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ORAL CANCER: AN OVERVIEW

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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 decapod. 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. [1,2] 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. [3] 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 decade in many European countries.[4] 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.[5] Oral cancer refers to cancers of the tongue, gingiva, floor of the mouth, palate, vestibule and retromolar area.[6] 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.[8] Cancer of the head and neck largely affects an older population, with males more frequently affected than females. Lifestyle factors, in particular tobacco smoking, [9,10] 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.[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.[11]

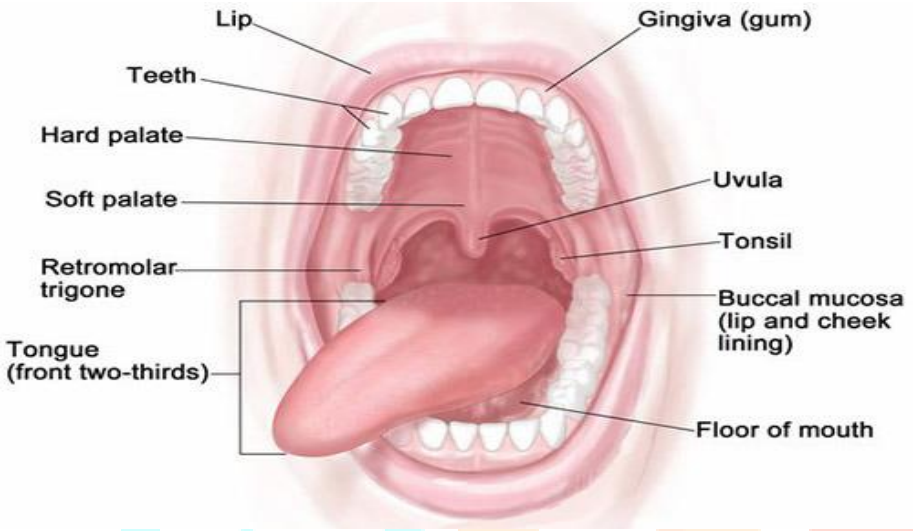
An Indian male prisoner's study, tobacco use and oral cancer knowledge, it was found that knowledge related to oral cancer did not impact on decisions regarding tobacco use. [12] Mouth self-examination to improve oral cancer awareness and early detection in a high-risk population was tested in an Indian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

Global annual incidence of oral cancer is estimated as 529,500 [14]. Oral cancers have shown little improvement in survival statistics across three decades [15,16]. An estimated 9750 deaths in the upcoming year are predicted in the United States alone.[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.[18] Tobacco use and alcohol are estimated to play a contributory role to 80% of all incident oral cancer.[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.[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.[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[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[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[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 [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 [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 [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 [23,24,25,28]. Early diagnosis is critical for the success of the treatment and long-term outcome [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.[29] Smoking accounts for 75% of oral cancers in the United States,[30] with higher risk for cancers of the larynx than for the pharynx and oral cavity.[31] Chewed tobacco, along with betel and areca nut, is more common in Asia, and areca nut alone in the pacific island. [32] 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.[33]

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.[34] In India almost 21 people per 100 000 of the population are affected.[35]

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. [36,37] 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. [38,39] 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. gingivalishas 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 induses epithelial mesenchymal transition (EMT) of normal oral epithelial cells by increasing phospho-GSK3ß, an important regulator of EMT.92 Besides, the presence of P. gingivalisis related to high serum level of C-reactive protein (CRP).[43]

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.120For example, gingival epithelium produces some cytokines such as IL-1, IL-8, , and TNF-αwhich 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]

INTERLEUIKIN-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 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

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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. Paces 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 ailment and multimodal treatment [64]. On the other hand, the roundabout expenses allude to the charges experienced because of loss of occupation/compensation, guardian and home-care costs, decreased work of people and decreased working hours with post-careful deformation causing lessened income [65]. W L Hicks et al. proposed 'repeat of oral malignant growth as a huge factor adding to the costs and increasing the monetary weight [66]. An ongoing report indicated that as far as inpatient costs, treatment of intermittent cases sums 151% more than the cases that remained malady free [64]. Writing recommends that roughly 60–80% patients in creating provinces like India present with cutting edge stage illness when contrasted with 40% in created nations [66]. Accordingly, early recognition would improve the endurance rate as well as diminish the monetary weight and help lessen treatment related bleakness.

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

1. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral Oncol 2009; 45: 309–16.

2. Ferlay J, Soerjomataram I, Ervik M et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: 2013.

3. Warnakulasuriya S. Causes of oral cancer – an appraisal of controversies. Br Dent J 2009; 207: 471–5.

4. Albuquerque RP, Lopez-Lopez J, Jane-Salas E, Rosa-Santos J, Ibrahim C. A pioneering epidemiological study investigating the incidence of squamous cell carcinoma of tongue in a Portuguese population. Med Oral Patol Oral Cir Bucal 2012; 17: e550–4.

5. Warnakulasuriya KA, Harris CK, Scarrott DM et al. An alarming lack of public awareness towards oral cancer. Br Dent J 1999; 187: 319–22.

6.National Cancer Registry Ireland. 2010. Available from: http://www.ncri.ie/data.cgi/client/generate_stats.php.

7. Vokes, E.E., Weichselbaum, R.R., Lippmann, S.M., Hong, W.K. Head and neck cancer. N Engl J Med 1993; 328: 184-194.

8. Kerdpon, D., Sriplung, H. Factors related to advanced stage oral squamous cell carcinoma in southern Thailand. Oral Oncol 2001; 37 (3): 216-221.

9. Blot, W.J., McLaughlin, J., Winn, D. Smoking and drinking in relation to oral and pharyngeal cancer. Cancer Res 1988; 48: 3282-3287.

10. Napier, S., Speight, P.M. Natural history of potentially malignant oral lesions and conditions: an overview of the literature. J Oral Pathol Med 2008; 37: 1-10.

11. Heck, J.E., Berthiller, J., Vaccaraella, S., Winn, D.M. Sexual behaviours and the risk of head and neck cancers: a pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. Int J Epidemiol 2010; 39 (1): 166-181.

12. Dahiya, M., Croucher, R. Male prisoner tobacco use and oral cancer knowledge: a case study of a local prison in India. Int Dent J 2010; 60 (2): 135-138.

13.Elango, K.J., Anandkrishnan, N., Suresh, A., Iyer, S.K., Ramaiyer, S.K., Kuriakose, M.A.Mouth self-examination to improve oral cancer awareness and early detection in a high risk population. Oral Oncol 2011; 47 (7): 620-624.

14. Shield KD, Ferlay J, Jemal A, et al. The global incidence of lip, oral cavity, and pharyngeal cancers by subsite in 2012. CA Cancer J Clin. 2017;67(1):51–64.

15. Oral Cancer Foundation. Oral Cancer Facts: rates of occurrence in the United States. 2018. https://oralcancerfoundation.org/facts/. Accessed 5 Apr, 2018.

16. American Cancer Society. Oral Cavity and Oropharyngeal Cancer 2016. Atlanta: American Cancer Society. 2018. http://www.cancer.org/acs/groups/ cid/documents/webcontent/003128-pdf.pdf. Accessed 5 Apr, 2018.

17. Villa A, Kreimer AR, Pasi M, et al. Oral cancer knowledge: a survey administered to patients in dental departments at large Italian hospitals. J Cancer Educ. 2011;26:505–9.

18. National Institute on Alcohol Abuse and Alcoholism. Alcohol and Tobacco. Alcohol Research & Health. 2006; 29(71). https://pubs.niaaa.nih.gov/ publications/aa71/aa71.htm. Accessed 5 Apr, 2018.

19. Rogers SN, Hunter R, Lowe D. Awareness of oral cancer in the Mersey region. Br J Oral Maxillofac Surg. 2010;49:176–81.

20. U.S. National Institutes of Health (NIH), National Cancer Institute (NCI). (2010). Cancer of the oral cavity and pharynx—SEER stat fact sheets. Bethesda, MD. http://www.seer.cancer.gov/stat facts/html/oralcav.html.

21. van der Waal, I., de Bree, R., Brakenhoff, R., & Coebergh, J. W. (2011). Early diagnosis in primary oral cancer: it possible? Medicina Oral Patologı´a Oral y Cirurgı´a Bucal, 16(3), e300–e305.

22. Shiboski, C. H., Schmidt, B. L., & Jordan, R. C. (2007). Racial disparity in stage at diagnosis and survival among adults with oral cancer in the US. Community Dentistry and Oral Epidemiology, 35(3), 233–240.

23. Conway, D. I., Petticrew, M., Marlborough, H., Berthiller, J., Hashibe, M., & Macpherson, L. M. (2008). Socioeconomic inequalities and oral cancer risk: A systematic review and metaanalysis of case-control studies. International Journal of Cancer, 122(12), 2811–2819.

24. Gourin, C. G., Kaboli, K. C., Blume, E. J., Nance, M. A., & Koch, W. M. (2009). Characteristics of participants in a free oral, head and neck cancer screening program. Laryngoscope, 119(4), 679–682.

25. Hashibe, M., Jacob, B. J., Thomas, G., Ramadas, K., Mathew, B., Sankaranarayanan, R., et al. (2003). Socioeconomic status, lifestyle factors and oral premalignant lesions. Oral Oncology, 39(7), 664–671.

26. Ragin, C. C., Langevin, S. M., Marzouk, M., Grandis, J., & Taioli, E. (2011). Determinants of head and neck cancer survival by race. Head and Neck, 33(8), 1092–1098.

27. Johnson, N. W., Warnakulasuriya, S., Gupta, P. C., Dimba, E., Chindia, M., Otoh, E. C., et al. (2011). Global oral health inequalities in incidence and outcomes for oral cancer: Causes and solutions. Advances in Dental Research, 23(2), 237–246.

28. Yellowitz, J. A., Goodman, H. S., & Farooq, N. S. (1997). Knowledge, opinions, and practices related to oral cancer: Results of three elderly racial groups. Special Care in Dentistry, 17(3), 100–104.

29. JohnsonN. Tobacco use and oral cancer: a global perspective. J Dent Educ 2001;65:328-39.11336118

30. WinnDM. Tobacco use and oral disease. J Dent Educ 2001;65:306-12.11336115

31. Bray F, Colombet M, Mery L, et al eds. Cancer incidence in five continents, Vol. XI. International Agency for Research on Cancer, 2017. http://ci5.iarc.fr/CI5-XI/Default.aspx.

32. LubinJH, PurdueM, KelseyK, etal . Total exposure and exposure rate effects for alcohol and smoking and risk of head and neck cancer: a pooled analysis of case-control studies. Am J Epidemiol 2009;170:937-47. . 10.1093/aje/kwp222 19745021

33. SinhaDN, AbdulkaderRS, GuptaPC. Smokeless tobacco-associated cancers: a systematic review and meta-analysis of Indian studies. Int J Cancer 2016;138:1368-79. . 10.1002/ijc.29884 26443187

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

35. WHO global report on trends in prevalence of tobacco smoking 2000-2025. 2nd ed. World Health Organization, 2018.

36. Speicher DJ, Ramirez-Amador V, Dittmer DP, et al. Viral infections associated with oral cancers and diseases in the context of HIV: a workshop report. Oral Dis 2016;

37. Suppl 1:181-92. 22. Morales-Sánchez A, Fuentes-Pananá EM. Human viruses and cancer. Viruses 2014;6:4047-79.

38. Correa P, Piazuelo MB. Helicobacter pylori Infection and Gastric Adenocarcinoma. US Gastroenterol Hepatol 2011;7:59-64.

39. Irani S,Monsef Esfahani A, Sabeti S, Bidari Zerehpoush F. Detection of Helicobacter pylori in Oral Lichen Planus and Oral Lichenoid Reaction. Avicenna J Dent Res 2014;6:e23213.

40. Gupta H, Youn GS, Shin MJ, Suk KT. Role of Gut Microbiota in Hepatocarcinogenesis. Microorganisms2019;7:5.

41. Katz J, Onate MD, Pauley KM, et al. Presence of Porphyromonas gingivalis in gingival squamous cell carcinoma. IntJOral Sci 2011;3:209-15.

42. Sayehmiri F, Sayehmiri K, Asadollahi K, et al. The prevalence rate of Porphyromonas gingivalis and its association with cancer: A systematic review and meta-analysis. Int J Immunopathol Pharmacol 2015;28:160-7.

43. Chen W, Alshaikh A, Kim S, et al. Porphyromonas gingivalis Impairs Oral Epithelial Barrier through Targeting GRHL2. J Dent Res2019:22034519865184.

44. Dye BA, Choudhary K, Shea S, Papapanou PN. Serum antibodies to periodontal pathogens and markers of systemic inflammation. J Clin Periodontol 2005;32:1189-99.

45.Sahingur SE, Yeudall WA. Chemokine function in periodontal disease and oral cavity cancer. Front Immunol 2015;6:214.

46. Hoare A, Soto C, Rojas-Celis V, Bravo D. Chronic Inflammation as a Link between Periodontitis and Carcinogenesis.Mediators Inflamm 2019;2019:1029857.

47. Naruishi K, Nagata T. Biological effects of interleukin-6 on Gingival Fibroblasts: Cytokine regulation in periodontitis. J Cell Physiol 2018;233:6393-400.

48. World Health Organization. WHO report on the global tobacco epidemic 2017: monitoring tobacco use and prevention policies. 2017. https://www.who.int/tobacco/global_report/en/ .

49. SpeightPM, EpsteinJ, KujanO, etal . Screening for oral cancer-a perspective from the Global Oral Cancer Forum. Oral Surg Oral Med Oral Pathol Oral Radiol 2017;123:680-7. . 10.1016/j.oooo.2016.08.021 27727113

50. SankaranarayananR, RamadasK, ThomasG, etal. Trivandrum Oral Cancer Screening Study Group. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. Lancet 2005;365:1927-33.

51. NevilleBW, DayTA. Oral cancer and precancerous lesions. CA Cancer J Clin 2002;52:195-215. 10.3322/canjclin.52.4.195 12139232

52. WaldronCA, ShaferWG. Leukoplakia revisited. A clinicopathologic study 3256 oral leukoplakias. Cancer 1975;36:1386-92.

53. AryaS, ChaukarD, PaiP. Imaging in oral cancers. Indian J Radiol Imaging 2012;22:195-208. 10.4103/0971-3026.107182 23599568

54. ColevasAD, YomSS, PfisterDG, etal . NCCN Guidelines Insights: Head and Neck Cancers, Version 1.2018. J Natl Compr Canc Netw 2018;16:479-90. 10.6004/jnccn.2018.0026 29752322

55. WoolgarJA, TriantafyllouA. A histopathological appraisal of surgical margins in oral and oropharyngeal cancer resection specimens. Oral Oncol 2005;41:1034-43. 10.1016/j.oraloncology.2005.06.008 16129652

56.HuangSH, O'SullivanB. Oral cancer: current role of radiotherapy and chemotherapy. Med Oral Patol Oral Cir Bucal 2013;18:e233-40. . 10.4317/medoral.18772 23385513

57. LiangL, ZhangT, KongQ, LiangJ, LiaoG. A meta-analysis on selective versus comprehensive neck dissection in oral squamous cell carcinoma patients with clinically node-positive neck. Oral Oncol 2015;51:1076-81. . 10.1016/j.oraloncology.2015.10.005 26500065

58.. GendenEM, FerlitoA, SilverCE, etal . Contemporary management of cancer of the oral cavity. Eur Arch Otorhinolaryngol 2010;267:1001-17. . 10.1007/s00405-010-1206-2 20155361

59. MartaGN, RieraR, BossiP, etal . Induction chemotherapy prior to surgery with or without postoperative radiotherapy for oral cavity cancer patients: systematic review and meta-analysis. Eur J Cancer 2015;51:2596-603. . 10.1016/j.ejca.2015.08.007 26318725

60.Cancer Research UK. Mouth cancer survival by stage. 2019. https://www. cancerresearchuk.org/about-cancer/mouth-cancer/survival.

61. Coelho KR. Challenges of the oral cancer burden in India. J Cancer Epidemiol 2012;2012. https://doi.org/10.1155/2012/701932. Article ID 701932.

62. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No.11 [Internet] Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan. iarc.fr, accessed on 6th August 2014.

63. Pollaers K, Massingham I, Friedland PL, Farah CS. The economic burden of oral squamous cell carcinoma in Australia. J Oral Pathol Med 2019;48(7):588–94.

64. Syse A, Tretli S, Kravdal Ø. Cancer's impact on employment and earnings—a population-based study from Norway. J Cancer Surviv 2008;2:149–58.

65. Hicks Jr WL, North Jr JH, Loree TR, et al. Surgery as a single modality therapy for squamous cell carcinoma of the oral tongue. Am J Otolaryngol 1998;19:24–8.

66. Coelho KR. Challenges of the oral cancer burden in India. J Cancer Epidemiol 2012;2012:701932https://doi.org/10.1155/2012/701932.