ORIGINAL ARTICLES

Oral and oropharyngeal malignancy: A clinicopathological study

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Abstract

Oral and oropharyngeal cancers are the commonest of head and neck malignancies. They share common etiological factors, which are often the personal habits of the patients. Human papillomavirus is increasingly being reported in patients with oral and oropharyngeal malignancies, especially in Western population. However in India, smoking, alcohol consumption and tobacco chewing are the common etiological factors. We conducted a retrospective study of 202 histopathologically confirmed cases of oral and oropharyngeal malignancies in Justice K.S. Hegde Charitable Hospital, Mangalore, during the three years period between January 2011 and December 2013. Majority of the patients were males. Buccal mucosa was the commonest site of lesions. Half of them had history of smoking, whereas the remaining had history of smokeless tobacco consumption. One-third of the patients had history of alcohol consumption. However, 10.8% of the patients had no addictions and this group was dominated by females.

Keywords: Oral cavity, oropharynx, malignancy, habits

Introduction

Head and neck cancers are among the common malignancies worldwide. These diseases, because of their location and symptoms, present early to the healthcare professionals. Oral cancer is one of the common cancers in the world. The annual estimated incidence is around 275,000 for oral and 130,000 for pharyngeal cancers excluding nasopharynx, with two-third of these cases occurring in developing countries.[1] Oral cancer is the most common cancer and cancer-related death in men in India.[2] Early diagnosis of most of these cancers have very good prognosis. However, a delay in diagnosis and intervention impairs the patients' quality of life.

Numerous studies have evaluated the clinicopathological profile of oral and oropharyngeal malignancies. The disease, which was once common in older age group, is being increasingly prevalent among the youth and large number of females. This change in trend can be attributed to the personal habits like smoking, alcohol consumption, and chewing tobacco. There is a strong positive correlation of oral cancer with alcohol consumption and tobacco use. The increase in risk noted with their combined use is well above than expected when compared to either alone. Studies have also shown significant association of oral cancer risk with oral hygiene, diet, nutritional status, sexual behavior, and genetic factors.

In the recent years, human papillomavirus (HPV) infection is found to be responsible for a subset of oropharyngeal cancers that arise predominantly from the lingual and palatine tonsils within the oropharynx. Oral HPV infection has recently been associated with sexual behavior, particularly with number of oral sex partners.[3]

Oral cancers are more common in males beyond 5th decade of life. However, there is a rising trend in the younger age group who has been influenced by a smokeless tobacco brand called Gutkha. The male to female ratio is also showing a slow decline, as there is rising incidence in oral cancers in women.[4, 5] Oral tongue is the most common site for intraoral cancer among European and the United States populations. Buccal cancer is more common among Indian population, which is likely to be due to betel quid and tobacco chewing habits. Lip cancers occur in patients with high exposure to sunlight.[1]

This retrospective study is aimed at determining the distribution of oral and oropharyngeal malignancies in terms of age, sex, personal habits, symptoms, site, histopathological type and differentiation.

Materials and Methodology

The retrospective study was conducted at Justice K.S. Hegde Charitable Hospital, Mangalore, Karnataka. The case records of 202 histopathologically confirmed cases of oral and oropharyngeal malignancies, during the three years period between January 2011 and December 2013, were reviewed. Details about the demographic profile, personal habits like smoking, consumption of alcohol, tobacco chewing, pattern of chewing, presenting complaints, site of the lesion, staging of the disease and histopathological type, and differentiation were recorded and analyzed.

Results

The study involved 202 patients of oral and oropharyngeal malignancies. Among these 150 (74.2%) were males and 52 (25.7%) were females. Majority of the patients were in the age group of 60-69 years (29.7%), followed by 50-59 years (27.7%) and 40-49 years (18.3%). The youngest patient in our study was a 17-year-old female. Regarding personal habits, 103 (50.9%) had history of smoking, 98 (48.5%) were consuming smokeless tobacco in the form of gutkha or chewing pan. Alcohol consumption was found in 67 (33.1%) patients. Consumption of alcohol and tobacco in the form of smoking or chewing was noted in 63 (31.1%) patients. Twenty-two (10.8%) patients had no habits, out of which 5 were males and 17 females. Out of 52 females in the study, 35 (17.3%) patients had one or the other habits. Chewing pan was observed in 34 (18.8%) patients and chewing gutkha in one patient (Table 1).

Presence of oral lesion in the form of ulcer, growth or nodule was the most common complaint noted, which accounted for 69.3% of cases. Other complaints included dysphagia (22.2%), pain (16.8%), neck swelling (9.4%), bleeding, and speech difficulty (2.4%). The figure 1 depicts the distribution of oral and oropharyngeal malignancies among the study subjects. Buccal mucosa was the most common site of oral cancer (55, 27.2%) (Fig 2a) followed by oral tongue (48, 23.7%) (Fig 2b), tongue base and tonsil (24, 11.8%).

The assessment of correlation between the site of the lesion and habits indicated that patients who had the habit of chewing smokeless tobacco had lesions predominantly on the buccal mucosa followed by tongue. Those who only smoke had lesion commonly on the tongue. Smoking with consumption of alcohol was the commonest combination observed and these patients had lesions commonly on the tongue base and tonsils, followed by oral tongue and buccal mucosa.

Squamous cell carcinoma was the most common histological type noted in the study, comprising 167 (82.6%) cases. Majority (49.7%) of the cases were moderately differentiated (Fig. 3a), followed by well differentiated in 34.7%, poorly differentiated in 14.9%, and undifferentiated in 0.4%. There were 2 cases each of spindle cell variant of squamous cell carcinoma and undifferentiated nasopharyngeal type carcinoma; one case each of basaloid and acantholytic variant of squamous cell carcinoma; 16 (7.9%) cases of verrucous carcinoma was encountered (Fig. 3b), of which 6 cases were seen in the lip. There were 8 cases of microinvasive squamous cell carcinoma.

Other than squamous cell carcinoma, five cases of minor salivary gland tumors were observed, one case each of polymorphous low-grade adenocarcinoma, adenoid

Table 1: Habits in oral and oropharyngeal cancer patients

Habits	No (%) n=202
Smoking	103 (51)
Alcohol	67 (33)
Tobacco chewing (pan/gutkha)	98 (48.5)
Alcohol and tobacco (smoking/pan/gutkha)	63 (31)
No habits	22 (10.8)

cystic carcinoma (Fig. 4a), mucoepidermoid carcinoma, mucinous cystadenocarcinoma (Fig. 4b), and papillary adenocarcinoma. The study also showed 3 cases of non-Hodgkin lymphoma (Fig. 5a), 2 cases of melanoma (Fig. 5b), and one case of pleomorphic sarcoma.

Discussion

In India, cancer of the oral cavity and oropharynx is the commonest cancer in men and third commonest cancer in women.[6] Oral cancers are more common in males than females. However, there is a rise in the incidence of these malignancies in females. In our study, majority (74.3%) were males with a male to female ratio of 3:1. This ratio is seen in most of the published studies in India. The corresponding prevalences of malignancy reported in a similar study by Muwonge *et al*. in Kerala, were 57.8% in males and 42.2% in females.[7] Patel *et al*. from Gujarat reported 75% of oral cancer patients were males.[4] Bhat *et*

Fig. 1: Distribution of oral and oropharyngeal malignancies

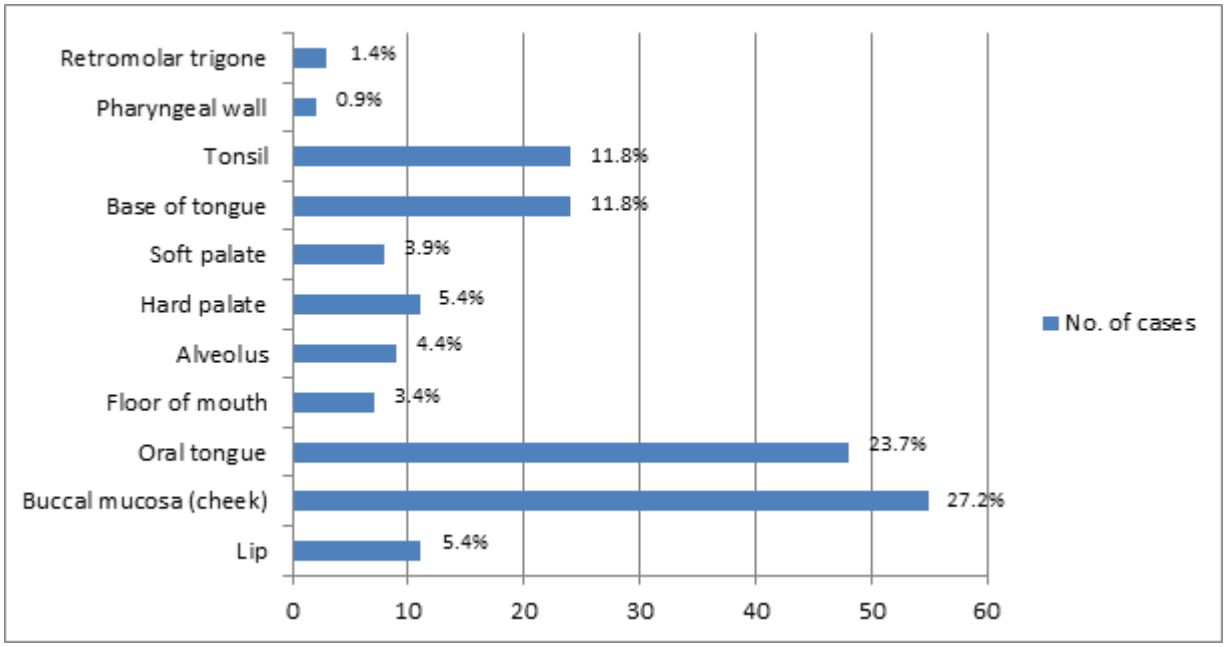
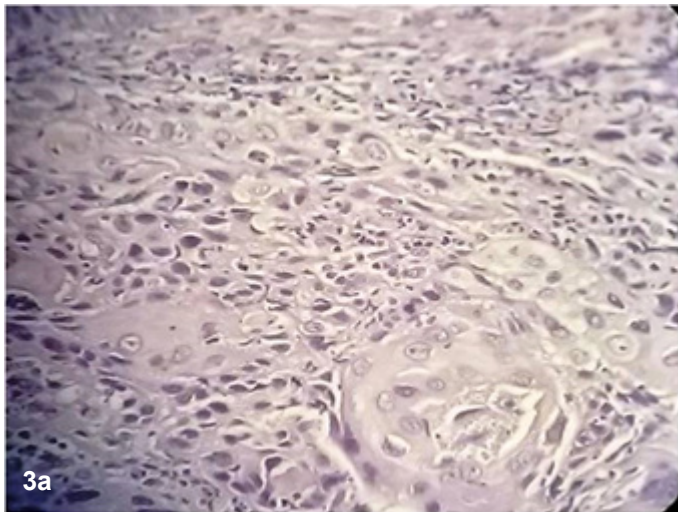
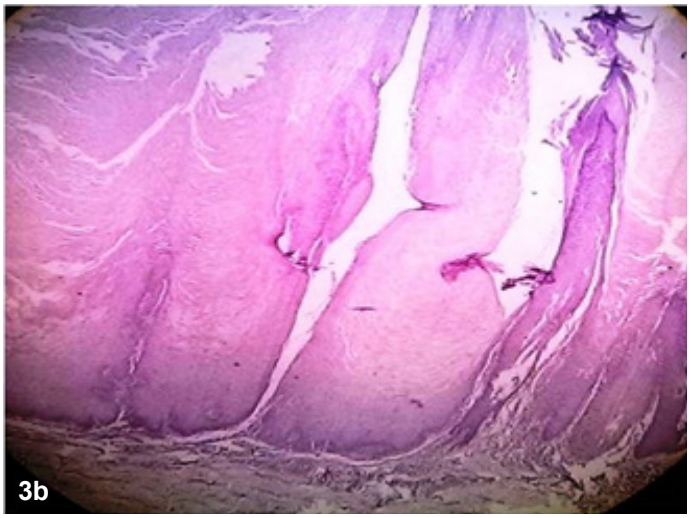


Fig. 2a: Carcinoma of right buccal mucosa Fig.2b: Carcinoma of tongue

Fig. 3a: H&E staining of moderately differentiated squamous cell carcinoma (10X) Fig. 3b: H&E staining of verrucous carcinoma (10X)





al. found that oral cancers have higher preponderance for males (77%).[8] Foreign studies indicate that the prevalence noted are not different from Indian scenario. Durazzo *et al*. from Brazil, reported that 68.2% of the study subjects were males, females accounted for 31.8% of cases.[5] The higher incidence of oral and oropharyngeal malignancies in males may be due to the increased rate of tobacco and alcohol consumption. Moreover, tobacco is consumed by males in both smoking and chewing form, whereas native Indian females usually do not indulge in smoking. This difference can also be attributed to more males seeking early medical consultation.[8]

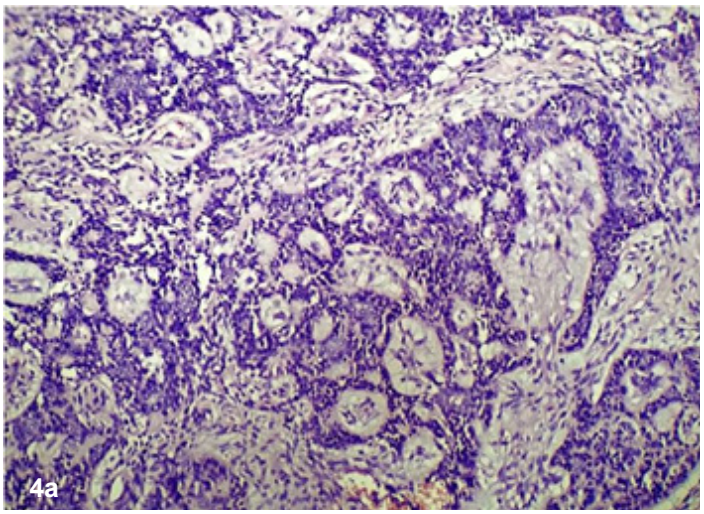
Most of the current study participants were between 60 and 69 (29.7%) years of age group, followed by 50-59 (27.7%) years and 40-49 (18.3%) years. The youngest patient in our study was of 17 years of age. Only 10.3% of patients were below 40 years. Brandizzi *et al*. in their study found that 28% of oral cancer patients were between 60-69 years, followed by 27% between 70-79 years and 18% between 50-59 years of age.[9] According to Abhinandan *et al*., the commonest age group affected was 6th decade (31.13% cases); 22.8% cases were in the 4th and 18% in 5th decade.[10] In a study by Ahluwalia *et al*., the peak incidence was noted among males in 6th decade of life (40.89%), while in females it was 5th decade comprising 37.31% case.[11] Patel *et al*. reported that 12.9% of oral and oropharyngeal malignancies were below 35 years of age, 23.8% between 35 and 45, and 63.3% cases over 45 years of age.[4] The mean age reported in a study done by Durazzo *et al*. was 57.4 years and only 8.6% of the patients were 40 years or less. [5] In conclusion, oral cancer commonly occurs in 5th- 6th decade of life. Though the incidence below 40 years is relatively low, they are not completely spared.

Among 103 (50.9%) subjects who had history of smoking in the present study, 98 (48.5%) were consuming smokeless tobacco in the form of gutkha or pan (betel quid). Alcohol consumption was found in 67 (33.1%) of our patients; 63 (31.1%) patients were consuming alcohol and tobacco in the form of smoking or chewing. Smoking and alcohol consumption were seen only in males. Out of 52 females in the study, 34 (18.8%) were chewing pan, one patient was chewing gutkha.

Tobacco chewing has emerged as a stronger risk factor of oral carcinoma than smoking, since there is a direct exposure of tobacco chewing on the mucosa for longer period, while smoking has more contact with pharynx, larynx, and lungs. Women have substantially high level of chewing habits than men in many rural areas, as they believe that tobacco has magical and medicinal properties.[6, 7]

In a study by Dias *et al*., 57.8% were tobacco users, 50% were alcoholics, 43.8% were both alcoholics and smokers.[12] The study by Durazzo *et al*. reported tobacco smoking in 80.8% of the patients. Alcohol consumption history was retrieved in 56.6% of the patients.[5] In Western

Fig. 4a: H&E staining of adenoid cystic carcinoma (10X), Fig. 4b: H&E staining of mucinous cystadenocarcinoma of cheek (40X)



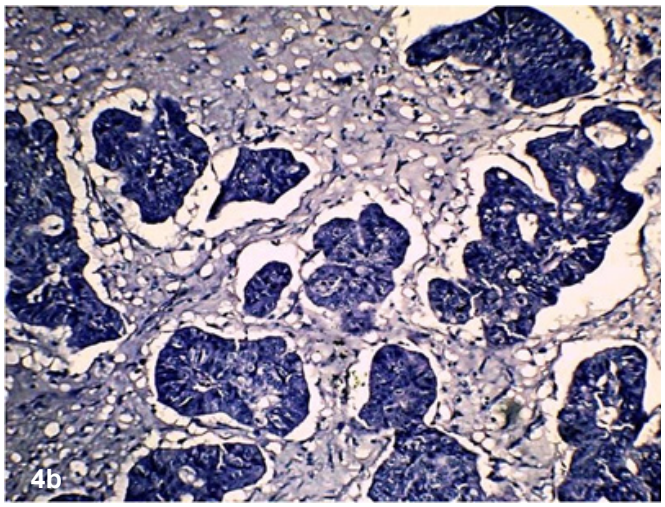
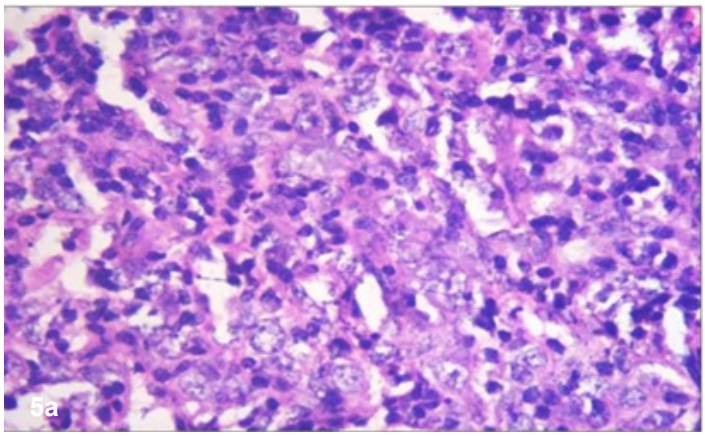
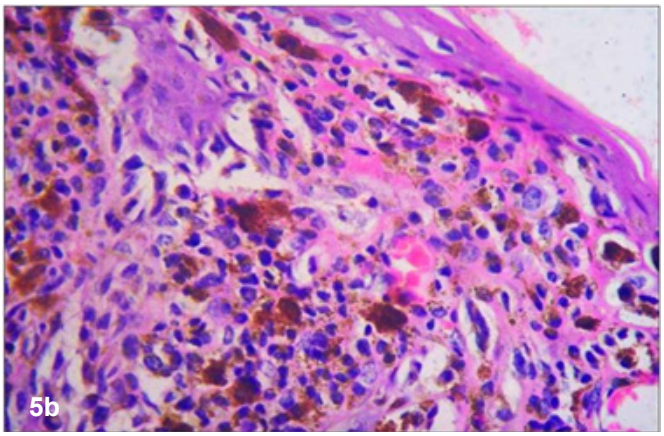


Fig. 5a: H&E staining of non-Hodgkin lymphoma (40X) Fig. 5b: H&E staining of mucosal melanoma (40X)





world, HPV is emerging as a common etiological factor for oral and oropharyngeal malignancies, mostly as a result of oral sex. In India, alcohol and tobacco use is still the strongest culprit. Oral cancer risk is seen to be significantly increasing with both quantity and duration of alcohol use. Risk of oral and oropharyngeal malignancy is higher for hard liquor and beer.[13] Alcohol may act as a solvent to enhance mucosal exposure to carcinogens, apart from being a direct carcinogen. Acetaldehyde, an alcohol metabolite, can form DNA adducts that interfere with DNA synthesis and repair.[14]

The relationship between use of smokeless tobacco products and oral cancers is complicated by heterogeneity in smokeless tobacco containing tobacco specific nitrosamines.[15] In India, smokeless tobacco is often mixed with other carcinogenic substances (betel, areca nut, and lime) and very strong dose response relationships were observed with increased intensity and duration of smokeless tobacco use and risk of premalignant and malignant lesions of the oral cavity.[16]

Strong and consistent inverse association between risk of oral cancer and consumption of fruits and vegetables has been observed, after controlling for the effects of alcohol and tobacco. This suggests that diet deficient in antioxidants is a factor that predisposes the development of oral cancer.[1] Poor oral hygiene is an independent risk factor for oral cancer, likely due to a chronic inflammatory state.[3]

Young age at onset is a cardinal feature of an inherited

predisposition to malignancy. Oral cancer at a young age has also been reported in families with functionally inactivated germline mutations in p16.[17] Fanconi anemia is a well-known genetic syndrome associated with 500-700 fold increased risk of oral cancers. A positive family history of head and neck squamous cell carcinoma also represents an inherited sensitivity to the genotoxic effects of mutagens in tobacco smoke and metabolites of alcohol.[15]

Oral lesion was the most common presenting symptom in the current study (69.3% of cases). This finding is in line with that of Durazzo *et al*. (88%).[5] Any growth or ulcer in the oral cavity should have a high index of suspicion and should be further investigated.

Site of involvement in oral malignancy has a variable geographical distribution. In our study, buccal mucosa was the commonest site of oral cancer, comprising 27.2% cases, followed by oral tongue in 23.7%, tongue base and tonsil in 11.8%. Other sites were hard palate and lip (5.4% each), alveolus (4.4%), soft palate (3.9%), floor of mouth (3.4%), retromolar trigone (1.4%) and pharyngeal wall (0.9%). Ahluwalia *et al*. from Allahabad, also found carcinoma of cheek to be commonest, representing 55.6% of cases.[11] Walid *et al*. from Pakistan, reported maximum (34%) oral cancer cases in buccal mucosa, followed by lip (26%) and tongue (21%).[18] Ahmed *et al*. from Bangladesh reported that buccal mucosa was the commonest site, followed by anterior two-third of tongue.[19] Muwonge *et al*. also reported buccal mucosa as the most frequent site (50.7%), followed by tongue (76%) and alveolus (8.9%).[7] Studies from Western world have reported tongue as the commonest site of malignancy in oral cavity. There are large number of studies reporting oral tongue as the commonest site.[4, 5, 9, 12, 20] More and D'cruz, in their review of oral malignancies across India, noticed buccal mucosa is the commonest site. [21] It is also observed that oral cancer affects mainly the anterior parts (buccal mucosa, anterior 2/3 of the tongue, alveolus) of oral cavity. Anterior part of the oral cavity is the area that comes largely in contact with the smokeless tobacco while chewing. Smokeless tobacco, which has carcinogenic agents like carbon monoxide, nicotine, hydrogen cyanide, ammonia, benzyl, phenol, benzanthrene and benzopyrene, on chewing can cause chronic inflammation and carcinogenesis.[4]

Squamous cell carcinoma was the most common histological type note in the present study (82.6% cases). There were 2 cases each of sarcomatoid squamous cell carcinoma and undifferentiated nasopharyngeal type carcinoma, one case each of basaloid and acantholytic variant of squamous cell carcinoma. Verrucous carcinoma was encountered in 7.9% cases, majority were seen in the lip in the age group range of 65-80 years. Minor salivary gland tumors were observed in 2.4% and majority were located in the palate. Non-Hodgkin lymphoma, melanoma, and soft tissue sarcoma were noted in 1.4%, 0.9% and 0.4% respectively.

The study by Bhat *et al*. found squamous cell carcinoma in 92%, 4% verrucous carcinoma, 3% adenoid cystic carcinoma, and 1% basal cell carcinoma.[8] Durazzo *et al*. reported squamous cell carcinoma in 90.3% and glandular carcinoma in 4%.[5] Ahluwalia *et al*. found squamous cell carcinoma in majority (89.9%) of cases.[11] Wahid *et al*. found squamous cell carcinoma in 94%, and 2% each of melanoma, adenocarcinoma and acinar cell carcinoma.[18] Iype *et al*. reported squamous cell carcinoma in 72%, minor salivary gland tumors in 3.8%, and 1.9% with soft tissue sarcomas.[22]

In the current study, maximum number of cases were moderately differentiated (49.7%), followed by well differentiated in 34.7%, poorly differentiated in 14.9%, and undifferentiated in 0.4%. Similarly, Mehrotra *et al*. also noticed moderately differentiated squamous cell carcinoma as the most prevalent type in males (13%), and well differentiated was common in females (5.3%).[23] However, there are several studies reporting well differentiated squamous cell carcinoma as the most prevalent.[8, 4, 12, 11, 19, 22] Though oral cancer are easily accessible for clinical examination and amendable to diagnosis and treatment, late reporting to the healthcare facility may be the reason for the maximum number of cases in the present study being moderately differentiated. Sankaranarayan *et al*. emphasized the importance of screening programs in early detection of oral malignancies, as even a non-medical person can detect any changes in the mucosa of the oral cavity by inspection alone.[2] A large number of oral cancers can be prevented through the implementation of available knowledge on the etiology of oral cancer, screening for early detection and preventive into clinical practice.

Conclusion

Oral and oropharyngeal cancers are among the most common malignancies encountered in clinical practice. Males are more commonly affected than females usually in 5th to 6th decade of life. However, there is a rising

incidence noted in female patients as they are hardcore tobacco chewers and less educated than men in the rural setup. Oral cancers are also increasing in younger population due to the habit of consuming alcohol and tobacco. Anatomically, the anterior portion of the oral cavity is commonly involved, possibly due to the longer duration of contact with the carcinogens in tobacco and alcohol. Squamous cell carcinoma is the most common histological type. Verrucous carcinomas have a good prognosis and should be reported as a distinct entity. Clinicians should be aware that minor salivary gland tumors, non-Hodgkin lymphomas, and melanoma can occur in oral cavity, more commonly on the palate. This study reflects that there is an urge to raise awareness and educate people regarding detrimental effects of alcohol and tobacco consumption, importance of dental hygiene, oral self-examination and the availability of preventive health care services.

Competing interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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