ORIGINAL ARTICLE OPEN ACCESS

Bridging Dysplasia to Diagnostic Oral Pathology: Comparative Evaluation of Leukoplakia as a Predictor of Oral Malignancy

Amna Sarfaraz[1], Mariam Fatima[2], Sahd Rashid[3], Saba Ejaz[4], Ayesha Siddiqa[2], Aiza Khan[5], Kainat Zafar[6]

[1]Department of Oral Pathology, Shifa College of Dentistry, Shifa Tamer - e- Millat University, Islamabad, [2]Department of Oral Medicine, Shifa College of Dentistry, Islamabad,[3]Department of Oral Medicine, Shifa College of Dentistry, Shifa Tamer - e- Millat University, Islamabad, [4]Department of Oral Pathology, Rawal Institute of Health Sciences, Islamabad, [5]Department of Oral Biology, Hazarat Bari Imam Sarkar Medical and Dental College, Islamabad, [6]Department of Pathology, Akhtar Saeed Medical College, Akhtar Saeed Hospital, Lahore, Pakistan.

ABSTRACT

Background: Oral leukoplakia is a frequently encountered premalignancy and potential source of oral dysplastic change, with the probable clinical manifestation in the form of an oral leukoplakia lesion. In this study, the authors endeavor to carry out the histological grading of dysplasia in leukoplakia and the relationship between the grades of dysplasia and malignant transformation.

Methods: One hundred and twenty clinically diagnosed oral leukoplakia patients were studied in a cross-sectional analysis. Demographic, tobacco history, and features of the lesions were documented. Histopathological analysis was used to decide on the existence and extent of epithelial dysplasia. Stratified cases were associated with dysplasia grade (none, mild, moderate, severe/CIS) and compared to the demonstration of malignant transformation during follow-up biopsy or surgical extirpation. SPSS version 26.0 was used to calculate % and estimate the values.

Results: Most patients (65%) were males, and the most dominant age group was among those aged 41-60. In 75 per cent of cases, tobacco use was reported. Histologically, there was mild dysplasia in 35 percent, moderate in 23.3 percent, and severe dysplasia/CIS in 13.3 percent of the organisms, with 28.3 percent being negative for dysplasia. The rate of malignant transformation was observed to be increased with dysplasia grade: 2.9 percent with no dysplasia, 9.5 percent with mild, and 32.1 percent with moderate dysplasia, and 81.3 percent in severe dysplasia ($p<0.01$). Tobacco use and gender were also positively correlated with dysplastic changes, malignant potential.

Conclusion: There is a quantifiable relationship between the malignant potential of oral leukoplakia depending on the severity of dysplasia as it appears in the histology.

Keywords: Leukoplakia, Oral, Mouth Neoplasms, Carcinoma, Squamous Cell, Epithelial Cells

Corresponding Author:
Dr. Kainat Zafar,
Department of Pathology,
Akhtar Saeed Medical College, Akhtar Saeed
Hospital, Lahore, Pakistan.
Email: kainatzafar@gmail.com
ORCID: https://orcid.org/0009-0000-4567-8833
Doi: https://doi.org/10.36283/ziun-pjmd14-3/026.

How to cite: Sarfaraz A, Fatima M, Rashid S, Ejaz S, Siddiqa A, Khan A, Zafar K Bridging Dysplasia to Diagnostic Oral Pathology: Comparative Evaluation of Leukoplakia as a Predictor of Oral Malignancy. Pak J Med Dent. 2025 July ;14(3): 167-172. Doi: https://doi.org/10.36283/ziun-pjmd14-3/026.

Received: Mon, June 23, 2025 **Accepted:** Fri, July 11, 2025 **Published:** Mon, July 21, 2025

INTRODUCTION

It has been acknowledged that oral leukoplakia is the most common potentially malignant disorder (PMD) of the oral cavity[1]. Leukoplakia is clinically characterized as a lesion that appears as a white patch or plaque, which has neither clinical nor pathological diagnosis as a disease, which makes it very important because it possesses a variable risk of oral squamous cells carcinoma (OSCC) transformation[2]. Although the phenomenon that accompanies it is common, its development is unpredictable, which is a problem in daily practice and clinical decision-making in terms of both diagnosis of the oral pathology and its formation [3]. Assessment of malignant potential Leukoplakia Histopathological assessment of leukoplakia can be said to be the gold standard in malignant potential [4].

The number and level of epithelial dysplasia are a prime predictor of future carcinogenic evolution. Nevertheless, in itself, dysplasia shows diverse histologic manifestations, ranging from cellular and architectural disorder, which can be both over-reported and under-reported, without there being a common grading scale [5]. Leukoplakia stratification into the levels of dysplasia is vital in determining the high-risk cases, which are sometimes closely monitored, treated by surgery, or chemoprevention [6]. There are other demographic and behavioral reasons that include age, gender, tobacco use, and lesion site as among the factors that have been correlated to increased malignant potential of leukoplakia [7]. Leukoplakia, particularly the tobacco-related one, has recorded an increased incidence of dysplasia and epithelial transformation, and therefore, early action is needed [8]. Mostly in developing countries, where lack of knowledge and availability of proper screening is the main problem, histopathological screening of leukoplakia lesions is paramount in countries such as Pakistan [9].

The goal of this study is to see the histopathological continuum of dysplasia in clinically identified leukoplakia and relate the degree of severity to established malignant change. This way, the study aims at reinforcing the diagnostic and prognostic value of dysplasia grading in oral pathology practice and opinions in favor of its contribution to the clinical setting as a predictor of malignancy in leukoplakia lesions.

METHODS

The cross-sectional study was conducted at the Department of Oral Pathology at a tertiary care dental teaching hospital, Akhtar Saeed, Shifa College of Dentistry, and Rawal Medical Institute (ref: 2315/24). One hundred and twenty patients with clinically diagnosed cases of oral leukoplakia within 06 months took part in the study (July 2024 to December 2024). Patients with leukoplakic lesion clinically evident and equal or greater than 20 years were included criteria. Patients who had a history of oral malignancy, systemic immune deficiency or any biopsy-documented cancer were excluded. Demographic factors were gathered using a structured proforma that comprised age, gender, and history of tobacco use. The clinical analysis was done on each of the leukoplakic lesions, and the area is noted in terms of location, size, and type. Incisional biopsy was done on all patients under aseptic conditions and the tissues were fixed in 10 % formalin and submitted to histopathology procedures. Slides with hematoxylin and eosin stains were determined through a light microscope by two oral pathologists.

The World Health Organization (WHO) 2005 grading system was used to categorize dysplasia as: no dysplasia, mild, moderate, and severe dysplasia/carcinoma in situ (CIS) as per cytological and architectural abnormalities. Clinical progression, as well as the malignant transformation of patients was tracked through further histopathology or surgical excision results proving malignancy. SPSS version 26.0 was used in the analysis of data. The demographics and the degree of dysplasia in the patients were described statistically. This approach was meant to fill the gap between clinical evaluation and histopathological evaluation by establishing relationships between dysplastic alterations and the possibility of predicting the development of the malignant process to the improvement of routine oral pathology diagnosis.

RESULTS

There was male predominance of 120 patients who had oral leukoplakia; most of them were in the age range of 41-60 years. The use of tobacco was substantially linked to the presence of leukoplakia. A significant sample of cases had dysplastic changes which were graded mild and severe. There was a gradual relationship that existed between the degree of dysplasia and the transformation into malignancy. Such results indicate the diagnostic expectations of particular histological grading.

Table 1: Demographic Characteristics of Study Population (n = 120)

Variable	Category	Frequency (n)	Percentage (%)
Age Group (years)	20–40	38	31.7%
	41–60	56	46.7%
	>60	26	21.6%
Gender	Male	78	65.0%
	Female	42	35.0%
Tobacco Use	Yes	90	75.0%
	No	30	25.0%

The study sample consisted of 120 individuals, with 65% being male. The most affected age group was 41–60 years, comprising 46.7% of the cases. Tobacco use was reported in 75% of the population, indicating a key risk factor. Females represented 35% of the total cohort. Higher prevalence in middle-aged males with a tobacco history supports epidemiological associations.

Table 2: Severity of Epithelial Dysplasia in Leukoplakia Lesions (n = 120)

Grade of Dysplasia	Male (n=78)	Female (n=42)	Total (n)	Percentage (%)
No Dysplasia	20	14	34	28.3%
Mild Dysplasia	28	14	42	35.0%
Moderate Dysplasia	20	8	28	23.3%
Severe Dysplasia/CIS	10	6	16	13.3%

Mild dysplasia was the most common finding, seen in 42 patients. Males presented more frequently with moderate to severe dysplasia than females. No dysplasia was noted in 34 cases, slightly more among males. Severe dysplasia or carcinoma in situ was found in 16 cases, 62.5% of which were male. A clear gradient was seen from mild to severe lesions, emphasizing risk stratification.

Table 3: Correlation of Dysplasia Severity with Malignant Transformation

Dysplasia Severity	Malignant Cases (n)	Non-Malignant Cases (n)	Malignancy Rate (%)
No Dysplasia	1	33	2.9%
Mild Dysplasia	4	38	9.5%
Moderate Dysplasia	9	19	32.1%
Severe Dysplasia/CIS	13	3	81.3%

Among 34 non-dysplastic cases, only 1 progressed to malignancy. Malignancy was seen in 81.3% of cases with severe dysplasia. Moderate dysplasia had a malignancy rate of 32.1%, showing a rising risk. Mild dysplasia demonstrated lower transformation (9.5%) but was not negligible. The data confirms a strong correlation between dysplasia grade and cancer progression.

This histopathology image presents the presence of severe epithelial dysplasia that is characterized by such features as hyperplasia of the basal cells, pleomorphism of the nucleus, and hyperchromatism. The epithelial structure is haphazard, stratification is gone, and the nuclear to cytoplasm ratio is high. All these changes are characteristic features of premalignancy at risk. As **Figure 1** indicates, arrows indicate important hemostatic alterations that are vital in diagnosis.

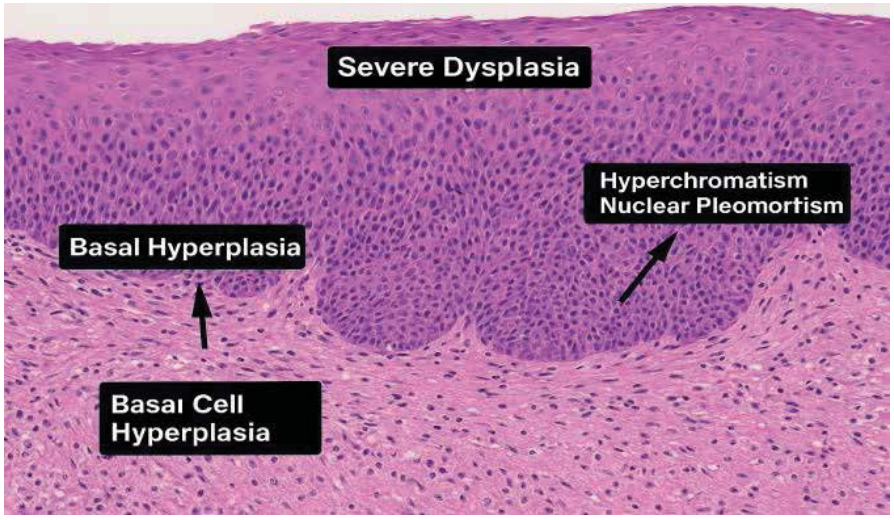

Figure 1. Hemostatic Alterations

DISCUSSION

In the present study, dental practitioners need to focus on the importance of dysplasia grading in the malignant potential of oral leukoplakia. Of the 120 clinically diagnosed cases, 57 percent were found to be showing one form of dysplasia or another by histopathological analysis, and a direct correlation between dysplasia and its intensity with the development of malignancy was established. The result is in line with the research of others who have found epithelial dysplasia to be a major indicator of the progression into OSCC. Cases of leukoplakia with severe dysplasia, carcinoma in situ, displayed maximal malignant transformation (81.3 %), whereas the zero and mild dysplasia cases had a much lower rate (2.9 and 9.5, respectively). This gradual course further strengthens the need for early biopsy and grading, particularly in the moderate or high-risk lesions.

The findings coincide with those of Warnakulasuriya et al. and Kujan et al., who pointed out that the severity of dysplasia is strongly associated with cancer risk and clinical prognosis [10,11]. A widespread risk factor, which is tobacco usage, was reported in 75 percent of the study population, and this again adds to the already substantiated causative relation between tobacco exposure and oral potentially malignant disorders (OPMDs) 12,13. Males were especially hit and might have reflected sociocultural contributions to tobacco use and access to healthcare [14]. The most affected age group was 41-60 years, which could be associated with prolonged risk factor exposure and late detection [15].

A histopathology assessment is the key to the assessment of malignant potential [16]. Interobserver variability, however, has been problematic in the grading of dysplasia. Subjectivity was curbed in this research with the help of duplication in reporting by the pathologists [17]. Additionally, non-dysplastic leucoplakias are not completely non-malignant even though their conversion risk is closer to zero, and they need to be monitored, at least in patients who use tobacco or have lesions of large size or non-homogeneous appearance [18]. The article also emphasizes the necessity of a combined use of clinical, histological, and behavioral information to implement effective risk stratification [19,20]. Some of its limitations are a cross-sectional design and follow-up that is rather short, which could result in negative biases towards the reporting of the long-term malignant transformations [21-23]. Also, molecular markers were not used, which would provide an improvement in the degree of prediction [24,25].

On the whole, the results are very highly indicative of the methods of regular biopsy of leukoplakic lesions and histological grading as instruments of oral cancer prevention. The resourceless conditions will enhance the basic histopathologic screening, especially in developing countries such as Pakistan where complex diagnostic tools are unavailable. Future research needs to be based on the integration of immunohistochemistry and genetic profiles in addition to the conventional histological assessments.

CONCLUSION

This study has established that leukoplakia which affects the epithelial cells is directly proportional to malignant potential of the epithelial dysplasia. The reversibility of severe dysplasia was 81.3%, bringing out the significance of an early biopsy and grading of a high-risk lesion. Possible risk factors were confirmed by the presence of tobacco use in the vast majority of affected patients who were middle aged males.

Histopathology has continued to be an important tool in the risk assessment of oral potentially malignant disorders. Regular follow-up on leukoplakia, regardless of the presence of dysplasia or not, should be carried out to eliminate a late diagnosis of cancer. It could also be possible that future incorporation of molecular markers would enhance the prediction and management of oral malignancies.

LIST OF ABBREVIATIONS

CIS: Carcinoma in Situ
OPMD: Oral Potentially Malignant Disorders
OSCC: Oral Squamous Cell Carcinoma
PMD: Potentially Malignant Disorder

ACKNOWLEDGMENTS

None

FUNDING

None

CONFLICT OF INTEREST

None

ETHICAL APPROVAL

The cross-sectional study was conducted at the Department of Oral Pathology at a tertiary care dental teaching hospital, Akhtar Saeed, Shifa College of Dentistry, and Rawal Medical Institute (ref: 2315/24).

AUTHORS' CONTRIBUTIONS

All participants participated equally as per ICMJE.

REFERENCES

1. Wils LJ, Poell JB, Peferoen LA, Evren I, Brouns ER, de Visscher JG, et al. The role of differentiated dysplasia in the prediction of malignant transformation of oral

leukoplakia. J Oral Pathol Med. 2023 Nov;52(10):930-8. Doi: 10.1111/jop.13483.
2. Wils LJ, Poell JB, Evren I, Koopman MS, Brouns ER, de Visscher JG, et al. Incorporation of differentiated dysplasia improves prediction of oral leukoplakia at increased risk of malignant progression. Mod Pathol. 2020 Jun;33(6):1033-40. Doi: 10.1038/s41379-019-0444-0.
3. Monteiro L, Mello FW, Warnakulasuriya S. Tissue biomarkers for predicting the risk of oral cancer in patients diagnosed with oral leukoplakia: A systematic review. Oral Dis. 2021 Nov;27(8):1977-92. Doi: 10.1111/odi.13747.
4. Tilakaratne WM, Jayasooriya PR, Jayasuriya NS, De Silva RK. Oral epithelial dysplasia: Causes, quantification, prognosis, and management challenges. Periodontol 2000. 2019 Jun;80(1):126-47. Doi: 10.1111/prd.12259.
5. Monteiro L, Rocha E, Ferreira S, Salazar F, Pacheco JJ, Warnakulasuriya S. Tissue Biomarkers for Predicting the Risk of Oral Cancer in Patients Diagnosed With Oral Leukoplakia: A Systematic Review of the Past 4 Years. J Oral Pathol Med. 2025 May;54(5):283-9. Doi: 10.1111/jop.13632.
6. Ranganathan K, Kavitha L. Oral epithelial dysplasia: Classifications and clinical relevance in risk assessment of oral potentially malignant disorders. J Oral Maxillofac Pathol. 2019 Jan 1;23(1):19-27. Doi: 10.4103/jomfp.JOMFP_13_19.
7. Warnakulasuriya S. Oral potentially malignant disorders: A comprehensive review on clinical aspects and management. Oral oncol. 2020 Mar 1;102:104550. Doi: 10.1016/j.oraloncology.2019.104550.
8. Soares AB, Warnakulasuriya S, da Silveira Terra Junqueira L, de Freitas AL, Schneider A, Silva AR, et al. Risk Assessment of Oral Leukoplakia by Individual Dysplasia Features. J Oral Pathol Med. 2025 May 29. Doi: 10.1111/jop.13633.
9. Celentano A, Glurich I, Borgnakke WS, Farah CS. World Workshop on Oral Medicine VII: Prognostic biomarkers in oral leukoplakia and proliferative verrucous leukoplakia—A systematic review of retrospective studies. Oral Dis. 2021 May;27(4):848-80. Doi: 10.1111/odi.13363.
10. Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, Bagan JV, González-Moles MÁ, Kerr AR, et al. 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):1862-80. Doi: 10.1111/odi.13704.
11. Odell E, Kujan O, Warnakulasuriya S, Sloan P. Oral epithelial dysplasia: recognition, grading and clinical significance. Oral Dis. 2021 Nov;27(8):1947-76. Doi: 10.1111/odi.13993.
12. Brouns ER, Evren I, Wils LJ, Poell JB, Brakenhoff RH, Bloemena E, et al. Oral leukoplakia classification and staging system with incorporation of differentiated dysplasia. Oral Dis. 2023 Oct;29(7):2667-76. Doi: 10.1111/odi.14295.
13. Tovaru S, Costache M, Perlea P, Caramida M, Totan C, Warnakulasuriya S, et al. Oral leukoplakia: A clinicopathological study and malignant transformation. Oral dis. 2023 May;29(4):1454-63. Doi: 10.1111/odi.14123.
14. Evren I, Brouns ER, Poell JB, Wils LJ, Brakenhoff RH, Bloemena E, et al. Associations between clinical and histopathological characteristics in oral leukoplakia. Oral dis. 2023 Mar;29(2):696-706. Doi: 10.1111/odi.14038.
15. Chaturvedi AK, Udaltsova N, Engels EA, Katzel JA, Yanik EL, Katki HA, et al. Oral leukoplakia and risk of progression to oral cancer: a population-based cohort study. JNCI: J Natl Cancer Inst. 2020 Oct;112(10):1047-54. Doi: 10.1093/jnci/djz238.
16. Rubert A, Bagán L, Bagán JV. Oral leukoplakia, a clinical-histopathological study in 412 patients. Journal of clinical and experimental dentistry. 2020 Jun 1;12(6):e540. Doi: 10.4317/jced.57091.
17. Jayasooriya PR, Dayaratne K, Dissanayake UB, Warnakulasuriya S. Malignant transformation of oral leukoplakia: a follow-up study. Clin Oral Investig. 2020 Dec;24:4563-9. Doi: 10.1007/s00784-020-03322-4.
18. Pinto AC, Carames 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 1;129(6):600-11. Doi: 10.1016/j.oooo.2020.02.017.
19. Jäwert F, Pettersson H, Jagefeldt E, Holmberg E, Kjeller G, Öhman J. Clinicopathologic factors associated with malignant transformation of oral leukoplakias: a retrospective cohort study. International J Oral Maxillofac Surg. 2021 Nov 1;50(11):1422-8. Doi: 10.1016/j.ijom.2021.01.012.
20. Rubert A, Bagán L, Bagán JV. Oral leukoplakia, a clinical-histopathological study in 412 patients. J Clin Exp Dent. 2020 Jun 1;12(6):e540. Doi: 10.4317/jced.57091.
21. Maymone MB, Greer RO, Kesecker J, Sahitya PC, Burdine LK, Cheng AD, et al. Premalignant and malignan oral mucosal lesions: Clinical and pathological findings. J Am Acad Dermatol. 2019 Jul 1;81(1):59-71. Doi: 10.1016/j.jaad.2018.09.060.
22. Pritzker KP, Darling MR, Hwang JT, Mock D. Oral potentially malignant disorders (OPMD): what is the clinical utility of dysplasia grade?. Expert Rev Mol Diagn. 2021 Mar 4;21(3):289-98. Doi: 10.1080/14737159.2021.1898949.
23. Walsh T, Macey R, Kerr AR, Lingen MW, Ogden GR, Warnakulasuriya S. Diagnostic tests for oral cancer and potentially malignant disorders in patients presenting with clinically evident lesions. Cochrane Database Syst Rev. 2021(7). Doi: 10.1002/14651858.CD010276.pub3.
24. Kokubun K, Nakajima K, Akashi Y, Yamamoto K, Katakura A, Matsuzaka K. Clinicopathological evaluation of oral leukoplakia: a single-center study of 676 cases in Japan. Oral Surg Oral Med Oral

Pathol Oral Radiol. 2024 May 1;137(5):529-36. Doi: 10.1016/j.oooo.2024.02.022.
25. Wils LJ, Poell JB, Brink A, Evren I, Brouns ER, de Visscher JG, et al. Elucidating the genetic landscape of oral leukoplakia to predict malignant transformation. Clin Cancer Res. 2023 Feb 1;29(3):602-13. Doi: 10.1158/1078-0432.CCR-22-2210.