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An Overview and Comparative Evaluation of Head and Neck Cancer Risk Factors in India and Australia

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Abstract

Aim: An overview and comparative evaluation of head and neck cancer risk factors in India and Australia. **Method:** In this review we included articles with information on head and neck cancer risk factors and its association based on: smoking tobacco, alcohol, smokeless tobacco, betel nut and areca nut chewing, viral infection like HPV, dental hygiene, diet, family history, socioeconomic status, other heavy metals and systemic conditions. Articles with clinical features, diagnosis, treatment and prognosis were excluded. **Results:** Head and neck cancer in India has different demographic, risk factors, dietary habits, personal and family history. Oral cancer is more common amongst all head and neck squamous cell cancers in males. This is mainly attributed with consumption of a variety of smokeless tobacco, smoking, alcohol, poverty, illiteracy, cultural, advanced stage at presentation; lack of good treatment infrastructure creates main challenge to India as compared to Australia. **Conclusion:** The knowledge about risk factors for HNC in public health education for general population supports health promotion and tobacco prevention, which is the main aim of the programs started by the government, as head and neck cancers are potentially preventable.

Keywords

Head and Neck Cancer, Oral Cavity, Oropharynx Smoking and Smokeless Tobacco, Alcohol, HPV, Oral Hygiene, Other Risk Factors

1. Introduction

Worldwide, the head and neck cancer (HNC) is the 6th most common cancer; as

it is considered a lethal disease affecting the upper aero-digestive tract and near about 0.9 million new cases have been diagnosed each year [1] [2]. With 0.47 million cases diagnosed per year in India alone, HNCs are the second most common cancers in the Indian population by National Institute of Cancer Prevention and Research [3]. India contributes up to more than 8% of the global cancer burden and deaths [4]. Developed countries like Australia present with a maximum 40% of patients with advanced disease whereas prevalence in developing countries like India is >60% of these patients [5].

The incidence of HNC seems to be 12.3 per 100,000 in Australia and 22 per 100,000 population in India, also accounts for about 30% of all types of Indian cancers [6] [7]. HNC is the most common cancer of males in India and the fifth most common in females [8]. Great difference in mean age of presentation lies in the 5th-6th decade for the Indian population as compared to 7th-8th decade among the Australian population, also more frequently diagnosed in males than females [9]. In India, 90% - 95%, whereas, in Australia more than 90% of HNC originates from the mucosal lining of the mouth and oropharynx, hypopharynx, larynx, sinonasal tract, and nasopharynx [10].

Most of the HNC cases and deaths are due to the cigarette smoking and alcohol consumption in the global population, which are the major risk factors, along that it has synergistic effect in increasing oral cancer risk whereas smokeless tobacco (SLT), betel nut, and human papilloma virus are etiological agents responsible for it in the Indian population [11] [12]. The various forms in which SLT is used in developing countries include khaini, mava, paan (betel quid), zarda, snuff, mashiri, etc. [13]. The prevalence of HNC in India has different demographic profiles, risk factors, dietary habits, socioeconomic conditions, lifestyles and family history [14]. High incidence of the oral and oropharyngeal cancer is observed among native Australians [15]. Many epidemiological evidences strongly report that many risk factors are not only causal but also associated with an increased risk of HNC occurrence [16].

In India, nearly two-thirds of patients present with advanced stages [17]. Despite advances in treatment methods for HNC, the present treatments improve the quality of life of head and neck cancer patients but the overall survival rate of 5 years has not improved in the past decades [18].

Major aim of this article is comparative evaluation of published data about the prevalence of risk factors for head and neck cancer in India and Australia.

2. Methods

We collected data from published literature by carried out a organized search using key words with risk factors, tobacco, alcohol, betel nut chewing, human papilloma virus, environmental factors and other risk factors for HNC from Medline, Pubmed and Google Scholar using a combination of subject headings and keywords.

In this review we included articles with information on head and neck cancer

risk factors and its association based on; smoking tobacco, alcohol, smokeless tobacco, betel nut and areca nut chewing, viral infection like HPV, dental hygiene, diet, family history, socioeconomic status, other heavy metals and systemic conditions.

We selected the articles carefully after reading abstract and titles to determine whether, they were completely fitted the inclusion criteria for the review. In addition to this, we also studied the references of related articles to find more literature. Articles with clinical features, diagnosis, treatment and prognosis were excluded. Figure 1 shows the flowchart for selection of the articles.

	Inclusion Criteria
1)	Web-based search from Medline, Pubmed and Google Scholar
2)	Carefully review of titles and abstract of selected articles are available in English and limited to human research
3)	Articles reporting data on association between HNC, HNSCC and risk factors: (about smoking tobacco, alcohol, smokeless tobacco, betel nut and areca nut chewing, viral infection like HPV, dental hygiene, diet, family history, socioeconomic status, other heavy metals and systemic conditions, HNC, HNSCC) completing inclusion criteria
4)	Selected relevant studies for this review article
	Exclusion Criteria
1)	Articles with clinical features, diagnosis, treatment, prognosis, and case reports were excluded.

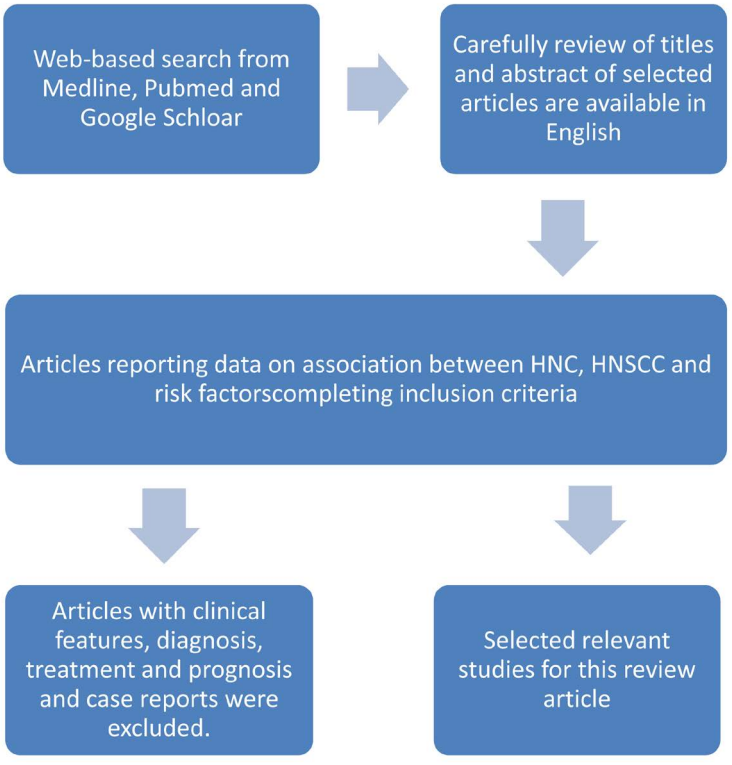

Figure 1. Flowchart for selection of the literature.

3. Risk Factors

3.1. Tobacco Use

Tobacco is deadly in any form and its use already has become responsible for more than 6 million deaths worldwide each year. According to the World Health Organization (WHO) estimates, globally, there were 100 million premature deaths due to tobacco in the 20th century, and if the current trends of tobacco use continue, this number is expected to rise to 1 billion in the 21st century [19]. Jha *et al.* have estimated that around 1 million deaths a year in India will be attributable to smoking by the early 2010s [20]. India's tobacco problem is very complex, with a large use of a variety of smoking forms and an array of SLT products are the most common cause of HNSCC [21].

In India tobacco smoking in the form of cigarettes, bidis, cigars/chutta/cheroot, dhumti (Goa), the water pipes/hookah (north India), reverse chutta smoking (in coastal regions in Andhra Pradesh and Orissa), hookli (Gujarat) and chillum (northeastern parts of India). Estimates indicate 57% of men and 11% of women between 15 - 49 years of age use some form of tobacco and an estimate of the Global Adult Tobacco Survey (GATS) conducted during 2009-10 indicate that 34.6% of the adults (47.9% males and 20.3% females) are current tobacco users. 14% of the adult smoke (24.3% males and 2.9% females) and similar number of students, whereas in Australia daily smoking rate for smokes is 17% in 2007 and around 70% of laryngeal cancers are attributed fully or in part to tobacco smoking [22] [23]. In Australia, the rate of smoking is approximately 15.1%, whereas in the Northern Territory is considered the highest smoking rate near 50% as compared to any state or territory in Australia [24].

Studies on bidi smoking, the most common form of tobacco smoking in India, provide a strong association of bidi smoking with risk of developing cancer is 5 - 9 times greater than for nonsmokers at various sites, such as oral cavity, pharynx, and larynx, which is further multiply about 17 times for heavy smokers of 80 or more per day [25]. Pednekar *et al.* in their Mumbai cohort found that the prevalence of oral cancers was 42% raised among bidi smokers as compared with cigarette smokers [26]. A study showed that cannabis smoke used in different Australian regions have a carcinogenic and mutagenic potential because it contains a higher level of carcinogens than cigarette smoke [27].

3.2. Smokeless Tobacco (SLT)

Many different forms of smokeless tobacco are used in India, which are very popular in large number of people. Among them, the use of betel quid chewing (pan) is extremely widespread in many regions of India. Along with this, gutka, khara, mawa, zarda, and khainni, are mixes by vendors and are all dry mixtures of areca nut flakes, lime, tobacco power [28]. It is also used as a moist snuff containing lime with tobacco, vegetable oil and water (Naswar/Nass), mainly according to local traditions and for the purpose of enhancing flavor and also in the form of dried tobacco powder applied on gums and teeth [29].

About 10% of the world's population chews betel quid regularly and most prevalent in Asia-Pacific region but use of betel quid is not quite relevant to Australia [30] [31]. Areca nut alone is a long-established carcinogen and causally connected with a premalignant condition known oral submucous fibrosis (OSMF) and oral cancer [32]. Areca nut use is very exceptional in the Western world due to its scarcity. In India alone, five million people (0.5% of the population of India) have OSMF [33]. In Australian native citizens are changing from alcohol to cannabis utilization since the restrictions on alcohol in remote communities; thus there is an epidemic of cannabis use in remote Indigenous communities in the Northern Territory [34].

Australian immigration statistics show that 30% of new arrivals in Australia (New South Wales) are from Indian subcontinent, China, and Taiwan, are more likely to be responsible for this tradition of tobacco chewing, as they are closely connected to sociocultural and religious activities long after they migrate to Australia [35]. Univariate analysis revealed that, in terms of oral dipping products, the risk was 7.3 for consumption of gutka, 5.3 for consumption of chewing tobacco and 4 for consumption of supari (pure areca nut) and the minor risk was found for mishiri [36].

3.3. Alcohol Consumption

Drinking alcohol on regular basis is an important risk factor for HNC and it is associated with an increased risk, which is dose-dependent. A regular consumption of 4 - 5 drinks daily, increase oral cancer risk by 2 - 3 folds than non-drinkers but, in case of heavy alcohol drinking risk increase up to 7% to 19% oral cavity cancer [37]. A prospective study in India has found that alcohol consumption increases the incidence by 49% among current users and 90% in past drinkers [38]. According to Ferlay, oral cavity cancer has its highest rates of incidence in Western Europe, India, South Africa and Australia. In 2008 the Australian Department of Health reported that Australia is 30th highest alcohol-consuming country of 180 countries worldwide [39] [40].

The consumption of alcohol was very high in India; in 2016 11.4 L per capita per year with age above 15 years old and among them 30% are regular and 11% moderate to heavy drinker. However, the consumption is very high in the Northern Territory: approximately 15 L and New South Wales 13 L of pure alcohol per year have been consumed by adults (≥15 years old) [41] [42].

3.4. Alcohol in Combination with Smoking

Taking alcohol in combination with tobacco in any form further enhances risk of oral cancer by 11 times [37]. A study conducted in northern India on oral cancer (buccal and labial mucosa) showed that alcohol alone had a nonsignificant odd ratio of 2.7, however there was a significant odd ratio seen with alcohol with bidi smoking (8.5), alcohol and pan tobacco chewing (20), and with alcohol, pan, and smoking altogether (31.4%) [29].

3.5. Human Papilloma Virus (HPV)

The human papilloma virus (HPV) has been identified as an etiological factor in HNC mainly oropharyngeal cancer [43]. The overall prevalence of HPV is about 50% globally and their incidence increased by 25% in last 20 years and is the third predominant risk factor for HNSCC with the highest prevalence in cancer of tonsil and base of tongue [44].

HPV-16 is the most common genotype, occurring in 90% of high risk HPV oropharyngeal carcinomas [45]. In India HPV incidence ranges from 33.6% in the Eastern region to 67% in South India and 15% in Western India. A study showed a rate of HPV infections of 56.3% in cancers of the mandible, 37.5% in cheek, and 38.6% in maxilla are reported in the advanced stages (III, IV) had higher infection rates as compared to earlier stage. Lesions of the tongue had the highest rate (9 of 11) of HPV infection [46].

Within Australia, 8844 cases of HPV-related oropharyngeal cancers were diagnosed between 1982 to 2005. This particular study reported that the incidence of HPV-related cancers significantly increased annually among both males (1.42% per annum) and females (1.04% per annum) P value < 0.01 [47].

Increase in incidence found with use of newer techniques that could be helpful for 45% (26 of 57) of tumors tested were positive for P16 in patients from the Northern Territory in Australia; however, 63% of those were Indigenous Australians [41] [48]. The prevalence of HPV-related HNC in Australia is currently increasing; this trend may be attributable to changes in sexual behaviors, particularly oral sex [47]. Synergistic association between HPV and other notable risk factors (alcohol consumption and smoking) remains controversial [49].

The vaccination of HPV has not been incorporated in the national immunization program of India. There is dispute about using the HPV vaccine in Australian men; it is currently indicated for use in young women. In Australia, the current HPV vaccination program for females aged 12 to 13 years was introduced in 2007 and may have an effect on the future incidence of these cancers [50].

3.6. Oral Hygiene

Poor oral hygiene also causes oral cancer. In one study, more than 85% of oral cancer patients had poor oral hygiene [7]. Poor oral hygiene related attributable risk is around 32% for men and 64% for women in India. Patients wearing poorly fitting or defective complete dentures for more than 15 years and not visiting a dentist regularly were highly associated with oral cancer but, least has occurred in Australian population who has received dental care [51] [52]. Periodontal disease has been found in connection with OSCC [53].

However, In India oral precancerous conditions are also prevalent which are helpful in diagnosing majority of oral cancer cases and exclusively present in tobacco users.

Oral lesions that have been identified clinically as having potential for malignant conversion include leukoplakia, erythroplakia, lichen planus, and submuc-

ous fibrosis. Reported rates of malignant transformation of leukoplakia range from less than 1% to 18% [54]. Erythroplakias are the most severe and carry a much greater risk of malignancy transformation followed by leukoplakia with 0.13% to 10% whereas in Australia malignant transformation rate of leukoplakia is approximately 1% but OSMF has highest transformation about 17% considered as important factor in the raising incidences of oral cancer in people 35 years and below in India [29].

3.7. UV Radiation

Ultraviolet (UV) light exposure may cause HNC, particularly lip cancer, is mainly caused by UVB (290 - 320 nm) irradiation due to increased exposure of the mucosal linning of the lips to the sun and cancer in the lower lip occurs in around 90% of all cases [55] [56]. A high incidence of lip cancer has been reported among whites and is about 3 times higher in men than in the women, which may be due to more outdoor occupations, smoking, and sun exposure among men. The variations in the incidence of lip cancer in the Australian states are probably attributable to differences in the rural and urban populations with respect to exposure to UV as a risk factor [55] [57].

In Australia, more than 50% of HNC in white people are located on the lip. [58]. However, HNC of the lip is not very common in nonwhite populations, in particular Indigenous Australians [59]. The reported incidence of skin cancer of HNC in India is less than 1% of all the cancers. BCC is the commonest skin cancer worldwide, but in India SCC as the most prevalent skin malignancy [60]. The incidence shows an inverse relation with the degree of pigmentation, presumably due to protective effect of eumelanin on ultraviolet light (UV)-induced damage [61].

In Western Australia annual incidence of lip cancer was 8.9 in 100,000 and 2.7 in 100,000 for males and females, respectively, from 1982 to 2006 [62].

3.8. Nutrition and Socioeconomic Status

Different studies in last few years showed diet has come into view as a risk factor of HNC along with tobacco smoking, alcohol intake and HPV [50]. A study in India showed that regular consumption of fruits and green leafy vegetables reduces risk by 2 folds as compare to butter and pulses for HNC [63]. Taking daily diet rich carbohydrates, vegetable oil, fish, fruits, vegetables and lean meat decrease risk of oral cancer by 50%, on the other side, too much meat consumption was considered to be a risk factor for many HNC [64].

According to the UN report published in 2017, India is home to 190.7 million underfed people, 51% women are anemic and more than 50% of elderly people of India are suffering from malnutrition but there is hardly any published quantitative data on the nutritional status of Indigenous Australians. Prevalence of malnutrition in Australia was reported at 2.5% in 2015, on average, daily smoking rate 3 times more in the lower socioeconomic group then higher [65] [66].

India is classified as a lower-middle-income group country by the World Bank. 90% of the oral cancer patients in rural areas belong to the lower or lower-middle socio-economic class, and 3.6% are below the poverty line based on Pareek's classification [67]. Around 80% of patients with cancers present with advance-stage incurable disease and hence increased mortality. Big reason for delayed diagnosis is the lack of easy access to healthcare, respectively further reasons included poor socio-economic status of the patient, cost of care, and high rate of illiteracy [68].

Brookes reported a significant difference between the survival of undernourished HNC patients (7.5% at 2 years) and the survival of adequately nourished patients (57.5% at 2 years) undergoing radiotherapy [69].

3.9. Family History and Genetic Susceptibility

Genetic susceptibility might play a role in the progression of cancer, but those that have revealed a high risk for HNC with respect to family history of cancer. A first-degree relative is a family member who shares about 50 per cent of their genes with a particular individual in a family beside this a higher risk of oral cavity cancer in males with a family history of smoking-related cancers than in females [70].

The prevalence of the p53 mutation is 81% in the Western world but rare in India. Multiple genetic abnormalities are common in head and cancers in India and Southeast Asia. These include a prevalence of Ha-ras mutations (35%), loss of heterozygosity of Ha-ras (30%), N-ras amplification (28%), and N-myc amplification (29%) [71].

4. Other Risk Factors

Environmental and occupational factors including asbestos, wood dust and leather dust can also contribute to some HNC, including in the larynx and pharynx [72].

In India large number of population dealing with Plummer-Vinson syndrome is associated with a high risk for development of carcinoma of oral cavity, oropharynx and esophagus [23].

Immunosuppressive conditions increase risk of developing oral cancers in a number of patient undergone kidney transplantation, lip cancer in patients suffering from AIDS oral carcinoma has been reported [73].

Australian diabetic patients consistently seemed to be more likely to have distant metastases of cancer at the time of diagnosis and it is involved as a risk factor not only for the development of HNC but also for oral premalignant lesions such as leukoplakia [74].

5. Conclusions

This review gives an idea that major risk factors are lifestyle, behavioral and environmental associated in developing various HNC in population of India and Australia.

In India, the illiteracy, lack of infrastructure and health care facilities, are major problems. Lack of awareness is more common in the lower socio-economic class about the side effects of tobacco, and prevalent cultural beliefs lead to delay in seeking treatment and result in advanced-stage presentation of disease. People in Australia more aware about symptoms and government provide better cancer treatment facilities and early diagnosis and treatment.

The knowledge about risk factors for HNC in public health education for general population supports health promotion and tobacco prevention programs by the government, as HNC are potentially preventable.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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