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Oral squamous cell carcinoma: early detection using brush scrape cytology and association with various risk factors

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ABSTRACT

Background

The incidence of oral cancers and oral premalignant lesions is very high in India. Although biopsy followed by histopathology is considered as gold standard in diagnosis of these lesions, it may not be possible to do biopsy in all suspected cases who may be medically compromised or refuse to undergo biopsy. In such cases, brush cytology may offer an attractive alternative.

Aims and Objectives

This study was undertaken to know the utility of oral brush scrape cytology in detection of oral squamous cell carcinoma and correlating the oral premalignant and malignant lesions with various risk factors.

Material and Methods

50 patients attending oral medicine and ENT outpatient department who exhibited oral lesions suspicious of premalignancy or malignancy were enrolled. All patients underwent oral scrapping using a toothbrush. Specimens were analyzed manually. Histopathological confirmation by biopsy was obtained wherever possible. Statistical tests were applied.

Results

Brush cytology technique showed a reasonable sensitivity and specificity in detecting oral premalignant and malignant lesions.

Conclusion

Oral brush cytology is simple, noninvasive, painless and rapid method in assessing oral premalignant and malignant lesions and useful particularly in population screening programme.

Keywords: Brush cytology, Oral premalignant lesions, Oral squamous cell carcinoma

INTRODUCTION

Oral cancer is a global health problem with increasing morbidity and mortality rate. Oral

squamous cell carcinoma accounts for 90% of the oral carcinomas. A key factor in the poor prognosis is the fact that these cases are not diagnosed and treated until they reach an advanced stage [1]. The

concept of a two-step process of cancer development in the oral mucosa ,i.e. The initial presence of a precursor (pre-malignant, precancerous) lesion subsequently developing into cancer, is well-established. A potentially malignant lesion is a morphologically altered tissue that has a greater than normal risk of malignant transformation. The presence of epithelial dysplasia is generally accepted as one of the most important predictors of malignant development in pre-malignant lesions [2]. Several oral lesions like leukoplakia, erythroplakia, lichen planus and actinic keratosis are considered to be pre-malignant lesions for oral squamous-cell carcinoma, since an increased risk of malignant transformation is associated with them. These lesions are often subtle and asymptomatic, requiring a high index of suspicion on the part of clinician, especially if the risk factors such as tobacco use or alcohol abuse are present [3,4] .Thus early diagnosis is needed to prevent this two-step process. Brush scrape cytology can be used as a tool for the early diagnosis. It is a non-invasive procedure which is well accepted by the patients and therefore is an attractive option. It provides a good cytological material, is relatively painless, inexpensive, a bed side option, can be done in any patients at any health care center and can be used in any location in the oral cavity [1]. This may have application in areas where limited resources are available [5].The higher incidences of oral cancer in India are mainly associated with tobacco chewing, smoking and other related factors. In patients with oral squamous cell carcinoma (OSCC), the survival rate is directly associated with early diagnosis, particularly in those with a potentially malignant disorder, including leukoplakia and erythroplakia, which may precede the development of OSCC or are present in association with it [5,6] .

The aim of this study is to device out a method that is efficient for the patient as well as the clinicians and aids in diagnosis of OSCC in its early stage. It also aims at correlating the disease with its various risk factors.

MATERIAL AND METHODS

This is a hospital based prospective study. Clinically suspected patients of oral pre-malignant and malignant lesions attending the department of ENT and Oral Medicine were studied. Patients of

all age group and both sexes with suspicious pre-malignant and malignant lesions were included.

Detailed history of the patient regarding their age, sex, presenting complaints, past medical / dental history and habits (tobacco chewing, smoking, alcohol consumption, betel quid use etc.) were asked and noted down. Local oral examination and soft tissue examination was done. The patient was further explained with the aims and procedure of the study and consent was taken. A scrape was taken using a tooth brush. The toothbrush was repeatedly brushed in the buccal mucosa in the affected site till adequate sample was obtained. A normal hard bristle nylon tooth brush was used. It was sterilized in 0.2% of chlorhexidinegluconate mouthwash for 24 hours and discarded after every use. The material from the brush was spread on a clean dry slide in the middle two third. For each case, 2-3 smears were prepared.

The smears were fixed using 95% alcohol and then stained with Haematoxyline and Eosin stain and Papanicolaou's stain. All smears were examined under the microscope.

The cytological smears were interpreted based on the following parameters:

Enlarged nuclei, variation in nuclear size and shape (pleomorphism), nuclear membrane irregularity, nucleocytoplasmic ratio and hyperchromatism.

Based on above parameters, brush scrape cytology specimens were classified as

Type 0-Inadequate specimen

Type 1-Benign (Those with nonspecific changes)

Type 2-Dysplastic changes

Type 3 –Malignant changes.

For analysis, dysplastic and malignant lesions (Type 2&3) were to be considered positive and Benign lesions (Type 1) as negative.

Feature variations which decrease with increased severity of dysplasia include

- Cellular cohesion
- Amount of cytoplasm
- Degree of maturation
- Normal flora

Feature variations which increase with increased severity of dysplasia include

- Mitosis
- Nuclear to cytoplasmic ratio

- Anisochromatism
- Nuclear membrane irregularity

Biopsies were obtained whenever possible and comparison was made between the cytological findings and the histopathological findings.

Cytology of homogenous leukoplakia demonstrated keratinised benign hypermature, polygonal cells or anucleated squamous cells.

The smears with dysplasia were graded as mild, moderate or severe. Those with malignancy were graded as well, moderately and poorly differentiated.

The results from the brush scrape cytology and histology were also studied according to various habits (kharra and tobacco chewing, smoking, betel quid, alcoholism) and associations were made.

Statistical analysis

Sensitivity and specificity were used for the statistical analysis of the samples. The true and false positives and negatives were determined.

RESULTS

In the present study out of 50 cases, squamous cell carcinoma was present in 12 cases (24%) while

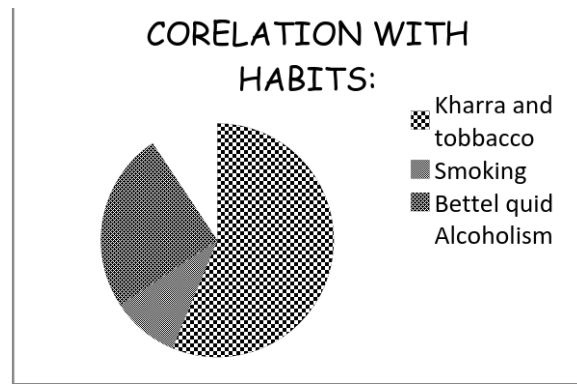
dysplasia was reported in 18(36%) cases.15 cases (30%) were reported as Benign with no specific changes and 5 cases (10%) were inadequate for interpretation. So total 45 cases were analyzed cytological (Table 1)

The cases of malignant conditions were those of ulcerative, ulceroproliferative lesions over buccal mucosa, tongue and alveolus.

The results were discussed under the following heads:

1. Correlation with age and sex
2. Correlation with habits
3. Comparison of brush scrape cytology and histopathology

Oral premalignant and malignant lesions were common in males as compare to females. The premalignant lesions were more common in 3rd -4th decade while malignant lesions were more common in 5th-6th decade. The maximum number of cases were associated with Kharra/tobacco chewing followed by smoking, betel quid use and alcoholism.(Img.1)



(Img.1)

The malignant cells showed nuclear enlargement, anisonucleosis, pleomorphism including tadpole shaped cells. (Fig.1,2)

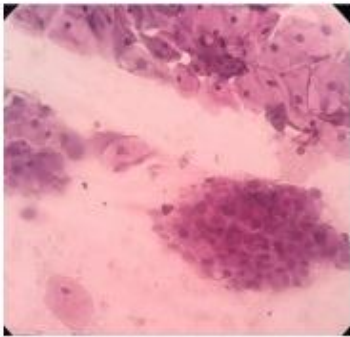


Fig.1 H&E 10x showing pleomorphic cells in squamous cell carcinoma

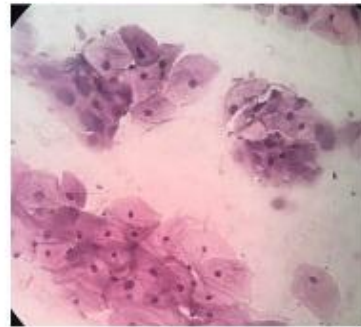


Fig.2 H&E 40x showing Squamous cell carcinoma

The cases of premalignant lesions and conditions obtained were those of Leukoplakia, Erythroplakia, Oral Submucous Fibrosis and Lichen Planus.

They showed mild, moderate or severe dysplasia.(Fig.3,4)

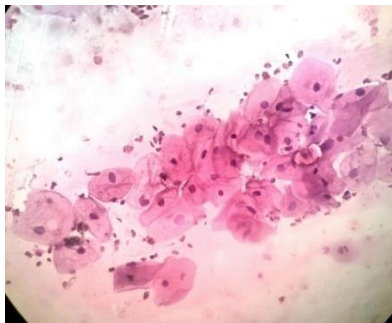


Fig.3 H&E 10x showing mild dysplasia



Fig.4 H&E 10x showing moderate dysplasia

Table-1--Cytology diagnosis of 45 cases

1.Cytologically negative	15
2.Cytologically positive	30
2a) Dysplasia	18
2b) Malignancy	12

Cytological, out of 30 cases, 12 were malignant and 18 cases were of various premalignant lesions.

Histopathologically, out of 20 available biopsies, 12 were from cytologically malignant cases and 8 were from cytologically premalignant lesions (8 out of 18).

Table 2-Histopathology diagnosis

Histopathology Diagnosis	Number Of Cases
Hyperkeratinised epithelium	4
Mild dysplasia	2
Moderate dysplasia	1
Severe dysplasia	1
Squamous cell carcinoma	

Well differentiated	5
Moderately differentiated	4
Poorly differentiated	2
Verrucous ca	<u>1</u>

Out of 30 cases, 18 were premalignant and 12 were malignant. Biopsy studies were available for 8 premalignant and all the 12 malignant cases (Table 1,2)

Table-3-Comparison of brush scrapes cytology and histopathology

Category	Cytology		Histopathology		Total
	Positive	Negative	Positive	Negative	
Dysplasia	3	5	4	4	8
Malignancy	10	2	12	0	12

Out of the 18 pre malignant cases, comparison was made only for the 8 cases whose biopsy studies were available. On cytopathology 3 were found positive and 5 were negative. On histopathology 4 cases were found positive and 4 negative.

Out of the 12 malignant cases, 10 were positive and 2 were negative on cytopathology and all 12 were positive and none was negative on histopathology.(Table 3)

Table-4 showing various statistical parameters

True positive	13
True negative	4
False positive	-
False negative	3
Sensitivity	81.25%
Specificity	100%

The sensitivity of the test was found to be 81.25% and the specificity was found to be 100%. i.e. the test is more specific and less sensitive.

DISCUSSION

The incidence of oral cancers and oral premalignant lesions is very high in India as compared with western population [7]. Though biopsy followed by histopathology is considered as gold standard in diagnosing these lesions, it may not be feasible to do biopsy in all suspected cases (the patient may be medically compromised or may refuse to undergo scalpel biopsy). In such cases, brush cytology may offer an attractive alternative [6,7]. This study was undertaken to assess the utility and reliability of oral brush cytology technique.

According to the study of Babshet [1], the males were predominantly affected with the large number of oral cancers developing in the fourth and fifth decades of life. In our study it was observed that more number of males reported with the premalignant lesions and conditions resulting to OSCC than the females and both being prevalent in the third to fourth decades of their lives. Males are affected more as compared to females because of their indulgence in various habits and risk factors. Spreading awareness about the signs and symptoms of the conditions that might convert into malignant cases and the early diagnosis made by the patients themselves or the doctors plays a key role in increasing the survival rate of these patients.

The study conducted by Thomas G [8], tobacco chewing is associated with the strongest increase in the risk of multiple oral premalignant lesions and may be the major source of field cancerization of the oral cavity in the Indian population.

In this study, 60% had the habit of tobacco chewing, 26.6% had smoking habit, and 10% of the patients had a combination of quid, tobacco or gutkha chewing habits along with alcohol consumption. However, 5% of the patients had no adverse habits. In the study performed by Mehrotra *et al.*, [2] tobacco consumption was the most common with 54% patients having used it in one form or another, 35.4% gave a history of exposure to more than one carcinogen, while 5% patients consumed heavy amounts of alcohol.

There are variations in the site of involvement of oral premalignant and malignant lesions. The most common site of involvement in our study was buccal mucosa followed by tongue and alveolus. This may be due to variation in placement of tobacco with prolonged contact with the carcinogen.

This is in accordance with the studies done by Mehrotra *et al* [2], Babshet *et al* [1]. In contrast to this posterior lateral border of the tongue and floor of the mouth are frequently involved in the western countries [5,6,9]. This differences in involvement of various sites in oral mucosa may be due to vast use of chewing tobacco in the India as compare to smoking in the west [6,8,10].

The distribution of premalignant and malignant lesions based on histopathology and cytopathology is done in the study. The comparison between them showed that out of the 30 cytologically positive cases, 12 were malignant and 18 were premalignant. All the 12 malignant cases were positive on histopathology and 10 out of the 12 were positive on cytology and 2 were negative. Out of the 18 premalignant cases, 8 were positive on cytology and 10 were negative and for the 8 biopsy available cases, 5 were positive on histopathology and 3 were negative. There were 4 such cases which were negative on brush scrape cytology but positive on histology and there was no such case which was positive on cytology and negative on histopathology. The sensitivity and specificity were calculated to be 81.25% and 100% respectively. The study was interpreted as being more specific than sensitive. In the study of Babshet M, [1] the sensitivity and specificity were 77% and 100%. Mehrotra *et al* [2] used modified brush cytology without computer-assisted analysis in their study in the detection of oral lesions and found the sensitivity was 76.8% and specificity was 93.3%.

The false negative results and errors in cytopathological interpretation can be attributed to several factors like sampling error, improper fixation, cytopreparation, subjective errors, and lack of clinical information may also lead to improper interpretation of the cytological smear.

A major limitation of this study is the lesser number of cases, inability to calculate the exact sensitivity and specificity because biopsy with histopathology results were not available for all patients particularly for benign samples.

But most important advantage of this study is that the technique is very simple, inexpensive, can be used in any setup and easy to carry. There are no complications or side effects and potentially important tool in resource challenged country like India.

Thus availability of an easy, noninvasive, quicker and efficient option like the brush scrape cytology can detect such cases earlier and improve quality of life [7, 9,11].

CONCLUSION

Early detection of oral carcinoma is possible even at precancerous stages because of its two stage theory. Cytological study of oral cells is a non-invasive technique that is well accepted by the patient, and is therefore an attractive option for the early diagnosis of potentially malignant and pre malignant lesions of oral mucosa. Brush cytology is more specific than sensitive and the negative brush cytology does not rule out malignancy in all cases. Thus, brush cytology with a commercially available tooth brush is an advantageous diagnostic procedure as it is non-invasive, relatively painless, inexpensive, less time consuming, reliable and requires minimum technical skill. It is useful in those situations when a patient refuses to have a biopsy performed or when medically compromised patients would be exposed to unnecessary surgical risks. Brush cytology is useful in screening of suspicious oral lesions and reducing the number of the malignant cases. Also spreading awareness about the harmful effects of tobacco and kharra chewing, smoking, betel quid and alcohol is essential. Certain measures taken at proper time can save lives. The study also shows the lack of awareness among people especially the females of these socioeconomic strata.

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