A study of Clinico-pathological Spectrum of Oral Cavity Lesions at a Tertiary Care Hospital

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Abstract
Introduction: Various inflammatory, autoimmune and infectious diseases show their expression in oral cavity. Benign tumours are more common than malignant tumours. High incidence of oral cancer has been associated with tobacco chewing and smoking habits, an important factor for oral cancers in India.

Materials and Methods: A cross sectional study was carried out in Department of Pathology, SMS Medical College, Jaipur (Rajasthan) during the year 2016-2017. Total 150 specimens of oral cavity lesions, received during study period were taken. Details about clinical history, histopathological examination and immunohistochemistry were taken and analyzed.

Results: Oral cavity lesions showed male predominance with highest prevalence in 30-59 years of life. Malignant tumours were 2.7 times as common as benign. Buccal mucosa was the most common site for malignant oral neoplasm followed by tongue. 64% of all malignant neoplasm appeared at these two sites. Squamous cell carcinoma was the most common histopathological lesion. A positive tobacco chewing history was found among three-fourth of cases (76.09%).

Conclusion: The present study concluded that majority of oral cavity lesions were malignant in nature. Tobacco chewing, in form of zarda/gutka was a major risk factor associated with oral cancers. Oral cavity is the easily accessible site for self-examination and clinical inspection at regular interval, so early diagnosis of malignant lesions can be possible. Any lesion in the oral cavity should be evaluated histopathologically to rule out malignancy.

Keywords: Oral cavity lesions, Histopathology, Benign, Malignant, Tobacco.

Introduction
Oral cavity lesions are usually common but ignored. They may be benign or malignant. Common benign lesions are lymphoid hyperplasia, retention cyst, inflammation, haemangioma, fibroma etc. and among malignant lesions squamous cell carcinoma is the most common. Oral cancer ranks the 8th most common cancer worldwide and 3rd most common cancer in India. Age standardized incidence rate of oral cancer is 12.6 per 100,000 population[1]. Variable distribution of cancer at various intraoral sites in different population suggests differences in risk factors. In India tobacco chewers constitute...
an important risk population and hence carcinoma of buccal mucosa and lateral tongue are most commonly seen in Indian population. The greatest risk for developing oral cancer is seen with the habit of “reverse smoking” (keeping the lit end of bidi or cigarette in mouth), frequently found in India. Tobacco use and excessive alcohol consumption have been estimated to account for about 90% of cancers in oral cavity. Tobacco contain more than 50 carcinogens that increases relative risk of cancer through causing various mutations disrupting the cell cycle regulations.[1-3]

Other risk factors include ill-fitting dentures, HPV infection, genetic mutations and alcohol. Prognosis of oral cancer is generally poor, with a five year survival less than 50%. Local recurrence as well as lymph node metastasis occurs in a significant percentage of patient. Distant metastasis is less common. Sometimes early stage of malignancy may mimic benign lesions which lead to incorrect management and fatal consequences for the patient. So, it is very important to make a proper diagnosis for proper management of oral cavity lesions. Histopathology is considered gold standard. The present study was planned to know the spectrum of oral cavity lesions.

Materials and Methods
A laboratory based cross sectional observational study was carried out in Department of Pathology, SMS Medical College, Jaipur (Rajasthan) during the year 2016-2017. After taking approval from institutional ethics committee, total 150 consecutive specimens of oral cavity lesions received during study period were included. Clinical data like age, sex, chief complaints, history of exposure to tobacco chewing, smoking, alcohol use and other associated illness were collected in a predesigned and semi-structured performa. Histopathological examination of all specimens was done and immunohistochemistry also used when ever required. Odontogenic tumours except peripheral ameloblastoma, tumours and tumour like lesions of lymphoid tissue, poorly preserved sample and size less than 2 mm were excluded from the study. Data were entered in Microsoft Excel 2010 and analyzed using chi square test of significance. P-value < 0.05 was considered significant.

Results
In the present study, total 150 specimens of oral cavity lesions were examined, out of them 70.67% were male and 29.33% were female. Age range of oral cavity lesions was quite large ranging from 6 days to 79 years with mean of 42.45±16.62 years. Maximum lesions (24.67%) were observed in 40-49 years age group followed by 30-39 years (20.00%) and 50-59 years (16.00%)(Figure-1). As shown in Figure-2, out of 150 tumours, 24% were benign, 4% were premalignant and 70% were malignant tumours. Commonest clinical presentation of oral lesions was ulceroproliferative growth (33.33%) in the oral cavity. Other presentations were ulcer (24.66%), nodular growth (23.33%), proliferative growth (15.33%) and white lesion (3.33%) (Table-1).

Table-2 shows the histological presentation of oral cavity lesions. It was observed that 2% tumours were inflammatory or infective in origin, 71.33% derived from surface epithelium, 14% were soft tissue tumours and 10.67% were minor salivary gland tumours. Out of 107 surface epithelial tumours, 85.98% were malignant (commonest squamous cell carcinoma), 8.41% were benign (most common squamous papilloma) and 5.61% were dysplasia. While out of 21 soft tissue tumours, 85.71% were benign (commonest hemangioma) and 14.29% were malignant. Among 16 minor salivary gland tumours, 43.75% were malignant, 6.25% was benign and 50% were non-neoplastic tumours.

Malignant tumours most commonly (37.14%) involved the buccal mucosa followed by tongue (25.71%), gingivobuccal sulcus (9.52%), hard palate (8.57%), floor of mouth (6.67%) and retromolar trigone (5.71). Lips and gingiva were involved only in 3.81% and 2.86% cases respectively (Table-3).
Present study included a detailed history of risk factors/ personal habits in all cases of oral squamous cell carcinoma (92 cases). Previous exposure to smoking, tobacco chewing, alcohol and any other chronic illness was noted. Out of 92 cases 76.09% gave history of tobacco chewing, 52.17% had exposure to smoking (bidi/cigarette). About 10.87% had no exposure to any risk factor. 1 case out of these 10 cases, had history of renal transplant one and half year back and was on immunosuppressive therapy. Dual habits were commonly noted in study (Table-4). Present study showed high exposure to tobacco chewing / smoking among all age groups. Single case of oral squamous cell carcinoma was found in 19-year female having history of tobacco chewing. In present study, higher occurrence of oral squamous cell carcinoma among cases below 30 years of age group was noted. Out of 10 such cases 9 were found to have tobacco/smoking habits.

Table-1: Clinical presentation of oral lesions

| Clinical presentation | No. of cases | Percentage |
|-----------------------|--------------|------------|
| Ulceroproliferative growth | 50 | 33.33 |
| Ulcer | 37 | 24.66 |
| Nodular growth | 35 | 23.33 |
| Proliferative growth | 23 | 15.33 |
| White lesion | 05 | 3.33 |
| Total | 150 | 100 |

Table-2: Histopathological distribution of oral lesions

| Type and sub types of oral cavity lesions | Number |
|------------------------------------------|--------|
| Infection / Inflammation (N=3) | |
| Histoplasmosis | 1 |
| Lichen planus | 1 |
| Chronic non-specific inflammation | 1 |
| Surface epithelium (N=107) | |
| Benign (N=9) | Sqamous papilloma | 5 |
| | Warty dyskeratoma | 1 |
| | Condylomaaccuminatum | 1 |
| | Benign verrucous hyperplasia | 1 |
| | Pseudoepitheliomatous hyperplasia | 1 |
| Dysplasia | 6 |
| Malignant neoplasm (N=92) | Sqamous cell carcinoma (N=81) | |
| Well differentiated SCC | 41 |
| Moderately differentiated SCC | 39 |
| Poorly differentiated SCC | 1 |
| | Verrucous carcinoma | 6 |
| | Papillary squamous cell carcinoma | 1 |
| | Basaloid squamous cell carcinoma | 1 |
| | Adenosquamous carcinoma | 1 |
| | Spindle cell (sarcomatoid ) carcinoma | 1 |
| | Lympheoepithelial carcinoma | 1 |
| Soft tissue tumours (N=21) | Benign (N=18) | Hemangima | 08 |
| | Lobular capillary hemangima | 03 |
| | Lymphangioma | 02 |
| | Neurofibroma | 02 |
| | Congenital epulis | 02 |
| | Fibroma/ fibroepithelial polyp | 01 |
| Malignant (N=3) | Low grade fibrocarcoma | 01 |
| | Leiomyosarcoma | 01 |
| | Ewings / PNET | 01 |
| Minor salivary gland tumours (N=16) | Non-neoplastic | Mucocele | 8 |
| | Benign | Pleomorphic salivary adenoma | 1 |
| | Malignant (N=7) | Mucoepidermoid carcinoma | 5 |
| | | Adenoid cystic carcinoma | 2 |
| Melanocytic tumours | Malignant | Mucosal malignant melanoma | 2 |
| Others | Tumour arising from odontogenic epithelium | Peripheral ameloblastoma | 1 |
| Total | 150 |
Table-3 Distribution of malignant oral cavity lesions according to site of origin

| Site of the lesion      | No. of cases | Percentage |
|-------------------------|--------------|------------|
| Buccal mucosa           | 39           | 37.14      |
| Tongue                  | 27           | 25.71      |
| Gingivobuccal sulcus    | 10           | 9.52       |
| Hard palate             | 09           | 8.57       |
| Floor of mouth          | 07           | 6.67       |
| Retromolartrigone       | 06           | 5.71       |
| Lip                     | 04           | 3.81       |
| Gingiva                 | 03           | 2.86       |
| **Total**               | **105**      | **100**    |

Table-4: Associated risk factors / personal habits in oral squamous cell carcinoma

| Personal habits/risk factors                              | No. of cases* (N=92) | Percentage |
|-----------------------------------------------------------|-----------------------|------------|
| Smoking (bidi / cigarette )                               | 48                    | 52.17      |
| Tobacco chewing (Zarda/ guthka/ pan)                      | 70                    | 76.09      |
| Smoking + Tobacco chewing                                 | 37                    | 40.22      |
| Smoking + Alcohol                                         | 10                    | 10.87      |
| Tobacco chewing + Alcohol                                 | 13                    | 14.13      |
| Immunosuppression (renal transplant patient)              | 1                     | 1.09       |
| No risk factor exposure                                   | 10                    | 10.87      |

* Multiple response table.

Figure-1: Distribution of oral cavity lesions according to age of subjects
Figure-2: Distribution of different types oral cavity lesions

Figure-3: (a) Oral Histoplasmosis: showing tiny, eosinophilic yeast bodies in an inflammatory granulation tissue. (b) Warty Dyskeratoma: show marked acantholytic, dyskeratotic cells. (c) Congenital Epulis: showing sheets of large, closely packed cells having abundant eosinophilic granular cytoplasm. (d) Lobular capillary hemangioma: Showing lobules of vascular proliferation with inflammation and granulation tissue formation.
Figure-4: (a) Verrucous carcinoma: showing hyperkeratosis, papillomatosis, enlarged, bulbous rete ridges. (b) Basaloid squamous cell carcinoma: showing nest of small basaloid cells. (c) Sarcomatoid (spindle) cell carcinoma: showing proliferation of atypical, hyperchromatic and pleomorphc spindle shape cells. (d) Papillary squamous cell carcinoma: showing proliferation of non-keratinizing type, transitional cell-like dysplastic epithelial cells.

Discussion
Present study was done to access the distribution of lesions found in oral cavity in relation to the age, sex and regional distribution. Personal habits or risk factors were also studied in malignant neoplasm. Study included 150 cases of various oral cavity lesions. Higher occurrence of oral lesions was observed in males. It was in contrast to previous studies by Modi et al[4] and Claudia et al[5], who reported a high incidence of oral lesions in females, however both study show male predominance for malignant neoplasm.

Present study showed a wide age range from 6 days to 79 years with mean of 42.45±16.62 years. Cases of congenital epulis were found in 6 day and 9 day old baby. Benign lesions did not show any predilection for specific age group and distributed randomly among all age groups from 1st decade to 7th decade. Akin to our observations, majority of malignant neoplasm were reported in 40-49 years, followed by 30-39 years, 50-59 years and 60-69 years. 84% cases were seen in 3rd to 6th decade of life which was consistent with Suri et al[6] study they reported 81% incidence of malignancy in 3rd to 6th decade. Youngest case
was a 19 year old female having squamous cell carcinoma of buccal mucosa. Previous study done by Agrawal et al\cite{7} also reported a case of squamous cell carcinoma of buccal mucosa in 19-year old female. Peak incidence of malignancy was seen in 40-49 years which was similar to the findings of Agrawal et al\cite{7} and Saraswathi et al\cite{8}. In present study 30% of malignant cases were found below 40-years of age. This rising occurrence of malignancy in early age was due to increased use of tobacco products in early age and other less known environmental and genetic factors contributing in developing malignancy.

In present study out of 150 cases, 70% were malignant, 26% were benign and 4% were precursor/premalignant. Kosam & Kujur\cite{9} found the similar frequency of malignant oral lesions in Raipur, India. Atram et al\cite{10} also reported the high incidence of malignancy in Maharasthra, India. Agrawal et al\cite{7}, Zaib et al\cite{11} and Dowerah & Bhuyan\cite{12} found a low incidence of malignancy in Bareilly, Rawalpindi and Guawahati respectively as compared to our study. Suri et al\cite{6} reported only 11.4% neoplastic cases in Bathinda, Punjab, out of which only 62.95 were malignant. Modi et al\cite{4} reported 32.8% malignant neoplasm in Manipur, India.

Present study showed a wide histopathological spectrum of lesions in oral cavity. 71.33% of cases in present study arise from surface epithelium, contributed major bulk of the morbidity. Out of these 6% were benign proliferations (included squamous papilloma, warty dyskeratoma, codylo-maaccuminatum and pseudoepitheliomatous hyperplasia), 4% were dysplasia and 61.33% (92 cases) malignant epithelial neoplasm. Among malignant, squamous cell carcinoma was the most common entity comprising of 81 cases. It was very close to the study by Kosam & Kujur\cite{9} (72.57%) and Atram et al\cite{10} (70%). Oral soft tissue tumours held the second most common histological entity which comprises of 21 cases (14%). Among these hemangiomia was the most common (8 cases) followed by lobular capillary hemangioma (3 cases), lymphangioma (2 cases), neurofibroma (2 cases), congenital epulis (2 cases), fibroepithelial polyp (1 case). Malignant soft tissue tumours comprises of leiomyosarcoma (1 case), low grade fibrosarcoma (1 case) and Ewings/PNET (1 case). Occurrence of leiomyosarcoma in oral cavity was extremely rare. In present study, a case of primary leiomyosarcoma of floor of mouth was reported. 28-years male presented with soft tissue mass in floor of mouth. MRI study of head & neck revealed a large lobulated lesion of size 46x59x69 mm, in floor of mouth causing superior displacement of tongue along with bilateral submandibular, sublingual, retromandibular and upper cervical lymph nodes. Present study included a case of low grade fibrosarcoma. 48-years male presented with a large 7x5x5 cm globular mass arising attached with mandible. Tumour was infiltrating into the underlying mandible. It was often difficult to determine whether the lesion primarily developed in the soft tissue or intraosseously in mandible. Yuwanati and Tupkari\cite{13} also report a case of fibrosarcoma of mandible in a 44-year old female while Reddy et al\cite{14} reported a case of maxillary fibrosarcoma in 45-year male. Present study included a case of Ewing’s sarcoma arising in mandibular bone, extending into retromandibular trigone and buccal mucosa. Patient was 27-year female. Margaixet et al\cite{15} presented a systemic literature review of oral cavity Ewing’s sarcoma reported during 1960-2014. Seventy-one cases of Ewing’s sarcoma of the oral cavity were documented. Ewing sarcoma of the oral cavity showed a slight female predominance (50.7%).\cite{15} In present study the case was also a female.

Tumours of minor salivary gland (MSGTs) constituted the third common broad histopathological category in oral lesions in our study comprising of 16 cases (10.67%). Mucocele was the most common non-neoplastic lesion. A single case of pleomorphic salivary adenoma was found on lower lip in 40-years female. Among the malignant MSGTs, there were mucoepidermoid carcinoma (5 cases) and adenoid cystic carcinoma...
Incidence of MSGTs in our study was 10.67%. Kosam & Kujur\(^9\) reported 1 case out of 350 cases (0.3%), Dilemmodi et al\(^4\) reported 1 case out of 119 case (0.8%), which was very less as compare to our study. Various studies including Mishra and Mishra\(^16\), Agrawal et al\(^17\) etc. reported hard palate was the most common site for MSGTs which was comparable to our study. Among the malignant, mucoepidermoid carcinoma was the most common followed by adenoid cystic carcinoma in our study, which was comparable to the literature. High grade and intermediate grade mucoepidermoid carcinoma found more as compare to low grade in our study, while Mishra and Mishra\(^16\) reported low grade mucoepidermoid as common finding in their study.

Present study reported 2 case of mucosal malignant melanoma out of 150 cases (1.33%). Primary malignant melanoma of oral cavity is very rare. Its prevalence ranges from 0.4% to 1.4% in oral cavity and 2% to 5% of all melanomas. Zaib et al\(^11\) reported 2 case of mucosal malignant melanoma out of 114 cases (1.7%) which was similar to our study and Kosam and Kujur\(^9\) reported 1 case of mucosal malignant melanoma out of 350 cases (0.28%).

In present study buccal mucosa was the most common site affected in malignant neoplasm comprising of 37.14%, followed by tongue (25.71%). Kosam & Kujur\(^9\),Modi et al\(^4\), Claudia et al\(^5\) also found buccal mucosa as common site.

So among the various regions in oral cavity, buccal mucosa was involved most frequently followed by tongue. Lateral border of tongue was affected most frequently as compared to dorsum and ventral surface in present study. This site specification for oral malignancy had an association with personal habits of keeping tobacco in mouth for long time and having smoking which affect the mucosa of lateral border of tongue and buccal mucosa. Long exposure of carcinogens makes the mucosa vulnerable to get change in the genetic material and developing malignancy. In our study lower lip was affected in almost all cases, no case was found on upper lip.

In present study, oral lesions showed varied spectrum of clinical presentation in form of growth, ulcer and a white patch. The most common growth pattern was ulceroproliferative growth. Ulcerative lesions in the oral cavity were next common presentation. Benign lesions like hemangioma, mucocele, neurofibroma, lobular capillary hemangioma and epulis showed a nodular growth pattern which can be sometimes ulcerate due to trauma and friction. Verrucous carcinoma, squamous papilloma and some squamous cell carcinoma cases showed a proliferative growth of varying size. White lesions were found on buccal mucosa and tongue only.

Present study included a detailed history of personal habits or exposure to known carcinogens in cases of malignant epithelial neoplasm in oral cavity. Out of 92 cases of oral squamous cell carcinoma, 52.17% gave history of bidi/cigarette smoking, 76.09% gave history of tobacco chewing in form of Zarda/Gutakha/Betal.40.22% had dual habits of smoking and tobacco chewing. Exposure to alcohol alone was not found in any case. Alcohol along with smoking and tobacco chewing was found in 10.87% and 14.13% respectively. About 10.86% cases had no exposure to any risk factor who were elderly females.

Youngest case of oral squamous cell carcinoma was a 19-year female, from rural area, had a history of tobacco chewing. Tobacco chewing and bidi smoking was common in females of rural population in Rajasthan. In our study, tobacco chewing was quite common in females as compare to smoking. Alcohol exposure was not seen in females. Increasing use of tobacco products in younger age was found in our study. Fairly 88% cases below 40-year of age gave history of tobacco use in any form. Rising incidence of oral squamous cell carcinoma at an early age contributed as a significant morbidity and mortality to the population. Iype et al\(^18\) found 56.4% of patients were habituated to either tobacco chewing, smoking or
alcohol. Bhat et al reported 58% of patients were smoker, 52% were consuming tobacco in form of pan or gutkha, 18% were both smoking and tobacco chewing, 37% were consuming alcohol, 44% were using alcohol with tobacco either smoking or chewing, 14% did not have any habit.

**Conclusion**

It was concluded from present study that awareness among population including young adults and females regarding harmful effects of tobacco products and clinical presentation of their oral lesions should be exercised. Every lesion in oral cavity is to be submitted for histopathology for correct diagnosis and assessment of malignant potential in early stage. This aids in better patient care, reduced morbidity and mortality and improves survival.

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