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Review

Oral cavity and lip cancer in the world: An epidemiological review

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ABSTRACT

Background: One of the most common cancers is squamous cell carcinoma of the head and neck which is a serious health challenge worldwide. Considering the importance of knowledge of incidence, death and risk factors in prevention programs, this study was conducted to investigate the incidence, mortality and risk factors for oral cavity and lip cancer in the world. **Methods**: A search was performed in Web of Science, PubMed and Scopus. The search keywords included: oral cavity or lip cancer, epidemiology, incidence, mortality, risk factors, and a combination of these terms. Studies that referred to epidemiological aspects of oral cavity and lip cancer epidemiology and risk factors were included in the review. **Results**: The five countries with the highest number of cancer of the oral cavity and lip included India, the United States, China, Pakistan and Bangladesh. The standard incidence of these cancers in the world was 4 per 100,000 people (in men versus women, 5.5 and 2.5 per hundred thousand, respectively). The five countries with the highest number of deaths from oral cavity cancer were India, China, Pakistan, Bangladesh and Russia. In 2012, the standardized death rate for this type of cancer was 1.9 per 100,000 people in the world (2.7 *vs.* 1.2 in every 100,000 of men *vs.* women, respectively). The most important risk factors for oral and lip cancer include tobacco smoke, alcohol drinking, viral infections, exposure to sunlight, and socioeconomic status. **Conclusion**: In order to reduce the burden of this cancer, there are the strategies for preventing risk factors such as tobacco and alcohol control, and vaccination against HPV infection to prevent oral cancers. Also, early detection by screening high-risk populations for oral cancer as well as risk reduction through training programs for physician and patients are effective.

Key words: incidence, epidemiology, oral cavity cancer, lip cancer, risk factor

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INTRODUCTION

Squamous cell carcinoma of the head and neck belong to a non-homogeneous group of cancers that are located at various places in the body[1] and are one of the most common cancers in the world with more than 450,000 new cases and 350,000 deaths annually[2]. Squamous cell carcinoma consists of oral cavity, oropharynx, nasal cavity, para nasal sinus, nasopharynx, hypopharynx, larynx, tongue, tonsils, parotid glands, salivary glands[3], and lip[4]. Each of the head and neck cancers is associated with various risk factors and prognosis[5]. The oral cavity is the most common cancer in the head and neck region[2], with an annual incidence of 300,373 and a mortality rate of 145,353[5]. Cancer of the lip is a typical malignant tumor that consists of 25 – 30 % of all cancers in the mouth[6]. Oral and lip cancer is a serious health challenge worldwide[4]. The incidence and mortality of this cancer is very different in various parts of the world and has a wide geographical variation. On the other hand, there is no comprehensive estimate of the incidence and mortality of this cancer. Considering the importance of being informed about the incidence, death and risk factors in prevention programs, this study aimed to determine the incidence, mortality and risk factors for oral cavity and lip cancer worldwide.

METHODS

A search was performed in Web of Science, PubMed and Scopus. The search keywords included: oral cavity or lip cancer, epidemiology, incidence, mortality, risk factors, and a combination of these terms. Studies that referred to epidemiological aspects of oral cavity and lip cancer epidemiology and risk factors were included in the review.

RESULTS

Incidence and mortality

Regarding the incidence and mortality rate of oral cavity cancer in the world, in 2012, there were a total of 300,373 cases of this cancer worldwide, of which 1989,755 were males and 101,398 were females[4]. The

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5 countries with the highest number of this cancer were India (with 77,003 cases), the United States (with 26,064 cases), China (with 21,413 cases), Pakistan (with 12,761 cases), and Bangladesh (with 10,550 cases)[4]. The standard incidence of oral cavity cancer in the world was 4 in every 3,000 people, 5.5 in men and 2.5 in women per 100,000 people[4]. In 2012, the global age-standardized rate (ASR) for lip cancer was 0.3 per 100,000 (0.4 in men and 0.2 in women)[7]. In terms of the number of new cases worldwide, most of the lip cancer cases (19.2 %) occurred in Central and Eastern Europe. At the national level, both Papua New Guinea and Australia had the highest ASR of this cancer, which was 8.9 and 2.6, respectively, per 100,000 people. Globally, Central and Eastern European countries such as Serbia and Ukraine ranked 4^{th} and 5^{th} highest, respectively, for lip cancer. The regions with the lowest incidence were in Eastern/ South-eastern Asia and sub-Saharan Africa. The incidence of lip cancer was higher among men than women, and this rate was 2.5 for men compared to women. Lip cancer in men and women older than 60 years old were 63.2 % and 69.9 %, respectively[7]. In 2012, the ASR for oral cavity cancer was 2.7 per 100,000 (3.7 in men and 1.8 in women per 100,000). New Zealand's Papua New Guinea had the highest ASR of oral cavity cancer, with 10.6 new cases per 100,000. However, the 2^{nd}, 3^{rd} and 4^{th} countries with the highest ASR for oral cavity cancer were Maldives, Sri Lanka and Pakistan (predominantly South Asian regions). The lowest incidence was observed in Oceania (for men) and in East/ South-east Asia (for women)[7].

In 2012, there was 145,353 mortalities from oral cavity and lip cancer worldwide, of which 97,940 were men and 47,413 were women. The five countries with the highest number of deaths from oral cavity cancer were India (with 52,067 deaths), China (with 11,333 deaths), Pakistan (with 7,266 deaths), Bangladesh (with 6,071 deaths), and Russia (with 5,658 deaths). In 2012, the standardized death rate for this cancer in the world was 1.9 per 100,000 people (2.7 in men and 1.2 in women for every 100,000)[4]. In 2012, cancer of the oral cavity and lip was the 12^{th} most common cancer in Asia and was the 8^{th} highest among cancers in men. Lip and oral cavity malignancy is the 2^{nd} most common cancer among men in South Asia. In fact, in 2012, Sri Lanka had the highest ASR of South Asia; this cancer was the most common among men in this country[8]. In Australia, lip and oral cavity ranked as the 9^{th} most common cancer among men with a standardized incidence age of 8.8%, while in New Zealand, it ranked as the 14^{th} most common cancer among men with an ASR of 5.5 per 100,000. Papua New Guinea and Solomon Islands reported a high incidence rate of oral cancer due to tobacco and paan, while Vanuatu Island showed lower incidence[8,9].

RISK FACTORS FOR ORAL CAVITY CANCER

Tobacco

Excessive use of tobacco (both smoked and chewable) is a potential risk factor for oral cavity cancer[10]. The onset of consumption, duration and frequency of chewing of bidis or smoked cigarettes on a daily basis are strongly linked to oral cancer[11].

Smoked tobacco

Smoked tobacco is a risk factor for the upper respiratory tract[12], and there is a positive relationship between the risk of using tobacco smoke and oral cavity cancer[13,14]. This relationship has been confirmed in several studies[15–17]. The risk for oral cavity cancer in people who use tobacco is 1.4 – 1.7 times higher than those who do not consume tobacco[15–18]. Several case-control studies have reported that the lower the age of tobacco consumption onset, the higher the risk for oral cavity cancer[19,20]. A study in India illustrated that the risk of oral cavity cancer in traditional tobacco (bidi, chutta and cheroot) users is twice as high as industrial tobacco users because traditional tobacco has a higher alkalinity and carcinogenicity[21].

Smoke-free tobacco

Toxicants in smoke-free tobacco appear to increase the risk of oral cavity cancer[12]. The risk of oral cavity cancer depends on the length of time[22], duration of use[12], and onset in the early age[22].

Exposure to tobacco smoke

Studies of the association between the effects of environmental exposure and tobacco smoke and the risk of oral cancer cavity are scarce[12]. In a study conducted on the relationship between tobacco smoke in the home or workplace with oral and pharyngeal cancers, it was found that the risk of oral cavity cancer

was lower than that of pharyngeal cancer (not significant), and that the unauthorized use of tobacco for more than 15 years had no risk for oral cavity at home or in the workplace[23].

Marijuana smoke

Marijuana increases the risk of oral and lip cancer[24]. Marijuana is mostly smoked with carcinogenic smoke included aromatic multi-ring hydrocarbons, which can be higher than those in tobacco smoke[25]. Generally, marijuana consumers are tobacco or alcohol consumers[26].

Alcohol consumption

The risk of oral cavity malignancy is increased by drinking alcohol; the higher the daily intake and duration of use, the higher the risk of oral cavity cancer[12]. Alcohol consumption of more than 150 g per day extends the risk of oral cavity cancer[27]. On the other hand, studies conducted on the relationship of age of onset of alcohol consumption and the risk of oral cavity cancer have shown that the risk of this cancer is elevated if the age of alcohol consumption begins in the teenage years[22,28].

Paan (betel quid chewing)

Paan consumption also increases the risk of oral cavity cancer. Paan contains arecanut, betel leaves, slaked lime (which may include tobacco); other ingredients (such as spices, sweets and essence) may be added to the paan, according to taste[29]. The use of paan and gutkha is abundant in most countries and is difficult to control it despite that fact that excessive use of both causes cancer[30]. In Asia, taking paan with or without tobacco is a stronger risk factor than tobacco or alcohol[31,32]. In fact, the risk of oral cavity cancer in people who consume paan is about 1.5 -3 times greater than that of tobacco consumption and about 2-11 times greater than that of alcohol consumption[31–33]. Due to the lack of awareness and education, people who generally use paan and gutkha are not aware of their harmful effects. Generally, they believe that these products are used to clean the mouth (like mouthwash), help digestion, aid germ astringency, and boost or relieve the mood[34].

Diet

It seems that inequality in the diet (or its misuse) is responsible for 11-15% of oral cavity and larynx cancers[12]. Low consumption of vegetables and fruits increases the risk of oral cavity malignancy[35,36]. As well, red meat consumption of greater than once a week elevates the risk of oral malignancy compared to white meats like chicken and fish[10]. Moreover, the use of hot drinks such as tea can increase the risk of oral cancer, which may be due to repeated heat damage due to mucosal contraction of the oral cavity[10,37]. Regarding the consumption of coffee, the results of the studies have been contradictory[12].

Body Mass Index (BMI)

In some studies, weight gain has been reported as a protective factor, but weight loss has been reported as a potential risk factor for oral cavity cancer[38].

Human papillomavirus and sexual behaviors

Viral papillomavirus infection is one of the most principal causes of squamous cell carcinoma of the head and neck[39,40]. The apparent increase in the incidence of oral HPV in the general population has been observed, which has led to an increase in concerns about human papillomavirus (HPV) infection and the risk of oral cavity cancer[41,42]. The number of sexual partners plays a main role in the transmission of the HPV virus, which can increase the risk of oral cancer[43]. About 25 % of cases of oral cavity cancer are related to HPV[44,45]. Given the recent global trend of oral HPV infections, the incidence of oral cancer is expected to increase in the coming decades[46].

Family history of cancer

Family history of oral malignancy in different populations may depend on various environmental and genetic factors, including the prevalence of genetic dissimilarity in genes and exposure to diverse environmental factors[47]. This variation is more dependent on differences in exposure to tobacco and alcohol, which are very significant factors for oral cavity cancer[48]. Furthermore, genetic polymorphisms can expand the sensitivity of oral carcinoma through interactions with alcohol, tobacco and possibly diet components[47]. Besides, the use of these can be the reason for oral cavity carcinoma[49]. These finding indicate genetic instability is a risk factor for oral carcinoma[49].

Oral and dental health

Oral health behaviors are a risk factor for oral cavity cancer[10]. Various factors have been used to assess oral and dental health; these include daily brushing, used materials, number of teeth lost, number of filled or damaged teeth, frequency of check-ups, gingival bleeding, and overall teeth status[12]. Missing more than five teeth is considered as an indicator of increased risk for oral malignancy[10]. Effective brushing eliminates dental plaques and subsequently improves oral and dental health; therefore, it reduces the risk of cancer of the head and neck region[50]. Dental plaque is a reservoir for the growth of pathogens and the production of nitrosamines that help to increase inflammation of the mouth[10]. Regular brushing can eliminate dental plaque, alcohol, nicotine, fungi, nitrosamines, and other toxic toxins, thereby delaying or preventing carcinogenesis[10].

Use of mouthwash

The relationship between alcohol mouthwash and oral cancer growth over the past decade has been the topic of debate[12]. Some studies have confirmed a positive relationship between mouthwash and oral malignancy[12]. However, the concentration of alcohol in the mouthwash has not been sufficiently evaluated[12].

Oral mucus diseases

Potentially malignant oral disorders such as leukoplakia, submucous erythroplasia T fibrosis, lichen planus, and chronic oral candidiasis may increase the risk of squamous cell carcinoma[51,52]. Some systemic diseases can have an effect on oral health, leading to malignancy or even cancer of the mouth[12]. Although most oral lesions are benign, many of them may appear with potential abnormalities in the mouth[46]. One of the most common oral lesions is squamous cell papilloma - a malignant, neuromuscular lesion that is swollen and usually has a monopoly of small white or red designs on the surface[53]. Also, lesions of the oral cavity of leukoplakia are also white plaques that can be considered as potential lesions[46].

Social inequality

According to the study, the risk of oral cavity cancer is higher in the lower classes[12].

Occupational exposure

In many occupations and industries, the risk of this cancer has been observed. The relationship between exposure to perchlorethylene (organic solvents used in cleaning laundry) and oral cavity cancer has been demonstrated[12]. An increased risk of this cancer in India has been confirmed among male farmers and industrial laborers[12]. Also, in one study, an elevated risk of this cancer was observed among male workers who worked at a cane factory in Puerto Rico[12].

RISK FACTORS FOR LIP CANCER

Exposure to sunlight

Exposure to sunlight is a principal risk factor for lip cancer[54]; it increases the incidence of illness in people who are working outdoors or live in the countryside[55]. In particular, UV — especially UVB (wavelengths of 320 – 900 nm) — is considered as the most salient environmental factor. UVA (wavelength 320-400 nm) may also play a role in carcinogenesis[56]. Evidence related to the association between exposure to sunlight and lip cancer has been shown through examinations of changes in lip cancer that are associated with sun rays and ethnic characteristics[55].

Tobacco smoke

Smoking is a principal risk factor for lip cancer, which can affect both lips equally[57]. Malignant lesions typically occur in a place where the cigar or pipe cigar is placed[58]. Traditional tobacco smoking, especially pipe smoking, is related with lip cancer. The nitrosamines found in tobacco are one of the main carcinogenic agents for cancer induction[56].

Viral infection

Viruses are one of the most important features in the development of this cancer[57]. The relationship between this cancer and herpes labialis infection has been observed. Herpes simplex virus type 1 and also HPV (especially HPV-16) have the potential for carcinogenicity[56]. The most common pathogenesis of lip cancer is the recurrence of herpes virus[57].

Race

People with bright eyes, hair and skin are at high risk of lip cancer[56,57]; about half of cancers occur in the North European countries[59]. Lip cancer is negligible in people with darker skin and among blacks and

Eastern folks[56,57]. This variation is due to the natural pigmentation of the natural melanin at the vermilion border, which is found in non-white races and creates a protection against sunlight[56].

Familial and genetic factors

Genetic or familial factors are one of the factors which contribute to the development of lip cancer[57]. Different diseases are more common among relatives than ordinary people[59] and it has been proven that there is an inherited basis for lip cancer. Also, the exposure to common risk factors, such as environmental exposure, increases the risk of inheritance and family life[56].

Immunosuppression and immunodeficiency

An increase in the prevalence of various malignancies has been reported in transplant recipients[56]. Kidney transplant patients in immuno-suppressive states have reported the most prevalence of obstructive and malignant lip lesions among renal transplant patients[57]; indeed, the risk of lip cancer increases with long-term treatment of immunosuppression[56].

Occupation

Exposure to sunlight, especially outdoor activity, is a risk factor for lip cancer[60]. Fishing, agriculture, forestry and agriculture, creosote exposure, and work in the greenhouse are linked to lip cancer[56,57]. The number of cases of lip cancer in men is greater than that of women, which may be related to occupation and behavioral differences between the sexes since a high percentage of men work outdoors[58]. Some researchers believe that using lipstick could act as a protective agent, contributing to the observed gender differences[61].

Residential area

Lip cancer is more common in people living in rural areas than those living in urban areas, and the most likely cause is exposure to sunlight[62].

Socioeconomic status

Low socioeconomic status is strongly related to the high risk of lip cancer. However, the correlation between socioeconomic status and other risk factors (such as high smoking, rural and occupational status) may increase the risk of lip cancer[56,57].

CONCLUSION

The aim of this study was to determine the epidemiological aspects and risk factors of oral cavity and lip cancer in the world. Findings of the study showed that the five countries with the highest number of oral cavity and lip cancers were India, the United States, China, Pakistan and Bangladesh. The standard incidence of these cancers in the world was 4 per 100,000 people (in men 5.5 and 2.5 in women per every 100,000). The five countries with the highest number of deaths from oral and lip cancer were India, China, Pakistan, Bangladesh and Russia. In 2012, the standardized death rate for oral and lip cancer in the world was 1.9 per 100,000 people (2.7 in men and 1.2 in women per every 100,000). Excessive use of tobacco (both smoked and chewable), marijuana smoke, alcohol consumption, diet, and body mass index are all risk factors for oral cancer. It seems that other factors, including HPV infection, genetic or family factors, oral health behaviors, systemic diseases, social inequalities and occupational exposures, are all considered as risk factors for oral cavity cancer. Exposure to sunlight, tobacco smoke, viruses, and racial variations play an important role in the progress of lip cancer. Also, genetic or family factors, immunosuppressive regimens, occupation, place of residence, and socioeconomic status are the most salient factors contributing to the development of lip cancer. In general, in order to reduce the burden of this cancer, strategies for preventing risk factors, including through controlling tobacco and alcohol use, vaccination against HPV infection to prevent oral cancer, early detection of screening of high-risk populations, and risk reduction through training programs for physician and patients, can all be effective.

ABBREVIATIONS

ASR: Age-standardized rate

BMI: Body Mass Index

HPV: Human papillomavirus virus

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COMPETING INTERESTS

The authors declare that they have no competing interests.

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