

# Exfoliative Cytology: An early diagnostic modality for detecting oral cancer.

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## ABSTRACT

Oral pre-cancerous lesions imitate various benign conditions in the oral cavity, which leads to delay in the diagnosis and treatment of further cancerous lesions. The need of the hour is to find out a diagnostic tool which is accepted by the patient, is minimally nvasive and would aid in early detection of the cancerous lesion. Exfoliative Cytology has time and again proven itself to be one such method. It acts as an important diagnostic aid in early oral carcinomas with ulcerative surfaces, unsuspected cases of malignancy etc. For this article, we discuss the future of oral cytological examination in the field of diagnosis, monitoring and furthermore, in the treatment area.

**Keywords :** Oralpre-cancerous,benign,malignancy,diagnosis.

## INTRODUCTION

Oral mucosa exhibits a rapid turnover of cells and these exfoliated cells have a valuable role in diagnosis of certain local and systemic diseases. Oral cavity reflects the various events occurring in the body and this is reflected by cytomorphological and nucleomorph logical variations in the exfoliated cells. Exfoliative cytology is based on the monitoring of exfoliated cells or cells flake off the mucosa wither through natural or artificial means (1). It is a diagnostic technique based on a microscopic evaluation of epithelial cells after a procedure of their fixation and staining. There are 2 methods in use: the indirect cell-collecting method, such as aspiration subjects with self-exfoliated cells, and the direct method, rubbing of cells of the mucosal surface. The exfoliated cells are put into a preservative fluid and the samples are processed according to the manufacturer directions, after staining using thePapanicolaumethod

## ORAL CANCER

Cancer is latinized from the Greek word “Karkinos,” meaning crab, denoting how carcinoma extends its claws like a crab into the adjacent tissues. Cancer involves multiple alterations of the genome progressively accumulated during a protracted period. Its overall effect surpasses the inherent reparative ability of the cell. During its progression, visible physical changes take place at the cellular level (atypia) and at the resultant tissue level (dysplasia). The sum total of these physical and morphological alterations is of diagnostic and prognostic relevance and is designated as “precancerous” changes. These changes are ultimately involved in driving cells further along the path to neoplastic transformation (3).Oral cancer is the most frequent neoplasm of the head and neck region. Among this the most common is oral squamous cell carcinoma (OSCC) (4). Cancerous lesions are usually benign in appearance and asymptomatic in nature in their early stages (5). The diagnosis of pre-cancers is primarily based on morphology of cells and its grading on histology, i.e., dysplasia. Even though this estimation is subjective, it is still widely practiced to assess the risk of malignant potential of such lesions. Due to this inherent discrepancy, such lesions may well be designated as potentially malignant(3).

## EPIDEMIOLOGY OF ORAL CANCER

Oral cancer is one of the prevailing issues around the globe. Oral cancer includes cancer of the lip, other parts of the mouth and the oropharynx. The global incidence of cancer of the lip and oral cavity is estimated at 4 cases per 100,000 people. However, there is wide variation across the globe, from 0 to around 22 cases per 100,000 people (6). In India, epidemiologically, Kerala has the lowest incidence of oral cancer while West Bengal reports the highest. In the western regions of Maharashtra, the highest occurrence of oral malignancy is reported in the age group of ≥60 years, followed by 40-59 years with a male-female ratio of 2:1 (7). In recent years, the occurrence of the tongue and buccal mucosa cancer has been increased in India with a higher number of buccal mucosa cancercases(8).

## CAUSATIVE FACTORS FOR ORAL CANCER

### A. RISK FACTORS (9)

1. Tobacco use: Using tobacco, including cigarettes, cigars, pipes, chewing tobacco, and snuff, is the single largest risk factor for head and neck cancer. Eighty-five percent (85%) of head and neck cancer is linked to tobacco use. Pipe smoking has been linked to cancer in the part of the lips that touch the pipe stem. Chewing tobacco or snuff is associated with a 50% increase in the risk of developing cancer in the cheeks, gums, and inner surface of the lips, where the tobacco has the most contact. Second-hand smoke may also increase a person’s risk of head and neck cancer.

2. Alcohol: Frequent and heavy consumption of alcohol increases the risk of head and neck cancer. Using alcohol and tobacco together increases this risk even more.

**B. BIOLOGICAL FACTORS (10)**

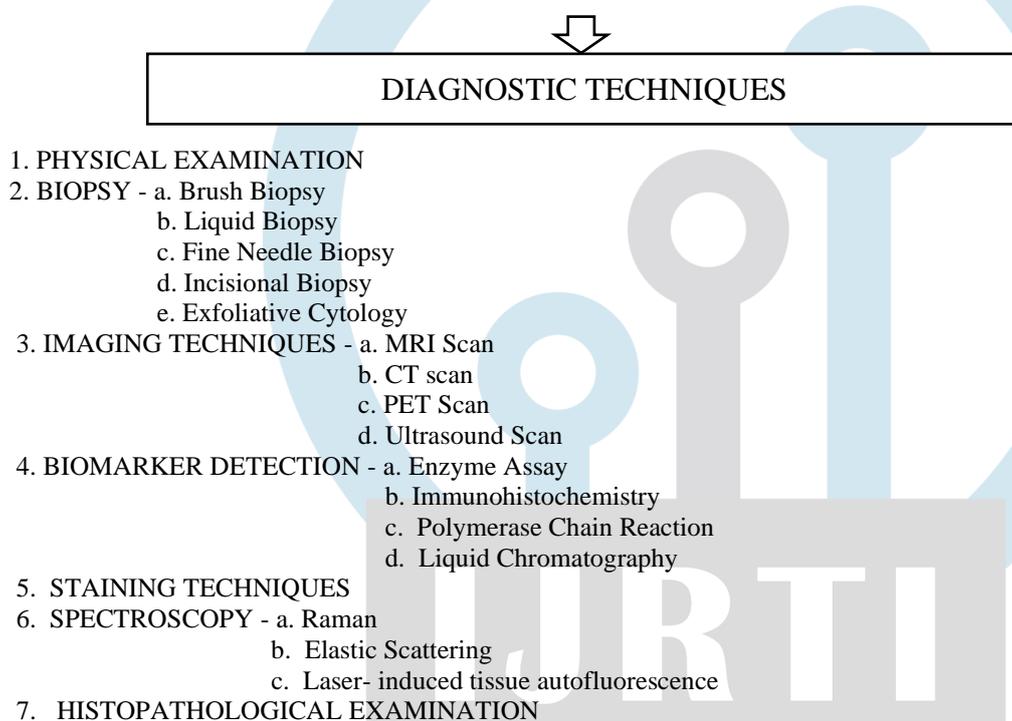
1. Viruses: Role of oncogenic viruses in human cancer is an emerging area of research. Viruses are capable of hijacking host cellular apparatus and modifying DNA and the chromosomal structures and inducing proliferative changes in the cells. HPV and Herpes simplex virus (HSV) have been established in recent years as causative agents of oral cancer.

**C. DENTAL HYGIENE FACTORS (11)**

There is inverse association between oral hygiene and incidence of oral cancer. Poor oral hygiene and prolonged irritation from sharp teeth have been viewed for their possible role in the development of oral cancer. Poor oral hygiene and dental sepsis is thought to promote carcinogenic action of tobacco. There are several scattered reports on the role of oro-dental factors in the causation of oral cancer, but the hypothesis still lacks major evidence.

**D. NUTRITIONAL FACTORS (12)**

Dietary deficiencies are also suggested to play a role in the development of oral cancer. This, however, requires more clinical and experimental evidence for establishment of causal association with the development of oral cancer. Some workers have reported lower risk of oral cancer with higher intake of fruits and vegetables.

**TECHNIQUES USED FOR DIAGNOSIS OF ORAL CANCER adapted from Borse V, Konwar A.N, Buragohain P. (13)****EXFOLIATIVE CYTOLOGY**

Amongst all these techniques, Exfoliative Cytology has proven to be much easier and reliable method for diagnosis of oral cancer. Exfoliated cytology is based on epithelial physiology and is a simple and non-invasive diagnostic technique for early detection of oral malignancy. Cellular cohesive forces are reduced due to the presence of benign disease or the formations of the malignant epithelial cells, leading to exfoliation; the exfoliated cells are collected for microscopic examination (3). The oral exfoliative cytology (OEC) is an easy, non-invasive technique that is affable for the patient and suitable for preliminary detection of oral cancer. OEC focuses on the morphological and staining characteristics of the individual cell, which requires skilled cytopathologists(14).

**RATIONALE OF EXFOLIATIVE CYTOLOGY**

The rationale of exfoliative cytology lies in the epithelial physiology. Due to physiological turnover, the normal epithelium undergoes exfoliation of its superficial cells. The cells of the deeper layer are adherent to each other normally. When there is any pathological condition, the cells may lose their cohesiveness and the cells in the deeper layer may also shed along with the superficial cells. These exfoliated cells as well as cells which are scrapped off by means of specific instruments, can be studied quantitatively or qualitatively(15).

**ADVANTAGES**

Exfoliative cytology till now has its fair share of opinions regarding its credibility in detecting the oral pathologies. Earlier, the divided views were based on the subjective interpretation of the abnormal mucosa cells and the false-negative results it showcased. It is advantageous, as it is a painless, bloodless, non-invasive, quick and simple 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 several times for diagnosis, follow-up, and research purposes. Exfoliative cytology usually plays a supportive role in a properly planned and carefully executed biopsy for the diagnosis of oral cancer (3).

### DISADVANTAGES

This technique is useful for preliminary diagnosis of many oral mucosal diseases but it is not a substitute for the routinely-used biopsy to obtain a definitive diagnosis. Lesions caused by reactive changes and inflammatory reactions are non-specific and non-diagnostic cytological findings. Exfoliative Cytology is not appropriate as a diagnostic tool for patients with clinical symptoms of desquamative gingivitis. It adds to the cost and delays the definite diagnosis (16). Some authors underline that we can eliminate them and increase its diagnostic value. The best way to do that is by making the procedures clearer and by standardizing them. A quantitative technique increases the diagnostic ability of exfoliative cytology. It is precise, objective, and reproducible. Quantitative methods include DNA cytophotometry (optical quantification of chemical substances incorporated into the DNA – the Feugen stain) and cytomorphology (characterizing the proliferative activity of the cell populations of oral mucosal squame (17).

### INDICATIONS (18,19,20)

1. Mucosal lesions that appear clinically innocuous and otherwise would not be biopsied.
2. Microbial diseases like herpes simplex infection, herpes zoster infection. Dermatological lesions like pemphigus vulgaris, benign familial pemphigus, keratosis follicularis.
3. Pernicious and sickle cell anaemia
4. Evaluation of extensive mucosal lesion when it is not possible to do enough incisional biopsies for adequate sampling.
5. Follow up for patients with prior diagnosis of either a malignant or premalignant mucosal lesion.
6. If the patient's medical status is too fragile for a biopsy or if the patients refuse.

### CONTRAINDICATIONS (21)

1. Majority of benign lesions do not lend themselves to cytologic smears.
2. Lesions having an intact surface like fibroma must never be smeared.
3. Leukoplakia does not lend itself to cytologic diagnosis because of scarcity of viable surface cells in the smear.

### RECENT ADVANCES

1. Exfoliative cytology was studied in patients with titanium implants. Metal-like particles were observed inside and outside epithelial cells and macrophages in cytological smears of peri-implant mucosa of both patients with and without periimplantitis. The concentration of titanium was higher in the peri-implantitis group as compared to the group without periimplantitis (22).
2. Ogden et al. suggested that quantitative techniques, based on the evaluation of parameters such as nuclear area (NA), cytoplasmic area (CA), and nucleus-to-cytoplasm area ratio (NA/CA), may increase the sensitivity of exfoliative cytology for early diagnosis of oral cancers, since these techniques are precise, objective, and reproducible (23).
3. Cowpe et al. demonstrated that exfoliative cytology can detect malignant changes, through estimation of NA/CA using the planimeter method in Papanicolaou-stained smears(24).
4. The validity of oral cytology or analysing the number of keratinised cells and the nucleolar activity (AgNORs) in smoking patients has recently been demonstrated (15).

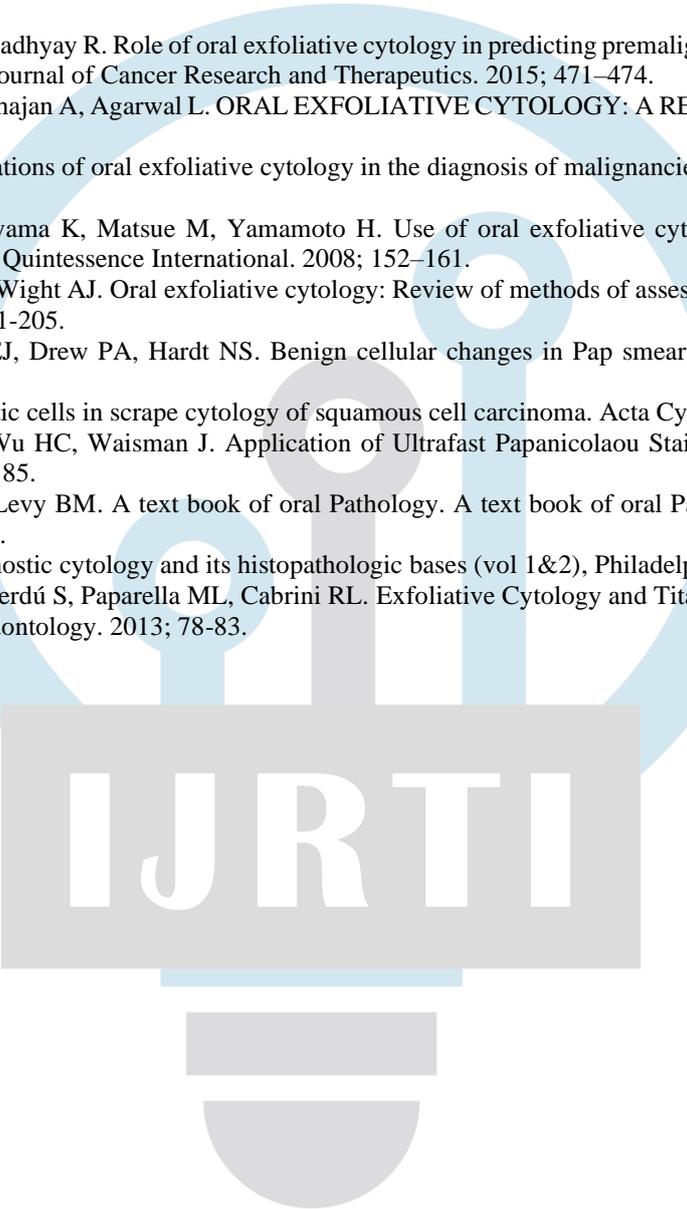
### CONCLUSION

Exfoliative cytology, orally, has always been considered as a simple yet convenient aid during chairside investigations. Although it has its own share of areas where improvements are needed but it can be treated as an excellent adjunct to other chairside tests like biopsy. The armamentarium has already been into several advances and so, has its value increased with time. More and more measures must be taken for deepening its usage in both dental education and private practice.

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