Quest Journals
Journal of Medical and Dental Science Research
Volume 12~ Issue 4 (April 2025) pp: 67-77
ISSN(Online): 2394-076X ISSN (Print):2394-0751
www.questjournals.org

Research Paper

Histopathological Spectrum of Oral Potentially Malignant Disorders and Risk of Malignant Transformation

[1.] Sailendra Nath Biswas, *Professor, Department of Oral & Maxillofacial Pathology and Oral Microbiology, Burdwan Dental College & Hospital, Burdwan, West Bengal, India*
[2.] Sayan Chattopadhyay , *Associate Professor, Department of Oral Medicine & Radiology, Dr. R. Ahmed Dental College & Hospital, Kolkata, West Bengal, India*
[3.] Rachita Arora, *Associate Professor, Department of Pediatric & Preventive Dentistry, Dr. R. Ahmed Dental College & Hospital, Kolkata, West Bengal, India*
[4.] Sumit Dutta, *Professor, Department of Oral Medicine & Radiology, Kalka Dental College, Partapur Bypass Road, Meerut, Uttar Pradesh, India*
Corresponding author: *Sailendra Nath Biswas*

Abstract
Background
Oral potentially malignant disorders (OPMDs) comprise a heterogeneous group of oral mucosal conditions that may exhibit varying degrees of epithelial dysplasia and may progress to oral squamous cell carcinoma (OSCC). Histopathological examination remains essential for assessing epithelial abnormalities and identifying lesions at increased risk of malignant progression. The present study evaluated the clinical and histopathological characteristics of OPMDs and examined their association with selected deleterious habits and malignant transformation.

Materials and Methods
A total of 200 patients with clinically diagnosed OPMDs were included in the study. Demographic characteristics, including age and sex, and reported tobacco and alcohol use were recorded. Clinical diagnoses included leukoplakia, oral submucous fibrosis (OSMF), oral lichen planus/lichenoid lesions, erythroplakia, and other OPMDs. Histopathological assessment of biopsy specimens classified lesions as hyperkeratosis/acanthosis without dysplasia, mild epithelial dysplasia, moderate epithelial dysplasia, severe dysplasia/carcinoma in situ (CIS), or invasive SCC. Associations between risk factors and epithelial dysplasia were assessed statistically, and malignant transformation was evaluated according to baseline histopathological severity.

Results
The mean age of the study population was 46.8 ± 11.7 years, with a predominance of males (64.0%). Tobacco use was reported by 66.0% of participants, while 39.0% reported alcohol consumption. Leukoplakia was the most frequently diagnosed OPMD (41.0%), followed by OSMF (24.0%). Histopathologically, hyperkeratosis/acanthosis without dysplasia was identified in 31.0%, mild dysplasia in 27.5%, moderate dysplasia in 18.5%, severe dysplasia/CIS in 12.5%, and invasive SCC in 10.5% of specimens. Overall, 69.0% demonstrated epithelial dysplasia or malignant changes. Tobacco use was significantly associated with epithelial dysplasia ($\chi^2 = 18.72$, $p < 0.001$), as was alcohol consumption ($\chi^2 = 5.02$, $p = 0.025$). Malignant transformation increased progressively with histopathological severity, from 1.6% in lesions without dysplasia to 32.0% in severe dysplasia/CIS.

Conclusion
The findings demonstrate a substantial burden of epithelial dysplasia among clinically diagnosed OPMDs and indicate significant associations between dysplasia and tobacco and alcohol exposure. Increasing histopathological severity was accompanied by a higher proportion of malignant transformation, emphasizing the importance of biopsy-based assessment and appropriate histopathological grading in the evaluation and risk stratification of OPMDs.

Keywords: *Alcohol, Epithelial dysplasia, Leukoplakia, Malignant transformation, Oral potentially malignant disorders, Oral squamous cell carcinoma, Oral submucous fibrosis, Tobacco*

R*eceived 09 Apr., 2025;* ***R****evised 26 Apr., 2025;* ***A****ccepted 28 Apr., 2025*
P*ublished with open access at* ***www.questjournals.org***

I. Introduction

Oral potentially malignant disorders (OPMDs) comprise a diverse group of oral mucosal conditions that are associated with an increased risk of developing oral squamous cell carcinoma (OSCC). Their clinical appearance and underlying tissue changes may vary considerably, ranging from minor epithelial abnormalities to pronounced dysplasia and, ultimately, malignant transformation. Early recognition and appropriate evaluation of these disorders are essential for improving oral cancer prevention and facilitating timely clinical management [1].

Oral leukoplakia is among the most commonly recognized OPMDs and is clinically characterized by a predominantly white mucosal lesion that cannot be attributed to another specific condition. The clinical course of leukoplakia is variable, with some lesions remaining stable while others progressively acquire features associated with malignant transformation. Clinical morphology, anatomical site, lesion size, tobacco exposure, and histopathological characteristics may contribute to differences in the biological behavior of individual lesions [2].

The histopathological evaluation of OPMDs provides important information regarding epithelial architecture, maturation, and cellular abnormalities. Biopsy specimens may demonstrate hyperkeratosis, epithelial hyperplasia, or other alterations without dysplasia, as well as different grades of epithelial dysplasia and invasive carcinoma. Although the severity of epithelial dysplasia is an important indicator of malignant potential, microscopic grading alone may not accurately predict the future behavior of every lesion. Consequently, histopathological findings should be interpreted in conjunction with relevant clinical characteristics when estimating malignant transformation risk [3].

Malignant transformation does not occur uniformly across OPMDs, and substantial variation may also exist among lesions within the same diagnostic category. This unpredictability makes it difficult to determine which patients require intensive surveillance or early intervention. Conventional assessment is primarily based on clinical examination and histopathological findings; however, evaluating individual variables separately may not adequately reflect the complex interactions involved in malignant progression. A multifactorial approach incorporating clinical, demographic, and pathological characteristics may therefore improve identification of lesions with increased risk [4].

The increasing application of artificial intelligence (AI) and machine-learning techniques has created new possibilities for improving diagnostic and predictive assessment in oral medicine. These technologies can analyze multiple variables simultaneously and identify complex relationships within clinical datasets. AI-based approaches have demonstrated promising applications in oral cancer detection and classification, potentially providing additional support to clinicians during diagnostic decision-making [5].

Deep-learning methods have further expanded the potential applications of AI in oral oncology by enabling automated analysis of clinical and imaging data. However, reported performance can vary according to the characteristics of the dataset, model architecture, image quality, validation strategy, and clinical setting. Consequently, appropriate methodological evaluation and independent validation remain important before AI systems can be incorporated into routine clinical practice [6].

Molecular and biological markers may also provide additional information regarding the malignant potential of OPMDs. Alterations in molecular pathways associated with epithelial carcinogenesis have been investigated as potential predictors of progression and may complement conventional clinical and histopathological assessment. Integrating such information with other patient and lesion characteristics could potentially improve individualized risk estimation [7].

Recent systematic reviews have demonstrated considerable interest in the use of AI for oral cancer diagnosis and risk assessment, while also emphasizing the need for standardized datasets, robust validation, and clinically representative study populations. These considerations are particularly relevant when developing predictive models intended to distinguish lesions with different levels of malignant potential [8].

Despite these advances, the use of AI specifically for predicting malignant transformation in OPMDs remains an evolving field. Further research is needed to determine whether AI-assisted models can effectively integrate clinical and histopathological information and provide clinically meaningful risk stratification. Well-

designed studies with standardized assessment criteria and appropriate validation are necessary to establish their reliability and practical utility [9].

Therefore, the present study was undertaken to evaluate the clinical and histopathological characteristics of oral potentially malignant disorders, identify factors associated with malignant transformation, and assess the potential utility of an AI-assisted predictive model for risk stratification.

II. Materials & Methods

Study Design and Study Population

A clinical and histopathological observational study was conducted at a single tertiary care centre among 200 patients with clinically diagnosed OPMDs from December 2024 to March 2025.

Participants were selected on the basis of predefined clinical and histopathological assessment criteria. The study population included adult patients presenting with clinically identifiable potentially malignant oral mucosal lesions.

Inclusion Criteria

- Adults aged 18 years or older
- Patients presenting with clinically identifiable OPMDs.
- Patients with lesions clinically diagnosed as leukoplakia, oral submucous fibrosis (OSMF), oral lichen planus/lichenoid lesions, erythroplakia, or other clinically suspected OPMDs.
- Patients who underwent biopsy of the clinically suspected OPMD for histopathological evaluation
- Patients whose biopsy specimens were adequate in quantity and quality for reliable histopathological examination
- Patients who provided relevant demographic and clinical information, including history of tobacco and/or alcohol use
- Patients who provided written informed consent to participate in the study and undergo the required clinical and histopathological evaluation.

Exclusion Criteria

Patients were excluded if they met any of the following criteria:

- Patients younger than 18 years
- Patients with oral lesions that were clinically diagnosed as conditions unrelated to OPMDs
- Patients with inadequate or insufficient biopsy tissue for definitive histopathological evaluation
- Specimens that were poorly preserved, extensively autolyzed, or otherwise unsuitable for microscopic examination
- Patients with incomplete clinical or demographic information
- Patients who did not provide consent for participation or biopsy
- Patients who had previously received treatment for the lesion that could significantly alter its clinical or histopathological characteristics
- Patients with a known history of previously treated oral squamous cell carcinoma at the biopsy site, where assessment of the original OPMD and its progression could not be reliably established

Clinical Assessment

A detailed clinical evaluation was performed for each participant. Demographic information, including age and sex, was documented. Patients were also assessed for the presence of potentially relevant deleterious habits. Particular attention was given to tobacco use and alcohol consumption, and the information was recorded based on the patient's reported history.

The clinically diagnosed OPMDs were categorized into leukoplakia, OSMF, oral lichen planus/lichenoid lesions, erythroplakia, and other OPMDs. The clinical diagnosis was established on the basis of the observed morphological characteristics and relevant clinical findings.

Histopathological Examination

Representative biopsy specimens obtained from clinically diagnosed OPMDs were submitted for histopathological evaluation. Tissue specimens were processed using routine histopathological techniques and stained with hematoxylin and eosin (H&E). The sections were examined microscopically for epithelial and stromal alterations.

Based on the microscopic findings, specimens were categorized into the following groups:

- Hyperkeratosis/acanthosis without epithelial dysplasia
- Mild epithelial dysplasia
- Moderate epithelial dysplasia
- Severe epithelial dysplasia/carcinoma in situ (CIS)
- Invasive SCC

The assessment focused on epithelial architectural and cytological abnormalities and the presence or absence of invasive malignant growth.

Assessment of Epithelial Dysplasia

For analytical purposes, specimens demonstrating mild, moderate, or severe dysplasia/CIS were considered to have epithelial dysplasia. Cases classified as hyperkeratosis/acanthosis without dysplasia were considered non-dysplastic. The distribution of histopathological grades was evaluated overall and according to the corresponding clinical OPMD category.

Assessment of Malignant Transformation

Malignant transformation was assessed in relation to the baseline histopathological category. The proportion of cases demonstrating malignant transformation was calculated separately for non-dysplastic lesions and for lesions exhibiting mild, moderate, and severe dysplasia/CIS. This allowed evaluation of the pattern of malignant progression across increasing grades of epithelial abnormality.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± Standard Deviation (SD), while categorical variables were presented as frequency and percentage. The Chi-square test was used to assess associations between clinical diagnosis, risk factors, and histopathological dysplasia, with Fisher's exact test used where applicable. Malignant transformation rates were calculated according to the baseline histopathological grade, and the trend in transformation with increasing dysplasia severity was assessed. A p-value <0.05 was considered statistically significant, with all tests being two-tailed.

III. Results

Table 1 & Figure 1 summarize the demographic characteristics and reported deleterious habits among the 200 study participants. The mean age of the participants was 46.8 ± 11.7 years. The 41–50-year age group constituted the largest proportion of the study population, comprising 58 participants (29.0%), followed by the 51–60-year group with 49 (24.5%) participants. Participants aged >60 years accounted for 36 (18.0%), while 35 (17.5%) were aged 31–40 years and 22 (11.0%) belonged to the 18–30-year age group.

A male predominance was evident, with 128 (64.0%) males and 72 (36.0%) females. With respect to deleterious habits, tobacco use was reported by 132 (66.0%) participants, making it the most prevalent habit, whereas 78 (39.0%) participants reported alcohol consumption. Overall, the study cohort predominantly comprised middle-aged males, with tobacco use being the most commonly reported deleterious habit.

Table 1: Distribution of patients according to demographic characteristics

	Parameter	**n (%) / Mean ± SD**
	Age (years)	46.8 ± 11.7
Age Group	18–30 years	22 (11.0%)
	31–40 years	35 (17.5%)
	41–50 years	58 (29.0%)
	51–60 years	49 (24.5%)
	>60 years	36 (18.0%)
Gender	Male	128 (64.0%)
	Female	72 (36.0%)
Habit	Tobacco use	132 (66.0%)
	Alcohol use	78 (39.0%)

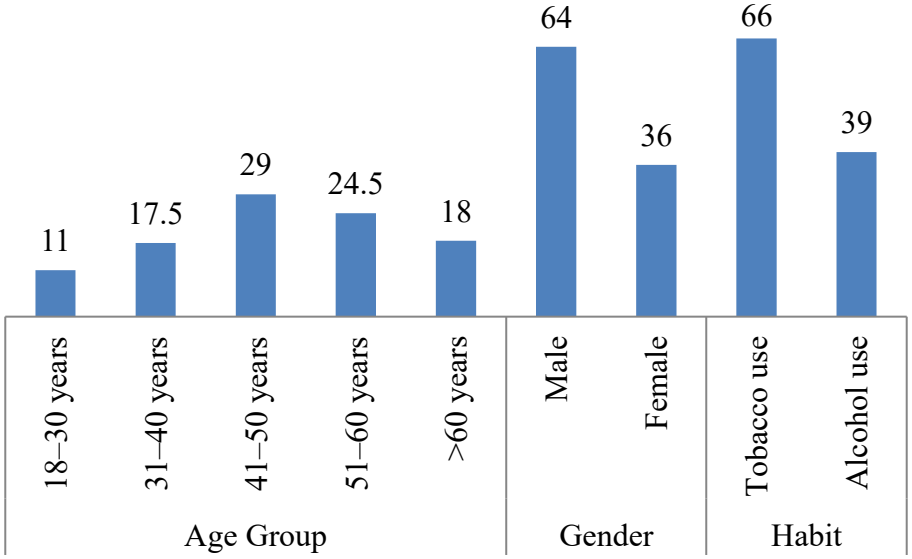

Figure 1: Age-wise, sex-wise, and deleterious habit-wise distribution of the study population

Table 2 & Figure 2 illustrate the distribution of different OPMDs among the 200 participants. Leukoplakia was the most commonly identified lesion, occurring in 82 (41.0%) patients. OSMF was the second most frequent condition, accounting for 48 (24.0%) cases. Oral lichen planus/ lichenoid lesions were documented in 31 (15.5%) participants, whereas other OPMDs comprised 28 (14.0%) cases. Erythroplakia was comparatively uncommon, with 11 (5.5%) cases. Overall, leukoplakia represented the largest proportion of clinically diagnosed OPMDs, comprising approximately two-fifths of the study population, while erythroplakia was the least frequently observed lesion.

Table 2: Clinical distribution of OPMDs

Clinical diagnosis	**Number (n)**	**Percentage (%)**
Leukoplakia	82	41.0
OSMF	48	24.0
Oral lichen planus /lichenoid lesion	31	15.5
Erythroplakia	11	5.5
Other OPMDs	28	14.0
Total	200	100.0

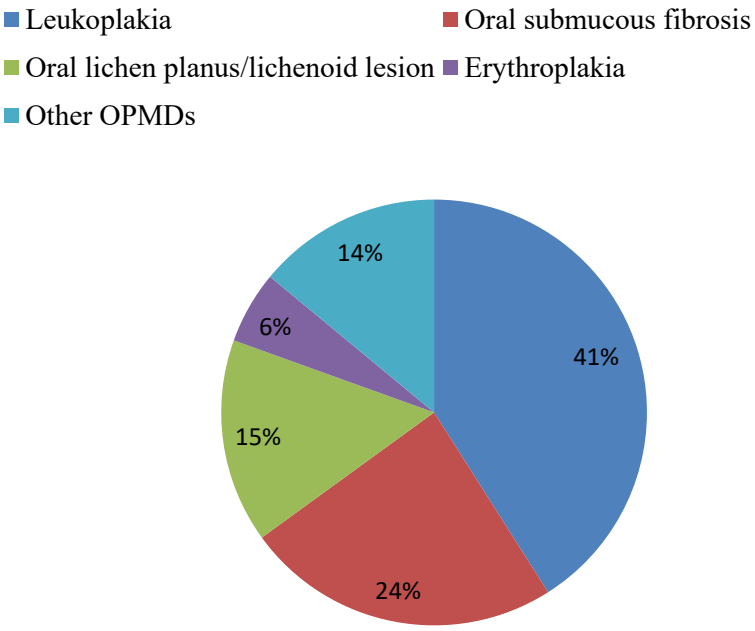

Figure 2: Frequency and percentage distribution of different OPMDs among the study participants

Table 3 & Figure 3 present the histopathological findings observed among the 200 study specimens. Microscopic examination revealed a broad range of epithelial alterations, extending from non-dysplastic changes to invasive SCC. Hyperkeratosis/acanthosis without dysplasia was the most common finding, recorded in 62 (31.0%) cases. Mild epithelial dysplasia was identified in 55 (27.5%) specimens, followed by moderate epithelial dysplasia in 37 (18.5%) cases. Severe epithelial dysplasia/CIS was observed in 25 (12.5%) specimens, whereas invasive SCC was detected in 21 (10.5%) cases.

Collectively, 138 (69.0%) specimens demonstrated epithelial dysplasia or malignant changes, while 62 (31.0%) showed no evidence of dysplasia. The histopathological findings therefore demonstrated a broad continuum of epithelial abnormalities, with lesions distributed across increasing grades of dysplasia and extending to invasive malignancy.

Table 3: Histopathological findings

Histopathological diagnosis	Number (n)	Percentage (%)
Hyperkeratosis/acanthosis without dysplasia	62	31.0
Mild epithelial dysplasia	55	27.5
Moderate epithelial dysplasia	37	18.5
Severe dysplasia/carcinoma in situ	25	12.5
Invasive SCC	21	10.5
Total	200	100.0

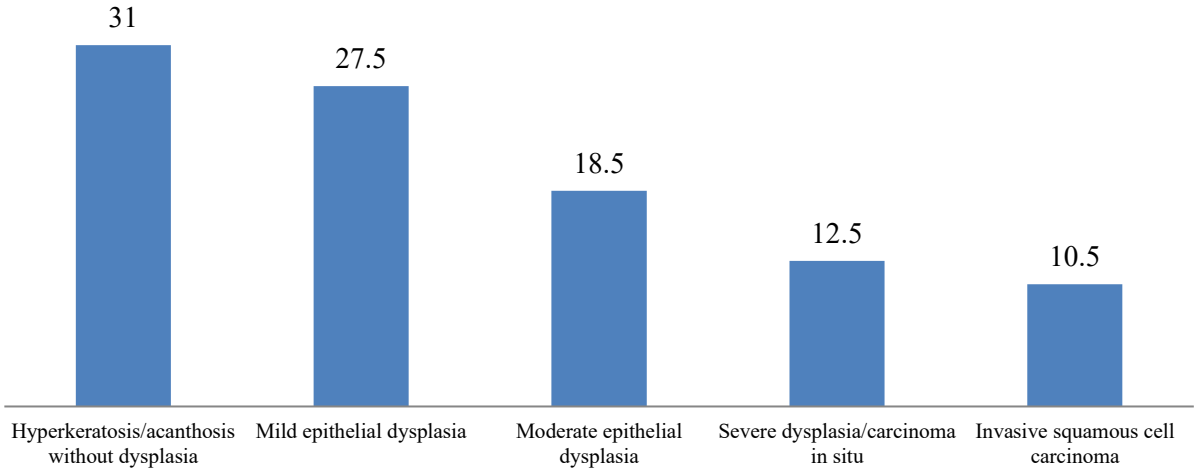

Figure 3: Histopathological spectrum of epithelial dysplasia and malignant transformation in the study population

Table 4 & Figure 4 demonstrate the relationship between the clinical types of OPMDs and their corresponding histopathological grades. Considerable variation was observed among the different clinical categories.

Among leukoplakia**,** 30 (36.6%) specimens showed no dysplasia. Mild, moderate, and severe dysplasia/CIS were identified in 23 (28.0%)**,** 15 (18.3%)**,** and 9 (11.0%) cases, respectively, while 5 (6.1%) specimens showed invasive SCC.

In the OSMF group, 20 (41.7%) cases were free of dysplasia. Mild dysplasia was observed in 13 (27.1%), moderate dysplasia in 8 (16.7%), and severe dysplasia/CIS in 5 (10.4%) cases. Invasive SCC was detected in 2 (4.2%) cases.

Among oral lichen planus/lichenoid lesions, 9 (29.0%) cases showed no dysplasia, while mild, moderate, and severe dysplasia/CIS were present in 9 (29.0%)**,** 6 (19.4%)**,** and 4 (12.9%) cases, respectively. Invasive SCC was identified in 3 (9.7%) cases.

Erythroplakia demonstrated a comparatively higher proportion of advanced histopathological abnormalities. Only 1 (9.1%) case showed no dysplasia, whereas mild and moderate dysplasia was each observed in 2 (18.2%) cases. Severe dysplasia/CIS and invasive SCC were each identified in 3 (27.3%) cases.

The other OPMDs category also demonstrated a substantial burden of advanced histopathological changes. Only 2 (7.1%) cases were without dysplasia, while mild dysplasia was observed in 8 (28.6%), moderate dysplasia in 6 (21.4%), severe dysplasia/CIS in **4 (14.3%)**, and invasive SCC in 8 (28.6%) cases.

Overall, the distribution indicates that erythroplakia and other OPMDs showed a greater relative frequency of severe dysplasia/CIS and invasive SCC, whereas leukoplakia and OSMF demonstrated comparatively higher proportions of non-dysplastic and lower-grade dysplastic changes. Across all clinical categories, 62 (31.0%) cases showed no dysplasia, while 138 (69.0%) demonstrated epithelial dysplasia or invasive SCC**.**

Table 4: Histopathological spectrum according to clinical diagnosis

Clinical diagnosis	No dysplasia	Mild	Moderate	Severe/CIS	SCC
Leukoplakia (n=82)	30 (36.6%)	23 (28.0%)	15 (18.3%)	9 (11.0%)	5 (6.1%)
OSMF (n=48)	20 (41.7%)	13 (27.1%)	8 (16.7%)	5 (10.4%)	2 (4.2%)
OLP/lichenoid (n=31)	9 (29.0%)	9 (29.0%)	6 (19.4%)	4 (12.9%)	3 (9.7%)
Erythroplakia (n=11)	1 (9.1%)	2 (18.2%)	2 (18.2%)	3 (27.3%)	3 (27.3%)
Other OPMDs (n=28)	2 (7.1%)	8 (28.6%)	6 (21.4%)	4 (14.3%)	8 (28.6%)

P value -0.001 (Sig)

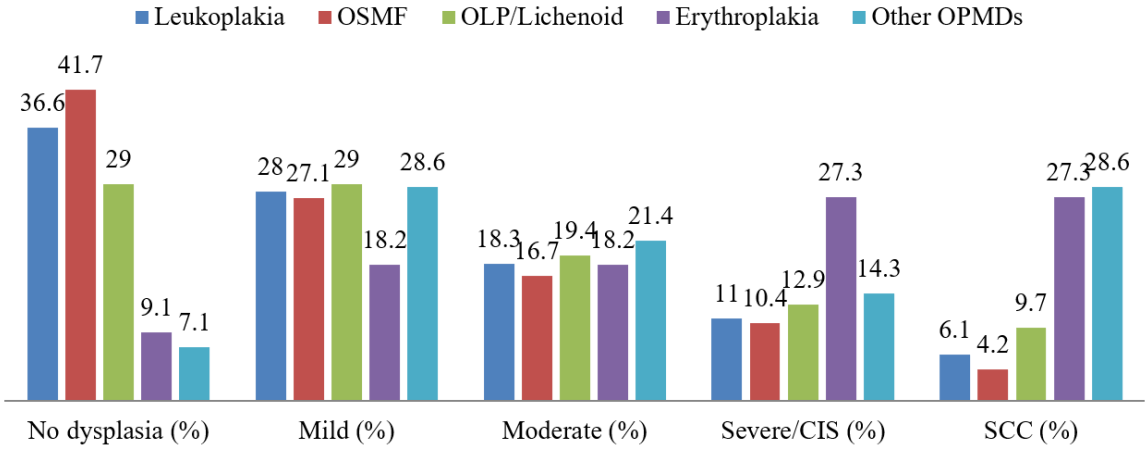

Figure 4: Comparative distribution of histopathological grades across different clinical types of OPMDs

Table 5 & Figure 5 present the relationship between reported deleterious habits and the presence of epithelial dysplasia among the study participants. A significant association was identified between tobacco use and epithelial dysplasia. Of the participants with dysplasia, 105 (76.1%) reported tobacco use, compared with 27 (43.5%) among those without dysplasia. Conversely, non-users constituted 33 (23.9%) of the dysplasia group and 35 (56.5%) of the non-dysplasia group. The difference was statistically significant ($\chi^2 = 18.72$, $p < 0.001$), demonstrating a substantially higher proportion of tobacco exposure among participants with epithelial dysplasia.

A significant relationship was also observed between alcohol consumption and epithelial dysplasia. Alcohol use was reported by 61 (44.2%) participants with dysplasia and 17 (27.4%) participants without dysplasia. The corresponding proportions of non-drinkers were 77 (55.8%) and 45 (72.6%), respectively. This association reached statistical significance ($\chi^2 = 5.02$, $p = 0.025$).

Overall, both tobacco and alcohol consumption were significantly associated with epithelial dysplasia. However, the stronger statistical association was observed for tobacco use, suggesting that tobacco exposure had a more pronounced relationship with dysplastic epithelial changes in the study population.

Table 5: Association of selected risk factors with epithelial dysplasia

Risk factor	**Dysplasia present n (%)**	**Dysplasia absent n (%)**	**χ^2/Fisher's test**	**p-value**
Tobacco use	105 (76.1%)	27 (43.5%)	18.72	<0.001
No tobacco use	33 (23.9%)	35 (56.5%)		
Alcohol use	61 (44.2%)	17 (27.4%)	5.02	0.025
No alcohol use	77 (55.8%)	45 (72.6%)		

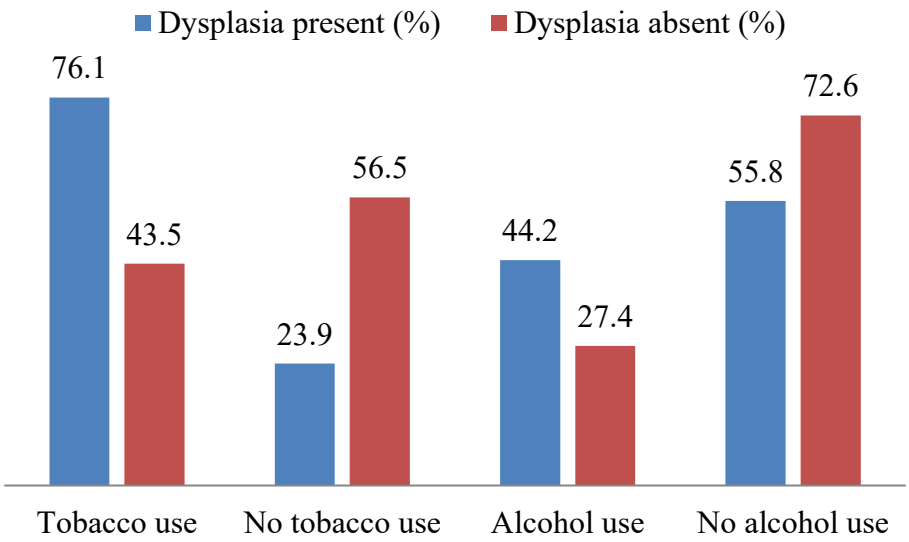

Figure 5: Comparative distribution of tobacco and alcohol consumption according to the presence or absence of epithelial dysplasia

Table 6 & Figure 6 illustrate the distribution of malignant transformation according to the initial histopathological severity of epithelial changes. A progressive increase in malignant transformation was observed with increasing grades of epithelial dysplasia.

Among the 62 specimens without epithelial dysplasia, malignant transformation occurred in only 1 (1.6%) case. In the group with mild dysplasia, transformation was identified in 3 of 55 (5.5%) cases. The frequency increased to 6 of 37 (16.2%) among specimens demonstrating moderate dysplasia. The highest proportion was recorded in the severe dysplasia/CIS group, where 8 of 25 (32.0%) cases showed malignant transformation.

Overall, the findings demonstrate a graded increase in malignant transformation corresponding to the severity of epithelial abnormalities, with the observed rate rising from 1.6% in non-dysplastic lesions to 32.0% in severe dysplasia/CIS. Severe dysplasia/CIS therefore represented the category with the greatest proportion of malignant transformation, whereas lesions without dysplasia demonstrated the lowest occurrence. These findings highlight the importance of histopathological grading as a useful indicator for identifying OPMDs with a greater likelihood of malignant progression.

Table 6: Malignant transformation according to baseline histopathological grade

Histopathological category	**Cases (n)**	**Malignant transformation n (%)**
No dysplasia	62	1 (1.6%)
Mild dysplasia	55	3 (5.5%)
Moderate dysplasia	37	6 (16.2%)
Severe dysplasia/CIS	25	8 (32.0%)

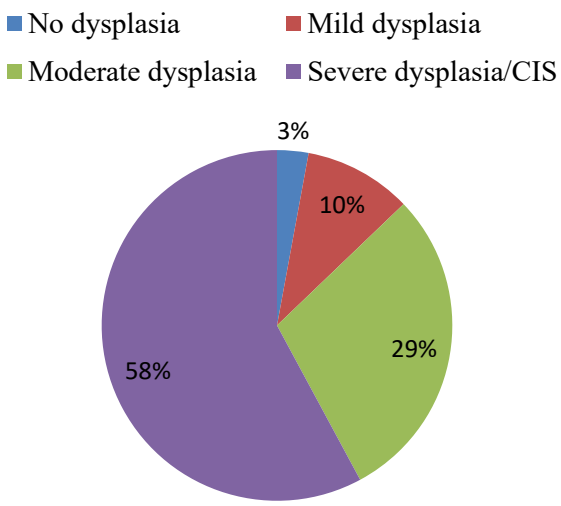

Figure 6: Progressive increase in malignant transformation across increasing grades of epithelial dysplasia

IV. Discussion

The present findings support the growing recognition that malignant transformation in OPMDs is a multifactorial process influenced by a combination of clinical, histopathological, and biological characteristics. Mello et al. (2020) [10] emphasized that numerous prognostic biomarkers have been investigated in OPMDs, reflecting the complex biological mechanisms underlying malignant progression. Their scoping review highlighted the potential value of biomarkers in identifying lesions at increased risk of transformation and suggested that molecular information may complement conventional clinical and histopathological assessment. These observations support the rationale for incorporating multiple variables rather than relying on a single clinical or microscopic characteristic when assessing malignant transformation risk.

Histopathological assessment remains a fundamental component of OPMD evaluation; however, its predictive capacity is influenced by the grading system used and by interobserver variability. Khoury et al. (2022) [11] demonstrated substantial variation among oral epithelial dysplasia grading systems and highlighted limitations in the reproducibility and prognostic consistency of existing approaches. This is particularly relevant because epithelial dysplasia represents an important indicator of malignant potential, but lesions with similar histopathological grades may demonstrate different clinical outcomes. Therefore, the incorporation of additional clinical and biological variables may provide a more comprehensive representation of an individual lesion's risk profile.

The prognostic importance of dysplasia grading was further demonstrated by de Freitas Silva et al. (2021) [12], who evaluated binary and World Health Organization (WHO) grading systems for predicting malignant transformation of oral leukoplakia and erythroplakia. Their findings support the association between increasing epithelial dysplasia and malignant transformation, while also demonstrating that grading systems differ in their ability to discriminate between lesions according to future risk. The present study therefore supports the concept that histopathological grading should not be interpreted in isolation. Combining histopathological findings with demographic and clinical characteristics may improve the identification of patients who require closer surveillance or earlier intervention.

Molecular alterations may provide additional prognostic information beyond conventional histopathological examination. Ramos-García et al. (2022) [13] reported that p53 overexpression was associated with an increased risk of malignant transformation in OPMDs. Their findings reinforce the concept that molecular abnormalities reflecting genetic instability and carcinogenic progression may help distinguish lesions with different biological behaviors. Although molecular biomarkers were not necessarily available for routine assessment in all clinical settings, their potential integration with clinical and pathological variables represents an important direction for individualized risk prediction.

The emergence of machine-learning approaches provides an opportunity to integrate these heterogeneous variables within a single predictive framework. Uppal et al. (2024) [14] systematically evaluated machine-learning methods for predicting malignant transformation in OPMDs and demonstrated the increasing application of computational approaches in this area. Machine-learning models may be particularly advantageous because they can simultaneously evaluate multiple interacting predictors and identify nonlinear

relationships that may be difficult to recognize using conventional statistical approaches. This supports the potential usefulness of AI-assisted risk stratification in the present study, particularly when clinical and histopathological parameters collectively contribute to the prediction of malignant transformation.

Nevertheless, the use of AI should complement rather than replace established clinical and pathological assessment. The reliability of machine-learning models depends on the quality, size, representativeness, and consistency of the training dataset, as well as on appropriate validation. Consequently, apparently high predictive performance in a single dataset does not necessarily indicate equivalent performance in independent clinical populations. The findings of Uppal et al. (2024) [14] therefore emphasize the importance of methodological rigor and external validation before machine-learning models can be translated into routine clinical decision-making.

The role of biomarkers in improving risk prediction was also reinforced by Turton et al. (2024) [15], whose updated systematic review and meta-analysis evaluated prognostic biomarkers associated with malignant progression of oral epithelial dysplasia. Their work demonstrates continued interest in identifying biological markers capable of improving risk estimation beyond conventional histopathological grading. The integration of such biomarkers with demographic, clinical, and microscopic characteristics may ultimately facilitate a more individualized assessment of malignant transformation risk.

Taken together, these studies support a multifactorial approach to OPMD risk assessment. Conventional histopathological grading remains clinically important, but its predictive limitations, together with the heterogeneous biological behavior of OPMDs, indicate a need for complementary approaches. Biomarkers such as p53 may provide additional biological information, while machine-learning techniques offer a means of integrating multiple predictors into a unified risk-stratification model. Therefore, the development of AI-assisted predictive systems represents a promising approach for improving individualized assessment of malignant transformation, provided that such models undergo rigorous validation and are interpreted alongside established clinical and histopathological findings.

V. Limitations

The present study has several limitations that should be considered when interpreting the findings. First, the study population consisted of 200 participants, which may limit the statistical power for subgroup comparisons, particularly for relatively uncommon lesions such as erythroplakia. Second, the study was conducted within a single centre, and therefore the findings may not be directly generalizable to populations with different demographic characteristics, patterns of tobacco and alcohol exposure, or healthcare access.

The assessment of tobacco and alcohol exposure was based on patient-reported information, which may be affected by recall or reporting bias. Detailed quantitative measures of cumulative tobacco exposure, duration of habit, frequency of consumption, and combined exposure patterns were not incorporated into the present analysis. Similarly, other potential confounding factors, including dietary variables, socioeconomic characteristics, genetic susceptibility, and additional environmental exposures, were not comprehensively evaluated.

The histopathological evaluation provided important information regarding epithelial dysplasia and malignant change; however, the study did not incorporate molecular, immunohistochemical, or genomic biomarkers that could provide additional information about malignant transformation risk. Furthermore, the assessment of malignant transformation should be interpreted cautiously because the available data do not establish causality between a particular histopathological grade and subsequent cancer development. Finally, the study was primarily based on clinical and histopathological observations. Long-term prospective follow-up would provide stronger evidence regarding the actual progression of OPMDs to OSCC and would allow evaluation of additional predictors of malignant transformation.

VI. Conclusion

The present study demonstrated a diverse clinical and histopathological spectrum among patients with OPMDs. Leukoplakia was the most frequently encountered clinical lesion, while histopathological examination revealed epithelial dysplasia or malignant changes in a substantial proportion of specimens. Tobacco and alcohol consumption were both significantly associated with the presence of epithelial dysplasia, with tobacco exposure demonstrating the stronger statistical association. A clear relationship was observed between increasing histopathological severity and malignant transformation, with the proportion of transformation rising progressively from non-dysplastic lesions to severe dysplasia/CIS. These findings reinforce the importance of histopathological examination in patients presenting with OPMDs and support the use of epithelial dysplasia grading for identifying lesions with greater malignant potential.

Early recognition, appropriate biopsy, accurate histopathological classification, and continued clinical surveillance remain important components of OPMD management. Future multicenter prospective studies incorporating molecular biomarkers, immunohistochemical markers, standardized risk-factor assessment, and long-term follow-up may provide further insight into the mechanisms and predictors of malignant transformation.

Conflicts of Interest: Nil
Financial Support: None

References

[1]. Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, Bagan JV, González-Moles MÁ, Kerr AR, Lodi G, Mello FW, Monteiro L, Ogden GR, Sloan P, Johnson NW. Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. Oral Dis. 2021 Nov;27(8):1862-1880. doi: 10.1111/odi.13704. Epub 2020 Nov 26. PMID: 33128420.

[2]. Aguirre-Urizar JM, Lafuente-Ibáñez de Mendoza I, Warnakulasuriya S. Malignant transformation of oral leukoplakia: Systematic review and meta-analysis of the last 5 years. Oral Dis. 2021 Nov;27(8):1881-1895. doi: 10.1111/odi.13810. Epub 2021 Apr 1. PMID: 33606345.

[3]. Pinto AC, Caramês J, Francisco H, Chen A, Azul AM, Marques D. Malignant transformation rate of oral leukoplakia-systematic review. Oral Surg Oral Med Oral Pathol Oral Radiol. 2020 Jun;129(6):600-611.e2. doi: 10.1016/j.oooo.2020.02.017. Epub 2020 Apr 2. PMID: 32249069.

[4]. Dost F, Lê Cao K, Ford PJ, Ades C, Farah CS. Malignant transformation of oral epithelial dysplasia: a real-world evaluation of histopathologic grading. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014 Mar;117(3):343-52. doi: 10.1016/j.oooo.2013.09.017. Epub 2013 Oct 17. PMID: 24388536.

[5]. González-Moles MÁ, Keim-Del Pino C, Ramos-García P. Hallmarks of Cancer Expression in Oral Lichen Planus: A Scoping Review of Systematic Reviews and Meta-Analyses. Int J Mol Sci. 2022 Oct 28;23(21):13099. doi: 10.3390/ijms232113099. PMID: 36361889; PMCID: PMC9658487.

[6]. Khanagar SB, Naik S, Al Kheraif AA, Vishwanathaiah S, Maganur PC, Alhazmi Y, Mushtaq S, Sarode SC, Sarode GS, Zanza A, Testarelli L, Patil S. Application and Performance of Artificial Intelligence Technology in Oral Cancer Diagnosis and Prediction of Prognosis: A Systematic Review. Diagnostics (Basel). 2021 May 31;11(6):1004. doi: 10.3390/diagnostics11061004. PMID: 34072804; PMCID: PMC8227647.

[7]. Warin K, Suebnukarn S. Deep learning in oral cancer- a systematic review. BMC Oral Health. 2024 Feb 10;24(1):212. doi: 10.1186/s12903-024-03993-5. PMID: 38341571; PMCID: PMC10859022.

[8]. Veeraraghavan VP, Minervini G, Russo D, Cicciù M, Ronsivalle V. Assessing Artificial Intelligence in Oral Cancer Diagnosis: A Systematic Review. J Craniofac Surg. 2024 Oct 29. doi: 10.1097/SCS.0000000000010663. Epub ahead of print. PMID: 39787481.

[9]. Sahoo RK, Sahoo KC, Dash GC, Kumar G, Baliarsingh SK, Panda B, Pati S. Diagnostic performance of artificial intelligence in detecting oral potentially malignant disorders and oral cancer using medical diagnostic imaging: a systematic review and meta-analysis. Front Oral Health. 2024 Nov 6;5:1494867. doi: 10.3389/froh.2024.1494867. PMID: 39568787; PMCID: PMC11576460.

[10]. Mello FW, Melo G, Guerra ENS, Warnakulasuriya S, Garnis C, Rivero ERC. Oral potentially malignant disorders: A scoping review of prognostic biomarkers. Crit Rev Oncol Hematol. 2020 Sep;153:102986. doi: 10.1016/j.critrevonc.2020.102986. Epub 2020 May 16. PMID: 32682268.

[11]. Khoury ZH, Sultan M, Sultan AS. Oral Epithelial Dysplasia Grading Systems: A Systematic Review & Meta-Analysis. Int J Surg Pathol. 2022 Aug;30(5):499-511. doi: 10.1177/10668969211070171. Epub 2022 Jan 7. PMID: 34994584.

[12]. de Freitas Silva BS, Batista DCR, de Souza Roriz CF, Silva LR, Normando AGC, Dos Santos Silva AR, Silva MAG, Yamamoto-Silva FP. Binary and WHO dysplasia grading systems for the prediction of malignant transformation of oral leukoplakia and erythroplakia: a systematic review and meta-analysis. Clin Oral Investig. 2021 Jul;25(7):4329-4340. doi: 10.1007/s00784-021-04008-1. Epub 2021 May 29. PMID: 34050426.

[13]. Ramos-García P, González-Moles MÁ, Warnakulasuriya S. Significance of p53 overexpression in the prediction of the malignant transformation risk of oral potentially malignant disorders: A systematic review and meta-analysis. Oral Oncol. 2022 Mar; 126:105734. doi: 10.1016/j.oraloncology.2022.105734. Epub 2022 Jan 25. PMID: 35091134.

[14]. Uppal S, Kumar Shrivastava P, Khan A, Sharma A, Kumar Shrivastav A. Machine learning methods in predicting the risk of malignant transformation of oral potentially malignant disorders: A systematic review. Int J Med Inform. 2024 Jun;186:105421. doi: 10.1016/j.ijmedinf.2024.105421. Epub 2024 Mar 22. PMID: 38552265.

[15]. Turton N, Payne K, Higginson J, Praveen P, Mehanna H, Nankivell P. Prognostic biomarkers for malignant progression of oral epithelial dysplasia: an updated systematic review and meta-analysis. Br J Oral Maxillofac Surg. 2024 Jun;62(5):415-425. doi: 10.1016/j.bjoms.2024.03.001. Epub 2024 Mar 7. PMID: 38677951.