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Original Research Article

Differential Diagnosis of Oral Malignant and Premalignant Lesions by Exfoliative Cytology with Emphasis on Demographic Factors

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ABSTRACT

Background: India alone accounts for one third of the world's oral cancer and has a high rate of potentially malignant disease (PMD). Most of patients 60-80% presents with advance stage which leading to high morbidity and mortality in comparison to developed country.

Objectives: To study the role of exfoliative cytology in diagnosis of malignant and potentially malignant lesion of oral cavity.

Materials and Methods: The data was retrieved from the records of the patients who presented with various oral cavity lesions and subsequently advised for oral exfoliative cytology over a period of one year from January 2016 to December 2016 in A. H. Reginal Cancer Centre, Cuttack.

Results: Total 1460 cases were encountered; out of which 865(59.24%) cases were malignant and 493(33.76% were benign. There were 102(6.98%) suspicious cases. Among malignant lesions, squamous cell carcinoma (SCC) was the only type encountered where as in benign group inflammatory lesions were most common (295=59.83%) followed by potentially malignant lesions (198=40.16%) comprising of leukoplakia 120 (60.6%) and oral sub mucous fibrosis 78 (39.39%). Males were predominantly affected in our series with M:F ratio 2.93:1.The age of the patients ranged from 19 years to 92 years, with mean age 49 years where as in malignant cases the peak incidence was observed in the age between 30 years and 70 years with mean age 52 years. History of smokeless tobacco use was predominant in this series. The cyto-histo correlation was available in 1047 cases. The sensitivity, specificity and diagnostic accuracy of OEC was 89.71%, 100%, and 91.4% respectively.

Conclusion: Exfoliative cytology is a rapid, easy and cost effective test for detection and categorization of different oral lesions.

Key words: Exfoliative Cytology, Oral Lesions, Leukoplakia, Squamous Cell Carcinoma.

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INTRODUCTION

Oral cancer is the 6th most common cancer in the world.[1] As estimated 300,400 new cases and 145,400 deaths from oral cavity cancer (including lip cancer) occurred in 2012 worldwide.[2] According to WHO, the incidence is increasing and expected to increase 50% by 2015.[3] India alone accounts for one third of the world's oral cancer and has a high rate of potentially malignant disease (PMD).[1] The most of patients 60-80% presents with advance stage which leading to high morbidity and mortality in comparison to developed country.[4]

In developing countries the increasing incidence with high mortality rates are most probably due to lack of awareness of common etiological factors such as smoking, alcohol use, various form of tobacco use, betel nut chewing, HPV infection, poor diet and poor oral hygiene denture. These contribute direct carcinogenic effect for development of oral cavity cancer or development of premalignant disorders such as leukoplakia, erythroplakia, nicotina palati and oral sub mucous fibrosis to further undergo malignant transformation.[1,2]

Although early detection by oral exfoliative cytology (OEC) is proved as non- aggressive, easy, inexpensive and early diagnostic technique of both oral precancer and cancer in some part of the world but It has not been widely practiced in developing countries due to paucity of knowledge on its sensitivity and specificity.[4-6] In India, oral cancer is a significant public health

problem and efforts towards early detection and prevention can reduce the high burden. But lack of knowledge on this topic is making health care strategy difficult.[4] So we aimed to study the role of exfoliative cytology in early diagnosis of malignant and potentially malignant lesions of oral cavity.

MATERIALS AND METHODS

This retrospective study was carried out over a period of one year from January 2016 to December 2016. 1460 cases were retrieved from the records of the patients who had presented with various oral cavity lesions and subsequently advised for oral exfoliative cytology in the Department of Pathology, Acharya Harihar Regional Cancer Centre, Cuttack.

The clinical presentation and history of tobacco use were documented. Scraping of the oral cavity lesion was done by a flat tongue metal spatula. The collected cells were immediately smeared on a clean glass slide and fixed in 95 % alcohol. Then the smears were stained according to pap method. The cyto-histological correlation was done where subsequent biopsy were available. The sensitivity, specificity and diagnostic accuracy of oral exfoliative cytology was done. The non-representative smears were excluded.

Table 1: Age and sex distribution in relation to various oral lesions.(n=1460)

Age range	Total		Total	Carcinoma		Leukoplakia/ Erythroplakia		SMF		Inflammatory		Suspicious/ Dysplasia	
	M	F	No.(%)	M	F	M	F	M	F	M	F	M	F
10-20	12	6	18 (1.23)	1	-	1	1	2	-	8	5	-	-
21-30	104	21	125 (8.56)	40	9	9	2	34	1	19	9	2	-
31-40	248	59	307 (21.2)	113	25	19	10	30	-	64	20	22	4
41-50	284	101	385 (26.36)	169	67	30	14	8	-	53	12	24	8
51-60	231	100	331 (22.67)	150	68	14	4	2	1	40	15	25	12
61-70	130	54	184 (12.6)	94	44	9	3	-	-	22	7	5	-
71-80	61	24	85 (5.82)	48	20	3	-	-	-	10	4	-	-
81-90	18	5	23 (1.57)	12	4	1	-	-	-	5	1	-	-
>91	1	1	2 (0.13)	1	-	-	-	-	-	-	1	-	-
Total	1089	371	1460	628	237	86	34	76	2	221	74	78	24

M: Male, F: Female, SMF: Submucus fibrosis.

Table 2: Site distribution of carcinomas. (n=865)

Site	No (%)
Tongue	170 (19.65)
Left buccal mucosa	186 (21.50)
Right buccal mucosa	110 (12.71)
Left lower alveolus	112 (12.94)
Right lower alveolus	45 (5.20)
Left upper alveolus	15 (1.73)
Right upper alveolus	6 (0.69)
Left RMT	20 (2.31)
Right RMT	18 (2.8)
Left GB sulcus	16 (1.84)
Right GB sulcus	15 (1.73)
Left angle of mouth	18 (2.8)
Right angle of mouth	20 (2.31
Lower lip	20 (2.31
Upper lip	4 (0.46)
Hard palate	28 (3.23)
Soft palate	15 (1.73
Anterior segment mandible	33 (3.81)
Left tonsilar fossa	6 (0.69)
Right tonsilar fossa	8 (0.92)

RESULTS

Out of total 1460 cases 865 (52.24%) were malignant, 198 (13.56%) potentially malignant disease (PMD) and 397 (38.28%) were from miscellaneous. Squamus cell carcinoma (SSC) was the only malignant type encountered in our study where as in PMD groups leukoplakia was the predominant lesion (20=60.6%), followed by oral submucus fibrosis (78=39.39%) (OSF). Males were predominantly affected i.e. 1089 (74.58%)) with M: F 2.93:1. The age of the patients ranged from 19 to 92 with mean age being 49 years overall where as in malignant cases the peak age of incidence ranged from 30 to 70 years with mean age being 52 years. The distribution of different oral cavity lesion with respect to age and sex are given in Table 1.

In the present study, the most common site of malignant cases were buccal mucosa 296(34.21%) followed by alveolous178 (20.57%) and tongue 170 (19.65%).[Table 2] Maximum patients were having history of tobacco use, among which males were commonly involved. [Table 3] Left side was the predominant side of involvement in our study due to habits of keeping gutkha in left side. Most of the patients (1109=75.95%) were of low socio economic status in this series. The cytohistological correlation was available in 1047 cases. Among these, 776 were true positive (TP), 182 true negative (TN), 89 false negative and no false positive cases; giving a sensitivity, specificity and diagnostic accuracy of 89.71%, 100%, 91.4% respectively in oral exfoloiative cytology.

Table 3: History of tobacco use in relation to sex and associated oral disease.(n=1460)

Variants	Male	Female	Total	Nicotine use
Squamous cell carcinoma	628	237	865	730
Leukoplakia/Erythroplakia	86	34	120	68
SMF/OSF (Oral sub mucus fibrosis)	76	02	78	76
Inflammatory	221	74	295	94
Suspicious/dysplasia	78	24	102	87
Total	1089	371	1460	1055

DISCUSSION

Oral cancer is the most frequent neoplasm of the head and neck region. Among this squamous cell carcinoma (SSC) is the most common comprising of 94% of all oral malignancy.[7,8] It most commonly affects males beyond 5th decade of life. According to US national cancer institute SEER programme, the mean age of diagnosis of oral cancer is 65 years.[6] In India Gupta et al.[9] and Mehrotra et al.[10] have also observed oral malignancies occurring in about two times more frequently in men, and 95% found in persons older than 40 years of age. Epidemiological study of oral cancer in India reported that in developing country oral cancer may affect younger men and women more frequently than seen in the western world.[6]

In our study group, OSCC comprised of 59.24% among all oral lesions and was the only malignant type. The males were predominantly involved with M: F ration 2.64:1 which was similar to the study done by Bhargava et al.[2] Shenoi et al.[6] reported that almost equal number of male and female were involved while others found a higher male to female ratio.[11-13] The peak incidence of age in our series was similar to the study done by Babshet et al.[14] The maximum number of cases were observed in 41-50 years age followed by 51-60 years while Singh et al.[13] have shown the maximum cases in 51-60 followed by 41-50 years age group. In Indian subcontinent, the buccal mucosa and gingiva-buccal sulcus are more commonly affected due to habit of placing tobacco quid like khaini, gutkha, betel quid etc. in oral cavity.[13] Buccal mucosa and gingiva-buccal sulcus were the most affected site in the present study. Other Indian epidemiological studies also found similar results.[6,10,13]

Next to buccal mucosa, the most common site involved were alveolus and tongue which was similar to the previous study.[6,11,13,14] This may be attributed to the extensive use of chewing tobacco in the Indian subcontinent compared to smoking in the West.[15] Tobacco consumption in various forms is culturally and socially accepted in our society. Tobacco is more easily available to males because of social factors. Tobacco consumption by females is however increasing gradually. Tobacco use occurs in all strata of society, such as illiterate to professional, adolescent to adults, poor to rich etc.; however, gender, occupation, and education influence tobacco use. The socially and economically weaker are more prone to consume tobacco because of lower educational level and lack of awareness about consequences of tobacco consumption.[13] In our series, among tobacco user, 69.97 % were labourers and all were below poverty line.

Worldwide initiation age of tobacco consumption is around 12 years. In India, initiation age of tobacco consumption varies from 8 years to 15 years. There is a time lag after the initiation of tobacco consumption and development of oral carcinoma which is well-exemplified in a study done by Singh et al.[13] In their study many patients of oral cancer were diagnosed in the 20–30 age group or subsequent decades. In our study there were 50 (5.78%) cases encountered in the age group 20-30 among which 90% were habituated to chewing tobacco such as gutkha and pan with mean duration 5 years.

Oral cancer is almost always preceded by some potentially malignant disorder (PMD). These PMD can be detected for up to 15 years before their change to an invasive carcinoma.[4] In the above study PMD comprised of 198 (13.56%) cases with maximum incidence in age between 21-50 years age where as Russel et al.[4] have shown the age between 15-40 years.[4] In Goel et al.[16] study most of the patients fall in 31-45 years of age group and next common age group was 46-60 years with strong male predominance.[16] The most common site involved was buccal mucosa, followed by tongue and buccal vestibule. In contrast, the tongue and floor of mouth are the more commonly involved sites in the West.[17] Among PMD, prevalence of leukoplakia varies from 0.2% to 5.2% with malignant transformation of 0.13% and 10% in India.[1] It most commonly is seen in age group between 5th to 7th decades of life with male predominance.[18] In this study, the prevalence rate was 6.36% and incidence was maximum in the age between 31-60 years with male predominance.

According to various studies, the prevalence of oral submucous fibrosis (OSMF) in India varies between 0.03% and 3.2% with a malignant transformation rate of 7.6%.[1] The most important consideration is the relation between the use of tobacco and related products and the development of lesions. In this study the prevalence rate of OSF was 5.34% .Whereas Misra et al.[19] reported higher rate (6.65%).In our study males were maximum whereas Senguven et al.[20] reported female predominance. Chronic inflammation was observed in 20.10% cases which was similar to the study done by Modi et al.[21] Detection of high-risk oral premalignant lesions and intervention at premalignant stages might represent a success towards reducing the mortality and morbidity associated with OSCC.[19] In this regard exfoliative cytology is advantageous, as it is a painless, bloodless non-invasive, quick simple and cheap procedure. It is suitable in patients with systemic disease who are contraindicated for biopsy. It guards against false negative biopsy and post-biopsy complications can be eliminated. This procedure can be repeated a number of times for diagnosis, prognosis and research purposes.[7]

In our study the overall sensitivity, specificity and diagnostic accuracy of oral exfoliative cytology in diagnosis of various oral cavity lesions was 89.71%, 100% and 91.49% respectively. The sensitivity was slightly higher in our study in comparison to Goel et

al.[16] who observed a sensitivity of 83.1%. However, specificity reported by Gupta et al.[9] was 100% which was similar to our study because they did not encounter any FP cases in their study.[1] Several studies had observed wide range of results in similar studies with PPV ranging between 10.6% and 100.0%, NPV between 60.0% and 100%, and accuracy between 13.2% and 96%.[11,22]

CONCLUSION

Oral exfoliative cytology can be safely and reliably used in diagnosis and prognosis of oral lesions and can also be used for follow up of treated cases. This study depicts the sensitivity, specificity and predictive value of this procedure which can be as a screening procedure of such lesions.

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