposure [71]. Smoking during pregnancy can harm fetal brain development, while cigarette smoking in individuals at an earlier age is associated with future cognitive impairment [72].

Smoking in AD patients is associated with oxidative stress, neuroinflammation, and impaired neuroprotection [73]. Structural abnormalities such as a thinner anterior cingulum and prefrontal lobe have also been noted in these patients [74].

**2.5 Arthritis**

The two main kinds are osteoarthritis (OA) and rheumatoid arthritis (RA). OA is the leading cause of pain and disability all over the world. It affects almost 1 in 3 people over age 65 [75]. OA is associated with cartilage loss while RA affects the synovial joints resulting in synovitis, joint erosion, and cartilage damage.

Smoking is considered a risk factor in knee and hip OA, causing an increased proliferation of chondrocytes [76]. It increases pain and cartilage loss in these patients. However, a meta-analysis of 48 observational studies and data from the 5th KNHANES study of individuals over the age of 50 suggested that smoking and osteoarthritis may not be significantly associated [77].

Some studies have shown that cigarette smoking intensity and duration are causally related to the risk of RA development [78]. This increased risk appears to persist even after smoking cessation.

## III. CONCLUSION

Tobacco use, especially cigarette smoking, is an important cause of global morbidity and mortality. Tobacco consumption in any form harms nearly every organ of the human body. It is adversely involved in the genesis and progression of all major NCDs. Smoking remains the leading preventable cause of death in the world. No amount of exposure to tobacco is safe. Abstinence from smoking is therefore an important step in the prevention and management of chronic NCDs.

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