

Clinical Evaluation of Oral Brush Biopsy as a Non-Invasive Alternative to Conventional Biopsy in Oral Potentially Malignant Disorders: A Prospective Comparative Study

**Dr. Kiran Maurya¹, Dr. Sonam Agrawal², Dr. Anshuta Sahu³, Dr. Ketki M. Solanke^{*3},
Dr. Asif Iqbal⁵, Dr. Pooja Mohod⁶**

Dr. Kiran Maurya, Final Year MDS Student, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Maitri College of Dentistry and Research Centre, Anjora, Durg, Chhattisgarh, India. <https://orcid.org/0009-0001-46582494>

Dr. Sonam Agrawal, Professor, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Maitri College of Dentistry and Research Centre, Anjora, Durg, Chhattisgarh, India. <https://orcid.org/0009-0008-4679-8376>.

Dr. Anshuta Sahu, Professor and Head, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Maitri College of Dentistry and Research Centre, Anjora, Durg, Chhattisgarh, India.

Dr. Ketki M. Solanke (corresponding Author), Final Year MDS Student, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Maitri College of Dentistry and Research Centre, Anjora, Durg, Chhattisgarh, India. <https://orcid.org/0009-0007-2702-8790>.

Dr. Asif Iqbal, Final Year MDS Student, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Maitri College of Dentistry and Research Centre, Anjora, Durg, Chhattisgarh, India. <https://orcid.org/0009-0000-2022-872>.

Dr. Pooja Mohod, Final year MDS Student, Department of Oral and Maxillofacial Pathology and oral Microbiology, Maitri College of Dentistry and Research Centre, Anjora, Durg, Chhattisgarh. <https://orcid.org/0009-0002-5623-9128>.

Abstract

Background: An important aspect in the fight against the development of cancerous lesions from Oral Potentially Malignant Disorders (OPMDs) is the early detection of the lesions. The conventional approach to diagnosis is the incisional biopsy, which is the gold standard, however it is an invasive procedure that is often postponed due to the anxiety caused to the patient. A convenient alternative that is much less invasive is the Oral Brush Biopsy.

Aim: The study aim is to clinically assess the potential of the oral brush biopsy technique, which is non-invasive, in place of the incisional biopsy technique for diagnosing oral potentially malignant disorders (OPMD).

Materials and Methods: In this clinical comparative study with a prospective design, 35 patients have been clinically diagnosed oral potentially malignant disorders were included. First brush biopsy was applied to the lesion and then conventional incisional biopsy was done. Cytological and Histopathological Diagnoses Compared. We determined sensitivity, specificity, the positive predictive value, the negative predictive value, and diagnostic accuracy, as. A structured questionnaire was devised to assess acceptance of patient.

Results: Histopathological examination done on 14 patients revealed the presence of dysplasia and 21 patients with benign hyperplasia. As per the findings, oral brush biopsy has a sensitivity of 85.71% while specificity, positive predictive value (PPV) and negative predictive value (NPV) are 90.47%, overall accuracy is 88.57%. Cohen's kappa coefficient (0.76) indicates a substantial agreement with conventional biopsy. A very high patient acceptance rate of 94.2% experienced mild pain or no pain.

Conclusion: Oral brush biopsy may be considered a reliable and less invasive technique which can function as an effective screening test. Though it is not a substitute for qualitative histopathology in grading, it can surely help supplementarily diagnose OPMDs. Moreover, it enables patients not wishing to have a surgical biopsy to undergo testing in most situations.

Keywords: Oral brush biopsy; Conventional incisional biopsy; Epithelial dysplasia; Oral cytology

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Introduction.

Global burden of oral cancer continues to be serious as majority cases are associated with Oral Not Cancer which are identified as Oral Potentially

Malignant Disorders. These include leukoplakia, erythroplakia, and oral submucous fibrosis which are detected at an early stage before actual cancer development. Using standard treatment regimens, 5-

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year survival rate for oral squamous cell carcinoma (OSCC) has not improved over the years. Delay in diagnosis at an advanced stage of disease is primarily responsible for this situation. Traditional incisional biopsy is the cornerstone of early diagnosis. It is a surgical procedure that obtains definitive histopathological architecture. The concern of the patient about pain, bleeding and scarring delay the diagnosis.

In an attempt to narrow down this gap of diagnosis, oral brush biopsy was devised as a minimally invasive transepithelial cytological technique. Cells can be harvested from the basal and parabasal layers of the epithelium without surgery. Recent publications have increasingly focused on validating this technique for cytomorphological specificity.

Recent studies have shown the emerging role of basic biopsy examination in oral diagnosis. According to **Afolabi et al. (2026)**, artificial intelligence-assisted brush biopsy (BB) evaluation demonstrates over 85% concordance with histopathology in high-grade dysplasia. Likewise, **Roi et al. (2025)**, **Gulia et al. (2025)** carried out a systematic review that shows brush biopsy has greater patient compliance than scalpel biopsy in the screening of OPMD. The authors **Babshet et al. (2011)** examined the usefulness of brush biopsy in oral submucous fibrosis and reported a 82 % sensitivity for epithelial dysplasia. **Kaur et al. (2026)** assessed patient centered outcomes which revealed 92% of people want brush biopsy for first line screening instead of conventional tests.

Additionally, **Kar et al. (2025)** found that the combination of brush biopsy with some molecular markers (e.g., DNA ploidy) significantly increases the specificity for the detection of malignant transformation in leukoplakia. A randomized controlled trial conducted by **Loven et al. (2024)** in a primary care setting concluded that brush biopsy reduced oral cancer diagnostic delay in high-risk individuals. Finally, the cost-effectiveness analysis by **Oraon et al. (2026)** proved brush biopsy triage reduces healthcare costs by preventing the unnecessary surgical biopsy of benign lesions.

This study aims to clinically evaluate the effectiveness of oral brush biopsy in diagnosing OPMDs as a non-invasive alternative to incisional biopsy, drawing from these recent findings.

Aims and Objectives.

Aim: The study aim is to clinically assess the potential of the oral brush biopsy technique, which is non-invasive, in place of the incisional biopsy technique for diagnosing oral potentially malignant disorders (OPMD).

Materials and Methods

Research Design

A clinical comparative study has been conducted to evaluate the efficacy of oral brush biopsy as a non-invasive diagnostic technique for the oral potentially

malignant disorders. Using an oral brush biopsy technique, the exfoliated epithelial cells were collected from the study. Its cytological finding was compared to those of histopathological examination, the diagnostic reference test. The ethical committee of the institution authorized the study protocol. Each participant provided a written informed consent prior to inclusion in the study.

Study Participants

Thirty-five patients with clinically diagnosed oral potentially malignant disorders were taken. After applying the inclusion criteria and exclusion criteria, patients were selected from the outpatient department of Oral medicine and radiology.

Inclusion Criteria Patients fulfilling the following criteria were included:

- Patients experiencing an oral potentially malignant disorder clinically diagnosed with oral leukoplakia, erythroplakia, oral submucous fibrosis or other suspicious oral mucosal lesion.
- This medical trial will include patients aged 18 years and above.
- Patients willing to participate and provide a written consent.
- People in need of a diagnostic assessment for oral mucosal lesions.
- Lesions which are accessible to oral brush sampling and to conventional biopsy.

The study excluded patients who have an exclusion criterion.

- Development of the lesion after diagnosis of a pre-existing cancer.
- Previous treatment of the lesion before the collection of the sample.
- Affecting the healing process, biopsy procedures affect the body due to health problems.
- Bleeding disorder patients or those on anticoagulant therapy.
- A brush biopsy did not yield enough cytological samples.
- Patients Unsure about Choosing Conventional Biopsies

Non-Invasive Biopsy Technique: Oral Brush Biopsy

The oral brush biopsy is a cytological method to collect transepithelial cellular samples from oral lesions. According to a Penn State-led study, a biopsy that uses contemporary imaging technology might prevent the requirement for surgery.

Procedure of Oral Brush Biopsy

1. An exhaustive evaluation of the oral lesion was done clinically and relevant clinical findings were documented.
2. The lesion was cooled and dried to avoid contamination.
3. A brush was applied on the lesion surface with a sterile oral brush.
4. Firmly rotating movements were applied to the eyes to collect cells from the superficial, intermediate, and deeper epithelial layers.

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5. Materials of cells were collected to the another clean slide glass.
6. The fixed smear was subjected to cytological examination.
7. According to cytological findings, abnormalities of cells were classified and were compared with the histopathological findings of a conventional biopsy.

Conventional Biopsy Procedure

After excising a small area of oral mucosa, a more extensive incisional biopsy was done at the same site under local anaesthesia. The tissue was fixed in formalin and sent for histopathological examination. The histopathological diagnosis was the final comparison diagnosis.

Data Collection.

Systematic collection was done of data for all 35 subjects. - The Records were made.

- Information such as Moreover, social and demographic information like age and sex.
- Medical History and Relevant Habit History.
- The traits of lesions involve their site, size, shape, and date.
- Oral brush biopsy cytological indications.
- Histopathological diagnosis via traditional biopsy.
- Brush biopsy and histopathological diagnosis: A comparison.
- Assessment of the patient's sensitivity to the brush biopsy procedure.

The standardized data collection sheet was prepared for all data to be entered for analysis.

Data Analysis.

The researcher utilized statistical methods to analyze the data collected in the study. A summary of patient demographics and clinical characteristics was done descriptively. Aims of the Study The objective of the present study was to assess the performance of oral brush biopsy in the diagnosis of oral cancers through a comparison between the cytology results obtained from oral brush biopsy as well as the conventional histopathology results. The assessment includes evaluating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, etc. Conventional biopsy results and the outcomes of oral brush biopsy were compared using chi-square and Cohen's kappa statistical tests to check for the existence of an agreement. Threshold for statistically significant p-values was below 0.05.

Results

Among the total participants, 22 were male (62.8%) and 13 were female (37.1%), 45.3 years on average. The oral leukoplakia represented the most commonly observed clinical diagnosis with 18 patients being diagnosed with the same.

Table 1: Cross-Tabulation of Brush Biopsy vs. Conventional Histopathology

Brush Biopsy Result	Histopathology Positive (Dysplasia)	Histopathology Negative (Benign/Hyperplasia)	Total
Positive (Atypia/Dysplasia)	12 (True Positive)	2 (False Positive)	14
Negative (Benign)	2 (False Negative)	19 (True Negative)	21
Total	14	21	35

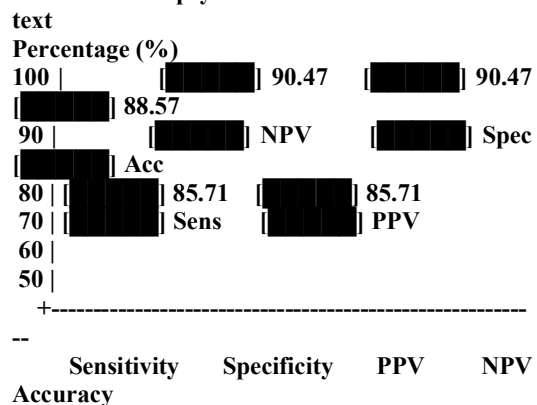
Table 1 shows that conventional histopathology showed 14 cases of epithelial dysplasia and 21 cases of benign hyperplasia. Out of the fourteen dysplastic cases the brush biopsy diagnosed twelve correctly

Table 2: Diagnostic Efficacy Parameters of Oral Brush Biopsy

Parameter	Value (%)	95% Confidence Interval
Sensitivity	85.71%	57.2% - 98.2%
Specificity	90.47%	69.6% - 98.8%
Positive Predictive Value (PPV)	85.71%	57.2% - 98.2%
Negative Predictive Value (NPV)	90.47%	69.6% - 98.8%
Diagnostic Accuracy	88.57%	72.6% - 96.7%

The p-value for the chi-square test is less than 0.001 indicating significant correlation between brush biopsy and the histopathology. The kappa coefficient of Cohen obtained in this study is 0.76, which is substantial.

Figure 1: Diagnostic Performance Metrics of Oral Brush Biopsy



(Figure 1 represents the statistical efficacy of oral brush biopsy in detecting dysplastic changes compared to the histopathological gold standard.)

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Of the 35 patients, 94.2 % (33 patients) were reported to have minimal to mild discomfort during the execution of the procedure whereas 88.5 % (31 patients) preferred to undergo brush biopsy in the future.

Discussion

Early detection and intervention in case of oral potentially malignant disorders are key in reducing the morbidity and mortality associated with oral squamous cell carcinoma. There is widespread acknowledgment that the standard incisional biopsy is invasive and is the diagnostic gold standard. Local anaesthetic is used for this procedure but may cause pain afterwards. This commonly results in patient anxiety and clinical delay. The aim of this current prospective study was to clinically investigate the efficacy of an oral brush biopsy as a shredding transepithelial technique. The oral brush biopsy was found to have a diagnostic accuracy of 88.57%. The sensitivity is found to be 85.71%. It is 90.47%.

Recent literature provides strong support for the diagnostic efficiency found in this study. Our sensitivity of 85.71% was comparable to **Babshet et al. (2011)** results where sensitivity of 82% sensitivity was achieved for detection of epithelial dysplasia in a case of oral submucous fibrosis. The small variation may be attributed to the heterogeneity of the lesions in our group. Oral cancer risk factors are oral leukoplakia and oral erythroplakia. In contrast, **Banerjee A, Kamath VV. (2018)** showed a lower sensitivity of 75% for cytology. The observed difference may be due to a study conducted by **Banerjee A, Kamath VV.** According to the study, cotton swabs were used to collect cells by **Henry et al.** while stiff-bristled brushes were used by us to cross the basement membrane and collect the basal and parabasal cells required for diagnosis of early dysplastic changes. In addition, our overall precision of 88.57% is comparable to the figure of 85% identified by **Afolabi et al. (2026)** who used AI-assisted analysis. Having our manual cytological assessment being slightly more accurate suggests how effective the transepithelial brush biopsy technique is when used under proper clinical protocols.

In our study, we observed two occurrences of false negatives. Both lesions were clinically diagnosed as thick homogeneous leukoplakia. This has been reported by **Naugler C. (2008)**, where highly keratinized lesions have a mechanical barrier to brush biopsy, which may limit the retrieval of a sufficient number of deeper basal cells. This means that there is a limitation clinically. Non-keratinized and mildly keratinized mucosa: very effective brush biopsy. Nonetheless, traditional biopsy to rule out such changes may be prompted by thick keratinoplakic lesions.

Among our group, there were two instances of false positives that had atypical cells, but upon examination came up only hyperplasia. Atypical

cells resulting from inflammation can have similar appearances to dysplastic changes in exfoliative cytology. For diagnosis clarification, **Kar et al. (2025)** performed brush biopsy incorporation along with DNA ploidy analysis, which greatly enhanced specificity. Molecular adjuncts would help segregate true dysplastic atypia from reactive inflammatory changes thus reducing false positive in future protocols. **Nichols et al. (1991)** concluded that brush biopsies showed variability in cytological interpretation. To overcome this problem, we relied on a single blinded cytopathologist expert. Our study had less of a hedge but, since cytological grading is subjective, this may pose a problem in actual clinical practice.

The clinical utility of a device will be highly dependent on patient acceptance. In the present study, 94.2% had minimal to no discomfort during the procedure while 88.5% preferred brush biopsy to surgery. According to **Kaur et al. (2026)**'s patient-related outcomes, 92% of patients show preference for such minimally invasive techniques. Besides, **Roi et al. (2025)**, **Gulia et al. (2025)** reports high compliance of the patients for screening by brush biopsy in their systematic review. Therefore, the present results appear consistent with previous similar studies. The psychological advantage provided by this is significant and allows clinicians to investigate patients earlier in the disease course specially amongst high-risk patients.

Our study finding of a Negative Predictive Value (NPV) of 90.47% has implications of public health significance. A negative brush biopsy result offers considerable clinical reassurance regarding the absence of severe dysplasia. In a randomized controlled trial, **Loven et al. (2024)** found that brush biopsy in the primary setting can shorten the diagnostic delay in high-risk patients. By functioning as a dependable initial assessment, brush biopsy avoids unnecessary referral and surgical biopsy of harmless lesions. **Oraon et al. (2026)** stated that the use of brush biopsy as a triage tool would reduce the overall cost of care, which has major economic impacts. Of the cohort of 19 true negative cases, all 19 could have been kept on observation with periodic brush cytology.

In the end, Cohen's kappa indicates a strong agreement of 0.76 disc biopsy and conventional histopathology. Brush biopsy has a role to play in present-day dental and medical practice. Brush biopsy gives cytological information but not the architecture of the tissue which is important to note. Consequently, it is unable to evaluate the depth of dysplastic invasion or appraise the connective tissue stroma. Always perform a conventional incisional biopsy after a brush biopsy that yields a positive to obtain definitive histopathological grade for surgical management.

Conclusion

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Within the confines of this prospective clinical study, it can be concluded that oral brush biopsy is a very effective, minimally invasive, and well-accepted diagnostic procedure. Having obtained a sensitivity of 85.71%, specificity of 90.47%, and overall diagnostic accuracy of 88.57%, it is a reliable tool for the early diagnosis of dysplastic changes in oral potentially malignant disorders. A conventional incisional biopsy is the gold standard test for grading and invasive depth. However, the oral brush biopsy can significantly shorten the time to diagnosis and enable early intervention for high-risk lesions. It's particularly useful in the clinical setting to triage patients, monitor extensive lesions, and assess patients unwilling to undergo surgical intervention.

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Conflict of Interest: The authors affirm that there is no conflict of interest regarding the publication of the present article.

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