Natural Resources for Human Health
eISSN: 2583-1194

Original Research

**Received** 20 May 2026
**Revised** 15 July 2026
**Accepted** 22 July 2026

Natural Resources for Human Health 2026, Vol. 6 (1s): 493–504

**KEYWORDS**:
Epithelial dysplasia, Oral potentially malignant disorders, Periodontal disease, Tobacco chewing

# Correlation of Periodontal Disease Severity with Clinical and Histopathological Features of Oral Potentially Malignant Disorders

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## ABSTRACT:

**Background:** Periodontitis is a chronic inflammatory condition that may contribute to alterations in the local oral inflammatory environment. Oral potentially malignant disorders (OPMDs) represent a heterogeneous group of mucosal lesions with variable potential for malignant transformation. The relationship between periodontal disease severity and the histopathological severity of epithelial dysplasia remains incompletely understood.

**Aim:** To evaluate the association between periodontal disease severity and histopathological dysplasia in patients presenting with OPMDs and to identify clinical and periodontal factors independently associated with epithelial dysplasia.

**Materials and Methods:** A total of 100 patients diagnosed with OPMDs were evaluated. Demographic characteristics, tobacco-chewing and smoking habits, type of OPMD, and periodontal parameters were recorded. Participants were categorized according to periodontal disease severity into mild/no periodontitis (n=34), moderate periodontitis (n=36), and severe periodontitis (n=30). Plaque Index (PI), Gingival Index (GI), probing pocket depth (PPD), clinical attachment level (CAL), and bleeding on probing (BOP) were assessed. Histopathological examination classified lesions as showing no, mild, moderate, or severe epithelial dysplasia. Group differences were evaluated using one-way Analysis of Variance (ANOVA) with Tukey's post-hoc test, while associations were assessed using the Chi-square test and Spearman's correlation. Multivariable logistic regression was performed to identify independent predictors of epithelial dysplasia.

**Results:** Periodontal parameters deteriorated progressively with increasing disease

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eISSN: 2583-1194

severity, with significant differences among the three groups for all evaluated variables ($p<0.001$). Histopathological examination identified epithelial dysplasia in 58% of lesions, comprising mild dysplasia in 31%, moderate dysplasia in 18%, and severe dysplasia in 9%. A significant association was observed between periodontal disease severity and dysplasia grade ($\chi^2=18.52$, $p<0.001$). CAL demonstrated the strongest correlation with dysplasia severity ($r=0.52$, $p<0.001$), followed by PPD ($r=0.48$, $p<0.001$). In multivariable analysis, severe periodontitis was independently associated with epithelial dysplasia (adjusted odds ratio (OR) =3.84, 95% confidence interval (CI): 1.42–10.38; probability (p) =0.008). Tobacco chewing (adjusted OR=2.46; p=0.029) and non-homogeneous lesion appearance (adjusted OR=2.71; p=0.034) were also significant predictors.

**Conclusion:** Greater periodontal disease severity was significantly associated with increasing histopathological severity of epithelial dysplasia among patients with OPMDs. Severe periodontitis, tobacco chewing, and non-homogeneous lesion morphology emerged as independent predictors of epithelial dysplasia. These findings suggest that comprehensive periodontal assessment may be relevant when evaluating patients with OPMDs, although prospective studies are required to establish temporal and causal relationships.

## INTRODUCTION

Oral potentially malignant disorders (OPMDs) comprise a heterogeneous group of oral mucosal conditions that are associated with an increased risk of developing oral squamous cell carcinoma (OSCC). Commonly recognized OPMDs include oral leukoplakia, oral submucous fibrosis (OSMF), oral lichen planus (OLP)/ lichenoid lesions, erythroplakia, proliferative verrucous leukoplakia, and other mucosal disorders with malignant potential. Their risk of progression varies according to the type of lesion, duration and intensity of etiological exposure, anatomical location, extent of involvement, and presence and severity of epithelial dysplasia. Early identification and appropriate evaluation of these lesions are therefore important for oral cancer prevention [1].

Periodontal disease is a chronic inflammatory disorder initiated by a dysbiotic microbial biofilm and mediated by an altered host immune response. Progressive periodontal inflammation can result in destruction of the periodontal ligament and alveolar bone and is accompanied by increased production of inflammatory cytokines, matrix metalloproteinases, reactive oxygen species, and other mediators of tissue injury. The periodontal pocket may also provide a favorable environment for microbial persistence and sustained inflammatory activity, thereby contributing to changes in the local oral environment [2].

The possible association between periodontal inflammation and OPMDs is of particular interest because chronic inflammation can promote oxidative stress, cellular damage, abnormal proliferation, and alterations in local immune surveillance. Persistent inflammatory activity may create a tissue environment that favors the accumulation or persistence of cellular abnormalities, particularly in individuals exposed to established carcinogenic factors such as tobacco, areca nut, and alcohol. Consequently, periodontal inflammation may act as a potential modifying factor in the biological behavior of potentially malignant oral lesions [3].

The relationship between periodontal disease and oral carcinogenesis has been investigated in epidemiological and biological studies, with chronic periodontal inflammation proposed as one of several factors that may influence oral cancer risk. Periodontal pathogens and their products can stimulate inflammatory signaling and may contribute to oxidative and genotoxic stress within the oral environment. However, the independent contribution of periodontal disease to the severity or progression of OPMDs remains incompletely established, particularly when important confounding factors such as tobacco and areca-nut exposure are considered [4].

Clinical assessment of OPMDs includes evaluation of lesion site, size, color, surface characteristics, distribution, and clinical appearance. Although these characteristics provide important diagnostic information, clinical examination alone cannot

reliably determine the degree of epithelial dysplasia or malignant potential. Histopathological examination is therefore essential for evaluating epithelial architecture and cytological abnormalities and for determining the presence and severity of epithelial dysplasia [5].

Microscopic alterations associated with epithelial dysplasia may include hyperkeratosis, epithelial hyperplasia or atrophy, basal cell abnormalities, nuclear hyperchromatism, cellular pleomorphism, increased or abnormal mitotic activity, loss of cellular polarity, and disturbed epithelial maturation. Increasing severity and extent of these abnormalities may indicate greater biological instability of the affected epithelium and may assist in identifying lesions requiring closer surveillance or intervention [6].

Assessment of periodontal status together with clinical and histopathological evaluation of OPMDs may provide a more comprehensive understanding of factors associated with lesion severity. Such an integrated approach is particularly relevant because periodontal disease and OPMDs may coexist in patients with common behavioral and environmental risk factors. Determining whether periodontal disease severity correlates with clinical or microscopic characteristics of OPMDs could therefore provide additional insight into the role of chronic oral inflammation in potentially malignant mucosal alterations [7].

From a clinical perspective, establishing such an association may emphasize the importance of comprehensive periodontal and mucosal examination. Patients presenting with severe periodontal inflammation, particularly those with established risk factors for oral cancer, may benefit from careful assessment of the oral mucosa. Similarly, individuals diagnosed with OPMDs should receive appropriate periodontal evaluation and management as part of their overall oral health care [8].

Despite increasing interest in the interaction between chronic inflammation and oral potentially malignant conditions, limited evidence is available regarding the direct relationship between periodontal disease severity and the clinical and histopathological characteristics of OPMDs. Further evaluation of this association may help clarify whether periodontal disease represents an independent inflammatory factor associated with more advanced mucosal alterations [9].

Therefore, the present study was undertaken to assess the correlation between periodontal disease severity and the clinical and histopathological features of OPMDs. The study specifically aimed to determine whether increasing periodontal disease severity is associated with greater clinical severity of OPMDs and more pronounced histopathological epithelial alterations.

## MATERIALS & METHODS

### Study Design and Study Population

The study included 100 patients diagnosed with OPMDs. Participants were evaluated clinically for periodontal status and oral mucosal lesions at a single tertiary care centre, followed by histopathological assessment of the OPMD specimens. The study population comprised 62 males and 38 females, with participants distributed across the age groups of 35–50, 51–60, 61–70, and >70 years. Leukoplakia was the most frequently identified OPMD, followed by OSMF, OLP/ lichenoid lesions, erythroplakia, and other OPMDs.

### Clinical and Habit Assessment

Relevant demographic and behavioral characteristics were recorded, including age, sex, tobacco-chewing habit, and smoking status. Tobacco chewing was reported by 54% of participants, whereas smoking was reported by 39%. The OPMDs were clinically categorized according to their recorded lesion type.

### Periodontal Assessment

A comprehensive periodontal assessment was performed, including measurement of Plaque Index (PI), Gingival Index (GI), probing pocket depth (PPD), clinical attachment level (CAL), and bleeding on probing (BOP). Based on periodontal findings, participants were categorized into three groups:

Mild/no periodontitis: n=34

Moderate periodontitis: n=36

Severe periodontitis: n=30

The mean periodontal parameters demonstrated progressive deterioration across these severity categories.

**Histopathological Evaluation**

Histopathological examination was performed on specimens obtained from the OPMDs. Based on the degree of epithelial alteration, lesions were classified into four categories: no epithelial dysplasia, mild dysplasia, moderate dysplasia, and severe dysplasia. Of the 100 specimens, 42 showed no dysplasia, while 31, 18, and 9 demonstrated mild, moderate, and severe dysplasia, respectively.

**Assessment of the Relationship Between Periodontitis and Dysplasia**

The distribution of histopathological dysplasia was compared across the three periodontal severity groups. The proportion of lesions without dysplasia decreased progressively with increasing periodontal severity, whereas moderate and severe dysplasia became increasingly prevalent in the severe-periodontitis group. The association between periodontal disease severity and dysplasia grade was evaluated statistically.

**Statistical Analysis**

The collected data were entered into a statistical package for social sciences (SPSS) software and analyzed using appropriate descriptive and inferential statistical methods. Categorical variables such as age group, gender, tobacco-chewing and smoking habits, type of OPMD, and histopathological grade were expressed as frequencies and percentages. Continuous periodontal parameters, including PI, GI, PPD, CAL, and BOP, were expressed as mean ± standard deviation (SD).

For comparison of periodontal parameters among the three periodontal disease severity groups (mild/no, moderate, and severe periodontitis), one-way analysis of variance (ANOVA) was applied. Following a statistically significant overall ANOVA, Tukey's HSD post-hoc test was used for pairwise comparisons between groups.

The association between periodontal disease severity and histopathological grade of epithelial dysplasia was assessed using the Chi-square test of independence. Histopathological dysplasia was categorized as no, mild, moderate, or severe dysplasia.

The relationship between periodontal parameters and histopathological dysplasia severity was assessed using Spearman's rank correlation coefficient, as the dysplasia grade represents an ordinal outcome. Correlation coefficients were interpreted according to the strength and direction of association.

To identify independent predictors of epithelial dysplasia, multivariable binary logistic regression analysis was performed, with the presence of epithelial dysplasia as the dependent variable. Relevant demographic, habit-related, clinical, and periodontal variables were included as independent variables. Results were expressed as OR with 95% CI.

A p-value $<0.05$ was considered statistically significant. The statistical analysis was designed to determine whether increasing periodontal disease severity was associated with increasing histopathological severity of OPMDs, while accounting for potential confounding factors such as age, tobacco chewing, and clinical characteristics.

**RESULTS**

Table 1 & Figure 1 summarize the demographic, behavioral, and clinical characteristics of the 100 participants diagnosed with OPMDs. The largest proportion of participants was in the 51–60-year age group (34.0%), followed by those aged 61–70 years (27.0%), 35–50 years (25.0%), and above 70 years (14.0%). Males represented 62.0% of the study population, while females accounted for 38.0%. Tobacco chewing was reported by 54.0% of participants, whereas 46.0% had no history of tobacco chewing. Smoking was documented in 39.0% of participants and was absent in 61.0%. Among the various OPMDs, leukoplakia was the most prevalent lesion (52.0%), followed by OSMF (22.0%), OLP/lichenoid lesions (10.0%), erythroplakia (8.0%), and other OPMDs (8.0%). Overall, the study population was predominantly composed of middle-aged and older males, with tobacco chewing being the most frequently reported deleterious habit and leukoplakia representing the predominant OPMD.

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eISSN: 2583-1194

**Table 1:** Demographic and Clinical Characteristics of the Study Population

| Characteristic | n (%) |
|---|---|
| Age | |
| 35–50 years | 25 (25.0) |
| 51–60 years | 34 (34.0) |
| 61–70 years | 27 (27.0) |
| >70 years | 14 (14.0) |
| Gender | |
| Male | 62 (62.0) |
| Female | 38 (38.0) |
| Tobacco chewing | |
| Present | 54 (54.0) |
| Absent | 46 (46.0) |
| Smoking | |
| Present | 39 (39.0) |
| Absent | 61 (61.0) |
| OPMD type | |
| Leukoplakia | 52 (52.0) |
| OSMF | 22 (22.0) |
| OLP/lichenoid lesion | 10 (10.0) |
| Erythroplakia | 8 (8.0) |
| Other OPMDs | 8 (8.0) |

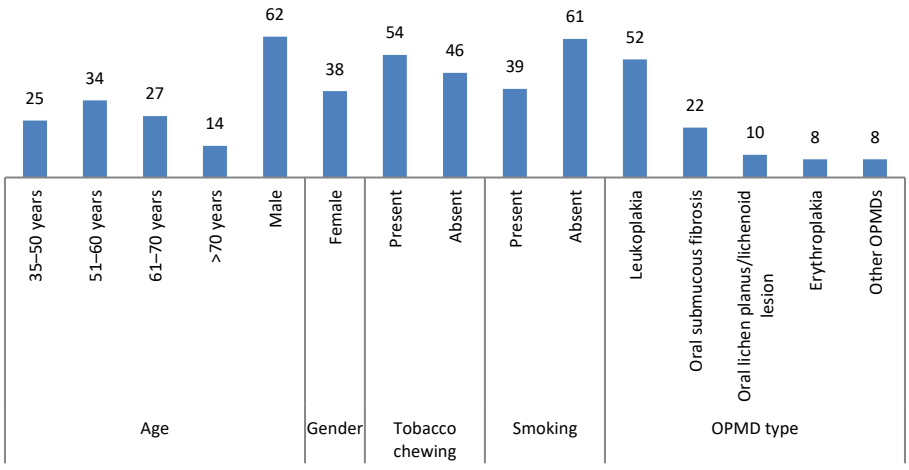


**Figure 1:** Demographic, Behavioral, and Clinical Characteristics of the Study Participants with OPMDs

Table 2 & Figure 2 present a clear and statistically significant gradient was observed across the three periodontal severity groups for all assessed periodontal parameters ($p < 0.001$). The mean PI increased from 1.42 ± 0.31 among participants with mild/no periodontitis to 1.71 ± 0.34 in the moderate group and 1.94 ± 0.36 in the severe group. A similar pattern was observed for the GI, which increased from 1.21 ± 0.28 to 1.48 ± 0.31 and 1.76 ± 0.35, respectively.

Indicators of periodontal tissue destruction also demonstrated a progressive increase with disease severity. Mean PPD increased from 2.74 ± 0.39 mm in the mild/no-periodontitis group to 4.12 ± 0.51 mm in the moderate group and 5.67 ± 0.72 mm in the severe group. Correspondingly, mean CAL increased from 2.83 ± 0.42 mm to 4.38 ± 0.57 mm and 6.21 ± 0.81 mm. BOP also showed a significant upward trend, increasing from 28.6 ± 9.4% to 47.3 ± 11.2% and 65.8 ± 13.1%, respectively.

Table 3 presents the results of Tukey's post-hoc analysis, confirming statistically significant differences between the periodontal severity groups for all evaluated parameters. For the PI, significant differences were observed between mild/no and moderate periodontitis (mean difference = 0.29, $p < 0.001$), moderate and severe periodontitis (mean difference = 0.23, $p = 0.014$), and mild/no and severe periodontitis (mean difference = 0.52, $p < 0.001$). Comparable significant pairwise differences were identified for the GI, PPD, CAL, and BOP. The largest differences were consistently observed when the mild/no-periodontitis group was compared with the severe-periodontitis group. Overall, the findings demonstrate a progressive worsening of periodontal clinical parameters with increasing disease severity.

**Table 2:** Periodontal Parameters According to Disease Severity

| Parameter | Mild/No periodontitis (n=34) | Moderate (n=36) | Severe (n=30) | p-value |
|---|---|---|---|---|
| PI | 1.42 ± 0.31 | 1.71 ± 0.34 | 1.94 ± 0.36 | <0.001* |
| GI | 1.21 ± 0.28 | 1.48 ± 0.31 | 1.76 ± 0.35 | <0.001* |
| PPD (mm) | 2.74 ± 0.39 | 4.12 ± 0.51 | 5.67 ± 0.72 | <0.001* |
| CAL (mm) | 2.83 ± 0.42 | 4.38 ± 0.57 | 6.21 ± 0.81 | <0.001* |
| BOP (%) | 28.6 ± 9.4 | 47.3 ± 11.2 | 65.8 ± 13.1 | <0.001* |

**Table 3:** Post Hoc Analysis

| Parameter | Pairwise comparison | Mean difference | Adjusted p-value | Significance |
|---|---|---|---|---|
| PI | Mild vs Moderate | 0.29 | <0.001 | Significant |
| | Moderate vs Severe | 0.23 | 0.014 | Significant |
| | Mild vs Severe | 0.52 | <0.001 | Significant |
| GI | Mild vs Moderate | 0.27 | <0.001 | Significant |
| | Moderate vs Severe | 0.28 | 0.002 | Significant |
| | Mild vs Severe | 0.55 | <0.001 | Significant |
| PPD (mm) | Mild vs Moderate | 1.38 | <0.001 | Significant |
| | Moderate vs Severe | 1.55 | <0.001 | Significant |
| | Mild vs Severe | 2.93 | <0.001 | Significant |
| CAL (mm) | Mild vs Moderate | 1.55 | <0.001 | Significant |
| | Moderate vs Severe | 1.83 | <0.001 | Significant |
| | Mild vs Severe | 3.38 | <0.001 | Significant |
| BOP (%) | Mild vs Moderate | 18.7 | <0.001 | Significant |
| | Moderate vs Severe | 18.5 | <0.001 | Significant |
| | Mild vs Severe | 37.2 | <0.001 | Significant |

Natural Resources for Human Health
eISSN: 2583-1194

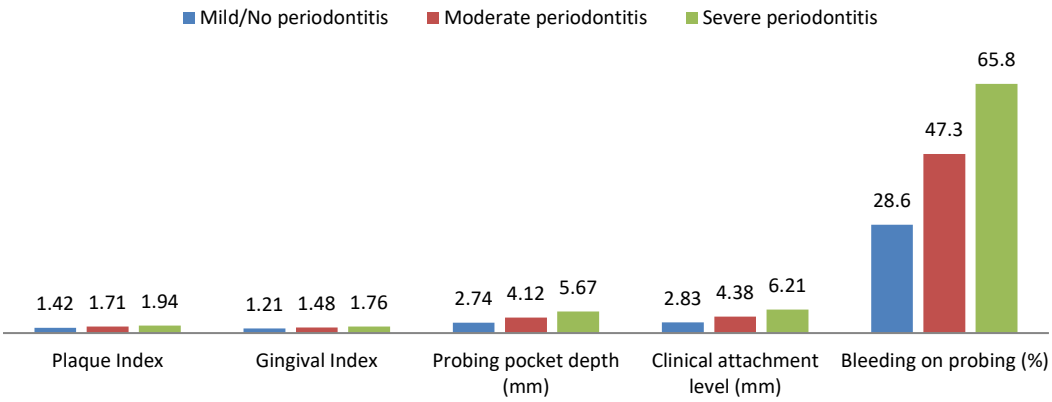


**Figure 2:** Comparison of Periodontal Parameters Across Different Levels of Periodontal Disease Severity

Table 4 & Figure 3 present histopathological assessment of the 100 OPMD specimens revealed that 42 cases (42.0%) had no epithelial dysplasia, whereas 58 cases (58.0%) demonstrated varying degrees of dysplastic change. Among the dysplastic specimens, mild dysplasia was most common, accounting for 31 cases (31.0%), followed by moderate dysplasia in 18 cases (18.0%) and severe dysplasia in 9 cases (9.0%). Overall, more than half of the evaluated lesions showed histopathological evidence of epithelial dysplasia, with 27.0% demonstrating moderate-to-severe dysplasia.

**Table 4:** Histopathological Grading of OPMDs

| Histopathological grade | n (%) |
|---|---|
| No epithelial dysplasia | 42 (42.0) |
| Mild dysplasia | 31 (31.0) |
| Moderate dysplasia | 18 (18.0) |
| Severe dysplasia | 9 (9.0) |

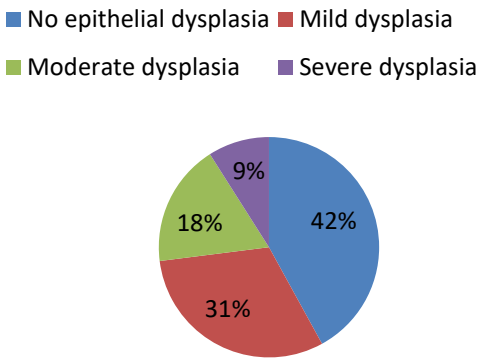


**Figure 3:** Distribution of Histopathological Grades of Epithelial Dysplasia Among OPMD Specimens

Table 5 & Figure 4 present significant relationship between periodontal disease severity and the histopathological grade of epithelial dysplasia ($\chi^2 = 18.52$, $p < 0.001$). Among participants with mild/no periodontitis, 64.7% showed no dysplasia, while mild, moderate, and severe dysplasia were identified in 23.5%, 8.8%, and 2.9%, respectively. In the moderate-periodontitis group, the proportion of lesions without dysplasia decreased to 38.9%, whereas mild, moderate, and severe dysplasia accounted for 33.3%, 19.4%, and 8.3%, respectively. The severe-periodontitis group demonstrated the highest prevalence of

dysplastic changes, with only 20.0% showing no dysplasia; mild, moderate, and severe dysplasia were present in 36.7%, 26.7%, and 16.7%, respectively. Overall, the findings demonstrated a progressive shift toward higher grades of epithelial dysplasia with increasing periodontal disease severity, particularly for moderate-to-severe dysplasia.

**Table 5:** Association Between Periodontal Disease Severity and Histopathological Dysplasia

| Periodontal disease severity | No epithelial dysplasia n (%) | Mild dysplasia n (%) | Moderate dysplasia n (%) | Severe dysplasia n (%) | Total |
|---|---|---|---|---|---|
| Mild/No periodontitis (n=34) | 22 (64.7) | 8 (23.5) | 3 (8.8) | 1 (2.9) | 34 (100) |
| Moderate periodontitis (n=36) | 14 (38.9) | 12 (33.3) | 7 (19.4) | 3 (8.3) | 36 (100) |
| Severe periodontitis (n=30) | 6 (20.0) | 11 (36.7) | 8 (26.7) | 5 (16.7) | 30 (100) |
| Total (n=100) | 42 (42.0) | 31 (31.0) | 18 (18.0) | 9 (9.0) | 100 (100) |

Chi-square test: $\chi^2 = 18.52$; $p < 0.001$*

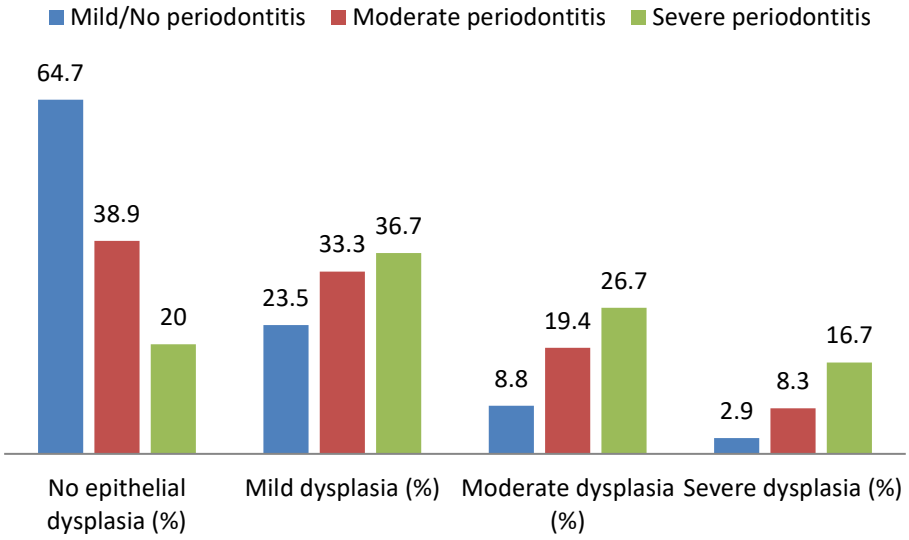


**Figure 4:** Distribution of Histopathological Epithelial Dysplasia According to Periodontal Disease Severity

Table 6 presents Spearman's rank correlation analysis revealed significant positive associations between each assessed periodontal parameter and the histopathological dysplasia score. The PI showed a weak positive correlation with dysplasia severity ($r = 0.29$, $p = 0.003$), while the GI demonstrated a slightly stronger association ($r = 0.34$, $p < 0.001$). A moderate positive correlation was observed between PPD and dysplasia severity ($r = 0.48$, $p < 0.001$). The strongest correlation was identified for **CAL** ($r = 0.52$, $p < 0.001$), suggesting that greater attachment loss was associated with higher grades of epithelial dysplasia. BOP also showed a significant positive correlation ($r = 0.39$, $p < 0.001$). Overall, increasing periodontal disease severity was significantly associated with greater histopathological dysplasia among the evaluated OPMD cases.

**Table 6:** Correlation Between Periodontal Parameters and Histopathological Dysplasia Score

| Parameter | Spearman's correlation coefficient (r) | p-value |
|---|---|---|
| PI | 0.29 | 0.003 |
| GI | 0.34 | <0.001 |

| | | |
|---|---|---|
| PPD | 0.48 | <0.001 |
| CAL | 0.52 | <0.001 |
| BOP | 0.39 | <0.001 |

Table 7 presents the results of the multivariable logistic regression analysis used to determine which demographic, behavioral, clinical, and periodontal factors were independently associated with epithelial dysplasia. Severe periodontitis was significantly associated with dysplasia, with affected patients showing nearly fourfold greater odds compared with the reference group (adjusted OR = 3.84, 95% CI: 1.42–10.38; p = 0.008). Tobacco chewing was also independently associated with dysplasia (adjusted OR = 2.46, 95% CI: 1.10–5.49; p = 0.029). Similarly, the presence of a non-homogeneous lesion was associated with increased odds of epithelial dysplasia (adjusted OR = 2.71, 95% CI: 1.08–6.81; p = 0.034). Although moderate periodontitis showed elevated odds (adjusted OR = 2.21, 95% CI: 0.92–5.30), the association was not statistically significant (p = 0.076). Likewise, age above 60 years did not demonstrate a significant independent association with dysplasia (adjusted OR = 1.72, 95% CI: 0.78–3.79; p = 0.179). Overall, severe periodontitis, tobacco chewing, and non-homogeneous lesion morphology were identified as significant independent predictors of epithelial dysplasia in the study population.

**Table 7:** Multivariable Logistic Regression for Predictors of Epithelial Dysplasia

| Predictor | Adjusted OR | 95% CI | p-value |
|---|---|---|---|
| Age >60 years | 1.72 | 0.78–3.79 | 0.179 |
| Tobacco chewing | 2.46 | 1.10–5.49 | 0.029 |
| Non-homogeneous lesion | 2.71 | 1.08–6.81 | 0.034 |
| Moderate periodontitis | 2.21 | 0.92–5.30 | 0.076 |
| Severe periodontitis | 3.84 | 1.42–10.38 | 0.008 |

## DISCUSSION

The present study evaluated the association between periodontal disease severity and the clinical and histopathological characteristics of OPMDs. The findings are of clinical interest because periodontal disease and OPMDs may coexist within the same oral environment, where chronic microbial dysbiosis and persistent inflammation can influence tissue homeostasis. Hajishengallis (2015) [10] described periodontitis as a dysbiotic inflammatory disease in which microbial immune subversion and sustained host inflammatory responses contribute to progressive periodontal tissue destruction. This inflammatory environment may also have implications for adjacent oral tissues.

The association between periodontal disease and OPMDs has been investigated epidemiologically. Bhat et al. (2019) [11] reported an independent association between periodontitis and OPMDs after accounting for recognized risk factors. Their findings are particularly relevant to the present study because they suggest that periodontal disease may represent an additional factor associated with OPMDs rather than simply occurring as a consequence of shared behavioral exposures. The observation that periodontal inflammation may coexist with potentially malignant mucosal changes supports the need for simultaneous assessment of periodontal and mucosal health.

Chronic inflammation provides a possible biological explanation for the relationship observed between periodontal disease and OPMDs. Hajishengallis (2015) [10] emphasized that periodontal inflammation involves persistent activation of innate and adaptive immune pathways, accompanied by the production of multiple inflammatory mediators. Prolonged exposure to such mediators may promote oxidative stress, extracellular matrix degradation, cellular injury, and changes in tissue homeostasis. In

patients already exposed to carcinogenic factors, these inflammatory effects could potentially contribute to an environment that favors the persistence or progression of abnormal epithelial changes.

The potential role of periodontal microorganisms in oral carcinogenesis has also received considerable attention. Li et al. (2022) [15] highlighted the possible involvement of periodontal pathogens in the biological link between periodontal disease and oral cancer. Bacterial components and virulence factors may interact with epithelial and immune cells, stimulate inflammatory signaling, alter cellular proliferation, and contribute to oxidative stress. These mechanisms provide biological plausibility for an association between severe periodontal inflammation and unfavorable mucosal changes. However, the presence of periodontal pathogens alone cannot establish that they directly cause malignant transformation.

The relationship between periodontitis and oral cancer has also been examined through integrated clinical and experimental evidence. Pigossi et al. (2025) [13] reported that interactions among periodontal dysbiosis, inflammatory pathways, immune responses, and epithelial alterations may contribute to the observed relationship between periodontitis and oral cancer. Their systematic review further emphasizes that the association is complex and involves multiple biological mechanisms rather than a single causative pathway. These observations support the interpretation that periodontal disease may function as a potential modifying factor within a multifactorial process.

Histopathological assessment is particularly important when evaluating the biological significance of OPMDs. Kujan et al. (2006) [14] demonstrated the usefulness of a binary grading system for oral epithelial dysplasia in predicting malignant transformation. Their findings reinforce the importance of identifying and grading epithelial dysplastic changes because histopathological abnormalities provide information that cannot be obtained reliably through clinical examination alone. In the context of the present study, evaluating periodontal disease severity together with epithelial dysplasia may therefore provide a more comprehensive assessment of factors associated with OPMDs.

The inflammatory and microbial mechanisms underlying periodontal disease may also be relevant to the histopathological findings observed in OPMDs. Li et al. (2022) [15] proposed that periodontal pathogens can influence host-cell signaling, inflammatory responses, epithelial integrity, and immune regulation. Persistent exposure to these microbial and inflammatory stimuli may theoretically contribute to cellular and architectural abnormalities within susceptible oral mucosa. Nevertheless, this proposed mechanism should be interpreted cautiously because epithelial dysplasia is influenced by multiple genetic, environmental, and behavioral factors.

An important consideration in interpreting the present findings is the possibility of confounding by shared risk factors. Tobacco use, alcohol consumption, areca-nut exposure, age, oral hygiene, and socioeconomic factors may influence both periodontal disease and OPMDs. Bhat et al. (2019) [11] demonstrated that the association between periodontitis and OPMDs persisted after adjustment for relevant covariates, supporting the possibility of an independent relationship. Nevertheless, residual confounding cannot be completely excluded, particularly in observational studies.

The clinical implications of these findings are relevant to routine dental practice. Patients diagnosed with OPMDs should receive a comprehensive periodontal examination in addition to detailed assessment of the mucosal lesion. Similarly, patients presenting with advanced periodontal disease and established oral cancer risk factors may benefit from careful inspection of the oral mucosa. Hajishengallis (2015) [10] emphasized the systemic and local consequences of persistent periodontal inflammation, reinforcing the importance of controlling periodontal inflammatory burden as part of comprehensive oral healthcare.

The potential relationship between periodontal inflammation and oral malignancy should not, however, be interpreted as evidence that periodontitis directly causes OPMDs or malignant transformation. Pigossi et al. (2025) [13] emphasized the multifactorial nature of the periodontitis–oral cancer relationship, involving microbial, inflammatory, immunological, and host-related factors. Therefore, periodontal disease should be considered a possible associated or modifying factor rather than an established independent cause of malignant transformation.

From a therapeutic perspective, effective periodontal management may reduce the local inflammatory burden and improve overall oral health, but periodontal treatment should not replace established management of OPMDs. Suspicious mucosal lesions require appropriate clinical evaluation, biopsy when indicated, histopathological examination, and continued surveillance according to their clinical and microscopic characteristics. Kujan et al. (2006) [14] demonstrated the importance

of dysplasia grading in assessing malignant transformation risk, emphasizing the continued role of histopathology in clinical decision-making.

Overall, the findings of the present study add to the growing evidence supporting an association between periodontal disease and OPMDs. The interaction is likely to be multifactorial, involving chronic inflammation, periodontal microbial dysbiosis, oxidative stress, immune dysregulation, and shared behavioral risk factors. Li et al. (2022) [15] suggested that periodontal pathogens may represent an important biological link between periodontal disease and oral cancer, while Pigossi et al. (2025) [13] highlighted the need to interpret this relationship within a broader biological framework.

Future prospective studies involving larger populations should incorporate standardized periodontal measurements, detailed assessment of tobacco and areca-nut exposure, longitudinal monitoring of OPMDs, standardized histopathological grading, and microbial or molecular biomarkers. Such studies may help determine whether periodontal disease severity independently influences epithelial dysplasia, progression of OPMDs, or subsequent malignant transformation. Until stronger longitudinal evidence becomes available, the relationship should be regarded as clinically important but not necessarily causal.

## LIMITATIONS

The findings should be interpreted in light of several limitations. First, the study included a relatively modest sample of 100 participants, which may limit the statistical power and generalizability of the findings to broader populations. Second, the observational nature of the analysis prevents determination of a temporal or causal relationship between periodontal disease and epithelial dysplasia. Although the regression model adjusted for selected demographic, behavioral, clinical, and periodontal variables, residual confounding by other factors cannot be excluded. In particular, tobacco exposure may involve differences in duration, frequency, and cumulative consumption that were not quantified in the available dataset. Furthermore, the study evaluated histopathological dysplasia as an outcome rather than subsequent malignant transformation; therefore, the findings should not be interpreted as demonstrating that periodontitis directly causes oral cancer. Larger multicenter prospective studies incorporating detailed tobacco exposure assessment, longitudinal follow-up, and molecular or immunohistochemical markers are warranted to validate these observations.

## CONCLUSION

Increasing periodontal disease severity was significantly associated with greater histopathological severity of epithelial dysplasia in patients with OPMDs. CAL and PPD demonstrated the strongest relationships with dysplasia severity, indicating that progressive periodontal tissue destruction may be associated with more pronounced epithelial alterations. Severe periodontitis remained an independent predictor of epithelial dysplasia, while tobacco chewing and non-homogeneous lesion morphology were also significantly associated with dysplastic changes. These findings emphasize the importance of comprehensive periodontal evaluation in patients with OPMDs and suggest that periodontal health may represent an important component of their overall clinical assessment. Although the observed associations are clinically relevant, they do not establish causality. Further prospective, multicenter studies with longer follow-up and molecular investigations are required to clarify the biological relationship between periodontal inflammation and epithelial dysplasia and to determine its potential implications for malignant transformation risk.

**CONFLICTS OF INTEREST:** Nil

**FIANCIAL SUPPORT:** None

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