Efficacy Of Oral Brush Cytology In The Detection Of Oral Malignant And Premalignant Lesions

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Abstracts: Introduction : Oral cancers account for approximately 3% of all malignancies and is a significant worldwide health problem. Globally, oral cancers are one of the 10 most common cancers and accounts for almost 40% of all cancers in Indian subcontinent. A key factor in the lack of improvement in prognosis is the fact that a significant proportion of oral squamous cell carcinomas are not diagnosed and treated until they reach an advanced stage. Material and Method: The present study has been carried out on 50 patients suffering from oral cavity lesion. In all patients oral brush cytology using a toothbrush was done prior to a planned surgical biopsy. The study was done to assess the efficacy of oral brush cytology in detecting the premalignant and malignant lesions and its use as an early diagnostic aid. Result: 25 Cases were true positive on both histopathology and oral brush cytology. 20 Cases were true negative and 5 Cases were suspicious for malignancy on brush cytology, they were diagnosed as malignant on further histopathological examination. A sensitivity of 80% , specificity of 100% , negative predictive value was 83.3% , positive predictive value was 100% and accuracy was 90%. Conclusion: Oral brush cytology is an accurate diagnostic tool that plays a significant role in early cancer detection. It is also useful as a screening procedure for a high risk population or also for the clinical follow up. [Sharma S Natl J Integr Res Med, 2018; 9(6):13-17]

Key Words: Brush cytology , Exfoliative cytology , Haematoxylin and Eosin , May Grunwald Giemsa.

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Introduction: Oral cancer refers to a subgroup of head and neck malignancies that develop at the lips, tongue, gingiva, floor of the mouth, oropharynx and buccal mucosa[4]. In India 83,000 new oral cancer Cases are detected and 46,000 deaths from it occur[5,6] every year. It comprises 30 – 40% of the total malignancies[7] and accounts for one quarter to one third of male cancers and one tenth of female cancers in India and ranks first among all cancer Cases in males and is the third most common among the females[8]. The estimated mortality is about 3.48 per 1,00,000 in males and 1.34 per1,00,000 in females[9]. Identification of high risk oral premalignant lesions and intervention at premalignant stages could institute one of the keys for reducing the mortality, morbidity and cost of treatment associated with squamous cell carcinomas. The early diagnosis and treatment of cancer are based on the concept that a carcinomadevelops over a long period of time, going through intermediate stages of different biological significance and the treatment at this early or preinvasive stage offers the [10] best prognosis and even the chances of cure.

The most definitive, accurate and reliable method for diagnosing oral mucosal abnormalities has been and remains the 'scalpel biopsy'. In recent decades, a dramatic switch from histopathological to molecular methods of disease diagnosis and exfoliative cytology has gained importance as a rapid and a[5] simple method. Exfoliative oral cytology is the study and interpretation of the characteristics of cells [11] that are shed off, whether naturally or artificially from the oral mucosa. Brush cytological study of oral cancer is a non invasive technique that is well accepted by patient and is therefore an attractive option for the early diagnosis of potentially malignant disorders and malignant lesions of oral mucosa. Oral brush cytology is a non invasive means of diagnosing dysplasia and early carcinoma in those patients who are either asymptomatic or in those with minor symptoms who do not warrant immediate biopsy.

The aim of this study is to evaluate the utility of oral brush cytology in the screening and early diagnosis of oral malignancies and to correlate the findings of oral brush cytology with the histopathological finding of surgical biopsy.

Material &Method: The present study has been carried out on 50 patients suffering from oral cavity lesion. In all patients oral brush cytology using a toothbrush was done prior to a planned surgical biopsy. Previously treated Cases of oral malignancies were excluded from the study. Patient were instructed to rinse their mouth with plain water, after which the oral cavity was cleaned, by wiping with a piece of gauge moistened in normal saline solution. Cells from the lesions were scraped using a gentle scraping

motion with the helpof hard bristle tooth brush, exerting little pressure allowing pin-point bleeding, and were spread on the glass slide and fixed in 95% alcohol.

Material obtained from lesions were smeared on a minimum of 2 glass slides. 1 slide was immediately fixed in 95% Ethyl alcohol, in a coplin jar, kept for minimum of 15 minutes followed by using standard Haematoxylin & Eosin stain. Other slide was air dried and later stained with May GrunwaldGiemsa stain. The smears were examined under microscope and were classified into one of three category:

(a) NEGATIVE – Adequate cellularity, neither suspicious nor malignant cells presentpresent.
(b) POSITIVE -The smears are highly cellular with following cellular characteristics: Ill-defined cell border , High cellular and nuclear atypia Enlarged nuclei with high N: C ratio , Condensation of nuclear chromatin forming strands, coarse clumps and dense peripheral nuclear outlines , Densely packed hyperchromatic nuclei in compact groups with no visible cell outline , Multiple and enlarged nucleoli , Multinucleated giant cells , Keratinised pearls of malignant cells are frequently seen , Necrotic background with blood and numerous leukocytes.
(c) SUSPICIOUS FOR MALIGNANCY - Abnormal epithelial changes of uncertain diagnostic significance.

Biopsy Procedure: The tissue were allowed to fix in 10% formalin for 24 – 48 hrs. After fixation , the tissue was processed and paraffin blocks were made. The blocks were cut at 3–5u thickness and stained with H & E stain and examined microscopically. Histopathological findings were noted and interpreted. The results of cytology and histopathology were correlated. The histopathological and cytological results were also correlated with clinical diagnosis.
Institute ethics committee approval was obtained before the start of study.

Results: Result are tabulated in table 1 to 6. Out of 50 Cases including both premalignant and malignant lesions 20 Cases were found to be positive on both histology and brush cytology. 25 Cases were found to be negative on both histology and brush cytology. 5 Cases were found to be suspicious on brush cytology and were considered as false negative. Though not a single case of false positive was found in the study conducted. . All 5 Cases which were reported as suspicious for malignancy were reported malignant on histopathology done after surgical biopsy.

All the Cases which were negative for malignant cells on brush cytology showed benign appearing squamous cells with acute inflammatory cells in background. The nucleus was of normal size , no hyperchromasia or nuclear pleomorphism was seen. There wasnoincrease in the N : C ratio. One case showed large number of macrophages and was reported as warty lesion on histopathology. One case was reported as tubercular lesion showed few clusters of epitheloid cells on brush cytology(Figure 1 to 4).

Fig 1 : Normal squamous cells on brush cytology.

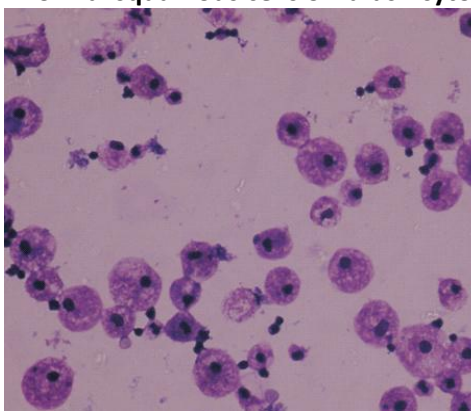
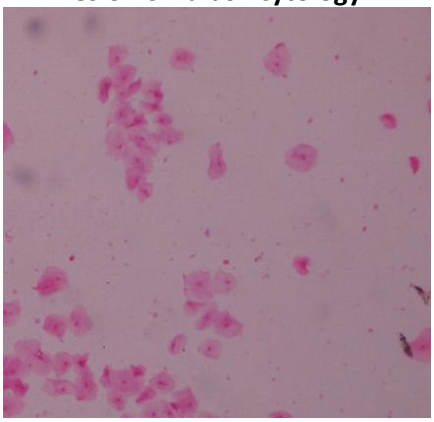


Fig 2 :Numerous macrophages from a cystic lesion on brush cytology.



All the malignant Cases revealed loose clusters and isolated cells with large hyperchromatic nuclei and marked nuclear pleomorphism. There was enlarged nuclei with high N : C ratio. 11 Cases showed bloody and necrotic background. All the 5 suspicious Cases on brush cytology had low squamous cellularity with large amount of inflammation. Squamous cells showed only mild pleomorphism andhyperchromasia, so we could not confidently ascertain the malignancy. Out of

these 5 suspicious Cases, 4 were diagnosed as Well differentiated squamous cell carcinoma and1 was diagnosed as Basal cell carcinoma on biopsy

Fig 3 :Cluster of epitheloid cells seen on brush cytology.

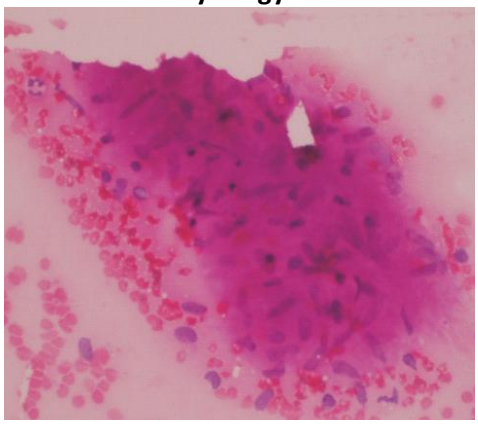
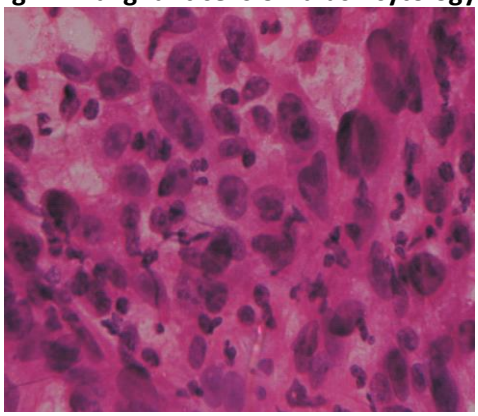


Fig 4 : Malignant cells on brush cytology.



Statistical Analysis: Sensitivity and specificity were used for the statistical analysis of the samples. The true and false positives and negatives were based on the following:

True positive : Samples that were positive on both histology and brush cytology.

True negative : Samples that were negative on both histology and brush cytology.

False positive : Samples that were negative on histology and positive on brush cytology.

False negative : Samples that were positive on histology and negative on brush cytology.

Table 1. Distribution based on clinical diagnosis

CLINICAL DIAGNOSIS	NO. OF CASES	%
Carcinoma	21	42
Papilloma	02	04
Leukoplakia	06	12
Ulcer	18	36
Wart	03	06
TOTAL	50	100

Table 2 : Histological diagnosis of oral cavity lesion

Histology Diagnosis	Cases	%
Poorly differentiated SCC	01	2
Moderately differentiated SCC	19	38
Well differentiated SCC	04	8
Basal Cell Carcinoma	01	2
Hyperplasia	04	8
Chronic non specific inflammation	19	38
Pyogenic granuloma	01	2
Tuberculosis	01	2
TOTAL	50	100

Table 3 : Comparison of histological and brush cytological diagnosis.

	HISTO-LOGICAL DIAGNOSIS	%	BRUSH CYTOLOGY DIAGNOSIS	%
Benign	25	50	25	50
Malignant	25	50	20	40
Suspicious	00	00	05	10
TOTAL	50	100	50	100

Table 4 : Comparison of clinical diagnosis with histological diagnosis.

	CLINICAL DIAGNOSIS	%	HISTOLOGICAL DIAGNOSIS	%
Benign	11	22	25	50
Malignant	21	42	25	50
Suspicious	18	36	00	00
TOTAL	50	100	50	100

Table 5 : Comparison of clinical diagnosis with Brush cytology diagnosis.

	CLINICAL DIAGNOSIS	%	BRUSH CYTOLOGICAL DIAGNOSIS	%
Benign	11	22	25	50
Malignant	21	42	20	40
Suspicious	18	36	05	10
TOTAL	50	100	50	100

Table 6 : Sensitivity and specificity of oral brush cytology (in percentage)

Sensitivity	80
Specificity	100
Negative Predictive Value	83.3
Positive Predictive Value	100
Accuracy (efficacy) of test	90

Discussion: Oral cancer is one of the 11th most common cancers in the world. WHO has reported [12] oral cancer as having one of the highest mortality rate amongst other malignancies. Early detection of oral cancers is not easy, because oral precancerous lesions and early oral cancers can mimic many benign conditions in the mouth, leading to delays in diagnosis and treatment.

Oral brush cytology is an accurate diagnostic tool that plays a significant role in early cancer detection. It is also useful as a screening procedure for a high risk population or also for the clinical follow up. 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 [13] malignant disorders of oral mucosa. The use of oral brush cytology for large , advanced and obviously highly malignant lesion is not indicated , since such growths always require a definitive biopsy obtained diagnosis.

The false negative results and errors or pitfalls in oral brush cytology interpretation can be attributed to several factors like: Sampling error , improper fixation , Hyperkeratotic lesions will not allow underlying malignant cells to be scrapped.So lesions should be scrapped till pinpoint bleeding is present , Lesion may not be fully accessible, Cancers with ulceration, fungation will not yield malignant cells in the smears because of presence of necrotic debris , Location and characteristics of the tumour-mucosa of oral cavity exhibits varying degrees of keratinisation at different sites leading to varied exfoliation in oral cancers.

Oral brush cytology is a powerful tool for early detection of malignant and premalignant lesions. Brush cytology has the potential to assist the diagnostic portion of the “screening gap” which currently challenges the early detection of many epithelial cancers including oral cancers. Biopsy is considered as the gold standard for diagnosing oral lesions, but it has its own drawbacks including poor patient compliance and the diagnosis being done in late Cases when the lesions looks clinically malignant.

Conclusion: Recently, Oral brush cytology has been advocated as a simple, non invasive screening technique. Oral brush cytology is reliable diagnostic tool in diagnosis of presence or absence of malignancy in a lesion with high accuracy rate. The high specificity and the high positive predictive value of oral scrape cytology makes it an ideal screening test for early detection of oral cancer. However, its low sensitivity means that it can miss Cases of carcinoma, and should be followed up with biopsy. The oral brush cytology technique is not intended to replace tissue biopsy, but it is a valuable supplement to surgical biopsy.

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