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Review

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Author for correspondence:

Hamid Salehiniya

e-mail: alesaleh70@yahoo.com

Tobacco Smoking and Cancer Types: A Review

Yousef Khani¹, Nima Pourgholam-Amiji²,
 Mohammad Afshar³, Omid Otroshi⁴,
 Mehran Sharifi-Esfahani⁵, Hamidreza
 Sadeghi-Gandomani⁶, Marjan Vejdani⁷
 and Hamid Salehiniya^{8,9}

¹Deputy of Health, Alborz University of Medical Sciences, Karaj, Iran

²School of Nursing & Midwifery, Tehran University of Medical Sciences, Tehran, Iran

³Department of Operating Room, School of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, Iran

⁴School of Medicine, Kashan University of Medical Sciences, Kashan, Iran

⁵Department of Oncology, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran

⁶Trauma Nursing Research Center, School of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, Iran

⁷Iranian Research Center on Healthy Aging, Sabzevar University of Medical Sciences, Sabzevar, Iran

⁸Zabol University of Medical Sciences, Zabol, Iran

⁹Department of Epidemiology and Biostatistics, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Objective: Tobacco smoking is one of the causes of the incidence and mortality of cancer in the world. This study aimed to review the relationship between TS and especially the use of cigarettes with common cancers of various organs of the body. **Methods:** This study was conducted in English by November 2017 through a search in databases of the PubMed, Scopus and Web of Science. The search strategy included the key words "cancer", "tobacco smoke", "tobacco smoke", and "smoking." Articles that looked at the relationship between each type of cancer and smoking were entered into the study and summarized in Review. **Results:** Tobacco smoking is associated with an increased risk of lung cancer, Upper aerodigestive tract, esophagus, stomach, bladder, kidneys, colorectal, prostate, and pancreas. However, further studies are needed to confirm the association between Tobacco smoking and liver, cervical, brain, gallbladder, Hodgkin's disease, non-Hodgkin's lymphoma and hematologic malignancies. However, Tobacco smoking plays a protective role in the development of thyroid cancers, skin and Kaposi's sarcoma. **Conclusions:** Given that almost all of the risk factors for most cancers are Tobacco smoking, increasing the public's awareness of the harmful effects of smoking, implementing programs and policies to reduce smoking, can lead to a reduction in smoking and consequently reduce the resulting harmful consequences.

1. Introduction

Tobacco smoking (TS) is one of the causes of the incidence and mortality of cancer in the world [1]. It is responsible for about 25% of all cancers in men, 4% of all cancers in women and about 16% of all cancers in both sexes in most developed countries and 10% in less developed countries [2]. In the United States, approximately 40% of the cancers diagnosed is related to tobacco consumption [3]. According to recent research evidence, tobacco causes a lot of cases of lung cancer [4]. It is the leading cause of cancers of oral and throat, vocal cords, esophagus, stomach, kidneys, pancreas, liver, bladder, cervix, colon and rectum, and types of leukemia [2] [5] [6] [7] [8]. According to the Center for Cancer Prevention (CDC), tobacco-related cancers have been diagnosed between 2008 and 2013 for some 660000 people in the United States, but 343,000 of these people have died [9].

It seems that only small organs in the TS have been immune to cancer. Available evidence has shown that there is an inverse relationship between endometrium cancer and TS [2]. Evidence also suggests that the association between TS and liver cancer has not been definitively confirmed. Confounding variables such as hepatitis B and C can affect this relationship [10]. Given the numerous studies on smoking and cancer, this study aimed to review the relationship between TS and especially the use of cigarettes with common cancers of various organs of the body, taking into account possible confounding variables for each organ based on available evidence and review of the literature.

2. Methods

This study was conducted in English by November 2017 to include epidemiological evidence from all available randomized control trials, case-control and cohort studies reporting tobacco-related cancer risks through a search in databases of the PubMed, Scopus and Web of Science. The search strategy included the key words "cancer", "tobacco smoke", and "smoking." In addition, the reference lists of relevant articles were manually searched to find any other potentially eligible articles. Articles about smoking intensity are also included in the present study. We excluded reviews, commentaries, articles from overlapping samples, conference abstracts, and articles printed in languages other than English. Articles that looked at the relationship between each type of cancer and smoking were entered into the study and summarized in review. Most studies evaluated exposure to tobacco smoke quantitatively by reporting number of cigarettes per day, duration of smoking or age at starting to smoke, or in a cumulative way in terms of pack years (number of packs of cigarettes smoked daily multiplied by the number of years of smoking). Similarly, the benefit of smoking cessation was evaluated either in comparing risks in former smokers with those in current smokers, or as a trend by years since quitting to smoke.

3. Results

(a) Study characteristics

In the initial electronic literature search, 2540 articles were obtained from databases and 12 articles were obtained using manual search. After removing duplicates using Endnote X7 (n =1200), the title and abstract of the remaining 1340 articles were reviewed. After this stage, 191 articles were included in the study and 1164 of these articles were removed because of scientific reasons and lack of eligible criteria or unrelated to our aim, in all, 176 full papers were reviewed.

The most important cancers related to Tobacco Smoking are summarized in **Table 1**.

(b) Lung

One of the main causes of lung cancer (LC) is TS (4). Smokers are at risk to LC approximately 20 times more than people who have never smoked regularly. Smoking is responsible for 80% of LC

Table 1. Relationship between TobaccoSmoking and Cancer Types.

Cancer Types	Protective	Risk factor	Controversial
Lung		*	
Upper aerodigestive tract (UADT)		*	
Esophagus		*	
esophageal adenocarcinoma			
the squamous cell carcinoma			*
Stomach		*	
Liver		*	*
Bladder		*	
Cervix			*
Kidney		*	
Blood Cancers			*
Colorectal		*	
Prostate		*	
Pancreas		*	
Brain			
Gallbladder			
Hodgkin’s disease			
Non-Hodgkin’s Lymphoma			
Kaposi’s Sarcoma	*		
Thyroid	*		
Skin	*		

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in men and 50% of LC in women [11]. TS is associated with the incidence of small lung carcinoma (SCLC) and squamous cell carcinoma (SCC) [12]. Cigarette smoke contains about 20 potentially dangerous carcinogens and 3,500 chemical substances. The most common LC-induced chemicals found in cigarette smoke are polycyclic aromatic hydrocarbons (PAH) like benzo (a) pyrenes, and the tobacco-specific N-nitrosamine 4- (methylnitrosamino) -1- (3-pyridyl) -1-butanone NNK [13]. Cigarette smoke also contains high levels of acrolin, which damages ciliated lining of the lung and helps to develop LC. Nitrogen oxides, acetaldehyde, phenols and formaldehyde are substances in cigarette smoke that indirectly contribute to LC [12]. Free radicals in cigarette smoke also cause oxidative damage in human and animal studies and contribute to the development of LC [14]. The risk of LC in the second hand smokers is also high [15] LC risk is 20-30% higher in non-smokers who marry smokers compared with others [11] [16] [17]. The risk of LC in heavy and continuous smokers is 20 to 50 times higher than non-smokers [18]. The most important risk index for LC is the duration of smoking [11].

(c) Upper aerodigestive tract (UADT)

UADT cancers include oral, pharyngeal, hypopharynx, larynx, esophagus, nasal cavities, nasal sinuses, pharynx and adenocarcinoma of esophagus [2] [19]. The findings of a case-control study in 10 European countries showed in 2009 compared to non-smokers, TS is associated with a risk of UADT in general (OR: 6.72; 95% CI, 5.45-8.30), oral cavity cancer (OR: 5.83; 95% CI; 4.5-7.54), pharyngeal cancer (OR: 12.19; 95% CI, 8.29-17.92), and laryngeal and hypopharyngeal cancer (OR: 4017; 95% CI, 2.45-7.10 for esophagus) [19]. The findings of the meta-analysis study also showed that non-selective involuntary exposure to tobacco is associated with head and neck cancers, especially throat and larynx [20]. Based on a review study of nine case-control studies and a cohort study on sinonasal cancer, this type of cancer is associated with increased TS. Also, TS is also associated with a significant decrease in sinonasal cancer [2]. A finding from a study by Bosetti *et al.* (2007) showed that discontinuation of smoking at any age has reduced the risk of UADT incidence [21].

(d) Esophagus

One of the major risk factors for esophageal cancer is TS [22]. The relationship between TS and esophageal cancer has been reported since 1985. It is also has been mainly related to squamous cell carcinoma of esophagus [2]. The findings of several case-control studies showed that TS is one of the proven risk factors for esophageal cancer [23] [24] [25]. Findings from several studies showed that the risk of developing ESCC in smokers is 3-7 times higher than non-smokers [26] [27]. According to a 2012 meta-analysis study, about 20-30% of esophageal cancer patients were addicted to cigarette smoking [28]. However, limited studies have directly evaluated the role of cigarette as a prognostic factor in esophageal cancer (22). Numerous studies in the United States, the incidence of esophageal adenocarcinoma in the United States and Britain in smokers has increased steadily compared with non-smokers. This process has been relatively constant for the squamous cell carcinoma and even has had a decreasing [29] [30].

(e) Stomach

One of the known causes of stomach cancer is TS [31]. A systematic review study on 23 epidemiologic studies investigated the relationship between TS and stomach cancer with 10,290 cases and 26,145 controls revealed that compared to non-smokers, Odd Ratio(OR) for ever was 1.20 (95% CI: 1.09-1.32), OR for former smokers 1.12 (95% CI: 0.99-1.27) and OR for current smokers 1.25 (95% CI: 1.11-1.40). Also, with an increase in TS duration, the incidence of stomach cancer was significantly higher (OR, 95.1% CI 95% CI: 1.14-1.54) [32]. The findings of the cohort showed more than 215,000 men and women of the five ethnic groups (African Americans, Japanese Americans, Latino Americans, Native Hawaiians, and Whites), for all five racial groups, the rate of stomach cancer in smoker men (HR = 1.98; 95% CI 1.46-2.70) and in smoker women (HR = 1.78; 95% CI 1.23-2.57) was higher than non-smokers [33]. The findings of meta-analysis on cohort studies showed tobacco is one of the most important risk factors for stomach cancer [31]. The findings of a systematic review study on 10 cohort studies and 6 case-control studies revealed that there is a positive and strong association between TS and stomach cancer in men and there is a positive and weak correlation between TS and stomach cancer in women [34]. Since the middle of the last century, the incidence and mortality rate of stomach cancer in most of the high-income countries has declined [35,36]. Reducing the incidence of stomach cancer can be due to a reduction in the prevalence of smoking in men [31]. A positive association between TS and stomach cancer can be affected by confounding variables such as the infection of the stomach and the helicobacter pylori infection [37]. However, the association is not well known and confirmed [2].

(f) Liver

Cohort and case-control studies have investigated the relationship between TS and liver cancer. Often, these studies have been conducted in areas where liver cancer is high, such as Southeast Asia and Europe [38,39]. Majority of these studies reported that the incidence of liver cancer among smokers was higher than non-smokers [40]. Other risk factors, such as hepatitis B or C and high alcohol intake, also play an important role in the development of liver cancer. Controlling these variables as a confounder also adjust the association between TS and liver cancer [39]. The International Agency for Research on Cancer also lists liver cancer in the list of tobacco-related malignancies [40]. A systematic review of 12 cohort studies showed that smoking is associated with an increase in the rate of liver cancer. However, there were no mention of potential confounders such as hepatitis B and C virus in these studies. In this study, 11 case-control studies were also studied and the findings showed that among the 11 case-control studies, 5 studies reported poor to moderate association between smoking and liver cancer, and the relation of dose response was only in one study. In the remaining 5 studies, the observed relationship was inverse or null due to the lack of data on the dose response variable [10]. Meta-analytical study findings in 2009 also supported the association between cigarette smoking and liver cancer [40].

(g) Bladder

The risk of developing bladder cancer in smokers is 2 to 4 times more than non-smokers [41]. By increasing the amount and duration of smoking, the risk increases in both sexes [42–44]. Risk in people who use non-smoked cigarettes with high tar or black tobacco is more than those who use filtered cigarettes and golden tobacco with low tar [42]. Second-hand smokers have a 30-60% lower risk compared to smokers [18]. Smoking is responsible for 23% of BC in women and 50% of BC in men [45]. Following the discontinuation of smoking, the risk of bladder cancer decreases by 30-20% within 5 years. Recently, it has been argued that women may have more risk at bladder cancer due to TS [41]. The precise method of developing BC is not clear by the use of cigarettes. BC risk seems to be related to some of the chemicals found in cigarettes such as naphthylamine-2 and aminobiphenyl-4, polycyclic aromatic hydrocarbons [46]. Tobacco combustion release at least 69 carcinogens including nitrosamine, polycyclic aromatic hydrocarbon, 2-naphthylamine and other aromatic amines, all of which are directly responsible for the role of mutagens in BC formation [47]. Also, the main routes of induction of cancer in smokers are the DNA adduct formation and genetic damage. They cause the change of specific cellular pathways, and subsequently uncontrolled cell growth and prevention of the activity of internal mechanisms inhibiting tumor growth [48].

(h) Cervix

Smoking is one of the known risk factors for cervical cancer [49]. This role of smoking is independent of sexual behavior. Some studies have shown a positive and significant relationship between the number of cigarettes consumed and the duration of smoking, and the incidence of cervical cancer. It seems that there is less danger in those who have left smoking [50,51]. However, other studies have not been able to relate their findings to smoking [52–54]. Meta-analysis findings in women with human papillomavirus revealed that smokers were twice as likely to have cervical cancer as non-smokers [55]. Cohort study findings in women with human papillomavirus also indicated that the risk of cervical cancer in women smokers and those who had previously smoked and now left smoking was at least three times more likely than other women [56]. The effect of direct TS carcinogens on cervix is based on the fact that nicotine metabolites can be found in the cervical mucus of women who smoke [57]. Another acceptable mechanism is the suppression of local immune responses to human papillomavirus infection [58,59]. In general, further studies are needed to confirm the definitive effects of TS on the incidence of oral cancer.

(i) Kidney

The findings of the epidemiological studies have shown the association between TS and the incidence of pelvis cancer. TS, especially cigarettes, has increased the risk of developing kidney cancers by 20%, which is seen more in middle-aged and elderly people. Cigarette smoking increases the risk of developing renal cell carcinoma (RCC). Meta-analysis study findings showed that the increased risk is associated with the number of cigarettes consumed [60]. The findings of another meta-analysis study showed that current smokers are at a 3 to 4-fold higher risk of developing urinary cancers than others. According to the study, in Europe about half of the cases of urinary tract cancer are detected in men and one third of women are attributed to TS [61]. With the cessation of smoking, the risk is reduced, but many years of time are needed to be as same as the risk level of people who quit smoking than the risk in people who have never smoked. The findings of several narrative studies have also recognized the significant role of smoking in the incidence of urinary tract cancer [62,63].

(j) Blood Cancers

TS is not a risk factor for the risk of malignancies, but some epidemiological evidence supports the claim that TS is a risk factor for leukemia [64]. Some cohort and case studies have shown an

increase in the incidence of hematologic malignancies, especially non-lymphoblastics, among smokers, while other studies have not shown significant correlation. However, the findings of Brownson et al (1993) [65], Siegel (1993) [66] and Sandler (1995) [67] showed that, despite the discrepancy in various studies, there is evidence that the relationship between TS and the development of blood malignancies. TS contains about 3800 chemical substances, most of which are mutagenic and carcinogenic [68] and contain radioactive compounds and benzene, both of which are known carcinogens in the development of leukemia [2,68,69]. It is estimated that smokers inhale benzene 10 times more than non-smokers [64]. Smoke also contains nitrosamines and urethane, which cause leukemia in animals, and also contain styrene and agricultural chemicals that are a potential source of leukemia in humans [68]. Available evidence also suggests that there is a relationship between TS and myeloid leukemia, and the risk increases with increasing the duration and amount of cigarette smoking [2].

(k) Colorectal

Smoking, and in particular smoking, is a common risk factor for CRC in both genders [70]. Cohort studies in Korea showed that CRC risk was higher in non-smokers than in non-smokers [71]. Findings from the meta-analysis studies suggest a positive relationship between smoking, and colorectal adenoma and colorectal cancer. The findings from comprehensive systematic review of batteri et al. showed a significant relationship between smoking and the occurrence of adenoma polyps, which are pre-cancerous lesions of colorectal cancer [72]. The meta-analysis findings by Chen et al showed that smoking is a major risk factor for colorectal cancer [73]. Another study found that CRC risk increased in people who smoked over 45 years, while there was no increase in the number of cigarette packs with CRC risk [74]. Smoking is responsible for 20% of all types of CRC in the United States [75]. Several studies also found that smoking has increased the risk of CRC by up to 30% in smokers and women [76-78].

(l) Prostate

Based on the findings of Paler *et al.*, 2013, the incidence and death rate of PCa increased significantly with the increase in smoking [79]. Various mechanisms have been proposed for prostate cancer due to smoking [79,80]. Among the known mechanisms of tobacco use, it is possible to increase serum estrogen metabolites, and subsequently stimulation of an invasive tumor phenotype, which ultimately leads to prostate cancer [81].

(m) Pancreas

One of the most important risk factors for pancreatic cancer is smoking [82,83]. Meta-analysis study findings revealed that the risk of pancreatic cancer in smokers is 2 times that of non-smokers. The risk of cancer is positively correlated with an increase in the number of cigarettes and duration of use [84]. About 20-30% of cases of pancreatic cancer are due to smoking. Most importantly, the risk of pancreatic cancer in people who leave smoking is reduced to near normal levels [85,86]. The findings of a meta-analysis study on 82 cohort studies and case-control cases published between 1950 and 2007 show that in current smokers, the relative risk (RR) of pancreatic septicemia is 1.7 (95% confidence interval [CI] 1.6-1.9) and in former smokers 1.2 (95% CI 1.1-1.3) [84]. According to the international cohort study, the pancreatic cancer included 1481 cases and 1539 controls, RR in former smokers was 1.1 (95% CI 0.9-1.3) and in current smokers was 1.8 (95% CI 1.4-2.3). This risk was also associated with an increase in the number of cigarettes and the duration of use. As in individuals who smoked 30 or more doses daily, RR was 1.75 and in those who smoked at least 50 years, while in people who had left smoking for more than 15 years, RR was similar to those who never smoked [87].

(n) Brain

Two types of common brain tumors are glioma and meningioma, accounting for approximately 75% of all brain tumors [88]. There is contradictory evidence regarding the relationship between smoking and gliomas or meningitis. In smokers, tobacco smoke is the largest source of N-nitroso compounds [89,90]. These compounds are associated with the development of tumors in the nervous system in animals [90,91]. Despite the role of nicotine in increasing the blood brain barrier permeability [92], whether N-nitrose penetrates into the brain or not is still unknown [93]. Considering that TS causes cancer in various organs of the body, tobacco smoke is thought to be effective in treating brain tumors [88]. However, the findings of most case-control studies have not shown evidence of increased glioma risk associated with TS [94–96]. Some other studies have shown RR increases, but these findings are not meaningful or limited to specific population subgroups [97–99]. In cohort studies, some findings also did not report a relationship between TS and brain tumors [100–102], while others reported a meaningful relationship only in women [103,104]. Meta-analysis study findings have recently shown that there is no relationship between cigarette smoke and glioma in general, though there was a slight, but significant increase in one cohort study entered into the analysis. For meningioma, some case-control studies did not report evidence of increased risk [96,102,105–108], and other studies reported association only in one sex [95,109,110]. In sum, there is no clear evidence of the link between tobacco smoke and glioma and meningitis, and further studies are needed.

(o) Gallbladder

Researchers believe that TS affects hepatobiliary system and is associated with increased risk of gallbladder cancer [111,112]. However, studies on the association between gallbladder disease and gallstone risk are as a mix. Several case-study and cross-sectional descriptive studies did not confirm the association [113–115] or even inverse relationship [116], while quantitative studies showed increased risk [117,118]. Some findings from these studies seem to be influenced by the selection or recall biased. Therefore, the final conclusion based on such studies is difficult and further studies are needed with more robust design, such as cohort studies.

(p) Hodgkin's disease

TS is one of the potential risk factors for the classic Hodgkin's lymphoma (CHL), which requires careful examination. Despite the limited number of studies in this regard, the findings of these studies are inconsistent. The findings of some studies have shown a significant decrease [119], some lack of association [120–123], and some significant increases [124–126] in overall HL risk in smokers. On the other hand, the discrepancy in the findings may be due to various methodological issues, including the low sample size of the study, the biases associated with the selection of the group, and the participants in the study and the uncontrollable confounders. Recently, the findings of three meta-analysis studies showed that TS increased the overall risk of HL [127–129]. Overall, it can be concluded that TS is one of the moderating risk factors for CHL types.

(q) Non-Hodgkin's Lymphoma

The findings of the early epidemiological studies on the role of smoking in non-Hodgkin's lymphoma have been disconnected. Some studies reported that smoking was associated with the incidence of this cancer [130–134], while others found that there was no relationship between cigarette smoke and non-Hodgkin's lymphoma [135–140]. Meta-analysis study findings in 2005 indicated that smoking is associated with a slight increase in non-Hodgkin's lymphoma (OR, 1.07; 95% CI, 1.00-1.15) [141]. Although smoking is generally unrelated to the risk of non-Hodgkin's lymphoma, there is much evidence that smoking can be associated with the follicular lymphoma subtype, especially in women [126,142–145]. More recently, cohort study findings showed that

people who were exposed to tobacco smoke 40 years or more became 50% more likely to develop non-Hodgkin's lymphoma than those who smoked 5 years or less [146]. There are more studies with more robust design like cohort studies in this area.

(r) Kaposi's Sarcoma

Kaposi's sarcoma is a relatively rare type of skin cancer that is common in humans. It is not activated in the normal state of the body, it can be considered an opportunistic disease [147]. The common feature of these diseases is its suppression by the immune system in the normal state of the body and its activation in the event of immunodeficiency. Unlike other cancers that smoke is a risk factor for them, it is known as a protective agent in this cancer [147,148]. However, many studies have not been done in this area.

The findings of the case-control study showed that there is a correlation between current cigarette smoking and a reduction in the incidence of Kaposi's sarcoma (OR, 0.20; 95% CI, 0.06-0.67) [149]. This inverse relationship is supported by reducing the risk of lung cancer in these patients [150-153]. In a cohort study, Nawar et al reported a lower relative risk (OR, 0.6, 95% CI, 0.5-0.9) in the incidence of Acquired Immune Deficiency Syndrome (AIDS) and Kaposi's syndrome in smokers [147]. Immunological effects of smoking are thought to reduce the risk of Kaposi's sarcoma. For example, nicotine can affect dendrite cellular function [154,155], and may cause cytokine changes and produce growth factor involved in Kaposi's sarcoma development [156]. However, according to a clinical trial that used nicotine skin patches for 15 weeks to improve skin lesions of Kaposi's sarcoma, it showed a small effect of nicotine [155]. Also, the findings of Guttman et al. And Conley et al. did not confirm the inverse relationship between smoking and Kaposi's sarcoma [157,158]. In general, given that most patients with Kaposi's sarcoma are often at an advanced age, their use of cigarettes increases the incidence of smoking-related illnesses and increases the mortality of these patients and thus cannot be considered as a completely protective factor to be considered [149]. On the other hand, in order to confirm the protective effect of smoking, the need for more comprehensive cohort studies is felt.

(s) Skin

Skin cancer is one of the most common and prevalent types of cancers in humans. Three major types of skin malignancies include basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and melanoma [148]. TS contains several carcinogenic compounds that affect at least 18 types of cancers [159] but have a reversible relationship with skin malignancies. Smoking can reduce the blood flow of the skin and stop the immune response, which increases the risk of skin cancer [160]; on the other hand, it can protect the inflammatory response induced by UV radiation and, therefore, reduce it. Risk of skin cancer [161-165]. his effect of smoking is relatively due to the prolonged effects of nicotine accumulation in human tissues that contain melanin [166]. Various studies have shown that transdermal delivery of nicotine suppresses inflammatory responses to sodium lauryl sulphate and UV-B [167,168]. Cohort study findings showed that in male ever smokers had less common risk of developing melanoma (RR = 0.72; 95% CI: 0.58-0.86) and BCC (RR = 0.94; 95) compared to those who never smoked. However, there was no significant relationship with SCC (RR = 0.99; 95% CI: 1.03-1.08) [148]. Findings from Mills Case Studies [168] and Kessides [164] also suggest that cigarette smoking has an inverse association with melanoma, although this relationship was not significant. Another study found that there was an insignificant decrease in the incidence of melanoma in men who were ever smokers (RR = 0.6; 95% CI: 0.3-1.1), but not seen in women (RR = 1.0; 95% CI: 0.3-1.1). [169].

(t) Thyroid

There is some evidence that smoking is a significant modifiable treatment that affects thyroid cancer. The findings of several case-control [170-173] and prospective [173,174] studies have

shown that there is an inverse association between thyroid cancer and smoking, but some studies did not confirm this relationship [175-177]. The findings of a meta-analysis study on five cohort studies indicate that there is an inverse association between current cigarette smoking and the risk of thyroid cancer. Based on this study, if the severity and duration of smoking is low in former smokers [178], the risk will be less. The findings of another meta-analysis study showed that the risk of thyroid cancer in current smokers decreased by 40% [179]. Compared to people who have never smoked or smoked, current smokers have lower levels of thyroid stimulating hormone (TSH) [180,181], Triiodothyronine (T3) [181] and thyroxine (T4) [180] and a lower prevalence of serum autistic thyroiditis [180]. T3, T4 and especially TSH play a major role in thyroid cancer [178,182]. Smoking is also effective in changing the levels of sex steroid hormones on thyroid cancer [183,184].

4. Conclusion

The purpose of this review study was to investigate the relationship between TS and especially smoking and common cancers. Based on the results of studies, TS is associated with an increased risk of lung cancer, Upper aerodigestive tract, esophagus, stomach, bladder, kidneys, colorectal, prostate, and pancreas. However, further studies are needed to confirm the association between TS and liver, cervical, brain, gallbladder, Hodgkin's disease, non-Hodgkin's lymphoma and hematologic malignancies. However, TS plays a protective role in the development of thyroid cancers, skin and Kaposi's sarcoma. Given that almost all of the risk factors for most cancers are TS, increasing the public's awareness of the harmful effects of smoking, implementing programs and policies to reduce smoking, can lead to a reduction in smoking and consequently reduce the resulting harmful consequences. There are also some limitations in this study. This review is not a systematic review and only English articles were reviewed.

5. List of abbreviations

AIDS: Acquired Immune Deficiency Syndrome; BCC: Basal cell carcinoma; CDC: Center for Cancer Prevention; CHL: Classic Hodgkin's lymphoma; CRC: Colorectal Cancer; LC: Lung cancer; PCa: Prostate cancer; RR: Relative risk; RCC: Renal cell carcinoma; SCLC: Small lung carcinoma; SCC: Squamous cell carcinoma; T4: Thyroxine; TS: Tobacco smoking; T3: Triiodothyronine; UADT: Upper aerodigestive tract.

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7. Funding

Not be applied

8. Authors' contributions

All authors contributed to the design of the research, Y.K, N.P.A, M.A, O.O, M.SE, extracted the data and summarized it. All authors drafted the first version. HSG, M.V and HS edited the first draft. All authors reviewed, commented and approved the final draft.

9. Ethics approval and consent to participate

Not be applied

10. Open Access

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11. Competing interests

The authors declare that no competing interests exist.

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