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Original Article

Pathology Section

Spectrum of Histopathological Diagnosis of Oral Lesions in a Tertiary Care Hospital at Miraj in Maharashtra State, India

RAHUL Y SAKPAL[1], BHUSHAN M WARPE[2], SHWETA JOSHI-WARPE[3]

ABSTRACT

Introduction: Oral cavity is a common site for many types of benign, precancerous conditions and malignant tumours as well as development of congenital and acquired lesions. Oral cancers are the most common type of cancer in Indian men and actually accounted for 40% of all forms of cancers due to tobacco addiction, representing 4% of total body cancers. In Indian females, 2% of all cancers are of oral cavity. The knowledge of aetiological factors for the development of oral cancers can make the disease preventable.

Aim: To study histopathological spectrum of various oral lesions.

Materials and Methods: This was a prospective observational study done, during the period from November 2013 to June 2017, 150 cases of oral lesions were studied at a tertiary care hospital in Miraj. All the cases were studied and histopathological diagnosis was correlated with clinical findings. The Microsoft Excel 2010 sheet was filled as per case proforma of patients. Analysis was done manually like age wise, gender wise, site wise and sex wise distribution based on the Excel sheet data.

Results: The age of study population ranged from 6-80 years. Most oral cavity lesions were found in the age group 51-60 years of age group with 46/150 (30.67%) cases. Male to female ratio was 1.78:1. Malignant epithelial tumours of oral cavity comprised 100/150 cases (66.67% cases). Amongst malignant tumours, Squamous Cell Carcinoma (SCC) comprised 92/100 cases (92% cases). There was history of addiction in 96/100 cases (96% cases) with 52/100 cases as tobacco chewers (52% cases). 4/100 cases did not have history of addiction (4% cases).

Conclusion: The clinical examination of the oral pathological lesions does not lead to appropriate diagnosis. The clinical diagnosis must be supplemented by 'gold standard' histopathological examination for confirming the malignant tendency of oral lesions.

Keywords: Oral-cavity, Precancerous lesions, Squamous cell carcinoma, Tobacco

INTRODUCTION

Oral cavity being a common site for benign and malignant tumours are also associated with the development of congenital and acquired lesions. The benign tumours do not invade other tissues and do not spread to other parts of the body whereas the malignant tumours can penetrate into surrounding tissues and spread to other parts of the body. There are also some oral precancerous conditions that start off harmless but can later develop into cancer [1].

Congenital lesions include dermoid cyst, odontogenic cyst, lingual thyroid. The majority of acquired, localised overgrowth of the oral mucosa is reactive rather than neoplastic in nature [2]. The likelihood of benign oral tumours and tumour-like conditions to recur are rare. Surgical removal helps in its treatment [2].

Malignant tumours of oral cavity include Squamous Cell Carcinoma (SCC), verrucous carcinoma, basaloid SCC, spindle cell carcinoma, acantholytic SCC, adenosquamous carcinoma, carcinoma cuniculatum, lymphoepithelial carcinoma, salivary gland carcinomas, malignant soft tissue tumours, malignant mucosal tumours like melanoma as well as haematolymphoid tumours [2,3].

Oral cancer is the eighth most common cancer in men and ranks 14th among women worldwide. Two-thirds of this burden is borne by developing countries and over 30% by India only alone [3]. Oral cancers are the most common type of cancer in India in men which accounted for 40% of all forms of cancers. In Indian males, oral cancers represent 4% of total body cancers whereas in Indian females it accounts for 2% of all cancers [4].

The knowledge of aetiological factors for the development of oral cancers can make the disease preventable by avoidance of risk factors like tobacco consumption, betel-quid chewing and alcohol abuse. Betel-quid and areca-nut chewing were major risk factors evaluated by International Agency for Research on Cancer (IARC) as carcinogenic to humans, more so in India [3]. In Western countries, tobacco usually is taken in the form of cigarette, cigar or pipe smoking. The aetiologic role of oncogenic Human Papilloma Virus (HPV) infections in the development of oral cancer is also being defined. The awareness of oral hygiene in prevention of oral lesions/HPV infections is of paramount importance.

Syphilis, nutritional deficiencies, sunlight (in cases of lip cancer), miscellaneous factors including heat (particularly heat from a pipe steam in cases of lip cancer), trauma, sepsis and irritation from sharp tooth and dentures also play a role in the aetiology of oral cancers [3]. Many oral carcinomas arises within regions that previously had premalignant lesions. The most common premalignant lesions seen in oral cavity are leukoplakia with related dysplasia [5]. An adequate incisional biopsy taken from the lesion can provide over 98% diagnostic accuracy as to whether the lesions are malignant or not [6]. This present study was undertaken to study the various lesions of the oral cavity.

It is important to have a patient profile/study of oral lesions which can vary in different regions of the world.

We studied the results of the present study in Miraj with the rest of the authors worldwide to know about the disease in our area, which was the prime novelty factor. Our objectives were: 1) To study gross and microscopic features of oral lesions in our region. 2) To study patient profile with respect to age, site, gender, addiction status and histopathological opinion.

MATERIALS AND METHODS

The present prospective, observational study of three years and seven months was conducted on 150 cases of oral lesions with simple random sampling. The study was conducted after obtaining the

Ethics committee Approval (IEC No. GMC Miraj/PATH/PATH 2015-2018/53/2015) from November 2013 to June 2017 in Department of Pathology at a tertiary care hospital in Miraj, Maharashtra.

Sample size calculation: Sample size was calculated using Open Epi statistical software with 95% confidence interval and 80% power.

Inclusion criteria: All oral cavity samples received during the study time period at Department of Pathology, Miraj, Maharashtra at histopathology section.

Exclusion criteria: The exclusion criteria were: 1) Patient with major salivary gland lesions; 2) Metabolic diseases of oral cavity; 3) Inadequate tissue on histopathology; 4) Localised lesions of the soft palate, tonsils, the side and posterior-wall of the throat.

All surgical resection specimen and oral biopsies were fixed in 10% formalin. The Formalin Fixed Paraffin Embedded (FFPE) tissue sections were stained with Haematoxylin and Eosin (H&E) and were reported.

STATISTICAL ANALYSIS

The case details were filled in case proforma of patients. The entries were later made in Microsoft Excel 2010 sheet and analysed by descriptive statistics as frequency (n) and percentages (%) manually.

RESULTS

The age of study population ranged from 6-80 years. Most oral cavity lesions were found in the age group 51-60 years of age group with 46 cases (30.67%). Amongst all oral cavity lesions, males were affected more than the females with male to female ratio of 1.78:1. Most common site involved in oral cavity lesions was buccal mucosa; 53 cases (35.33%).

Most common clinical presentation in oral cavity lesions was oral swelling. The spectrum of various histopathological categorisations of oral lesions with respect to age group, gender distribution, addiction status, location and histopathological diagnosis (n=150) are discussed in [Table/Fig-1]. Cysts of oral cavity were most common in 21-30 years of age group. Amongst all cysts of oral cavity, males were affected more than the females with male to female ratio of 1.2:1. Most common site involved in cysts of oral cavity was lip. Most common pathological subtype of cyst of oral cavity was mucocele [Table/Fig-2,3]. Amongst all oral cavity lesions, oral malignant epithelial lesions account for maximum cases; 100 (66.67%) cases. A 92 out of these 100 cases were oral SCC. A 66 out of 92 cases were well-differentiated SCC.

DISCUSSION

Oral tumours are common tumours of India. This changing pattern of malignancy in developing India is due to higher consumption of tobacco in the form of chewing as well as smoking.

A variety of oral lesions summing up to 150 cases, both non-neoplastic and neoplastic were analysed for the purpose of studying the clinical aspect as well as histopathological patterns of oral tumours.

Age incidence of all lesions of oral cavity ranged from 6 to 80 years with 30.67% of cases occurred between 51-60 years of age group. Zaib N et al., in their study found most common age group as 51-60 years with 35.96% cases [9]. This finding is comparable with the present study as per [Table/Fig-4] [7-16].

In the present study, as per [Table/Fig-4], oral lesions showed male preponderance with male to female ratio of 1.78:1 and this is in accordance with most of the studies; especially; Muhsen HJ et al., with male to female ratio of 1.89:1 [8]. The present study as per [Table/Fig-4] shows that majority of cases occurred in buccal mucosa (35.33%) which is in accordance with the result in the study conducted by Ali M and Sundaram D (26.8%), Mehta NV et al., (32%) and Mishra V et al., (54.5%) in which the most common site was buccal mucosa [13-15]. In the present study as per [Table/Fig-5] [8,11,14,16-18], malignant epithelial tumours of oral cavity were the most common oral cavity lesions (66.67%) which is in accordance with the result in the study conducted by Parikh S et al., in which the most common lesion was malignancy (61.83%) [11]. Ulcerative lesion was the most common gross finding for malignancies [Table/Fig-6].

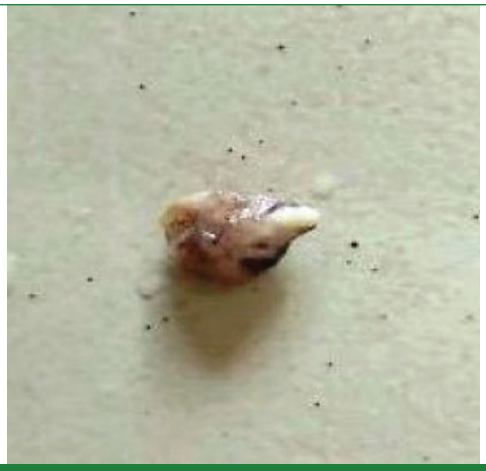
Most oral SCC was well-differentiated SCC with 66 cases out of 92 cases [Table/Fig-7]. This was followed by moderately differentiated SCC with 21 cases out of 92 cases [Table/Fig-8]. Only five cases out of 92 cases were poorly differentiated SCC.

As per [Table/Fig-9] [19-22], the present study findings of reactive hyperplastic lesions were comparable to study done by Reddy V et al., and Kashyap B et al., [21,22]. In both studies, females were common than males. Just like study by Kashyap B et al., pyogenic granuloma was the most common reactive hyperplastic lesion of oral cavity which is comparable with the present study [Table/Fig-10] [22].

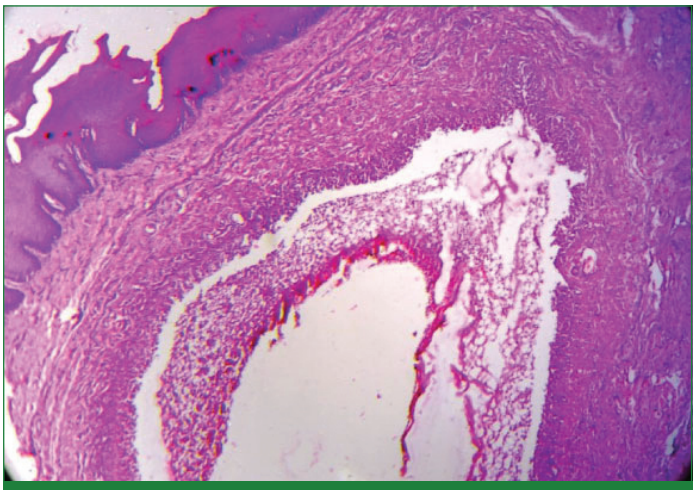
As per [Table/Fig-9], the most common age group affected in study by Awange DO et al., was 20-29 years which is similar to that found in the present study [19]. Most common site was gingiva, as studied

Parameters	Reactive, inflammatory, and tumour-like lesions	Benign epithelial tumours	Epithelial precursor lesions	Malignant epithelial tumours
No. of cases	**19**	**23**	**8**	**100**
Most common age group affected	21-30 years of age with 6 cases (31.58%)	21-30 years of age with 8 cases (34.78%)	51-60 years of age with 3 cases (37.5%)	51-60 years of age with 39 cases (39%).
Male to female ratio	1: 1.37	1.4: 1	1.67: 1	2.3: 1
Location of lesions	• Gingiva with 8 cases (42.11%). • Buccal mucosa with 6 cases (31.58%). • Retromolar trigone with 5 cases (26.32%).	• Tongue with 8 cases (34.78%). • Buccal mucosa with 7 cases (30.43%). • Gingivo-buccal sulcus with 6 cases (26.09%). • Lip with 2 cases (8.7%).	• Tongue with 5 out of 8 cases (62.5%). • Gingivo-buccal sulcus with 3 out of 8 cases (37.5%)	• Buccal mucosa with 40 cases (40%). • Tongue with 25 cases (25%). • Gingivo-buccal sulcus with 20 cases (20%). • Retromolar trigone with 15 cases (15%)
Histopathological diagnosis	• Pyogenic granuloma with 9 cases (47.37%). • Fibrous epulis with 7 cases (36.84%). • Peripheral giant cell granuloma with 2 cases (10.53%). • Fibrous hyperplasia with 1 case (5.26%)	• Squamous papilloma with 14 cases (60.87%). • Haemangioma with 7 cases (30.43%). • Mucocele with 2 cases (8.7%)	• Mild dysplasia with 3 cases each (37.5%). • Moderate dysplasia with 3 cases each (37.5%). • Severe dysplasia with 1 case (12.5%). • Carcinoma in-situ with 1 case (12.5%)	• Squamous Cell Carcinoma (SCC) with 92 cases (92%). • Mucoepidermoid carcinoma with 2 cases (2%). • Basaloid carcinoma with 2 cases (2%). • Acantholytic carcinoma with 2 cases (2%). • Spindle cell carcinoma with 1 case (1%). • Verrucous carcinoma with 1 case (1%)
Tobacco chewers	-	-	4 out of 8 cases (50%)	52 out of 100 cases (52%)
All addictions (smoking, pan-chewers, alcoholism, gutkha)	-	-	All 8 cases (100%)	96 out of 100 cases (96%)

[Table/Fig-1]: Spectrum of various histopathological categorisations of oral lesions with respect to age group, gender distribution, addiction status, location and histopathological diagnosis (n=150).



[Table/Fig-2]: Gross photograph-Excisional biopsy of Mucocele on lower lip measuring 2×1 cm.



[Table/Fig-3]: Microphotograph-Microscopy showing an area of mucin surrounded by granulation tissue, consistent with mucocele. (H&E stain, x100).

Study	Most common age group in Years (% of cases in that age group)	Male:Female ratio	Most common site (% in this group)
Mehrotra R et al., (2006) [7]	31-40 (45.05%)	2.78:1	-
Muhsen HJ et al., (2009) [8]	40-49 (14.4%)	1.89:1	-
Zaib N et al., (2012) [9]	51-60 (35.96%)	-	-
Luqman M et al., (2012) [10]	20-29 (51.6%)	-	-
Parikh S et al., (2013) [11]	31-40 (23.66%)	2.74:1	-
Moridani SG et al., (2014) [12]	31-50 (62%)	-	-
Ali M and Sundaram D (2012) [13]	-	1.1:1	Buccal mucosa (26.8%)
Mehta NV et al., (2013) [14]	-	2.44:1	Buccal mucosa (32%)
Mishra V et al., (2009) [15]	-	-	Buccal mucosa (54.5%)
Agrawal R et al., (2015) [16]	-	-	Tongue (39%)
Present study	51-60 (30.67%)	1.78:1	Buccal mucosa (35.33%)

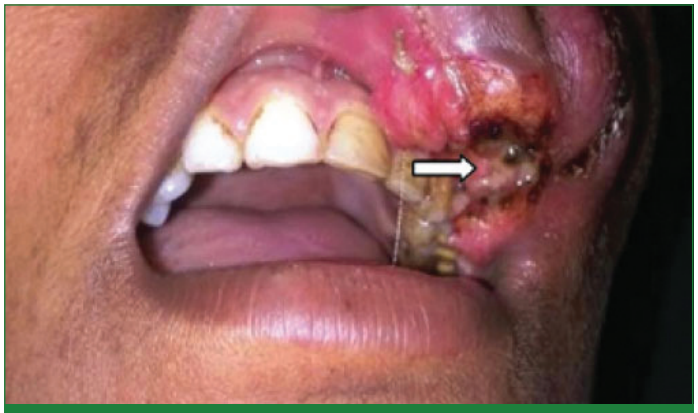
[Table/Fig-4]: Comparative analysis of common age incidence, gender wise and site wise distribution of all lesions of oral cavity [7-16].

by Awange DO et al., Naderi NJ et al., and Reddy V et al., which is comparable with the present study [19-21].

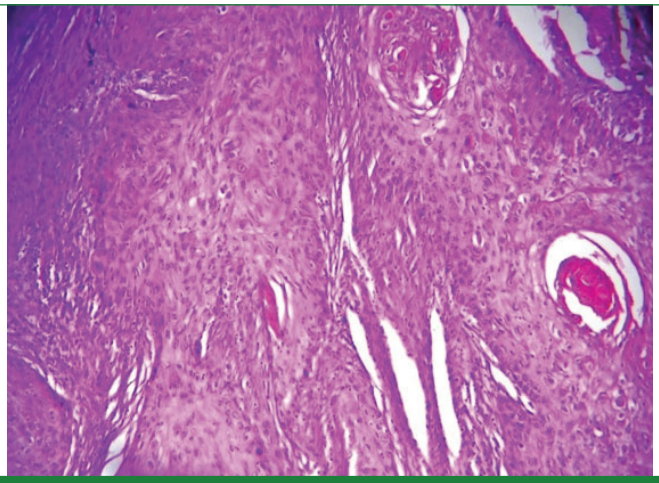
In the present study, the most common benign epithelial tumour of oral cavity was squamous papilloma (58.34%) [Table/Fig-11]. This is in

Study	Non-neoplastic (%)	Neoplastic (%)		
		Benign	Epithelial precursor lesions	Malignant
Muhsen HJ et al., (2009) [8]	74	8.6	3.9	13.5
Shivshetty BS, (2009) [17]	-	9.14	4.3	86.56
Hassawi BA et al., (2010) [18]	69.63	16.5	0.99	12.8
Mehta NV et al., (2013) [14]	53	5	17	25
Parikh S et al., (2013) [11]	23.66	2.30	12.21	61.83
Agrawal R et al., (2015) [16]	39.1	13.53	-	47.36
Present study	12.67	15.33	5.33	66.67

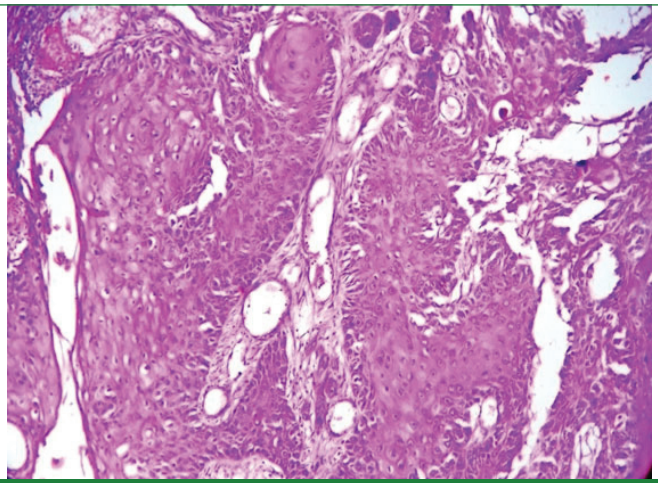
[Table/Fig-5]: Comparison of percentage prevalence of major histopathological types of oral cavity lesions [8,11,14,16-18].



[Table/Fig-6]: Clinical photograph of ulcero-proliferative swelling of Squamous Cell Carcinoma (SCC), of size 4×3 cm, on left buccal mucosa.



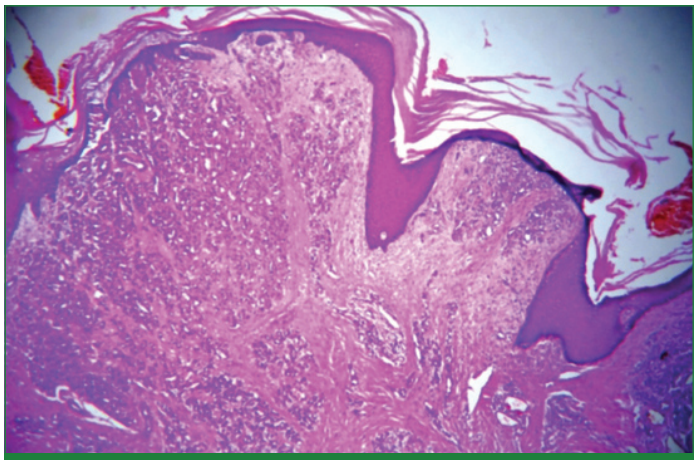
[Table/Fig-7]: Microphotograph of well-differentiated Squamous Cell Carcinoma (SCC) showing round to polygonal tumour cells with individual cell keratinisation and keratin pearls (H&E stain, x 400).



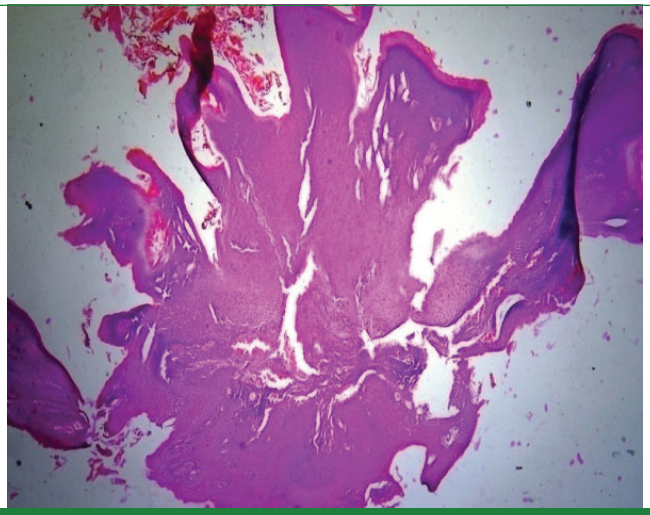
[Table/Fig-8]: Microphotograph of Moderately differentiated squamous cell carcinoma showing pleomorphic tumour cells with hyperchromatic nuclei and minimal keratinisation (H&E stain, x 400).

Study	Mean age (years)	Male:Female ratio	Common site	Common subtype
Awange DO et al., (2009) [19]	30.5	1:2.11	Gingiva (77.2%)	Fibrous epulis (38.7%)
Naderi NJ et al., (2012) [20]	39.56	1.4:1	Gingiva (64.36%)	Peripheral giant cell granuloma (30.12%)
Reddy V et al., (2012) [21]	31.56	1:1.5	Gingiva (81.8%)	Fibrous hyperplasia (57.4%)
Kashyap B et al., (2013) [22]	36	1:1.14	Mandible-region (45%)	Pyogenic granuloma (42%)
Present study	47.49	1:1.37	Gingiva (42.11%)	Pyogenic granuloma (47.37%)

[Table/Fig-9]: Comparison between studies of reactive, hyperplastic conditions of oral cavity lesions [19-22].



[Table/Fig-10]: Microphotograph of Pyogenic granuloma-Microscopy showing lobules of capillary sized blood vessels lined by endothelial cells and separated by fibrous septae with neutrophilic infiltrate (H&E stain, x 100).



[Table/Fig-11]: Microphotograph of Squamous papilloma: Microscopy showing proliferation of keratinised stratified squamous epithelium arranged in finger-like projections with fibrovascular connective tissue cores (H&E stain, x 100).

accordance with the result in the study conducted by Muhsen HJ et al., Parikh S et al., Mehta NV et al., and Agrawal R et al., [8,11,14,16].

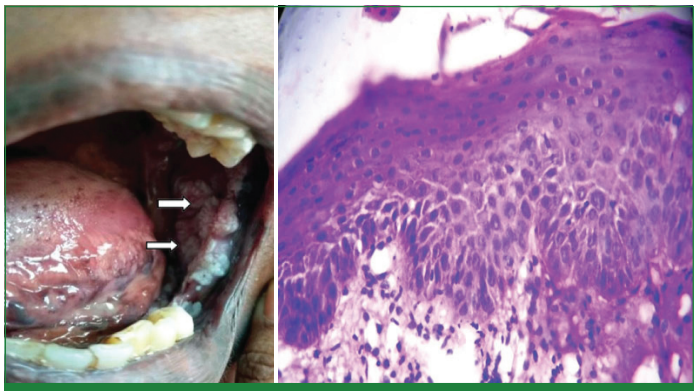
Thakur BS et al., in their study found that tongue was the most common site for benign epithelial tumours in oral cavity (38%) which is comparable with present study (33.33%) [23].

According to Hassawi BA et al., in their study, most common age group of benign epithelial tumours in oral cavity was 11-20 years and 21-30 years with 30% cases each of all benign epithelial tumours [18]. In the present study, the most common age group of benign epithelial tumours was 21-30 years (33.33%) followed by 11-20 years (16.67%). Benign epithelial tumour of the present study was slightly more common in males than in females with male to female ratio of 1.4:1 [8]. Muhsen HJ et al., in their study found male to female ratio of 2.28:1 [8].

In the present study as per [Table/Fig-12] [24-26], dysplasia is commonest epithelial precursor lesion which was in accordance with the result in the study conducted by Prithal G [26]. Gross photograph of leukoplakia and microphotograph of mild oral squamous dysplasia are displayed in [Table/Fig-13,14], respectively.

Study	Dysplasia (%)			Carcinoma in-situ (%)	Hyperkeratosis without dysplasia (%)
	Mild	Moderate	Severe		
Lee JJ et al., (2006) [24]	22.6	26.44	4.86	-	46.1
Allegra E et al., (2009) [25]	21.05	13.16	15.79	10.53	39.47
Prithal G (2013) [26]	56.25	18.75	12.5	6.25	6.25
Present study	37.5	37.5	12.5	12.5	-

[Table/Fig-12]: Comparison of histological subtypes of epithelial precursor lesions of oral cavity [24-26].



[Table/Fig-13]: Clinical photograph of leukoplakia -localised white patch of 3×2 cm size on the left side of buccal mucosa. **[Table/Fig-14]:** Microphotograph of Mild oral squamous dysplasia-Microscopy showing drop-shaped rete ridges, basal cell hyperplasia with loss of polarity limited to lower third of the epithelium (H&E stain, x 400). (Images from left to right)

In this study, mean age for malignant epithelial tumours was 49.82 years. Maximum numbers of patients were in the age range 51-60 years (39%). The youngest and oldest patient in our study was 29 years and 80 years respectively. The present study is in concordance with Mehrotra R et al., Shivshetty BS, Prithal G, Dhar PK et al., and Abhinandan B [7,17,26-28], according to these studies, malignant epithelial tumours were commonly seen in 6th decade. Atram MA et al., reported highest incidence of malignant epithelial tumours in 5th decade, a decade earlier compared to the present study.

Most of the studies found maximum incidence of oral malignant epithelial tumours in people over 50 years of age. Hence, screening programs targeting men over 50 years, would help in early diagnosis of oral cancer and therefore improve the treatment outcome.

From [Table/Fig-15] [17,26,29-32], it can be observed that most of the authors found a male preponderance in their studies. In the present study, 70% were males and 30% patients were females which is similar with the study reported by Durazzo MD et al., with relatively higher incidence in male population. Gender is not a risk factor per se in oral cancers [29].

Study	Males (%)	Females (%)
Durazzo MD et al., (2005) [29]	68.2	31.8
Khandekar SP et al., (2006) [30]	61.3	38.7
Brandizzi D et al., (2008) [31]	55	45
Shivshetty BS (2009) [17]	63.98	36.02
Prithal G (2013) [26]	60.71	38.29
Bhat SP et al., (2015) [32]	74.2	25.7
Present study	70	30

[Table/Fig-15]: Comparative study of malignant epithelial tumours amongst males and females [17,26,29-32].

The difference may be due to the high rate of tobacco, smoking and alcohol consumption in males compared to Indian females [33].

Buccal mucosa (40%) was the commonest site for oral malignancies. Similar findings were observed by various authors like Shivshetty BS, Prithal G, and Bhat SP et al., [17,26,32]. Tongue was the most common site involved in Mehrotra R et al., and Bhattacharjee A et al., studies [7,34]. This can be attributed to cultural difference in the use of tobacco which has led to the variation in the geographic and anatomic incidence of oral cancers in accordance with dose response principle [7].

From [Table/Fig-16], it was observed that with 92%, SCC was the most common malignancy in the present study [17,26,30,34,35].

Study subtype	Shivshetty BS (2009) [17]	Prithal G (2013) [26]	Khandekar SP et al., (2006) [30]	Bhattacha-rjee A et al., (2006) [34]	Bushra A et al., (2011) [35]	Present study
Squamous cell carcinoma	98.76	92.87	72.5	85.12	95.5	92
Verrucous carcinoma	0.62	5.94	27.5	7.14	-	1
Spindle cell carcinoma	-	-	-	-	-	1
Acantholytic SCC	-	-	-	-	0.75	2
Basaloid carcinoma	0.62	1.19	-	-	-	2
Mucoepider-moid carcinoma	-	-	-	-	0.75	2
Others	-	-	-	7.74	3	-

[Table/Fig-16]: Comparison of histopathological subtypes of malignant lesions of oral cavity [17,26,30,34,35].

As per [Table/Fig-17] [11,17,26,36], out of 100 patients of oral malignant epithelial tumours, in the present study, 52% patients were tobacco chewers, 15% were smokers, 2% were alcoholics, 12% were habituated to pan, 15 % had combined habit of tobacco chewing with either smoking or alcohol. Only 4% did not have any habit. This finding is comparable with Parikh S et al., and Shivshetty BS [11,17].

Habits	Shivshetty BS (2009) [17]	Prithal G (2013) [26]	Parikh S et al., (2013) [11]	Akram S et al., (2013) [36]	Present study
Tobacco chewing	47.56	33.33	68.35	420	52
Pan/Gutkha	17.07	-	-	47	12
Smoking	28.05	35.71	21.51	-	15
Alcohol	2.44	2.38	-	1	2
Tobacco+Smoking/ Alcohol	-	2.38	-	5	15
Smoking+Pan/Gutkha	-	20.24	-	22	-
Smoking+Alcohol	3.66	-	6.32	-	-
Nil	1.22	5.95	3.79	5	4

[Table/Fig-17]: Comparison of addiction habits in malignant epithelial tumours of oral cavity [11,17,26,36].

In the present study, most common age group of SCC was 51-60 years with 42.39%. This finding is comparable with Shivshetty BS, Prithal G and Bhattacharjee A et al., [17,26,34]. According to these studies, SCC was commonly seen in 6th decade. Male to female ratio of SCC of oral cavity was 2.54:1. This finding is comparable with Bhattacharjee A et al., and Akram S et al., [34,36]. Buccal mucosa (43.48%) was the most common site for oral SCC. Similar findings were observed by authors like Shivshetty BS, Prithal G, Akram S et al., and Wahid A et al., [17,26,36,37].

The studies conducted by Shivshetty BS, Prithal G, Atram MA et al., and Kiran G et al., [17,26,38,39], found well-differentiated SCC as the most common histological grade among all cases of invasive SCC, which is in accordance with present study (71.74%).

Dragomir LP et al., study, however, showed majority of the tumours as well-differentiated SCC but showed an almost equal percentage of poorly differentiated SCC [40], whereas a study conducted by Bushra A et al., showed majority of cases of moderately differentiated SCC of oral cavity [35].

Limitation(s)

Pathological Tumor-Node-Metastasis (pTNM) staging was not discussed as primary focus of the study was on histopathological pattern based primary diagnosis of the malignant oral lesions. The follow-up of patients was not done as our study is an observational prospective research article and not an analytical study. Clinicopathological correlation for concordance rate and disconcordance rate was not the aim of the study.

CONCLUSION(S)

Oral and oropharyngeal cancers are the one of the most common malignancy in developing countries. The incidence of oral SCC remains high due to the bad habits like pan and tobacco chewing in Miraj region. Any mass lesions especially in the oral cavity should be biopsied to rule out malignancy. A detailed clinical workup with histopathology study can help in diagnosing most of the oral cavity epithelial precursor lesions. This potentially reduces the morbidity and mortality arising out of subsequent malignant transformation.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Pathology, B.K.L Walawalkar Rural Medical College, Sawarde, Maharashtra, India.
2. Associate Professor, Department of Pathology, B.K.L Walawalkar Rural Medical College, Sawarde, Maharashtra, India.
3. Associate Professor, Department of Pathology, B.K.L Walawalkar Rural Medical College, Sawarde, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Shweta Joshi Warpe,
Associate Professor, Department of Pathology, B.K.L. Walawalkar Rural Medical College and Hospital, Shree-kshetra Dervan, Dist-Ratnagiri, Sawarde, Maharashtra, India.
E-mail: shwetajoshi4422@yahoo.com

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