Clinical and Histopathological Profile of Tobacco-Associated Oral Mucosal Lesions: A Cross-Sectional Observational Study

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ABSTRACT:

Background: Tobacco use is a major preventable risk factor for oral mucosal diseases and is strongly associated with the development of oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC). The present study aimed to evaluate the clinicopathological spectrum of tobacco-associated oral mucosal lesions and correlate the pattern of tobacco use with histopathological findings in a tertiary care dental hospital.

Methods: A prospective cross-sectional study was conducted at the Department of Oral & Maxillofacial Pathology and Oral Microbiology, Santosh Dental College and Hospital, Ghaziabad, from June 2024 to June 2025. A total of 2,850 patients were screened, of whom 658 were tobacco users. One hundred and forty eligible tobacco users with clinically identifiable oral mucosal lesions were enrolled. Comprehensive clinical examination was performed, and all 160 lesions underwent incisional biopsy followed by histopathological evaluation using hematoxylin and eosin staining. Epithelial dysplasia was graded according to the World Health Organization (WHO) criteria.

Results: Of the 140 participants, 119 (85%) were males and 21 (15%) were females. Smoking was the predominant tobacco habit (62.1%), with cigarette smoking being the most common form (33.5%), followed by beedi smoking (27.1%). Smoker's melanosis (25.6%) and leukoplakia (23.1%) were the most frequently diagnosed lesions, followed by oral submucous fibrosis (OSMF) (10.0%). Histopathological examination of 160 lesions revealed no dysplasia in 75 (46.9%) lesions, mild dysplasia

in 45 (28.1%), moderate dysplasia in 26 (16.2%), and severe dysplasia in 14 (8.8%). Four cases (2.5%) of OSCC identified, comprising two well-differentiated, one moderately differentiated, and one poorly differentiated carcinoma. Erythroplakia and speckled leukoplakia demonstrated the highest frequency of moderate-to-severe epithelial dysplasia.

Conclusion: Tobacco use is associated with a wide spectrum of oral mucosal lesions, including lesions with significant malignant potential. Histopathological evaluation remains indispensable for identifying epithelial dysplasia and guiding early intervention. Regular oral screening of tobacco users, prompt biopsy of suspicious lesions, and effective tobacco cessation strategies are essential to reduce the burden of oral cancer.

Keywords: Epithelial dysplasia, Leukoplakia, Oral mucosal lesions, Oral potentially malignant disorders, Oral squamous cell carcinoma, Oral submucous fibrosis, Tobacco

Introduction

Tobacco use remains a major public health challenge and is recognized as the most important preventable risk factor for diseases affecting the oral cavity. Repeated exposure of the oral mucosa to the carcinogenic constituents of smoked and smokeless tobacco results in cellular injury, oxidative stress, epithelial alterations, and molecular changes that increase the likelihood of developing oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC) [1,2].

India accounts for a substantial proportion of the global tobacco-consuming population, where the use of cigarettes, beedis, khaini, betel quid with tobacco, and other smokeless tobacco products is common. Variations in the type, frequency, and duration of tobacco consumption contribute to differences in the clinical presentation of tobacco-related oral lesions. These lesions include reversible pigmentary and keratotic alterations as well as potentially malignant disorders such as leukoplakia, erythroplakia, speckled leukoplakia, and oral submucous fibrosis (OSMF), which possess varying risks of malignant transformation [3, 4].

Among OPMDs, the probability of progression to malignancy differs according to the clinical subtype and underlying histopathological changes. Erythroplakia and non-homogeneous leukoplakia frequently exhibit higher grades of epithelial dysplasia, whereas OSMF is characterized by progressive fibrosis with an established risk of transformation into invasive carcinoma. Histopathological grading of epithelial dysplasia remains the most reliable method for assessing biological behaviour and estimating the likelihood of malignant progression [5–7].

Early recognition of tobacco-associated oral lesions through comprehensive clinical examination and histopathological confirmation is essential for preventing the development of advanced oral cancer. Although several epidemiological studies have documented the burden of tobacco-related oral lesions in India, regional variations in tobacco habits necessitate institution-based clinicopathological investigations to better understand local disease patterns and associated histological changes [8, 9].

Accordingly, the present prospective cross-sectional study was designed to evaluate the clinicopathological spectrum of tobacco-associated oral mucosal lesions among tobacco users attending a tertiary care dental teaching hospital in northern India. The study assessed the pattern of tobacco consumption, frequency of various oral mucosal lesions, and

histopathological grading of epithelial dysplasia and OSCC, with the objective of generating evidence that may facilitate early diagnosis, risk stratification, and effective tobacco cessation and oral cancer prevention strategies.

Materials & Methods

This prospective, cross-sectional study was conducted at the Department of Oral & Maxillofacial Pathology and Oral Microbiology, Santosh Dental College & Hospital, Ghaziabad, between June 2024 and June 2025, following Institutional Ethical Committee approval. From 2,850 systematically screened patients, 658 tobacco users were identified, of whom 140 met the inclusion criteria: age ≥18 years, documented tobacco use (current or past), and the presence of at least one clinically identifiable oral mucosal lesion. Patients without tobacco habits or without discernible oral lesions were excluded.

Tobacco habits were categorized as smoking (cigarettes, beedis, chillum) or smokeless (khaini, arecanut-tobacco combinations, pan with betel nut and tobacco, tobacco dentifrices), with combined users classified separately. All participants underwent systematic oral examination under standardized illumination. Incisional biopsies were performed under local anesthesia (2% lignocaine with 1:80,000 adrenaline) for all 160 identified lesions. Specimens were fixed in 10% formalin and processed for hematoxylin and eosin staining. Dysplasia was graded as absent, mild, moderate, or severe per World Health Organization (WHO) criteria; OSCC was graded as well-, moderately, or poorly differentiated. Statistical analysis was performed using SPSS v23.0, with significance set at $p < 0.05$.

Results

The cohort comprised 119 males (85%) and 21 females (15%), with mean ages of 44.3 ± 9.1 and 42.7 ± 7.6 years, respectively. Tobacco smoking was the predominant habit in 87 participants (62.1%), exclusive smokeless use was reported by 39 (27.9%), and combined habits were documented in 14 (10%). Among smokers, cigarette use was most frequent (33.5%), followed by beedi smoking (27.1%). Tobacco with lime (khaini) was the leading smokeless form (11.5%), followed by arecanut-tobacco combinations (10.7%). Tables 1–3 summarize the distribution of habits, lesion types, and histopathological grades.

Table 1: Distribution of Tobacco Habits

Tobacco Habit	n	%
Cigarette smoking	47	33.5
Beedi smoking	38	27.1
Chillum	2	1.5
Tobacco with lime (Khaini)	16	11.5
Pan with betel nut and tobacco	7	5.0
Tobacco with arecanut	15	10.7
Tobacco dentifrices	1	0.7
Combined (smoking + smokeless)	14	10.0
Total	140	100

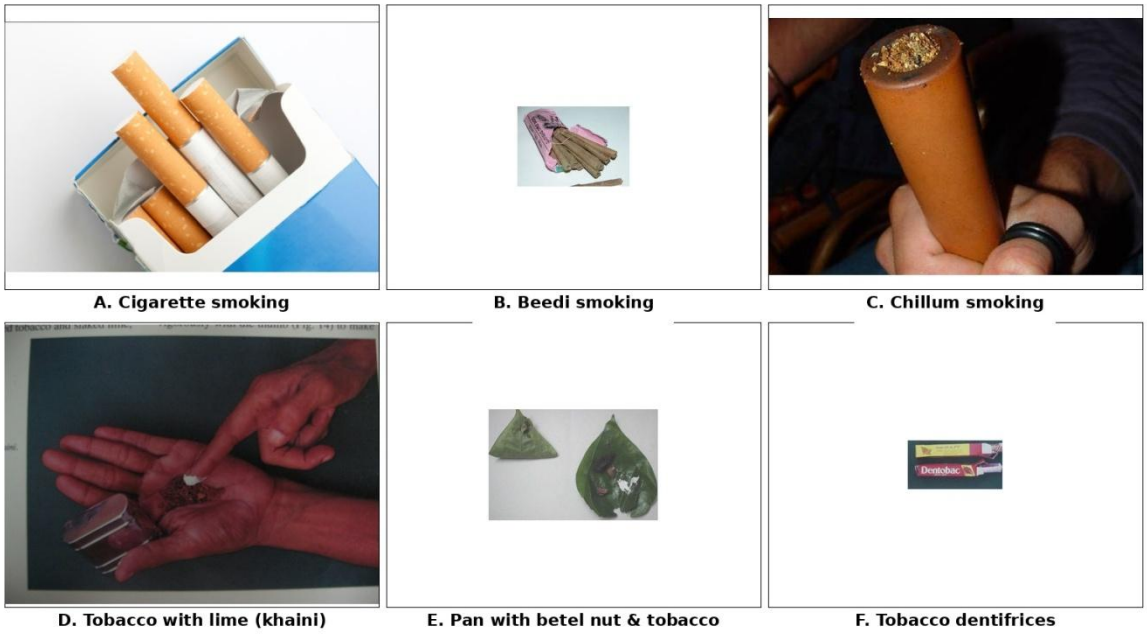

Figure 1: Clinical photographs of tobacco habits observed among the study participants (A) Cigarette smoking, (B) Beedi smoking, (C) Chillum smoking, (D) Tobacco with lime (Khaini), (E) Pan with betel nut and tobacco, (F) Tobacco dentifrices

Table 2: Types and Frequency of Oral Mucosal Lesions

Lesion	n	%
Smoker's Melanosis	41	25.6
Leukoplakia	37	23.1
OSMF	16	10.0
Frictional Keratosis	13	8.1
Speckled Leukoplakia	12	7.5
Smoker's Palate	11	6.9
Erythroplakia	10	6.6
Lichenoid Reaction	8	5.0
Tobacco Pouch Keratosis	7	4.4
OSCC	4	2.5
Total	160	100

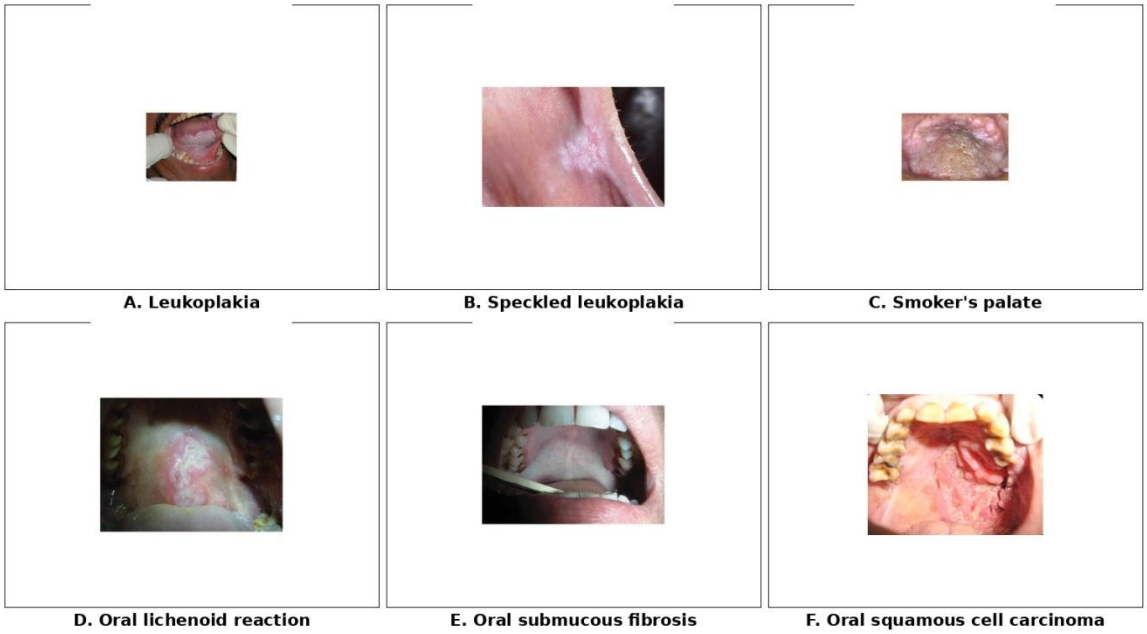

Figure 2: Clinical photographs of tobacco-associated oral mucosal lesions (A) Leukoplakia (B) Speckled leukoplakia (C) Smoker's palate (D) Oral lichenoid reaction (E) OSMF,(F) OSCC

Table 3: Histopathological Grading of Epithelial Dysplasia

Dysplasia Grade	n	%
No Dysplasia	75	46.9
Mild Dysplasia	45	28.1
Moderate Dysplasia	26	16.2
Severe Dysplasia	14	8.8
Total	160	100

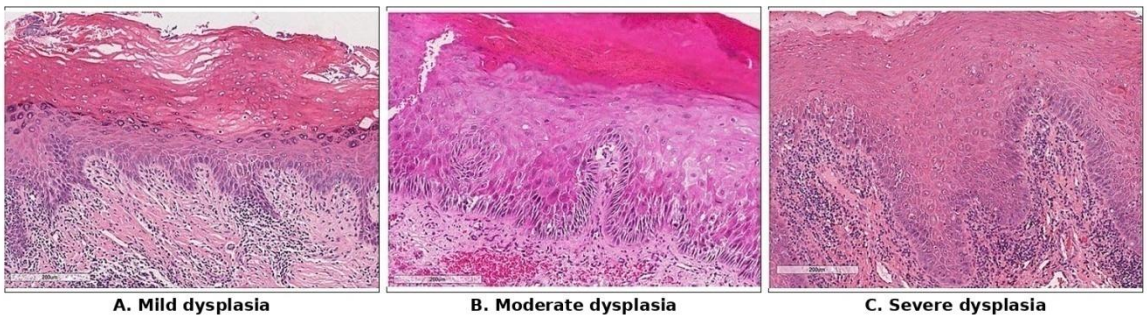

Figure 3: Photomicrographs illustrating histopathological grading of epithelial dysplasia (A) Mild dysplasia (B) Moderate dysplasia (C) Severe dysplasia (H&E stain)

Of the four OSCC cases, two (50%) were well-differentiated, one (25%) moderately differentiated, and one (25%) poorly differentiated. Erythroplakia showed the highest proportion of moderate-to-severe dysplasia, followed by speckled leukoplakia and OSMF. Smokeless tobacco users were overrepresented among severe dysplasia cases.

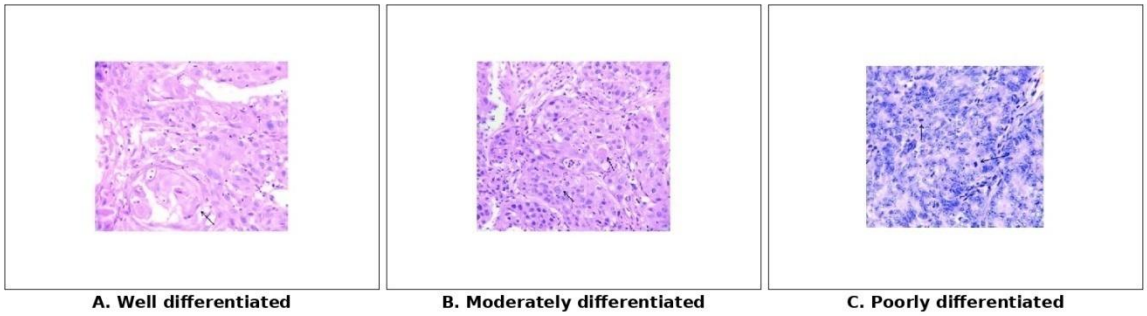

Figure 4: Photomicrographs illustrating histopathological grading of OSCC (A) Well differentiated (B) Moderately differentiated (C) Poorly differentiated (H&E stain)

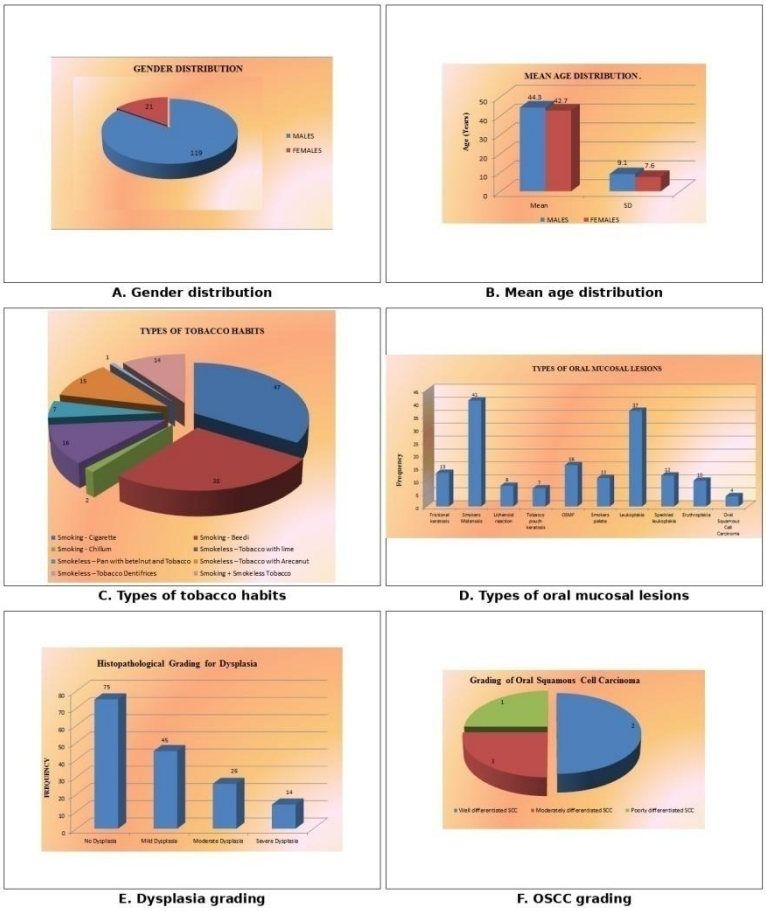

Figure 5: Graphical summary of study findings (A) Gender distribution (B) Mean age distribution (C) Types of tobacco habits (D) Types of oral mucosal lesions (E) Dysplasia grading (F) Grading of OSCC

Discussion

The present study evaluated the clinicopathological characteristics of tobacco-associated oral mucosal lesions among tobacco users attending a tertiary care dental hospital in northern India. The findings demonstrate that tobacco consumption continues to be strongly associated with a wide spectrum of oral mucosal lesions, ranging from benign pigmentary alterations to OPMDs and OSCC. Histopathological examination revealed epithelial dysplasia in more than half of the lesions, highlighting the importance of biopsy and microscopic evaluation for early diagnosis and prevention of malignant transformation.

A marked male predominance (85%) was observed in the present study. This finding is consistent with the observations of Warnakulasuriya et al. (2007) [10], who reported that the higher prevalence of tobacco-associated

oral lesions among males reflects gender differences in tobacco consumption patterns and exposure to established risk factors for OPMDs. The predominance of smoking over smokeless tobacco use, with cigarette smoking exceeding beedi smoking, may also reflect changing tobacco consumption trends in urban and peri-urban populations of northern India.

Smoker's melanosis was the most frequently diagnosed lesion in the present study. This lesion is considered a benign mucosal response to chronic tobacco exposure and results from increased melanin synthesis by basal melanocytes stimulated by tobacco constituents. Although smoker's melanosis has negligible malignant potential, its presence serves as an important clinical indicator of chronic tobacco use and has been reported to regress following cessation of smoking. Such lesions therefore provide clinicians with a useful marker for monitoring behavioural modification and tobacco cessation outcomes (Neville and Day, 2002) [11].

Leukoplakia represented the second most common lesion identified in the study. The biological behaviour of leukoplakia is highly variable and depends on its clinical subtype and histopathological characteristics. According to Warnakulasuriya et al. (2007) [10], leukoplakia is the most common OPMD, while non-homogeneous variants such as speckled leukoplakia possess a substantially greater risk of malignant transformation than homogeneous lesions. In the present study, speckled leukoplakia exhibited a greater proportion of moderate-to-severe epithelial dysplasia, emphasizing the need for careful surveillance and early biopsy of these lesions.

OSMF was observed exclusively among smokeless tobacco users and individuals consuming areca nut-containing preparations. The disease is characterized by progressive fibrosis of the oral mucosa resulting from arecoline-induced stimulation of fibroblasts and excessive collagen deposition. van der Waal (2009) [12] described OSMF as one of the most clinically significant OPMDs because of its irreversible nature and recognized malignant transformation potential. The occurrence of OSMF exclusively among smokeless tobacco users in the present study further supports the established etiological role of areca nut and smokeless tobacco products.

More than half (53.1%) of the lesions in the present study demonstrated epithelial dysplasia, including 8.8% with severe dysplasia. These findings indicate a substantial burden of premalignant epithelial change among chronic tobacco users. Reibel (2003) [13] emphasized that histopathological grading of epithelial dysplasia remains the most reliable predictor of malignant transformation, despite the contribution of emerging molecular biomarkers. Similarly, the WHO classification proposed by Warnakulasuriya et al. (2007) [10] recognizes epithelial dysplasia as the cornerstone for risk assessment and clinical decision-making in OPMDs.

Four cases of OSCC were diagnosed during the study period, with most occurring in individuals with smokeless tobacco habits. This observation is consistent with the findings of Neville and Day (2002) [11], who reported that prolonged exposure to tobacco-specific carcinogens, particularly nitrosamines present in smokeless tobacco products, plays a central role in oral carcinogenesis through cumulative genetic and epigenetic alterations.

The findings of the present study reinforce the importance of comprehensive oral screening among individuals with tobacco habits. Mehrotra and Gupta (2011) [14] highlighted that early recognition of OPMDs, combined with histopathological confirmation, significantly improves opportunities for early intervention and enhances patient survival by facilitating diagnosis before progression to invasive carcinoma. Likewise, the landmark community-based randomized trial conducted by Sankaranarayanan et al. (2005) [15] demonstrated that systematic oral visual screening among high-risk tobacco users significantly reduced oral cancer mortality, supporting the implementation of organized

screening programmes in populations with a high prevalence of tobacco use.

Limitations

The findings of this study should be interpreted in light of several limitations. Since the investigation was carried out at a single tertiary care centre and included a relatively limited number of participants, the results may not be representative of the wider population of tobacco users. Moreover, only patients with clinically detectable oral mucosal lesions were enrolled, which may have introduced selection bias. The cross-sectional nature of the study further restricted the evaluation to a single time point, preventing assessment of lesion progression, recurrence, or malignant transformation over time.

Information regarding tobacco use was obtained through participant self-reporting and, therefore, may have been influenced by recall errors or underreporting. Additionally, the study did not comprehensively quantify tobacco exposure in terms of duration, frequency, or cumulative lifetime use. Several other variables known to influence the occurrence and progression of oral mucosal lesions, including alcohol intake, nutritional deficiencies, viral infections, socioeconomic factors, and genetic susceptibility, were beyond the scope of the present investigation. Advanced laboratory techniques, such as molecular biomarker assessment and immunohistochemical evaluation, were also not incorporated, limiting insights into the biological characteristics and malignant potential of the lesions.

Future research should focus on well-designed multicentre prospective studies with larger and more heterogeneous populations, extended follow-up periods, and community-based participant recruitment. The inclusion of molecular and immunohistochemical markers, together with comprehensive assessment of behavioural and biological risk factors, would facilitate more accurate risk stratification and improve understanding of the pathogenesis and malignant transformation potential of tobacco-associated oral mucosal lesions.

Conclusion

The findings of the present study highlight the substantial impact of both smoked and smokeless tobacco on oral mucosal health, with a considerable proportion of lesions exhibiting epithelial dysplasia and a small but clinically important number of cases diagnosed as OSCC. These observations emphasize the importance of routine oral examination of tobacco users, timely biopsy of clinically suspicious lesions, and histopathological assessment for early identification of potentially malignant changes. Strengthening tobacco cessation initiatives, increasing public awareness, and implementing targeted screening programs, particularly in regions with a high prevalence of tobacco use, may contribute to earlier diagnosis and a reduction in the burden of tobacco-associated oral cancer.

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