



## Association of Common risk factors and duration of exposure with histopathological gradings of Oral Epithelial Dysplasia – A Prospective cross-sectional single center study

Authors

**Dr Usha Sarma, Dr Manjula Choudhury, Dr Sanjoy Krishna Handique,  
Dr Aradhana Saikia, Dr Priyanka Baishya**

Department of Pathology, Gauhati Medical College and Hospital, Narakasur Hilltop,  
GMC Hospital Rd, Bhangagarh, Guwahati, Assam 780132

Corresponding Author

**Dr. Sanjoy Krishna Handique**

### Abstract

**Aim:** *This study aimed to evaluate the association between common risk factors, their duration of exposure, and the histopathological grading of oral epithelial dysplasia (OED).*

**Materials and Methods:** *A cross-sectional prospective study was conducted on 60 histologically confirmed cases of OED diagnosed over one year. Patients were evaluated for risk factors such as tobacco habits, alcohol consumption, and exposure duration using a standardized proforma. Biopsy specimens were processed and graded into mild, moderate, or severe dysplasia. Statistical analysis, including Chi-square tests, was performed to assess the associations, with a significance level set at  $p < 0.05$ .*

**Results:** *The study population included 45 males and 15 females (3:1 ratio) aged 30–60 years. Buccal mucosa was the most affected site (35%), and Leukoplakia was the predominant clinical presentation (66.6%). Histopathological grading revealed mild (36.6%), moderate (31.7%), and severe (31.7%) dysplasia. Betel nut quid with tobacco was the most frequently associated risk factor across all grades, while its combination with smoking correlated significantly with severe dysplasia. Longer exposure durations (44–50 years) were strongly associated with severe dysplasia ( $p < 0.05$ ).*

**Conclusion:** *This study highlights the significant association between risk factors, exposure duration, and OED grades. Betel nut quid with tobacco emerged as a critical risk factor, with smoking compounding its severity. These findings emphasize the need for targeted prevention strategies and early intervention to reduce the progression to malignancy.*

**Keywords:** *Oral epithelial dysplasia, Risk factors, Tobacco, Betel nut, Alcohol, Histopathological grading.*

## Introduction

Oral cavity cancers are the most common in the head and neck region, 90% of which are oral squamous cell carcinoma (OSCC).<sup>1</sup> OSCC are preceded by lesions clinically termed as oral potentially malignant disorders (OPMD). Histological evidence of oral epithelial dysplasia is the most reliable indicator of malignant transformation in OPMD.<sup>1</sup>

WHO defines oral epithelial dysplasia (OED) as “a spectrum of architectural and cytological epithelial changes caused by the accumulation of genetic changes, associated with an increased risk of progression to squamous cell carcinoma”.<sup>2</sup> The OED are graded according to WHO into three-tier grading as: mild, moderate and severe dysplasia based on the presence of eight architectural and eight cytological features.<sup>2</sup> The risk of malignant transformation is highest with moderate and severe dysplasia.<sup>3</sup>

Oral carcinogenesis is characterized by a sequence of molecular and cellular changes, some of which may be reversible, ultimately leading to neoplasia. Consequently, it is expected that some known causative factors of OED will overlap with those of OSCC.<sup>4</sup> Few of the common risk factors are mentioned that may drive oral epithelial dysplasia. Tobacco: Tobacco use is a widely recognized risk factor for oral cancers, with various forms of intake, including chewing and smoking, linked to the development of OED.<sup>5-7</sup> Tobacco and tobacco smoke contain over carcinogens that include aromatic hydrocarbon benzo-pyrene and specific tobacco-related nitrosamines (TSNs), such as 4-(nitroso methylamino)-1-(3-pyridyl)-1-butanone (NNK) and N'-nitrosornicotine<sup>8</sup>. Tobacco is consumed in both smoking forms such as cigarettes, cigar and smokeless forms such as betel quid (betel leaf, slated lime, and areca nut), khaini etc<sup>8</sup>. The use of smokeless forms is more prevalent in Asian countries owing to the high burden of oral cancer cases in these regions.

Alcohol: Alcohol is a recognized risk factor for various cancers, including head and neck cancers.<sup>4</sup>

A number of studies have found a strong association of alcohol and OED<sup>9,10</sup>.

Other risk factors, such as infection with HPV (particularly HPV-16), genetic disease (Bloom disease, Fanconi anemia), infections (Candida, Treponema) may also contribute to the development of OED.

There is less data available on the grades of OED and different risk factors. Therefore, this study aims to establish an association between the common risk factors and the grades of OED.

## Materials and Methods

A cross-sectional prospective study carried out for a period of one year. A total of 60 cases of histologically confirmed cases of OED were included in the study. The most common clinical presentation was leukoplakia followed by erythroplakia. A standard proforma was prepared that included i] Patients' personal habits, ii] Types of tobacco used (chewing, smoking, betel quid with tobacco) and iii] Total duration of tobacco and alcohol exposure. The proforma was filled up during the clinical examination in the OPD. The suspicious lesions were evaluated, and the biopsy specimen was fixed in 10% buffered formalin and sent for histopathological examination. The tissues were processed according to the standard operating procedure followed by staining with Hematoxylin & Eosin and reporting was done.

## Statistical Analysis

The data was entered into a computerized spreadsheet using IBM SPSS software, version 22. Chi-square tests were applied and the p-value of <0.05 was considered statistically significant.

## Results

A total of sixty cases of histologically diagnosed cases of OED were included in the present study. The age of patients varied from 3<sup>rd</sup> – 6<sup>th</sup> decade with 45 males and 15 females with a male: female ratio of 3:1. The most affected site was buccal mucosa followed by tongue.

Forty (66.6%) cases presented with leukoplakia and the remaining twenty (33.4%) cases presented with erythroplakia.

Histopathological analysis revealed that twenty-two (36.6%) cases exhibited mild dysplasia, nineteen (31.7%) cases showed moderate dysplasia, and the remaining nineteen cases (31.7%) had severe dysplasia.

Most patients with mild dysplasia were exposed to betel nut quid with tobacco, while those with severe dysplasia were mostly exposed to both

betel nut with tobacco and smoking. A significant association was observed between the risk factors and grades of oral epithelial dysplasia. ( $\chi^2$ -value: 15.90 with p value of 0.014). (Table 1)

Patients with 20-25 years of exposure predominantly showed mild dysplasia, while those with 44-50 years of exposure had severe dysplasia. A statistically significant association was observed between the duration of risk factors and grades of oral epithelial dysplasia. ( $\chi^2$ -value: 30.63 with p value of 0.00016). (Table 2)

**Table 1:** Characteristics of Oral epithelial dysplasia patients (n=60)

Patients	N (%)
Male	45 (75%)
Female	15 (25%)
<b>Location</b>	
Buccal Mucosa	21 (35%)
Tongue	14 (23.3%)
Gingivobuccal Sulcus	10 (16.6%)
Hard Palate	6 (10%)
Lip	5 (8.3%)
Retromolar Trigone	4 (6.8%)
<b>Dysplasia Grade</b>	
Mild	22 (36.6%)
Moderate	19 (31.7%)
Severe	19 (31.7%)

**Table 2:** Association of risk factors with different grades of oral epithelial dysplasia (n=60)

Degree of Dysplasia	Mild	Moderate	Severe	Total	d.f.	$\chi^2$ -value	p-value
<b>Risk Factors</b>							
Betel nut quid with Tobacco	15	5	5	25	6	15.90	0.014
Betel nut quid with Tobacco and Smoking	2	3	8	13			
Alcohol	3	6	2	11			
Betel nut quid with Tobacco and Alcohol	2	5	4	11			
Total	22	19	19	60			

**Table 3:** Association of duration of risk factors and different grades of oral epithelial dysplasia

Degree of Dysplasia	Mild	Moderate	Severe	Total	d.f.	$\chi^2$ -value	p-value
<b>Duration of risk factors</b>							
20-25 years	13	5	2	20	8	30.63*	0.00016
26-31 years	4	4	1	9			
32-37 years	3	6	0	9			
38-43 years	2	4	8	14			
44-50 years	0	0	8	8			
Total	22	19	19	60			

**Discussion**

We evaluated a total of sixty cases of OED diagnosed over a period of one year along with their exposure to common risk factors and

duration of exposure of the same. The majority of cases displayed mild dysplasia, while the remaining cases were evenly distributed between moderate and severe dysplasia.

In our study there was a male preponderance with a male to female ratio of 3:1. The observations were similar to the studies done in other parts of Asia.<sup>11-13</sup> This is likely attributed to the higher consumption of tobacco-related products among males compared to females.

The age at presentation is a crucial clinical factor to consider when developing a differential diagnosis for a lesion. In our study the age of the patients ranged from 30 to 60 years with a peak incidence in the fifth decade. The age of our study population was similar to that of other reports.<sup>11-14</sup>

In the present study the most frequently affected site was buccal mucosa (35%), similar to the findings of other studies in different states of India.<sup>11,13</sup> This may be attributed to the patterns of tobacco use, particularly the widespread practice of chewing tobacco and placing the quid at specific sites.

Leukoplakia was the most common clinical diagnosis, as it is typically associated with dysplastic changes, predominantly mild and moderate OED, consistent with findings from other studies.<sup>3,12,15,16</sup>

On analysis of risk factors, patients with exposure to Betel nut quid with Tobacco form the largest group across all severity levels, indicating its strong association with dysplasia. In addition to this, the present study also revealed that mild dysplasia is more prevalent in cases involving betel nut quid with tobacco. Betel nut quid with Tobacco and Smoking shows a higher proportion of severe dysplasia cases, suggesting a compounding effect of smoking with betel nut quid. There was a significant association between grades of OED and risk factors ( $p < 0.05$ ) (Table 2). This significant relationship highlights the role of specific risk factors in the progression of dysplasia severity, emphasizing the need for targeted preventive measures and clinical awareness of these associations.

The duration of exposure to risk factors was also assessed. Cases with shorter exposure durations predominantly exhibited mild dysplasia, while

those with longer exposure durations developed severe dysplasia. A significant association was observed between the duration of risk factor exposure and the grades of OED ( $p < 0.05$ ) (Table 3), indicating that prolonged exposure to risk factors is strongly correlated with more severe dysplasia.

### Conclusion

This study highlights the significant association between common risk factors, their duration of exposure, and the histopathological grades of oral epithelial dysplasia (OED). Betel nut quid with tobacco was the most frequently associated risk factor across all grades of dysplasia, while the combination of betel nut quid with tobacco and smoking was strongly linked to severe dysplasia, suggesting a compounding effect of smoking. Moreover, longer durations of exposure to risk factors were significantly correlated with the development of severe dysplasia, underscoring the role of chronic exposure in disease progression.

These findings emphasize the importance of identifying and mitigating risk factors through targeted preventive measures and raising clinical awareness to curb the progression of OED to malignancy.

### Acknowledgements

The authors would like to thank Dr. Gautam Kumar Nayak for the support given to this research.

### References

1. Bernard C, Zhang JZ, Klieb H, Blanas N, Xu W, Magalhaes M. Clinical outcomes of oral epithelial dysplasia managed by observation versus excision. *Head & Neck*. 2023;45(12):3096–106.
2. WHO. Head and neck tumours. 5th edition. Lyon: International Agency for Research on Cancer, World Health Organization; 2024. 2 p. (WHO classification of tumours).

3. Hsue SS, Wang WC, Chen CH, Lin CC, Chen YK, Lin LM. Malignant transformation in 1458 patients with potentially malignant oral mucosal disorders: a follow-up study based in a Taiwanese hospital. *Journal of Oral Pathology & Medicine*. 2007;36(1):25–9.
4. Porter S, Gueiros LA, Leão JC, Fedele S. Risk factors and etiopathogenesis of potentially premalignant oral epithelial lesions. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2018 Jun;125(6):603–11.
5. Jaber MA, Porter SR, Gilthorpe MS, Bedi R, Scully C. Risk factors for oral epithelial dysplasia—the role of smoking and alcohol. *Oral Oncology*. 1999.
6. Lee CH, Ko YC, Huang HL, Chao YY, Tsai CC, Shieh TY, et al. The precancer risk of betel quid chewing, tobacco use and alcohol consumption in oral leukoplakia and oral submucous fibrosis in southern Taiwan. *Br J Cancer*. 2003 Feb 10;88(3):366–72.
7. Chung CH, Yang YH, Wang TY, Shieh TY, Warnakulasuriya S. Oral precancerous disorders associated with areca quid chewing, smoking, and alcohol drinking in southern Taiwan. *J Oral Pathol Med*. 2005 Sep;34(8):460–6.
8. Li Y, Hecht SS. Carcinogenic Components of Tobacco and Tobacco Smoke: A 2022 Update. *Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association*. 2022 May 25.
9. Morse DE, Psoter WJ, Cleveland D, Cohen D, Mohit-Tabatabai M, Kosis DL, et al. Smoking and drinking in relation to oral cancer and oral epithelial dysplasia. *Cancer Causes Control*. 2007 Nov 1;18(9):919–29.
10. Li L, Psoter WJ, Buxó CJ, Elias A, Cuadrado L, Morse DE. Smoking and drinking in relation to oral potentially malignant disorders in Puerto Rico: a case-control study. *BMC Cancer*. 2011 Jul 29;11(1):324.
11. Singh S, Singh J, Chandra S, Samadi F. Prevalence of oral cancer and oral epithelial dysplasia among North Indian population: A retrospective institutional study. *J Oral Maxillofac Pathol*. 2020;24(1):87.
12. Pereira J dos S, Carvalho M de V, Henriques ACG, de Queiroz Camara TH, Miguel MC da C, Freitas R de A. Epidemiology and correlation of the clinicopathological features in oral epithelial dysplasia: analysis of 173 cases. *Ann Diagn Pathol*. 2011 Apr;15(2):98–102.
13. Kannan SK, Sherubin JE, Priya MS, H S, Uthappa R, Alnemare AK. Prevalence Of Epithelial Dysplasia In Oral Leukoplakia And Its Clinical Correlation; A Retrospective Study. *Annals of Dental Specialty*. 2019;7(1–2019):6–11.
14. Ellonen R, Suominen A, Kelppe J, Willberg J, Rautava J, Laine H. Histopathological findings of oral epithelial dysplasias and their relation to malignant transformation. *Cancer Treatment and Research Communications*. 2023 Jan 1.
15. Reibel J. Prognosis of oral pre-malignant lesions: significance of clinical, histopathological, and molecular biological characteristics. *Crit Rev Oral Biol Med*. 2003;14(1):47–62.
16. Arduino PG, Surace A, Carbone M, Elia A, Massolini G, Gandolfo S, et al. Outcome of oral dysplasia: a retrospective hospital-based study of 207 patients with a long follow-up. *J Oral Pathology Medicine*. 2009 Jul;38(6):540–4.