ORAL CANCER: AN OVERVIEW

1Dr. Imran Ahmad, 2Mrs. Rakhi Ahuja, 3Dr. Mukesh Savaria, 4Ram Iswar Sah, 5Dr. Shabnam Ansari
1Post-Graduate Student of Master in Public Health, 2Assistant Professor in DPSRU, 3Post-Graduate Student of Mater in Public Health, 4Post-Graduate Student of Master in Hospital Management, 5PHD (Scholar)
1Department of Public Health, 2School of Allied Health Sciences, 3Department of Public Health, 4Department of Hospital Management, 5Dept. of Biotechnology
12345Delhi Pharmaceutical Sciences and Research University, New Delhi, India

ABSTRACT

Oral cancer is the 6th most common malignancy in whole world. Oral cancer is the biggest deal with in Southeast Asia primarily because of the prevalent oral habits of betel quid chewing, smoking, and alcohol intake. Although recent advances in cancer diagnoses and therapies, the 5-year survival rate of oral cancer patients has remained at a dismal 50% in the last few decades. This paper is an overview of the various etiological agents and risk factors involved in the development of oral cancer.

KEY WORDS
Oral cancer, risk factors, pathology, investigation, treatment.

INTRODUCTION

Oral cancer constitutes a major public health problem, with more than 300,000 cases reported annually worldwide. Exposure to tobacco, smokeless tobacco products (including areca nut and betel quid) and alcohol constitute the main risk factors associated with the development of oral cancer. High-risk human papillomavirus (HRHPV) has also been identified as an important emerging risk factor for oral cancer. Despite advances in the diagnosis and treatment of cancer, a low survival rate for tobacco and alcohol associated oral cancers (about 50%) has been observed during the past few decades in many European countries. The lack of information about the causes and knowledge of signs and symptoms of oral cancer is often stated to be a factor related to the late diagnosis of this tumor. In a national study conducted in the United Kingdom a serious lack of public awareness of this cancer was reported. Oral cancer refers to cancers of the tongue, gingiva, floor of the mouth, palate, vestibule and retromolar area. The five-year survival rates for oral cancer range between 50 and 80% depending on the stage of the disease, varying from 86% for stage I to 12-16% for stage IV. Cancer of the head and neck largely affects an older population, with males more frequently affected than females. Lifestyle factors, in particular tobacco smoking, alcohol consumption and use of betel quid are implicated in the etiology. Alcohol intake may be
related with a higher prevalence of cancers involving the floor of mouth, tongue and buccal mucosa and a synergistic effect between alcohol and tobacco use has been documented.\cite{10} The evidence for the involvement of human papillomavirus in the etiology of oral cancers suggests that it may be a co-factor, particularly in the development of carcinoma of the oropharynx in younger populations.\cite{11}

An Indian male prisoner’s study, tobacco use and oral cancer knowledge, it was found that knowledge related to oral cancer did not impact on decisions regarding tobacco use. \cite{12} Mouth self-examination to improve oral cancer awareness and early detection in a high-risk population was tested in an Indian community. \cite{13}

Global annual incidence of oral cancer is estimated as 529,500\cite{14}. Oral cancers have shown little improvement in survival statistics across three decades \cite{15,16}. An estimated 9750 deaths in the upcoming year are predicted in the United States alone.\cite{17} A gap in patient knowledge and health literacy surrounding oral cancer, specifically related to risk factors and symptomology, is posited to be among the key modifiable factors contributing to high morbidity and mortality.\cite{18} Tobacco use and alcohol are estimated to play a contributory role to 80% of all incident oral cancer.\cite{19} Additional contributory risk factors, including oral hygiene and dietary habits are also frequently under-recognized by patients. Symptomology surrounding oral cancer also tends to be poorly understood by the patient population. Established symptoms of oral cancer include a non-healing ulcer, visible red or white patches, mouth swelling, and tongue soreness.\cite{19}

Oral cancer is considered to be a major public health issue due to the relatively low 5-year survival rate of 61 %, the lowest of all major cancer types.\cite{20} Late diagnosis, usually in stages III and IV, has been implicated as the primary reason for the low survival rate for patients with oral cancer\cite{21,22}. With roughly one person dying of oral cancer each hour and an estimated 7,900 total deaths in the United States in 2010, it is a major burden within the overall disease incidence in our population\cite{20}. Use of tobacco and alcohol products, as well as infection with the human papillomavirus (HPV), have been implicated as the primary risk factors for oral cancer. Thirty to forty years ago the ratio of men to women with oral cancer was 6:1, now it is 2:1\cite{20}. Individuals with low socioeconomic status (SES), elderly, and African-American males are disproportionally over-represented in the incidence rates of late-stage oral cancer at diagnosis, resulting in high mortality for these individuals \cite{24,25}. Low SES, defined by low education attainment and income levels, is a major oral cancer determinant due to associated factors such as limited access to care, increased exposure to environmental carcinogens, poor nutrition, and higher tobacco and alcohol consumption\cite{25,26}. According to the Surveillance Epidemiology and End Result (SEER) data for the years 2005–2009, median age at diagnosis for oral cancer was 62 years old and 70.7 % of those diagnosed were over 55 years old \cite{20}. While the socioeconomically disadvantaged individuals are at highest risk for oral cancer, they are also typically the population with minimal access to preventative and screening care \cite{23,24,25,28}. Early diagnosis is critical for the success of the treatment and long-term outcome \cite{21,22}. 
DEFINITION

The oral cavity is defined as the anatomical space which lies between an imaginary coronal plane drawn from the junction of the soft and hard palate and the circumvallate papillae of the tongue to the vermillion of the lips. There are seven oral cavity subsites that are used to classify the oral cavity cancer (lip, tongue, floor of mouth, buccal, hard palate, alveolar, retromolar trigone and soft palate).

HOW IS IT CAUSED?

Tobacco use, alcohol consumption, and poor diet together possibly explain about 90% of head and neck cancers. Smoking accounts for 75% of oral cancers in the United States, with higher risk for cancers of the larynx than for the pharynx and oral cavity. Chewed tobacco, along with betel and areca nut, is more common in Asia, and areca nut alone in the pacific island. A similar risk was observed with smokeless forms of tobacco in a meta-analysis of observational studies from India, where its use is more prevalent.

WHO IS AFFECTED?

The highest incidence of tobacco related oral cancer is seen in low- and middle-income countries. People in the lower socioeconomic strata are more commonly affected. In India almost 21 people per 100 000 of the population are affected.

PATHOLOGY

The contribution of microorganisms to carcinogenesis

Different viruses contribute to the development of cancers. For instance, the association between human papilloma virus (HPV) and cervical cancer and oropharyngeal cancer has been demonstrated. Also, the association between Epstein-Barr virus (EBV) and Hodgkin’s lymphoma has been reported. In addition to viruses, research has established a strong link between cancer and bacteria. Helicobacter pylori (H. pylori) is one the most well-recognized pathogenic bacteria associated with cancers such as stomach and intestine cancers. Also, the intestinal dysbiosis promote sheath carcinogenesis. Porphyromonas gingivalis (P. gingivalis) which colonizes in
the oral epithelium is associated with digestive system cancers. Interestingly, P. gingivalis has been indicated in gingival SCC tissue samples.\[40\]

**The mechanisms by which Porphyromonas gingivalis may promote head and neck cancer**

Activation of some immunologic and inflammatory reactions in the host by P. gingivalis has been considered as the underlying mechanism. Besides, it has been found that P. gingivalis is capable to invade and penetrate different epithelial cells which enables it to alter some genes in response to chronic infection.\[41\] A very recent investigation has demonstrated that P. gingivalis penetrates oral mucosa by targeting Grainyhead-like 2 (GRHL2), an epithelial specific transcription factor. Later, GRHL2 causes epithelial barrier damage by inhibition of tight junction protein expression which results in increased periodontium tissue destruction.\[42\] P. gingivalis promotes the secretion of cytokines such as IL-6 which in turn activates tumorigenic transcription factors such as STAT1.

P. gingivalis also induces epithelial mesenchymal transition (EMT) of normal oral epithelial cells by increasing phospho-GSK3β, an important regulator of EMT.\[43\] Besides, the presence of P. gingivalis related to high serum level of C-reactive protein (CRP).\[44\]

**The role of inflammatory cells in periodontitis and cancer development**

Various inflammatory cell types contribute to the inflammatory responses. Macrophages are one of the most important inflammatory cells which have significant roles in the host innate response to periodontal pathogens. Macrophages are classified into two groups: M1-type and M2-type.

**Involvement of some other cytokines and chemokines in periodontitis and oral cancer**

Cytokines is classified as pro-inflammatory and anti-inflammatory groups. Any imbalances between their relative concentrations may result in tissue destruction. Chemokines recruit leukocytes and other immunological mediators in periodontal inflammatory foci. Besides, chemokines and their receptors are involved in the cell proliferation, cell motility, angiogenesis, cancer development and metastasis.\[44\] Endothelial cells, epithelial cells and mast cells.\[120\] For example, gingival epithelium produces some cytokines such as IL-1, IL-8, , and TNF-α which in turn can recruit the macrophages.\[45\] Additionally, IL-6 plays a crucial role in the development of periodontitis through a crosstalk of fibroblasts and macrophages.\[46\]

**INTERLEUKIN-8 AND ORAL CANCER**

Previous studies of in vitro human cell lines as well as malignant tumours have demonstrated that concentration of certain proinflammatory, proangiogenic cytokines such as TNF-α, IL-1, IL-6, and IL-8 are increased in oral cancer.\[42,40\] It has been known that cellular genes including IL are uniquely associated with oral squamous cell carcinoma. These cytokines have also been linked with increased tumour growth and metastasis, and could thus contribute to the pathogenesis of oral disease. Elevated concentrations of IL-8 in cell line supernatants, tumour specimens, and the serum of patients with oral squamous cell carcinoma have also been documented.\[46\] Recent studies have documented that salivary levels, as well as gene polymorphisms of IL-8 and environmental carcinogens, might be highly related to the risk of oral cancer. Therefore, it is important to study association between inflammation and oral squamous cell carcinoma development through the potential mediator, IL-8.
HOW CAN ORAL CANCER BE PREVENTED?

PUBLIC HEALTH MEASURES TO REDUCE TOBACCO USE

Nearly 10% of countries have completely prohibited all forms of promotion. In India, tobacco products are labelled as hazardous, and advertisements are used to create awareness about tobacco related oral cancer. Higher taxation on tobacco products can potentially decrease consumption, particularly in low- and middle-income countries.\[48\]

SCREENING

This is performed for population screening in communities with high tobacco use to detect early signs of disease.\[49\] In a cluster randomised controlled trial (96 517 participants) in India oral visual examination by trained health workers resulted in a 35% reduction in overall mortality among high risk users of tobacco and alcohol.\[50\]

WHAT TO LOOK FOR ON INITIAL ASSESSMENT?

A history of tobacco uses and findings on oral visual examination help establish the diagnosis. Ask about the duration, type, and quantity of tobacco use—cigarettes, cigars, bidis, or forms of chewed tobacco common in your area. Inspect the mouth and oral cavity for lesions. White (leukoplakia) and red (erythroplakia) patches on the buccal mucosa, lips, gums, or tongue are considered potentially malignant. These represent morphological changes due to chronic exposure to carcinogens.\[51\] Lesions on the floor of the mouth were more likely to have malignant changes, followed by the tongue and lips.\[52\] Palpate the gums, teeth, inside of the cheeks, tongue, palate, and sublingual region with a gloved finger. Examine the neck for enlarged lymph nodes suggestive of metastasis.

WHAT INVESTIGATIONS ARE REQUIRED?

Refer patients with a suspected lesion on examination or with “red flag” features to a specialist. Imaging followed by a biopsy of the lesion will be required to establish the diagnosis. Contrast enhanced magnetic resonance imaging (MRI) is preferred for lesions on the tongue and soft palate, whereas computed tomography (CT) is more sensitive to delineate bone involvement. In patients with a history of smoking and in those with advanced disease, a plain CT scan of the chest will in addition help identify lung cancer or metastasis.\[53\]

WHAT ARE TREATMENT OPTIONS?

SURGERY

Once cancer is confirmed on biopsy, surgical excision is the mainstay of treatment. The tumour may be inoperable in advanced disease, with involvement of the skull base, the internal carotid artery, and/or the prevertebral fascia.\[54\] Facial appearance and functional recovery are important outcomes for patients after surgery. An adequate margin of normal tissue around the tumour is excised (10-15 mm).\[55\] After excision, the tumour is staged based on histopathology to decide if adjuvant therapy is needed.34 Neck dissection is required in patients with metastasis to the cervical lymph nodes.\[56,57\]
RADIOTHERAPY OR CHEMOTHERAPY

External beam radiotherapy or brachytherapy may be considered in patients intolerant to surgery or with advanced, unresectable tumour.[58] It is uncertain if chemotherapy given before surgery to reduce the volume of tumour improves clinical outcomes such as recurrence and survival.[59]

WHAT IS THE PROGNOSIS?

With prompt treatment, 90-95% of patients with early lesions (tumours <4 cm across and no spread to nearby tissues, lymph nodes, or organs) survive their cancer for a year or more, and around 80% survive their cancer for three years or more. The prognosis is worse for advanced disease (larger or more invasive tumours or with spread to lymph nodes or other organs). About 65-70% of patients with advanced oral cancer survive for one year or more, and only half survive beyond three years.[60]

ORAL AND OROPHARYNGEAL CANCER: STATISTICS

Approved by the Cancer.Net Editorial Board, 01/2020

This year, an expected 53,260 grown-ups (38,330 men and 14,880 ladies) in the United States will be determined to have oral and oropharyngeal disease. Rates of these malignant growths are more than twice as high in men as in ladies. Oral and oropharyngeal malignant growth are the eighth most basic disease among men. The normal time of determination is [61]. About 25% of cases happen in individuals more youthful than 55, yet these tumors are uncommon in kids.

Frequency rates for oral and oropharyngeal malignancies in individuals of color have diminished by 1% to 2% every year from 2007 to 2016. Be that as it may, in a similar period, human papillomavirus (HPV)- related oral and oropharyngeal diseases among non-Hispanic white individuals have expanded by around 1% every year. It is evaluated that 10,750 passings (7,760 men and 2,990 ladies) from these 2 sicknesses will happen this year. From 2008 to 2017, the passing rate declined by roughly 2% among individuals of color and expanded by under 1% every year in white individuals.

The 5-year endurance rate mentions to you what percent of individuals live at any rate 5 years after the malignant growth is found. Percent implies what number of out of 100. Endurance rates for oral and oropharyngeal malignant growth fluctuate broadly relying upon the first area, regardless of whether the disease is identified with HPV, and the degree of the malady.

Measurements adjusted from the American Cancer Society's (ACS) distribution, Cancer Facts and Figures 2020, and the ACS site (January 2020).

GLOBAL CANCER DATA (W.H.O.2018)

Disease trouble ascends to 18.1 million new cases and 9.6 million malignant growth passings in 2018. One out of 5 men and one of every 6 ladies overall create malignancy during their lifetime and one out of 8 men and one of every 11 ladies pass on from the illness. Around the world, the absolute number of individuals who are alive inside 5 years of malignancy finding, called the 5-year pervasiveness, is assessed to be 43.8 million.
WORLDWIDE CANCER PATTERNS BY SEX (W.H.O. 2018)

Lung malignant growth is the most regularly analyzed disease in men (14.5% of the all out cases in men and 8.4% in ladies) Followed by prostate malignant growth (13.5%) colorectal disease (10.9%) liver malignant growth (10.2%) stomach malignancy (9.5%) for mortality. Bosom malignant growth is the most regularly analyzed disease in ladies (24.2%).

FINANCIAL BURDEN OF ORAL CANCER IN INDIA

Oral malignant growth is the 6th most basic disease with a yearly frequency coming to more than 300,000 cases out of which 62% cases emerge in creating countries [62]. It was evaluated that India would have north of 1,19,992 new instances of oral disease in 2018 which would wind up in the loss of 72,616 lives because of the poor guess of the illness [63]. The financial weight of malignant growth can be isolated into immediate and backhanded expenses. Direct expenses are brought about by the pre-treatment examinations and imaging followed by treatment medical procedures and auxillary chemo/radiotherapy, while, roundabout costs originate from the fallout of oral malignant growth.

Pollaers K et al. in an ongoing paper looked into the immediate expense of oral malignancy care and inferred that there exists an immediate connection between's malignancy arranging and treatment cost, where the board of beginning period oral malignancy is minimal effort and increments altogether with late-stage ailme

CONCLUSION

Oral malignant growth is a difficult ailment with high death rates, dental specialists assume a basic job at all phases in the administration of patients. Anticipation through training about smoking discontinuance and safe liquor utilization is basic, location and early referral of premalignant injuries and oral malignant growths and continuous reconnaissance, development and protection of oral wellbeing are only a couple of the numerous jobs of the dental specialists in the administration of oral disease. Every single patient with oral malignancy ought to be overseen inside a multidisciplinary group spent significant time in the administration of head and neck tumors and early referral for any dubious sore ought to be made to an Oral and Maxillofacial Surgeon. In the event that we talk about administration of oral malignant growth, at that point investigation is performed with an uncovered eye, without the utilization of uncommon gear and takes around 1 moment. Because of the idea of their work, dental specialists are in the perfect situation to look at their oral mucosa to every one of their patients and to send them to
expert treatment if there should arise an occurrence of any presumed changes. A convenient finding and treatment of oral malignant growth can essentially improve the guess and personal satisfaction of these patients. If there should arise an occurrence of monetary weight of oral malignancy, the proportion of normal pay to average expense is slanted which demonstrates the absence of moderateness for disease care. A significant hole along these lines, exits between pay levels and cost of malignant growth care obviously demonstrating enormous hole among reasonableness and cost of treatment, which unmistakably shows the requirement for an arrangement and state mediation for a mass disease care program.

REFERENCES


34. Warnakulasuriya S. Significant oral cancer risk associated with low socioeconomic status. Evid Based Dent 2009;10:4-5. . 10.1038/ebd.6400623 19322216


