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A clinicopathological study of squamous cell carcinoma of oral cavity and oropharynx in non-smoker and non-drinker patients

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ABSTRACT

Background: To describe the clinicopathological variables of the Squamous cell carcinoma (SCC) of oral cavity and oropharynx in non-smoker and non-drinker patients (NSND).

Methods: A retrospective review of thirty NSND patients with proven SCC of oral cavity and oropharynx in ENT department at Government Medical College Patiala. Data collected included demographics, aetiological factors, site, symptoms, nodal metastasis, histopathological grading and TNM staging at presentation.

Results: In oral cavity cancers, patients presented commonly in 4th decade whereas in oropharynx, commonly in 6th decade. NSND patients were more likely to be female, male female ratio being 43:56. In NSND women, 82% had oral cavity SCC and 18% had oropharyngeal SCC. 13% of NSND patients reported sharp tooth, 10% reported regular environmental exposure, and 10% reported occupational exposure followed by lichen planus (6.67%). In oral cavity SCC, maximum incidence was that of oral tongue (59.1%) and in oropharyngeal SCC, base of tongue (62.5%) was most commonly involved. Overall, well differentiated SCC predominated in both oral cavity and oropharyngeal carcinoma in our study. In oral cavity SCC, maximum patients presented in early tumor staging i.e T1 and T2 (81.8%) and early overall staging (stage I and II). In oropharyngeal SCC, maximum patients presented in advanced tumor staging i.e T3 and T4 (62.5%) and advanced overall staging (stage III, IV).

Conclusions: In NSND patients, potential factors like sharp tooth, environmental smoke, occupational exposure and lichen planus may contribute to SCC in oral cavity and oropharynx.

Keywords: Oral cavity, Oropharynx, Non-smoker, Non-drinker, Squamous cell carcinoma

INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) is an anatomically heterogenous group of neoplasms arising from the mucosal surface of the oral cavity, oropharynx, hypopharynx, larynx, sinuses and other sites within the upper aerodigestive tract.1 The international incidence of HNSCC (particularly of the oral tongue and oropharynx), has increased in young adults.2

Role of tobacco smoking and alcohol drinking is well established in oral cavity and oropharyngeal SCC. However, there remains a small minority of head and neck cancer patient population who have no history of either smoking tobacco or drinking alcohol.³ In these patients, other risk factors may contribute to development of SCC. Although a growing number of reports exist that examine head and neck cancers in non users of tobacco and head and neck cancers in young patients, the current literature examining the adult NSND head and neck cancer patient population is limited.⁴⁻¹²

Cancers of oral cavity are generally easily amenable to early detection during routine screening examinations. On the other hand, tumors of the oropharynx remain relatively asymptomatic and may not be easily accessible to early detection.

The objective of this study was to gain appreciation of the clinical manifestation of SCC of oral cavity and oropharynx in NSND patients and to study the underlying etiology, pathological variants and TNM staging of the disease, with the ultimate goal of improving the treatment outcomes, so that prognosis can be better understood in this unique head and neck cancer patient population.

METHODS

The retrospective study described in this paper consists of thirty patients of newly diagnosed and previously untreated cases of SCC of oral cavity and oropharynx who met the selection criteria. These patients were identified at the department of ENT of Government Medical College and Rajindra Hospital, Patiala between the time period of October 2012 to September 2014.

The criteria for inclusion in our study population were the following: history of no tobacco use (cigarette smoking, pipe smoking, cigar smoking, or tobacco chewing), history of no alcohol consumption.

The criteria for exclusion was: history of head and neck irradiation, history of betel nut chewing, current or previous history of immunosupression (disease or treatment related), prior history of head and neck cancer, growth involving the lip.

Detailed history of patient was taken, including history of any occupational exposure to carcinogens/toxins, any history of environment tobacco smoke exposure and family cancer history. Thereafter, general physical examination, detailed ENT examination including examination of oral cavity and oropharynx, indirect laryngoscopic examination, anterior rhinoscopy, posterior rhinoscopy, and ear examination was done. Biopsy was taken and proven cases of squamous cell carcinomas of oral cavity and oropharynx by histopathological examination was taken up and reviewed to gather data on multiple clinicopathological variables. Clinical and pathological data were abstracted. Tumor data, including site, subsite, grade and TNM stage was collected. Statistical analysis was not used in current study.

RESULTS

We identified thirty cases of SCC of oral cavity and oropharynx, who were NSND, from the department of ENT, Government Medical college and Rajindra Hospital, Patiala.

In our series, maximum number of cases of SCC of oral cavity and oropharynx were seen in 4th to 6th decade with peak in 4th decade of life. Youngest in series was 34 years old and oldest 80 years old. In oral cavity cancers, patients presented most commonly in 4th decade whereas

in oropharynx, most common presentation was in 6th decade. The age distribution of cases of SCC of oral cavity and oropharynx in NSND patients is shown in Figure 1.

Table 1: Distribution of SCC of oral cavity and at various subsites according to sex.

Subsites		Male (%)	Female (%)
Oral cavity		8 (36.36)	14 (63.63)
Oral tongue	Lateral border	3	8
	Ventral surface	1	1
	Dorsal surface	-	-
Mandibular gingival		-	1
Buccal mucosa		4	2
Maxillary gingival		-	1
Hard palate		1	1

Table 2: Distribution of SCC of oropharynx and at various subsites according to sex.

Sub sites	Male (%)	Female (%)
Oropharynx	5 (62.5%)	3 (37.5%)
Base of tongue	4	1
Tonsil	1	2

Table 3: Tumour characteristics.

	Oral cavity	Oropharynx		
Histopathological grading				
Well differentiated	15	4		
Moderately differentiated	7	4		
Poorly differentiated	-	-		
T classification				
T_1	8	1		
T_2	10	2		
T ₃	2	2		
T_4	2	3		
N classification				
N_1	16	3		
N_2	4	3		
N ₃	2	2		
Stage				
I	6	1		
II	7	1		
III	5	3		
IV	4	3		

Out of thirty patients, 56% were female and 43% were males. However, we observe difference in tumor site distributions between men and women. We found that, 82% of NSND women had oral cavity SCC and 18% had oropharyngeal SCC, whereas 61.5% of NSND men had oral cavity SCC and 38.5% had oropharyngeal SCC. The sex distribution of cases of SCC of oral cavity and

oropharynx in NSND patients is shown in Figure 2. Maximum number of cases were recorded amongst housewives (56.67%) followed by labourer (16.67%).



Figure 1: Ulceroproliferative growth left lateral border of tongue.



Figure 2: Ulcerative growth involving left side of hard palate.

In the present study, sharp tooth (13.34%), regular environmental smoke exposure (10%), and occupational exposure (10%) are found to be associated with SCC of oral cavity and oropharynx followed by lichen planus (6.67%). However, these factors need to be further explored to understand the etiology in NSND patients. Predisposing factors for oral cavity and oropharygeal SCC in NSND patients is shown in figure 3.

In oral cavity cancers, maximum number of cases were that of oral tongue (59.1%) followed by buccal mucosa (27.3%) (Table 1). Furthermore, in oral tongue SCC, lateral border was most commonly involved. In oropharyngeal SCC, maximum number of cases were that of base of tongue (62.5%) followed by tonsils (37.5%) (Table 2).

In oral cavity SCC, mass/growth (50%) and non-healing ulcer (23.3%) were the most common and in

oropharygeal SCC, odynophagia (36.6%) was the most common presentation.

In case of well differentiated SCC, 78.9% had oral cavity cancers and 21% had oropharyngeal cancers. Among moderately differentiated SCC, 63.3% had oral cavity SCC and 36.3% had oropharyngeal SCC.

In oral cavity SCC, maximum patients presented in early tumor staging i.e T1 and T2 (81.8%) and early overall staging i.e stage I, II (60%). In oropharyngeal SCC, maximum patients presented in advanced tumor staging i.e T3 and T4 (62.5%) and advanced overall staging i.e stage III, IV (75%). Tumor characteristics are shown in Table 3.

DISCUSSION

The casual association between tobacco consumption and alcohol intake with the development of OSCC is well established; however a considerable portion of OSCC occurs in non-smokers and non-drinkers, indicating the presence of other risk factors.¹³

Current literature evaluated that NSND patients with oral cavity cancers presents at younger age whereas oropharyngeal cancers present at older age. In case of oral cavity cancers, it is likely that NSND patients are more attuned to oral symptoms and thus present earlier. Dahlstrom et al described a cohort of 172 NSND patients and found that SCC tend to occur in younger and peak age incidence is in 4th decade which is comparable to our study. Wiseman et al described a cohort of 1648 invasive head and neck cancer cases, 40 patients were identified as NSND and they observed mean age of presentation as 60 years in NSND patients which is contrary to our study. 3

Our study comprised of 30 patients, out of which, 13 patients were male and 17 patients were female and male to female ratio was 43.4:56.6.

In the study conducted by Wiseman et al and Harris et al male to female ratio in NSND patients was 22:78 and 25:75 respectively. ^{1,3} They did not analysed further sex incidence rates based on location of cancer in oral cavity and oropharynx. However, we observed differences in site distributions between men and women. This predominance of females in NSND population may be due to greater environmental tobacco smoke exposures than men, as women may be exposed to more smoke by virtue of having a spouse who smokes at home than that of men who would be exposed only at workplace.

This gender distribution was incomparable with study by Dahlstrom et al, which found male to female ratio to be 55.2: 44.8 in NSND patients where male population is slightly on higher side.¹⁴

Knowing the role of aetiological factors is important because NSND patients are accounting for a rising proportion of patients with SCC and disease is not restricted to smoking and alcohol abuses. However these aetiological factors needs to be further explored as it may help in better understanding of the disease process.

Occupational exposures to carcinogens/ toxins like rubber, paints, pesticides, fertilizers can be related to SCC in labourers. Despite the difficulties inherent in obtaining accurate occupational and environmental exposure histories, numerous studies have suggested that several agents encountered in the workplace may lead to an increased risk for head and neck malignancies.¹⁵

Dahlstrom et al reported that more than 40% of NSND patients had regular exposure to environmental tobacco smoke at home (most often), work or both. In addition, we found that sharp tooth (13.34%), environmental smoke exposure (10%), occupational exposure (10%) and lichen planus (6.67%) are associated with SCC in NSND patients. These factors need to be further explored.¹⁴ Potential factors like nutritional deficiency, gastrointestinal reflux disease and lichen planus may contribute to head and neck cancer development. Some authors have also suggested for a role of HPV in the development of head and neck cancer in NSND patient population. 16-20

In our series, incidence of oral cavity and oropharyngeal SCC were recorded maximum in housewives (56.67%) and next common in labourers (16.67%). This may also be attributed to environmental smoke exposure at home in housewives which needs to be evaluated in further studies. Regarding distribution according to subsites, we found that the most frequent oral cavity subsite (n=22) was the oral tongue 59.1% (n=13) followed by buccal mucosa 27.3%. Most of the series in literature have reported oral tongue as most common subsite in oral cavity SCC. Dahlstrom et al, Wiseman et al and Harris et al also reported oral tongue as the most frequent site in NSND patients in oral cavity. Furthermore, we found that, among the oral tongue growths, lateral border of tongue was most commonly involved that may be attributed to sharp tooth as causative agent which needs to be further explored. The dental professionals as well as ENT surgeons should be cognizant of the increasing incidence of SCC of oral cavity and consider oral tongue SCC when evaluating patients with tongue lesions and non healing ulcers of tongue even when history of smoking and alcohol abuse is not present.

On the other hand, we found that the most common oropharyngeal subsite in our patients was base of tongue 62.5% followed by tonsillar fossa 37.5%. In accordance with our study Dahlstrom et al and Wiseman et al also found base of tongue as most common subsite followed by tonsils in oropharyngeal tumors in NSND patients. In contrast Harris et al found an inverse pattern in subsite of

oropharynx, in which tonsils was found to be most common site followed by base of tongue.

In our study oral cavity cancers, most commonly presented with mass/growth (50%) followed by non healing ulcer (23.3%) and in oropharyngeal cancers most commonly presented as odynophagia (36.6%) followed by lump in the neck (6.67%). To the best of our knowledge, no other study has discussed about the presenting symptomatology and duration of symptoms in NSND patients.

In the present study, cervical nodal metastasis in oral tongue cancer was found to be 30.76% and in buccal mucosa was 33% whereas in base of tongue cancer was 80% and in tonsillar region was 33%. Harris et al and Wiseman et al found 43% and 45% of NSND patients to be having node positive disease respectively. In our study, we found slightly lower incidence i.e 36.67% of patients having node positive disease. Early presentation in case of oral tongue SCC may be ascribed to lower incidence of cervical lymph nodal metastasis.

The degree of differentiation is considered as one of the important prognostic factor in head and neck cancers. Dahlstrom et al observed that, out of well differentiated tumors, 79% had oral cavity cancers and among poorly differentiated tumors, 68% had oropharyngeal cancers in NSND patients. In our study, it was observed that majority of patients presented with either well differentiated or moderately differentiated SCC.

In present study, we found that, maximum patients presented in early tumor staging i.e T1 and T2 (81.8%) in oral cavity SCC. In oropharyngeal SCC, maximum patients presented in advanced tumor staging i.e T3 and T4 (62.5%). Harris et al also reported maximum number of patients presented in T1 and T2 stage (72%) but they did not analyzed TNM staging incidence rates based on location of cancer in oral cavity and oropharynx. ¹

Wiseman et al and Dahlstorm et al found that most patients presented with advanced stage disease 55% and 71.5% respectively. Both studies did not analysed staging incidence based on location of cancer in oral cavity and oropharynx. In present study, it was found that 50% of cases presented in early stage and 50% of cases presented in advanced stage.

The clinical stage at the time of presentation has been shown to be significantly related to the overall prognosis, with advanced stage disease having worst prognosis.

In addition we found that, oral cavity SCC most commonly presented with early stage (stage I, II) whereas oropharynx SCC most commonly presented with stage III, IV i.e advanced stage disease.

We also acknowledged some limitations to our study. One limitation of our study was relatively small patient cohort. Second limitation was that we did not included HPV status in our patients, which in recent times had been found to be associated with oral cavity and oropharyngeal SCC in NSND patients.

CONCLUSION

In conclusion, NSND patients are more likely to be young women with oral tongue cancer and young to middle aged men with oropharyngeal cancer mainly involving base of tongue. Furthermore, this study suggests that sharp tooth, environmental smoke, occupational exposure and lichen planus may contribute to SCC in NSND patients. High index of suspicion is required to diagnose these lesions early, even when history of smoking and drinking is absent. Thus, it will help in improving the treatment outcomes and prognosis in this unique NSND population. Further study of NSND population in HNSCC seems to be warranted.

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Institutional Ethics Committee

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