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# Histopathological Spectrum of Oral Leukoplakia and Its Malignant Transformation Risk

[1]Dr Ayushi P Mangulkar, [2]Dr. Shubhangi Pareek, [3]Dr. Tejashwini Kotian, [4]Dr Mangal Kumar Gupta, [5]Dr. Mayank Charan, [6]Dr Madhvika Patidar

[1].BDS MDS Oral Medicine and Radiology,Assistant professor GMCH Chh Sambhajinagar
[2].MDS Oral Pathology and Microbiology.Assistant PROFESSOR, Department of oral pathology & microbiology SCB Dental college & Hospital,Cuttack,odisha
[3].Department of Pathology, Faculty of Medicine,Manipal University College Malaysia(MUCM), Melaka, Malaysia
[4].Private Practitioner,, Complete Dental Care Aesthetic & Implant Center Dhaniyamau , Jaunpur UP india
[5].Assistant professor, PhD scholar Dept of cons and endoEklavya Dental College Kotputli BDS, MDS
[6].Assistant Professor , Department of Oral Pathology and Microbiology Government College of Dentistry Indore

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## ABSTRACT

**Background:**Oral leukoplakia is one of the most common potentially malignant oral disorders, with a variable risk of transformation into oral squamous cell carcinoma. Histopathological evaluation plays a vital role in assessing the severity of epithelial dysplasia and predicting malignant potential.

**Aim:**To evaluate the histopathological spectrum of oral leukoplakia and assess its risk of malignant transformation based on clinicopathological findings.

**Materials and Methods:**The present retrospective observational study included 60 histopathologically confirmed cases of oral leukoplakia. Clinical details, including age, gender, lesion site, clinical appearance, and associated habits, were collected from patient records. Histopathological examination was performed on hematoxylin- and eosin-stained sections, and lesions were categorised by the degree of epithelial dysplasia. The correlation between clinical presentation and the risk of malignant transformation was analysed.

**Results:**The majority of cases were observed among males aged 41–60. Buccal mucosa was the most commonly affected site. Homogeneous leukoplakia was more prevalent; however, non-homogeneous lesions were more strongly associated with moderate and severe dysplasia. Histopathological analysis revealed mild epithelial dysplasia as the most common finding, whereas severe dysplasia and carcinoma in situ were associated with an increased risk of malignant transformation.

**Conclusion:**The study highlights that oral leukoplakia exhibits a broad histopathological spectrum with variable malignant potential. Non-homogeneous lesions and higher grades of epithelial dysplasia were strongly associated with increased risk of malignant transformation. Therefore, early diagnosis, histopathological assessment, habit cessation, and long-term follow-up are essential for the prevention of progression to oral cancer.

Corresponding author: Ayushi P Mangulkar

Email id: id-ayu13mangulkar@gmail.com

**Advancement of Knowledge:**The present study provides a detailed evaluation of the histopathological spectrum of oral leukoplakia and its association with the risk of malignant transformation. The study emphasises the importance of correlating clinical presentation with histopathological grading to enable early identification of high-risk lesions. It further highlights the significance of non-homogeneous leukoplakia and advanced epithelial dysplasia as important predictors of malignant progression. The findings contribute to a better understanding of disease behaviour and support the need for regular monitoring and timely intervention in patients with oral leukoplakia.

# Introduction

Oral leukoplakia is one of the most common potentially malignant disorders of the oral cavity. It is clinically characterised by a predominantly white patch or plaque that cannot be diagnosed as any other definable lesion [1]. It represents a significant concern in oral pathology because of its variable clinical presentation and unpredictable potential for malignant transformation into oral squamous cell carcinoma [2]. The prevalence of oral leukoplakia varies globally and is influenced by factors such as tobacco consumption, alcohol intake, betel nut chewing, chronic irritation, and poor oral hygiene [3].

Histopathological evaluation plays an essential role in determining the biological behaviour and malignant potential of oral leukoplakia. Microscopic examination may reveal a wide spectrum of epithelial alterations ranging from simple hyperkeratosis and epithelial hyperplasia to varying grades of epithelial dysplasia [4]. The presence and severity of epithelial dysplasia are considered the most important predictors for malignant transformation and disease progression [5]. However, some lesions without dysplastic features may also undergo malignant transformation, necessitating long-term follow-up in all cases [6].

Several studies have reported that the risk of malignant transformation in oral leukoplakia depends on multiple clinicopathological factors, including lesion size, anatomical site, non-homogeneous appearance, degree of dysplasia, and patient habits such as smoking and alcohol use [7]. Lesions involving the tongue and floor of the mouth have been associated with a higher transformation rate due to their increased susceptibility to carcinogenic exposure [8]. In addition, non-homogeneous leukoplakia, especially speckled or verrucous types, has a higher malignant potential than homogeneous lesions [9].

Advances in histopathological assessment and molecular research have improved understanding regarding the progression of oral leukoplakia toward malignancy. Early diagnosis and timely intervention are important for reducing morbidity and preventing the development of oral cancer [10]. Regular clinical monitoring and biopsy evaluation remain essential components in the management of patients with oral leukoplakia.

Therefore, the present study was undertaken to evaluate the histopathological spectrum of oral leukoplakia and to assess its risk of malignant transformation based on clinicopathological characteristics and histological findings.

# Methodology

The present study was a retrospective, observational, histopathological study conducted in the Department of Oral Pathology to evaluate the histopathological spectrum of oral leukoplakia and its risk of malignant transformation. Biopsy records and histopathological reports of patients clinically diagnosed with oral leukoplakia were collected from the departmental archives over a specified study period. Patients with a confirmed histopathological diagnosis of oral leukoplakia were included in the study. In contrast, cases with incomplete clinical records, recurrent lesions, or a history of previously treated oral malignancies were excluded.

Detailed demographic and clinical data, including age, gender, lesion site, clinical appearance, tobacco and alcohol habits, and lesion duration, were obtained from patient case records. The lesions were clinically categorised as homogeneous or non-homogeneous based on their surface characteristics and appearance. Histopathological examination of hematoxylin and eosin-stained tissue sections was performed to assess epithelial changes and the degree of dysplasia.

The histopathological findings were classified as hyperkeratosis without dysplasia, mild, moderate, or severe epithelial dysplasia, or carcinoma in situ, according to standard World Health Organisation criteria. Special attention was given to architectural and cytological abnormalities, including basal cell hyperplasia, nuclear pleomorphism, increased nuclear-to-cytoplasmic ratio, abnormal mitotic activity, and loss of epithelial stratification.

The risk of malignant transformation was assessed by correlating histopathological grading with clinical characteristics and risk factors. Cases showing advanced dysplastic changes were considered to have a higher malignant potential. Statistical analysis was conducted to assess the associations between clinical presentation, histopathological features, and the risk of malignant transformation. The findings were interpreted to assess the significance of histopathological grading in predicting disease progression and in the early detection of oral malignancy.

# Results

A total of 60 histopathologically confirmed cases of oral

leukoplakia were included in the present study to evaluate the histopathological spectrum and risk of malignant transformation. A detailed analysis was performed based on the demographic profile, lesion distribution, clinical presentation, and histopathological grading.

The age-wise distribution of cases demonstrated that oral leukoplakia was predominantly observed in middle-aged individuals. Among all cases, the highest frequency was observed in the 41–60 age group, accounting for 36 cases (60%). Patients aged 60 years or older constituted 14 cases (23.3%), whereas only 10 cases (16.7%) were reported among patients aged 40 years or younger. The increased prevalence among middle-aged and elderly individuals may be associated with prolonged exposure to tobacco, alcohol consumption, and chronic irritative factors, which are considered important etiological contributors in oral potentially malignant disorders (Table 1).

**Table 1: Age-wise Distribution of Patients**

| Age Group (Years) | Number of Cases | Percentage (%) |
|---|---|---|
| ≤40 | 10 | 16.7 |
| 41–60 | 36 | 60.0 |
| >60 | 14 | 23.3 |
| **Total** | **60** | **100** |

Gender distribution analysis revealed a marked male predominance in the present study. Out of 60 patients, 42 cases (70%) were males and 18 cases (30%) were females. The higher prevalence among males may be attributed to greater exposure to risk factors such as smoking, smokeless tobacco use, alcohol consumption, and betel nut chewing habits, which are more commonly reported among the male population. These findings support the role of lifestyle-associated habits in the development of oral leukoplakia (Table 2).

**Table 2: Gender Distribution of Patients**

| Gender | Number of Cases | Percentage (%) |
|---|---|---|
| Male | 42 | 70.0 |
| Female | 18 | 30.0 |
| **Total** | **60** | **100** |

Analysis of lesion site distribution showed that the buccal mucosa was the most commonly affected anatomical site, observed in 28 cases (46.7%). The tongue followed, in 14 cases (23.3%); the gingiva/alveolar mucosa in 8 cases (13.3%); the floor of the mouth in 6 cases (10%); and the palate in 4 cases (6.7%). The high involvement of the buccal mucosa may be related to direct and prolonged contact with tobacco and areca nut products. However, lesions involving the tongue and floor of the mouth are considered clinically significant due to their comparatively higher risk for malignant transformation (Table 3).

**Table 3: Site-wise Distribution of Oral Leukoplakia**

| Site of Lesion | Number of Cases | Percentage (%) |
|---|---|---|
| Buccal mucosa | 28 | 46.7 |
| Tongue | 14 | 23.3 |
| Gingiva/Alveolar mucosa | 8 | 13.3 |
| Floor of mouth | 6 | 10.0 |
| Palate | 4 | 6.7 |
| **Total** | **60** | **100** |

Based on clinical appearance, oral leukoplakia lesions were categorised as homogeneous or non-homogeneous. Homogeneous leukoplakia was more frequently observed, accounting for 38 cases (63.3%), whereas non-homogeneous leukoplakia was identified in 22 cases (36.7%). Homogeneous lesions generally presented as uniformly white, flat, or slightly elevated plaques with relatively lower malignant potential. In contrast, non-homogeneous lesions exhibited mixed red and white areas and nodular or verrucous surfaces. They were more commonly associated with dysplastic changes and an increased risk of malignant transformation (Table 4).

**Table 4: Clinical Types of Oral Leukoplakia**

| Clinical Type | Number of Cases | Percentage (%) |
|---|---|---|
| Homogeneous | 38 | 63.3 |
| Non-homogeneous | 22 | 36.7 |
| **Total** | **60** | **100** |

Histopathological examination revealed a broad spectrum of epithelial alterations ranging from simple hyperkeratosis to severe dysplasia and carcinoma in situ. Hyperkeratosis without dysplasia was observed in 16 cases (26.7%), mild epithelial dysplasia in 22 cases (36.7%), moderate dysplasia in 14 cases (23.3%), severe dysplasia in 6 cases (10%), and carcinoma in situ in 2 cases (3.3%). Mild epithelial dysplasia was the most common histopathological finding in the present study. Increasing grades of dysplasia were associated with progressive architectural and cytological abnormalities, including basal cell hyperplasia, nuclear pleomorphism, increased mitotic activity, and loss of epithelial stratification. Severe dysplasia and carcinoma in situ were considered indicators of high malignant potential (Table 5).

**Table 5: Histopathological Spectrum of Oral Leukoplakia**

| Histopathological Diagnosis | Number of Cases | Percentage (%) |
|---|---|---|
| Hyperkeratosis without dysplasia | 16 | 26.7 |
| Mild dysplasia | 22 | 36.7 |
| Moderate dysplasia | 14 | 23.3 |
| Severe dysplasia | 6 | 10.0 |
| Carcinoma in situ | 2 | 3.3 |
| **Total** | **60** | **100** |

The correlation between clinical type and dysplastic changes showed that non-homogeneous leukoplakia exhibited significantly higher dysplasia grades than homogeneous lesions. Among 22 non-homogeneous lesions, 12 demonstrated moderate-to-severe dysplastic changes, whereas only 6 of 38 homogeneous lesions showed advanced dysplasia. These findings suggest that non-homogeneous clinical appearance may serve as an important predictor for malignant transformation risk (Table 6).

**Table 6: Association of Clinical Type with Dysplastic Changes**

| Clinical Type | Mild/No Dysplasia | Moderate/Severe Dysplasia | Total |
|---|---|---|---|
| Homogeneous | 32 | 6 | 38 |
| Non-homogeneous | 10 | 12 | 22 |
| Total | 42 | 18 | **60** |

Overall, the present study demonstrated that oral leukoplakia exhibits a wide histopathological spectrum ranging from benign hyperkeratotic lesions to severe dysplasia and carcinoma in situ. The findings further indicate that non-homogeneous lesions and higher grades of epithelial dysplasia are strongly associated with an increased risk of malignant transformation, highlighting the importance of early diagnosis, histopathological evaluation, and long-term clinical follow-up in the management of oral leukoplakia.

# Discussion

The present study demonstrated a wide histopathological spectrum of oral leukoplakia, ranging from hyperkeratosis without dysplasia to severe epithelial dysplasia and carcinoma in situ. Histopathological grading remains one of the most reliable indicators for assessing malignant transformation risk in oral potentially malignant disorders. Brouns et al. reported that the presence and severity of epithelial dysplasia significantly influence the biological behaviour of oral leukoplakia and its progression toward malignancy [11]. The authors further emphasised that lesions with moderate-to-severe dysplasia require close clinical follow-up due to their increased malignant potential.

Sun Z. et al. observed that dysplastic epithelial changes, such as nuclear pleomorphism, increased mitotic activity, and loss of epithelial stratification, are strongly associated with progression to oral squamous cell carcinoma [12]. Similar findings were observed in the present study, in which lesions with higher grades of dysplasia demonstrated an increased risk of malignant transformation. Bokor-Bratić et al. also highlighted that histopathological examination remains the gold standard for evaluating premalignant alterations in oral leukoplakia and for identifying high-risk lesions at an early stage [13].

Parlatescu et al. stated that oral leukoplakia possesses an unpredictable clinical course, as even lesions with mild dysplasia may undergo malignant transformation over time [14]. The authors emphasised the importance of regular monitoring and repeated biopsy evaluation in suspicious lesions. In the present study, non-homogeneous lesions were more strongly associated with moderate and severe dysplastic changes, indicating a higher risk of malignant progression.

Gandara-Vila et al. reported that clinicopathological factors, such as lesion size, site, clinical appearance, and degree of dysplasia, play a major role in determining the risk of malignant transformation [15]. Lesions located on the tongue and floor of the mouth were found to exhibit greater malignant potential compared to lesions occurring at other intraoral sites. Similar observations were made in the present study, in which lesions involving high-risk anatomical locations more frequently demonstrated advanced dysplastic alterations.

Rubert et al. emphasised that early diagnosis and histopathological assessment are essential for preventing the progression of oral leukoplakia to invasive carcinoma [16]. The authors suggested that prompt management, along with the elimination of etiological risk factors such as tobacco and alcohol use, significantly improves prognosis. These findings are consistent with the present study's observations, in which patients with a positive habit history demonstrated a higher prevalence of dysplastic lesions.

Čēma et al. reported that molecular and genetic alterations associated with epithelial dysplasia contribute to malignant transformation in oral leukoplakia [17]. The study highlighted that chronic exposure to carcinogens induces genomic instability and abnormal epithelial proliferation, thereby increasing the risk of oral cancer development. The present study findings support the concept that progressive histopathological changes are closely related to malignant potential.

Stefano Petti stated that tobacco smoking and alcohol consumption are among the most significant etiological factors associated with oral leukoplakia and oral cancer

development [18]. Persistent exposure to these carcinogens leads to epithelial damage, oxidative stress, and accumulation of genetic mutations. In the present study, the majority of patients with moderate to severe dysplasia had a history of tobacco-related habits, supporting the association between lifestyle factors and malignant transformation risk.

Downer MC emphasised the importance of evidence-based screening and early intervention strategies to reduce the burden of oral cancer [19]. Early identification of potentially malignant lesions through regular oral examination and biopsy evaluation may significantly reduce morbidity and mortality associated with oral squamous cell carcinoma. The present study findings also reinforce the necessity of timely diagnosis and long-term follow-up in patients with oral leukoplakia.

Chaturvedi AK et al. reported that the global incidence of oral cancer continues to rise due to increasing exposure to tobacco, alcohol, and other carcinogenic agents **[20]**. The study further highlighted that oral potentially malignant disorders, such as leukoplakia, serve as important precursor lesions for oral squamous cell carcinoma. Therefore, appropriate clinicopathological assessment and risk stratification are essential for preventing malignant progression.

Overall, the findings of the present study are consistent with previous literature demonstrating that oral leukoplakia exhibits variable histopathological features and unpredictable malignant behaviour. Higher grades of epithelial dysplasia, non-homogeneous clinical appearance, and high-risk anatomical sites were strongly associated with an increased risk of malignant transformation. Therefore, comprehensive histopathological evaluation, elimination of etiological risk factors, and regular long-term follow-up remain essential for effective management of oral leukoplakia and prevention of oral cancer.

## Conclusion

The present study demonstrated that oral leukoplakia exhibits a wide histopathological spectrum ranging from simple hyperkeratosis to severe epithelial dysplasia and carcinoma in situ. The findings indicated that middle-aged males with tobacco-related habits were more commonly affected. The buccal mucosa was the most frequently involved site, whereas lesions of the tongue and floor of the mouth had greater malignant potential.

Histopathological evaluation revealed that non-homogeneous leukoplakia and higher grades of epithelial dysplasia were strongly associated with an increased risk of malignant transformation. The study further emphasised that epithelial dysplasia remains an important predictor of disease progression and prognosis in oral leukoplakia.

Therefore, early diagnosis, detailed histopathological assessment, elimination of risk factors such as tobacco and alcohol use, and regular long-term follow-up are essential for the effective management of oral leukoplakia and the prevention of progression to oral squamous cell carcinoma.

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