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RECENT TRENDS IN THE CLINICOPATHOLOGICAL CHARACTERISTICS OF ORAL SQUAMOUS CELL CARCINOMA – AN INSTITUITIONAL STUDY

Oral Pathology

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ABSTRACT

Oral cancer accounts for approximately 5% of all cancers globally, while in India it is about 40%. It is considered as a disease of elderly. This study analyze the recent trends in oral squamous cell carcinoma and to describe the clinicopathological characteristics of OSCC over a period of 7 years in a tertiary health care center in Southern India. Out of 495 histologically proven cases, 52 (10.5%) were under 40 years. The mean age for males was 70.3 and for females 68.6. Most common site was tongue (46%). Moderately differentiated carcinoma was the most common histological subtype (75.5%). Habit had a significant influence in male patients when compared to females (p value<0.012). p16 protein expression profile was studied in cases below 40 years of age and observed that 31 (59.5%) out of the 52 patients showed p16 positivity.

KEYWORDS

Oral squamous cell carcinoma, recent trends, p16.

INTRODUCTION

Oral cancer is a significant health problem globally with an overall incidence of 16.1 adults per 100, 000 populations [1]. In India, most common among all cancers in males and third in females [2]. Oral Squamous cell carcinoma (OSCC) is the commonest of all oral malignancies (90 -95%). Despite the amenability of oral cavity for early detection through visual inspection, these cancers are often diagnosed at advanced stages, resulting in poor survival outcomes.

Despite traditional risk factors, oral cancer may also occur due to poor oral hygiene and poor diet which is low in fruit and vegetable [3,4]. The etiology of OSCC in individuals without a history of drinking and or smoking is unclear[5,6]. A possible association with other factors like chronic irritation [7] viral infections like EBV [8], HPV [9, 10], immunosuppression [11], familial factors [12], genetic [13], and hormonal factors [14,15] have been proposed.

The purpose of this study was to determine the recent trends in oral squamous cell carcinoma cases and to describe the distribution according to gender, site, habits, and histopathologic types reported over a period of last 7-years in a tertiary dental health care center in Southern India.

MATERIALS AND METHODS

The archival records of patients reported to the Department of Oral Pathology and Microbiology, between **2010** and **2016** were retrospectively reviewed. It has been found that among the **5250** oral mucosal biopsies, **495** cases were **OSCC**. The data extracted were analyzed to determine its distribution according to age, gender, site, habits and histopathologic types. The anatomical sites reviewed in this study included buccal mucosa, alveolus, hard palate, tongue and floor of mouth (FOM). Variables analyzed for each patient included age, gender, site, habits, and histologic grading. All variables were entered in a database for analysis. p16 expression profile was studied in patients <40 years patients.

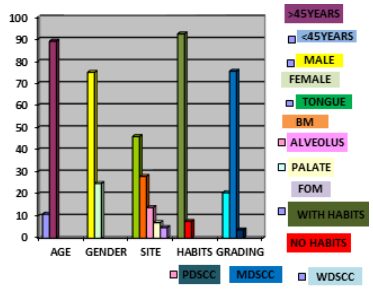
RESULTS

A total of 495 patients with OSCC in the 7-year period from 2010 to 2016 were retrospectively analyzed. Among this, 443 patients (89.49%) were above 40 and 52 patients (10.5%) were below 40 years. A significantly high male preponderance was noted with 75% of total cases. The mean age of presentation for males was 70.3 and for females 68.6 years. A site predilection was noted for tongue with 171 in males, 55 in females followed by buccal mucosa in 104 males (28%) and 49 females, alveolus in 52 males (13.9%) and 5 females, palate in 27 males (7.07%) and 3 females and FOM in 18 males (4.84%) and 11females. Histopathological examination showed that among these, 374 (75.5%) were moderately-differentiated tumors, 102 (20.6%) were well differentiated, and 19 (3.8%) were poorly differentiated tumors. 92.4% of patients were having deleterious habits and 7.6% of patients were non habituate. The data is represented in table and graph (table 1 & graph 1)

Table 1.Percentage distribution of variables among OSCC cases in the period of 2010 – 2016

Age	<40 years – 52 (10.5%)	
	>40years – 443 (89.09%)	
Gender-Male	372 (75%)	
Female	123 (24.8%)	
Site	Male	Female
Tongue	171(46%)	55(44.7%)
BM	104 (28%)	49(39.8%)
Alveolus	52 (13.9%)	5(4.07%)
Palate	27(7.07%)	3(2.43%)
FOM	18 (4.84%)	11(8.9%)
Grading	102 (20.6%)	
WDSCC	374(75.5%)	
MDSCC	19(3.8%)	
PDSCC		
Habit With habits	457(92.4%)	
Without habits	38 (7.6%)	

BM: buccal mucosa, FOM: floor of mouth, WDSCC: well differentiated SCC, MDSCC: moderately differentiated SCC, PDSCC: poorly differentiated SCC



Graph 1.Graphical representation of distribution of variables among OSCC reported in the period of 2010 – 2016

Further analysis was done in the data for patients younger than 40 years, and found that there was a significant number of OSCC cases in this age group. A male sex predilection (75.9%) which was comparable to that of total cases noted. In cases below 40 years of age, the mean age at presentation was 39.1 years for males and 34.25 years for females (P=0.436). For patients below 40 years of age, more cases were seen in tongue (58.4%) followed by buccal mucosa (39.6%) and palate (1.98%). Males show a site predilection for tongue with 23 cases (56%) followed by buccal mucosa 17 cases(41.4%) and palate 1 (0.02%).No cases were reported to occur in FOM and alveolus. In females more cases were

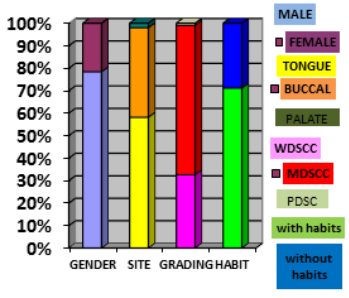
seen in tongue (63.6%) and buccal mucosa (36.3%). Histopathological grading also shows distribution with MDSCC (66.3%), WDSCC (32.6%) and PDSCC (0.9%) in males and MDSCC (63.6%) and WDSCC (36.3%) in females. Among the cases, 68.5% of patients had deleterious habits with a male dominance (87.8%). Rests of the patients were non habituate with a female predilection of 54.2%. Considering habit as a risk factor for OSCC among males and females below 40 years , it was found that, the association of habit with OSCC in males is significant than the association in females with a p value of <0.012. The above data is shown in table 2 & graph 2.

TABLE 2:Percentage distribution of variables among OSCC in patients <40 years

Gender Male Female	41(75.9%) 11(20.7%)	
Site Tongue Buccal mucosa Alveolar ridge Palate Floor of the mouth	Male 23 (56%) 17(41.4%) 0(0%) 1(0.02%) 0(0%)	Female 7 (63.6%) 4 (36.3%) 0 0 0
Grading WDSCC MDSCC PDSCC	13(32.6%) 27(66.3%) 1(0.9%)	4 (36.3%) 7 (63.6%) 0
Habit With deleterious habits Without deleterious habits	36(87.8%) 5(12.1%)	1(9.09%) 10(90.9%)

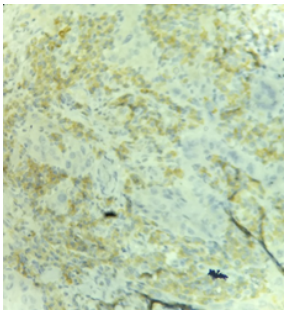
BM: buccal mucosa, FOM: floor of mouth, WDSCC: well differentiated SCC, MDSCC: moderately differentiated SCC, PDSCC: poorly differentiated SCC

Graph 2 : Graphical representation of distribution of variables among OSCC in patients <40 years.



As the incidence of OSCC in patients below 40 years was found to be more than the global average, it was decided to do further studies. Since our study was a retrospective "one" immunohistochemistry was the best possible option. Thus p16 expression profile was studied and it was observed that 31 patients (59.5%) among the 54 patients below 40 showed p16 positivity.

p16 protein expression in patients younger than 40 years



DISCUSSION

Worldwide nearly half a million patients a year are diagnosed with oral cancer. The epidemiology of oral cancer is complex because this condition shows multiple etiologic factors and the data are not available for all the countries. In a review of SEER data from 1973 to 1985, Silverman and Gorsky found that more than 95% of oral cancers occurred in persons older than 40, with a median age at diagnosis of 63 years 16. The data analyzed in our study shows that approximately 90% of cases have documented in individuals above 40 years which is in agreement with the global statistics. There is a higher incidence of OSSC cases in the young patients (10.5%) than that reported by other authors, which has varied from 0.4% to 3.6%[17, 18, 19].In the present cohort, the gender predilection is similar to reports of other dental and medical institutions [20,21]and the Indian cancer registry data [22].There is an overall male predominance in all intra-oral sub sites in both age groups of patients which is in agreement with most of earlier studies.

Oral carcinogenesis shows multifactorial etiology which includes both endogenous and exogenous factors. The changing trends of habits and the rate of occurrence of OSCC have been reported in the literature[23,24].

This study re-confirms and further contributes to establish the role of deleterious habits in the causation of OSCC which is in fact an avoidable exogenous factor. However, numerous cases of OSCC occurring in nonsmokers and non-alcoholic consumers or patients who were not associated with the traditional risk factors were seen in approximately 15-20% of all oral cancer cases as reported in some literature25. Identification of these uncommon risk factors is vital for the diagnosis of oral squamous cell carcinoma especially in cases where there is a long-standing ulcer or a smaller tumour size. The factors that could contribute to this phenomenon could include hormonal or viral infection such as HPV. The higher occurrence of OSCC in patients over 40 years old seems to be due to a longer exposure and heavier consumption of tobacco and/or alcohol than to the habit itself. Although men and women in the older group were almost equally exposed to abnormal habits, men were more prone to consume tobacco, alcohol or pan chewing heavily, which explains the predominance of OSCC in older male patients [26,27]. In our cohort, histopathological grading of tumors in both age groups showed that the majority of them were moderately differentiated. This was not of much statistical significance and was consistent with the other studies done over the years [28]

The effect of conventional etiological factors such as usage of tobacco and alcohol has been well established in the literature and it was evident in our cases also even in younger age groups. It indicates that these risk factors carry greater significance for young patients considering that the conventional risk factors like alcohol consumption and tobacco usage need a longer period of exposure for OSCC to develop. This points out that other factors such as genetic susceptibility, viral infection, immunologic modulations, and other systemic factors could have a greater role in initiating and promoting OSCC in this age group. Many investigators consider p16 over expression as an indirect marker of HPV infection in stratifying patient and thus considers it to be the most important marker as it negatively regulates cell proliferation by suppressing inactivation of pRb protein. In our cohort of young individuals we could find out nearly 60% cases with p16 positivity; which is in agreement with the data available for Indian samples when compared with that of other countries.

CONCLUSION

Oral cancer is an important public health problem. This study has highlighted the important role of tobacco and alcohol consumption in oral carcinogenesis, but nearly 10% of OSCC cases were without these conventional habits. There have been an increased number of cases among individuals without history of smoking and/or alcohol consumption; mostly in females. Another interesting aspect refers to the potential role of HPV associated with OSCC especially in younger individuals. It is important to investigate other possible factors associated with the development of OSCC, enabling appropriate clinical management and monitoring which requires a multi-level structural approach. More in-depth studies are needed to investigate the etiology of intraoral cancer in younger patients. A high index of clinical suspicion should be attached in high incidence areas that would lead to further investigation and detection of the disease in an early stage, which is perhaps the only way to ensure a good prognosis.

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