



# Malignant transformation in oral epithelial dysplastic lesions: An observational study

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## ABSTRACT

**Introduction:** This research study is a comprehensive analysis of cases oral epithelial dysplasia (OED) to oral squamous cell carcinoma (OSCC) over the past decade, with a particular focus on eliciting the frequency of malignant transformation (MT) of OED within this group of 328 patients in a tertiary center of Karnataka. Aim of this study is to investigate the likely correlation between OSCC and OED with demographic details, clinical parameters, and risk factors, highlighting the frequency of MT of OED to OSCC.

**Methods:** This study, retrospectively analyses 328 cases of OSCC (n = 236) and OED (92) using the medical records of the patients over 10 years, out of which 29 cases of OED had undergone MT. Statistical analysis was conducted using the Chi-square and Wilcoxon rank sum tests.

**Results:** The median IQR of MT (n = 29) was found to be 34 months (within a range from 27 to 38 months). 51.7% of dysplastic cases had transformed into well-differentiated squamous cell carcinoma and 48.3% of dysplastic cases had transformed into moderately differentiated squamous cell carcinoma the risk of cancer increased with severe dysplasia, the median age was found to be 54, which was prevalent in the buccal mucosa and male patients with a habit history.

**Conclusion:** Severe dysplasia could serve as a significant indicator for evaluating MT risk in patients with potentially malignant lesions; Moreover, our data indicated that patients with OED require long-term monitoring and clinical follow-up, thereby aiding in early intervention.

**Keywords:** Carcinoma; squamous cell; mouth neoplasms; hyperplasia

## INTRODUCTION

Oral cancer is the sixth leading cause of cancer-related deaths globally having a survival rate of around 50% within 5 years despite the progress made in treatment modalities during the past 30 years (1). The pathogenesis of oral squamous cell carcinoma (OSCC) is a complex process that involves various stages, starting from alterations in the normal oral mucosa and culminating in invasive cancer and metastasis (2). The development of OSCC is often preceded by dysplastic changes which is crucial for early diagnosis and for better outcomes. Risk factors include tobacco use, alcohol consumption, HPV infections, chronic inflammation, UV radiation, immunosuppression, genetic predisposition, and dietary factors (3).

Our study aims to elucidate the duration of malignant transformation (MT) of oral epithelial dysplasia (OED)

in patients who reported to a tertiary health care center in Karnataka, their demographic details, and the association of time of MT of OED to OSCC. This study offers a pioneering analysis of the MT of OED into OSCC within a substantial cohort of 328 patients in a tertiary healthcare center, from Karnataka, India. Its primary contribution lies in elucidating the frequency and temporal dynamics of MT, revealing a median transformation duration of 34 months (about 3 years). The research identifies severe dysplasia as a significant indicator for MT and enhances our understanding on the prevalence and demographic correlations, such as age, gender, and lifestyle habits, of OED and OSCC. The study's emphasis on rigorous long-term monitoring and follow-up protocols for OED patients represents a significant advancement, facilitating earlier intervention and improved clinical outcomes for potentially malignant lesions. By focusing on the Indian population, this research provides critical context-specific data that can help in the targeted prevention and intervention strategies. It underscores the necessity of habit cessation programs and the consideration of local irritational factors, often underappreciated yet influential in the progression of oral cancer. The rigorous

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statistical methodologies employed, and the detailed examination of clinical parameters further underscore the study's intellectual merit, offering substantial contributions to the field's understanding and management of OED and OSCC within high-risk populations.

## METHODS

This study was conducted after obtaining ethical approval from the Kasturba Medical College and Kasturba Hospital, Institutional Ethics Committee (IEC2 111/23).

A retrospective analysis was carried out on all the histopathological diagnosed cases of OED and OSCC in the Department of Oral and Maxillofacial Pathology and Oral Microbiology. The grading was according to diagnostic criteria mentioned in the fourth edition of the World Health Organization classification of head-and-neck Tumors (4). Histopathologic data of OSCC was divided into 3 grades: well-differentiated squamous cell carcinoma (ICD-O-3,8071/3), moderately differentiated squamous cell carcinoma (ICD-O-3, 8070/3), and poorly differentiated squamous cell carcinoma (ICD-O-3, 8074/3) and OED cases were graded as: Minimal/mild dysplasia (ICD-O-3, 8077/0), moderate dysplasia (ICD-O-3, 8077/1) and severe dysplasia/carcinoma-*in-situ* (ICD-O-3, 8077/2), that were reported in the past 10 years. An organized data collection document was prepared to gather and compile the information of each patient. The medical records were assessed in terms of frequency/duration of MT (OED to OSCC), age, gender, site mainly buccal mucosa (ICD-O-3, C06.0), lip (ICD-O-3, C00.9), tongue (ICD-O-3, C02.9), palate (ICD-O-3, C05.0) gingiva (ICD-O-3, C03.9), and also looked for any associated local irritating factors such as ill-fitting dentures, sharp tooth, and overhanging restorations. The recurrent cases of OSCC were excluded. Incomplete records and scattered data were excluded from the study.

Statistical analysis was carried out using Jamovi (version 2.3) software. Descriptive statistics were used to examine the distribution of OED, OED transforming into malignancy, and OSCC cases by patients' gender and age at diagnosis, habit history where available, site of lesion, histologic diagnosis, treatment, and outcome. Continuous variables were reported as median IQR whereas categorical variables were reported as counts and percentages. The frequency of cases that progressed to cancer (Yes/No) and the time to progression were calculated. The association of categorical variables across OED and OSCC categories was examined using the Chi-square test. Wilcoxon rank sum test was done to compare the medians across the categories of OED and OSCC.

## RESULTS

The analysis of age across the three grades of OED (n = 63) revealed the median age for mild dysplasia to be 55 years (with a range of 49-63), for moderate dysplasia, it was 60 years (ranging from 50 to 65), and for severe dysplasia, it was 60 (with a range of 52-68). The *p*-value was 0.45 and the *q* value was found to be 0.75. Whereas in the analysis of OSCC (n = 236) well-differentiated squamous cell carcinoma (WDSCC), patients (n = 91, 39%) had a median age of 62 years (with the range of 50-70),

moderately differentiated squamous cell carcinoma (MDSCC) (n = 131, 5%) had a slightly lower median age of 60 years (with a range of 52-69), and poorly differentiated squamous cell carcinoma (PDSCC) patients (n = 14, 5.9%) exhibited the median age of 51 years (with a range of 45-56). The overall *p*-value was found to be 0.022 and a *q*-value of 0.043.

The gender distribution in our study for OED showed male predominance in all three grades compared to females with a *p* = 0.22 and a *q*-value was 0.75. Correspondingly, the gender distribution for OSCC (n = 236) also showed male predominance compared to females with a significant difference (*p* = 0.015).

Regarding habit history, in patients with mild dysplasia (n = 21, 33%), 29% used areca (n = 6). In moderate dysplasia (n = 29, 46%), the combination of all three habits (n = 7, smoking, areca, gutka) was maximum. Conversely, patients with severe dysplasia (n = 13, 21%) also showed the prevalence of all three habits (n = 4) in 31% of patients. In patients who presented with OSCC (n = 236), WDSCC group (n = 91, 39%), and PDSCC (n = 3, 21%) the combination of all three habits predominated. In the MDSCC group (n = 131, 56%), the majority 24% (n = 31) had a history of areca chewing.

Concerning the site, the majority of OED was found on buccal mucosa (46-76%), with a decreasing trend observed in other anatomical sites, *p*-value being 0.77 and the *q* value was 0.94. The patients with OSCC (n = 236) also had the majority of the lesions on the buccal mucosa (50-67%), the overall *p*-value was found to be 0.55 and the *q* value was 0.71.

Out of 236 OSCC cases, in WDSCC, the distribution across stages was 20% (n = 18) in TNM (Tumor Node Metastasis) Stage 1, 31% (n = 28) in Stage 2, 34% (n = 31) in Stage 3, and 15% (n = 14) in Stage 4. Similarly, in MDSCC, the distribution across stages was, 13% (n = 17) in Stage 1, 35% (n = 4) in Stage 2, 31% (n = 40) in Stage 3, and 21% (n = 28) in Stage 4. Conversely, PDSCC exhibited 14% (n = 2) stage 1, 29% (n = 4) in Stage 2, 3% (n = 6) Stage 3 and 14% (n = 2) in Stage 4.

The treatment of choice for dysplasia was wide local excision. For OSCC (n = 91, 39%), 23% of cases (n = 21) of WDSCC had undergone surgery, and 77% (n = 70) were treated with surgery and adjunct therapy (chemotherapy/radiotherapy). In MDSCC (n = 131, 56%), surgery with adjunct therapy was employed, representing 71% (n = 93) of cases, while surgery alone accounted for 29% (n = 38). Similarly, for PDSCC (n = 14, 5.9%), in the majority of cases, 71%, (n = 10) underwent surgery with adjunct therapy, with surgery alone comprising 29% (n = 4).

In the total sample size of 63 cases of OED, in mild dysplasia (n = 21, 33%), 48% showed good prognosis (n = 10), and 4.8% (n = 4) presented with recurrence and there was a loss of follow-up for 48% of cases with mild dysplasia (n = 10). In moderate dysplasia (n = 29, 46%), 59% had a good prognosis and 3.4 showed recurrence (n = 3.4), there was a loss of follow-up in 38% of cases (n = 11). In severe dysplasia, 46% showed loss to follow-up, 54% (n = 7) showed good prognosis and there was a loss of follow-up of 46% (n = 6). The overall *p*-value and *q*-value are 0.94.

In OSCC (n = 236), for WDSCC (n = 91, 39%) 45% of cases had good outcomes (n = 41), while 46% were lost to follow-up (n = 42). In MDSCC (n = 131, 56%) 37% had a good outcome (n = 49) and there was a loss of follow-up of 58% cases (n = 76). For PDSCC a substantial 21% (n = 3) of cases resulted in death, indicating a more unfavorable prognosis compared to the other groups. 36% had a good prognosis (n = 5) and 43% (n = 6) had lost the follow-up. The overall *p*-value for OSCC was found to be 0.004 and the value was 0.025 (Tables 1 and 2).

Association between transformed cases of OED to OSCC and demographic details.

In this retrospective study, out of 328 cases that were retrieved, 236 cases were reported with OSCC, 92 cases were of OED, out of which 29 cases had undergone MT. In our study, we observed 41.7% (n = 5) of cases of moderate dysplasia cases transformed into WDSCC and 58.3% (n = 7) transformed to MDSCC. For severe dysplasia, 62.5% (n = 10) transformed into WDSCC, and 37.5% (n = 6) transformed to MDSCC. The results of the Chi-square test gave a *p* = 0.316. The median IQR for the transformation of OED cases to OSCC was found to be 34 months (with a range of 27-38). The *p*-value was found to be 0.88 and the value was >0.99.

The median IQR for age was found to be 58 (with a range of 44-62) with a *p*-value being >0.99 and q value of 0.99. Male predilection was observed with 80% (n = 12) transformed to Well differentiated OSCC and 71% (n = 10) transformed to MDSCC. Among females, the distribution was found to be 20% (n = 3) transformed to WDSCC and 29% (n = 4) transformed to MDSCC. The overall *p*-value was 0.68 and the value was >0.99.

The majority of the transformed cases were associated with the habit history. 57% (n = 8) of cases had transformed

to MDSCC, and 33% (n = 5) transformed to WDSCC, the history of areca nut was noted. This was followed by the usage of Gutka 33% (n = 5, transformed to WDSCC), and 21% (n = 3, transformed to MDSCC), smoking 13% (n = 2, transformed to WDSCC) and 7.1% (transformed to MDSCC), a combination of all habits comprised of 6.7% (n = 1, transformed to WDSCC) and 7.1% (n = 1, transformed to MDSCC). About 3 cases did not give any habit history showing the transformation into malignancy (13% n = 2 - WDSCC, 7.1% n = 1 - MDSCC). The overall *p*-value was found to be 0.81 and the q-value was >0.99.

The most common site was buccal mucosa for the cases transformed into MDSCC (79%, n = 11) and WDSCC (67%, n = 10). The 2<sup>nd</sup> most common site was tongue, 33% (n = 5) had transformed into WDSCC and 14% (n = 2) had transformed into MDSCC. In 7.1% (n = 1), palate was involved. The overall *p*-value was 0.39 and the q value was >0.99.

The mode of treatment was surgery with adjunct therapy (67%), follow-up was lost for a few of the patients, 36% of cases showed good prognosis. The *p*-value associated with these outcome distributions is 0.45 and the q-value was found to be >0.99 (Table 3).

## DISCUSSION

In the present study, comprising 328 cases (OED = 92, OSCC = 236), the prime focus was to find the mean duration of MT of OED to OSCC (n = 29). We found the median IQR of MT to be 34 months (range of 27-38 months). Severe dysplastic lesions had a high risk for MT. Majority of the malignant transformed cases were seen in males, having habit history, and were more prevalent in patients with the usage of areca. The buccal mucosa was found to be the most common site, with some cases

**TABLE 1.** Association of OED with the clinical parameters

Characteristic	n	Mild dysplasia=21 (33%)	Moderate dysplasia=29 (46%)	Severe dysplasia=13 (21%)	<i>p</i> -value	q-value
Age	63	55 (49, 63)	60 (50, 65)	60 (52, 68)	0.45	0.75
Gender	63				0.22	0.75
Male		14 (67)	25 (86)	9 (69)		
Female		7 (33)	4 (14)	4 (31)		
Habits	63				0.37	0.75
NO habits		3 (14)	4 (14)	4 (31)		
Areca		6 (29)	8 (28)	0 (0)		
Ghutka		3 (14)	5 (17)	4 (31)		
Smoking		5 (24)	5 (17)	1 (7.7)		
All 3 habits		4 (19)	7 (24)	4 (31)		
Site	63				0.77	0.94
Buccal mucosa		16 (76)	20 (69)	8 (62)		
Tongue		4 (19)	6 (21)	2 (15)		
Lip		1 (4.8)	2 (6.9)	1 (7.7)		
Palate		0 (0)	0 (0)	1 (7.7)		
Gingiva		0 (0)	1 (3.4)	1 (7.7)		
Rx	63					
Wide local excision		21 (100)	29 (100)	13 (100)		
Outcome	63				0.94	0.94
Lost follow up		10 (48)	11 (38)	6 (46)		
Good		10 (48)	17 (59)	7 (54)		
Recurrent		1 (4.8)	1 (3.4)	0 (0)		

OED: Oral epithelial dysplasia, n: Number of cases, *p*-value: Probability value, q value: False discovery rate

**TABLE 2.** Association of SCC with clinical parameters

Characteristic		1N-Well differentiated Squamous cell carcinoma=91 (39%)	2N-moderately differentiated squamous cell carcinoma=131 (56%)	3 N- Poorly differentiated squamous cell carcinoma=14 (5.9%)	p-value	q-value
Age	236	62 (50, 70)	60 (52, 69)	51 (45, 56)	0.022	0.043
Gender	236				0.015	0.043
Male		66 (73)	114 (87)	13 (93)		
Female		25 (27)	17 (13)	1 (7.1)		
Habits	236					
No habits		20 (22)	26 (20)	5 (36)		
Areca		18 (20)	31 (24)	0 (0)		
Ghutka		17 (19)	28 (21)	5 (36)		
Smoking		11 (12)	22 (17)	1 (7.1)		
All 3 habits		25 (27)	24 (18)	3 (21)		
Site	236				0.55	0.71
Buccal mucosa		55 (60)	88 (67)	7 (50)		
Tongue		28 (31)	38 (29)	7 (50)		
Lip		1 (1.1)	0 (0)	0 (0)		
Palate		4 (4.4)	3 (2.3)	0 (0)		
Gingiva		3 (3.3)	2 (1.5)	0 (0)		
Rx	236				0.60	0.71
Surgery		21 (23)	38 (29)	4 (29)		
Surgery with adjunct therapy		70 (77)	93 (71)	10 (71)		
Outcome	236				0.004	0.025
Lost follow up		42 (46)	76 (58)	6 (43)		
Good		41 (45)	49 (37)	5 (36)		
Recurrent		6 (6.6)	0 (0)	0 (0)		
Metastasis		0 (0)	2 (1.5)	0 (0)		
Died		2 (2.2)	4 (3.1)	3 (21)		
TNM	236				0.71	0.71
Stage 1		18 (20)	17 (13)	2 (14)		
Stage-2		28 (31)	46 (35)	4 (29)		
Stage-3		31 (34)	40 (31)	6 (43)		
Stage 4		14 (15)	28 (21)	2 (14)		

OSCC: Oral squamous cell carcinoma, WDSCC: Well differentiates squamous cell carcinoma, MDSCC: Moderately differentiated squamous cell carcinoma, PDSCC: Poorly differentiated squamous cell carcinoma, n: Number of cases, p-value: Probability value, q-value: False discovery rate

**TABLE 3.** Characteristics of OED cases that have transformed into malignancy

Dysplasia	OSCC		
	Well differentiated squamous cell carcinoma	Moderately differentiated squamous cell carcinoma	Total
Mild dysplasia			
Observed	0	1	1
% within row	0.0%	100.0%	100.0%
Moderate dysplasia			
Observed	5	7	12
% within row	41.7%	58.3%	100.0%
Severe dysplasia			
Observed	10	6	16
% within row	62.5%	37.5%	100.0%
Total			
Observed	15	14	29
% within row	51.7%	48.3%	100.0%

OED: Oral epithelial dysplasia, WDSCC: Well differentiates squamous cell carcinoma, MDSCC: Moderately differentiated squamous cell carcinoma, n: Number of cases, p: Probability value, q-value: False discovery rate

associated with long-term local irritational factors such as sharp tooth and ill-fitting restorations. The findings of

our study are in concordance with in the study by Kierce et al. (2020), involving 201 cases with a 17% dysplasia rate over a mean follow-up of 33.4 months, factors such as the degree of dysplasia, smoking habits, and history were found to be significant in lesions occurring on the ventrolateral tongue (1).

McCord et al. (5) in their study population (n = 5036) found the rate of MT to be 6.4% (322/5,036 cases). The mean time for cancer development was 51.2 months. 33.6% of cases (107/322) progressed after over 60 months. The MT rate was found to be highest in the tongue (11.4%), followed by the floor of mouth (7.1%) and gingiva.

Similar findings were noted in the study done by Nevanpaa et al. (6) where they found OED patients had a 44.7-fold higher risk (95%) of developing OSCC than the general population they also found that the risk was at its highest within 2 years of OED diagnosis with a mean follow-up of 5.5 (range 0.1-29.0) years 10.9% of OED patients developed OSCC.

Jaber and Elameen (7) in their retrospective study on 359 patients with histologically confirmed OED found twenty (5.5%) of the 359 patients developed an invasive squamous cell carcinoma (SCC) of the oral mucosa over

a period of 2-274 months with mean transformation time of 3.3 years. The risk was higher in patients older than 50 years and floor of mouth was the common site.

Mahmood et al. (2022) developed models predicting MT (AUC 0.86) and recurrence (AUC 0.81) in OED using 120 cases, leveraging architectural and cytological features (8).

Tovaru et al. (9) conducted a corresponding study, noting that 7.5% of nine cases of epithelial dysplasia underwent a MT over a mean period of 75 months. This transformation encompassed both treated and untreated patients. The patients mean age was 65.4 years. Similarly, Chuang et al. (10) reported the average time for transformation as 5.7 years. The summary of the comparison of our study results with other previous studies also the comparison of same and different points of our study and other studies is mentioned in Tables 4 and 5.

The strengths of our study contribute significantly to the understanding of Oculopharyngeal Muscular Dystrophy (OPMD) and their MT. The inclusion of a substantial

cohort of 328 cases provides a robust dataset for analysis, offering a comprehensive view of the trends and patterns within this specific population. The longitudinal design, spanning a decade, allows for the observation of changes over time, enhancing the study's depth and providing valuable temporal insights into the progression of OED to OSCC. Other than the habit history, another important factor the clinician has to look for is, local irritating factors such as long-term exposure to the sharp tooth, overhanging restorations, and ill-fitting dentures that may have an overall influence on the general health of the patient. In our study, we found buccal mucosa to be the most common site. The buccal mucosa is associated with cheek biting due to certain irritational factors (sharp tooth, ill-fitting restorations). Studies have shown that chronic irritational factors do play a role in oral cancer, they may not be able to produce genetic mutations by themselves but may promote epigenetic changes that ultimately inhibit DNA repair and apoptosis. That is if the cancer has started from other causes, these irritational factors could accelerate the process. Thus, suggesting that

**TABLE 4.** Comparison of our study results with other previous studies

Study	Sample size (OED/OSCC)	MT rate (%)	MT duration	Risk factors identified	Common sites
Present study	328 (92/236)	31.5% (29/92)	Median 34 months (27-38 months)	Severe dysplasia, male gender, habit history (areca chewing), and local irritational factors	Buccal mucosa
Kierce et al. (1),(2020)	201	17%	33.4 months	Degree of dysplasia, smoking, habit history	Ventrolateral surface of tongue
McCord et al. (5) (2023)	5036	6.4% (322/5036)	Mean 51.2 months	Severe dysplasia, habits	Tongue (11.4%), floor of mouth (7.1%)
Nevanpaa et al. (6) (2022)	Not specified	10.9%	Mean 5.5 years (0.1-29 years)	Severe dysplasia, high risk within 2 years post-OED diagnosis	Not specified
Jaber et al. (7) (2021)	359	5.5% (20/359)	Mean 3.3 years (2-274 months)	Older age (>50 years), severe dysplasia	Floor of mouth
Tovaru et al. (9) (2023)	9	7.5% (9/120)	Mean 75 months	Treated and untreated patients	Not specified
Chuang et al. (10) (2015)	8501	8.4%	Mean 5.7 years	Alcohol, Betel Quid consumption	Buccal Mucosa

**TABLE 5.** Comparison of the details of our study at the same and the different points to the previous studies

Category	Similarities	Differences
Risk factors	Severe dysplasia identified as a critical MT risk factor. Similar findings were noted by Kierce et al. (1), Nevanpaa et al. (6) and Jaber et al. (7)	Higher MT rate in this study (31.5%) compared to McCord et al. (5) (6.4%) and Nevanpaa et al. (6) (10.9%)
Habit history	Common risk factors like areca nut chewing, tobacco use, and alcohol consumption noted across studies by McCord et al. (5)	Not mentioned
Gender predilection	Male predominance in MT cases noted across studies.	Male predominance seen in other studies as well (Kierce et al. (1) Jaber et al. (7))
Common sites of MT	Buccal mucosa as the most frequent transformation site.	Differences in common sites: McCord et al. (5) and Jaber et al. (7) noted the tongue and floor of the mouth as higher-risk sites, possibly due to regional oral habits.
MT duration	Median MT duration (34 months) aligns with Chuang et al. (10), 33.6 months and Jaber et al. (7), 3.3 years.	Follow-up periods varied significantly: McCord et al. (5) (51.2 months), Tovaru et al. (9) (75 months), potentially missing late-stage transformations in this study.
Chronic irritational factors	Chronic irritants like sharp teeth and ill-fitting restorations identified as promoters of MT, was persistent with study by Tovaru et al. (9)	None noted in this category
Prevalence of high-grade dysplasia	Severe dysplasia consistently found to be a high-risk factor for MT.	Severe dysplasia -as high risk factor noted in other studies as well Kierce et al. (1) Nevanpaa et al. (6) Jaber et al. (7)
Role of age	Older age recognized as a risk factor in previous studies (Jaber et al., (7) Nevanpaa et al. (6))	Present study observed median age of 54 years for MT, possibly due to early exposure to areca nut and other risk factors in the Indian population.

these factors could act as promoters in the progression of oral cancer (11).

Our study's specific focus on MT rates distinguishes it, shedding light on a critical aspect of OED that may inform clinical practice. The statistical analyses applied add rigor to our findings, establishing a quantitative foundation for the observed trends. Moreover, the identification of risk factors and associations with clinical parameters, such as age, gender, site, and TNM staging, provides a nuanced understanding of the multifaceted nature of these oral lesions. The clinical relevance of our findings is underscored by the emphasis on long-term monitoring and follow-up for patients with potentially malignant lesions, aiding in early intervention. This aspect of the study holds practical implications for healthcare practitioners and reinforces the importance of vigilant clinical management.

Despite the strengths of our study, some limitations need consideration. The retrospective design, inherent to our approach, introduces potential biases due to reliance on historical data, and the accuracy and completeness of past medical records may vary. In addition, the study's single-centre focus on a tertiary center in Karnataka raises concerns about the generalizability of our results to broader populations. Furthermore, a larger sample size could provide more robust statistical power and strengthen the reliability of our analyses. Finally, the study's 10-year timeframe and cases lost to follow-up might not capture longer-term trends or changes in clinical practices, limiting the scope of our insights.

## CONCLUSION

This study contributes to the existing knowledge by providing data on the specific context of the Indian population, potentially guiding targeted prevention and intervention strategies. The study emphasizes the importance of continued research on habit cessation interventions as well as the local irritating factors for high-risk individuals with OED. To conclude, this study underscores the significance of OED as a precursor to oral cancer. By concentrating on high-risk groups (severe dysplasia) personalized treatment approaches, effective habit cessation programs, giving importance to the chronic irritating factors and public awareness campaigns, we can envision a future where OED is effectively managed, and the risk of MT significantly reduced.

## Key insights and implications

1. High-risk factors: Our study identifies males with a history of tobacco and/or areca use, and those with OED on the buccal mucosa, as facing a heightened risk of MT. This emphasizes the necessity for targeted prevention efforts, particularly among these high-risk groups. Tailored campaigns promoting tobacco and areca cessation should be prioritized.
2. Transformation rate and duration: The median time for OED to progress into OSCC was 34 months, highlighting the significance of regular follow-up and close monitoring of OED patients. Establishing effective surveillance protocols with intervals tailored to

individual risk profiles is important for early detection of potential cancer development.

3. Habit history and chronic irritating factors: Consistent with prior research, our data underscores the challenge of modifying tobacco and alcohol habits along with the equal importance to be given to local irritating factors such as sharp tooth and defective restorations. Developing and implementing effective habit cessation interventions specifically targeted at high-risk OED patients is essential for reducing their risk of MT.

## Future directions

### *Continued research*

More comprehensive studies are required to deepen our understanding of the intricate mechanisms underlying OED progression to OSCC. This will pave the way for the development of new and advanced predictive tools and targeted therapeutic interventions.

### *Personalized medicine*

Future research should concentrate on personalized medicine approaches for OED management, taking into account individual risk factors, genetic susceptibility, and molecular pathways involved in MT. Tailoring treatment plans based on these insights can potentially enhance patient outcomes.

### *Habit cessation interventions*

Effective programs tailored to the Indian context and addressing cultural aspects of tobacco and areca use are necessary to support behavioral change among high-risk populations. Developing accessible and culturally sensitive interventions will be crucial for long-term success.

### *Public awareness*

Raising public awareness about OED, its risk factors, and the importance of early detection through regular oral examinations is critical for promoting early diagnosis and timely intervention.

## DECLARATION OF INTERESTS

Authors declare no conflict of interest.

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