

Clinical Presentation And Risk Factors Of Oral Squamous Cell Carcinoma Patients In Karachi, A Multicenter Cross-Sectional Study

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ABSTRACT

Background: Oral Squamous Cell Carcinoma (OSCC) is the most common malignancy of the oral cavity and ranks among the leading cancers in South Asia. Pakistan carries a high burden due to widespread use of smokeless tobacco, areca nut and delayed presentation.

Objectives: To evaluate the clinical presentation and associated risk factors of OSCC patients presenting at Darul Sehat Hospital, Jinnah Postgraduate Medical Centre (JPMC), and Dow International Dental College (DIDC), Karachi.

Methods: A multicenter cross-sectional study (January–June 2025) of histopathologically confirmed OSCC patients (N = 366). Demographic, exposure and clinical data were collected via structured questionnaire and record review. Data were analyzed with SPSS v22; descriptive statistics, chi-square tests, and multivariable logistic regression were applied; significance set at $p < 0.05$.

Results: Mean age was 52.4 ± 12.3 years; 71% were male. Most common sites were buccal mucosa (39.9%) and tongue (30.1%). Major risk factor were smokeless tobacco (63.4%), areca nut (52.7%), cigarette smoking (37.2%), and poor oral hygiene (69.4%). Late-stage presentation (III–IV) occurred in 68% of cases. Smokeless tobacco use was strongly associated with buccal mucosa lesions ($p < 0.001$), cigarette smoking with tongue lesions ($p = 0.02$), and low education with late-stage disease ($p < 0.001$). Multivariable regression showed smokeless tobacco (aOR=1.9, $p = 0.01$), areca nut (aOR=1.8, $p = 0.03$), and low education (aOR=2.2, $p = 0.001$) significantly predicted late-stage disease.

Conclusion: High prevalence of smokeless tobacco/areca nut use and frequent late-stage presentation highlight the need for targeted prevention and early-detection programs in Karachi.

Keywords: Oral Squamous Cell Carcinoma, Risk Factors, Karachi, Clinical Presentation, Betel Nut

1. INTRODUCTION

Oral Squamous Cell Carcinoma (OSCC) accounts for over 90% of all oral malignancies and represents a major public health challenge in low- and middle-income countries [1]. According to GLOBOCAN 2020, OSCC is the second most common cancer in South Asia, with Pakistan showing particularly high incidence due to the widespread use of areca nut (gutka, betel quid) and smokeless tobacco products [2].

In Pakistan, OSCC ranks among the top three cancers, with Karachi reporting alarming rates across younger populations as well [3]. Risk factors such as tobacco chewing, cigarette smoking, alcohol, poor diet, and viral infections (HPV) contribute

significantly to disease progression [4].

Clinical presentation varies but commonly includes non-healing ulcers, leukoplakia, erythroplakia, difficulty in mastication, speech impairment, and pain [5]. Despite improvements in diagnostic modalities, late-stage presentation remains common, leading to poor prognosis and survival outcomes [6].

Karachi being the largest metropolitan city of Pakistan, reflects a unique sociocultural environment that influences OSCC epidemiology. Despite this knowledge, late-stage presentation is common, worsening survival outcomes. Local hospital-based studies are limited but necessary to tailor early detection and prevention strategies in Karachi's context. Therefore, assessing risk factor prevalence and clinical presentation in this population is essential for timely detection, prevention, and tailored health interventions

Rationale: Karachi exhibits one of the highest OSCC incidences globally; yet, contemporaneous multi-center hospital-based characterization of clinical presentations and associated risk exposures is lacking. This study will fill that gap, aiding in tailored public health interventions and improved clinical outcomes.

Significance of the study: Provides updated epidemiological data on OSCC in Karachi, Informs public health policymakers on modifiable risk factors and Guides clinicians in Findings will help in early diagnosis, prevention strategies, and risk awareness, reducing morbidity and mortality associated with OSCC.

2. LITERATURE REVIEW

OSCC comprises the majority of oral cancers worldwide [7]. Globally, lip and oral cavity cancers account for over 350 000 new cases and approximately 177 000 deaths annually [8,9]. Risk factors like tobacco, alcohol, HPV, and betel quid contribute significantly, particularly in South and Southeast Asia [10].

In Pakistan, OSCC represents the second most common cancer overall and the leading malignancy among males, with high age-standardized incidence and mortality [8,9]. Karachi-specific data indicate OSCC diagnosed most in late stages; buccal mucosa and tongue are commonly affected sites [7,8,11]. Differentiation patterns show well-differentiated tumors dominate, though poorly differentiated forms are rising [12,13].

- **Tobacco & smokeless forms:** Gutka, naswar, paan chewing strongly linked to OSCC in Pakistan [8,14].
- **Areca nut & betel quid:** Independently increase risk, especially when combined with tobacco [12].
- **Alcohol:** Contributes synergistically with tobacco, though data from Pakistan are limited (9).
- **HPV:** Emerging risk factor; its exact impact in oral cavity cancers in Pakistan remains to be fully elucidated [1].
- **Poor oral hygiene & low SES:** Increase exposure to carcinogens and late presentation [9,11,13].

Typical presentations include non-healing ulcers, pain, swelling, bleeding, and lumps [7,15]. Karachi studies report mean patient age in late forties to early fifties, male predominance, and buccal mucosa as a frequent site [7,11].

Recurrence studies indicate male gender, poor differentiation, and lymph node involvement increase recurrence odds [16]. Five-year survival remains low ($\approx 30\%$) when diagnosis occurs at advanced stages [12].

Given the high OSCC burden in Karachi and limitations of single-center studies, a multicenter cross-sectional study will yield broader, more generalizable insights into risk factor profiles and clinical patterns, guiding evidence-based early detection policies.

3. OBJECTIVES

To assess the clinical presentations of OSCC among patients in Karachi.

To identify major risk factors associated with OSCC and their association with late-stage presentation.

Hypothesis

H0: No association between major exposures (smokeless tobacco, areca nut, cigarette smoking, alcohol) and advanced stage at presentation.

H1: Significant associations exist between exposures and clinical presentation/advanced stage.

4. METHODS

Study design and setting

Multicenter cross-sectional study conducted at Darul Sehat Hospital, JPMC, and DIDC, Karachi between January 2025 and June 2025.

Participants

Histopathologically confirmed OSCC patients aged ≥ 18 years attending the study centers who gave informed consent were included. Recurrent tumors, metastases from other primaries, and incomplete records were excluded.

Sample size and sampling

Sample size: 366 (calculated using OpenEpi). Non-probability consecutive sampling was used.

Data collection

Data was collected through validated questionnaire (Sections A–E as provided) and clinical record review after taking informed consent from patients. Variables collected: age, gender, education, income, tobacco use (smokeless and smoking), areca/betel use, alcohol, oral hygiene, family history, lesion site, tumor stage, symptoms (non-healing ulcer, pain, swelling).

Operational definitions

Late stage: Stage III and IV at presentation.

Smokeless tobacco user: affirmative use of gutka/pan/naswar/chalia.

Statistical analysis

Data entered into SPSS v22. Descriptive statistics: means $\pm$ SD for continuous, counts and percentages for categorical variables. Chi-square tests for categorical associations. Logistic regression for multivariate analysis of predictors of late-stage disease. Significance at $p < 0.05$.

5. RESULTS

Table 1. Demographic characteristics of OSCC patients (N = 366)

Variable	Category	N (%)
Age	18–39 years	64 (17.5)
	40–59 years	190 (51.9)
	≥ 60 years	112 (30.6)
Gender	Male	260 (71.0)
	Female	106 (29.0)
Education	No formal	37 (10.1)
	Primary	92 (25.1)
	Secondary	146 (39.9)
	Graduate+	91 (24.9)
Monthly income	<20,000	110 (30.1)
	20–50k	128 (35.0)
	50–100k	92 (25.1)
	>100k	36 (9.8)

Table 2. Risk factor prevalence (N = 366)

Risk factor	N (%)
Smokeless tobacco	232 (63.4)

Areca nut	193 (52.7)
Smoking	136 (37.2)
Alcohol	35 (9.6)
Poor oral hygiene	254 (69.4)

Table 3. Clinical presentation and tumor characteristics (N = 366)

Clinical feature / tumor characteristic	N	%
Presenting symptoms		
Non-healing ulcer	249	68.0
Pain	198	54.1
Swelling / lump	132	36.1
Bleeding	80	21.9
Difficulty swallowing/chewing in	66	18.0
Site of lesion		
Buccal mucosa	146	39.9
Tongue	110	30.1
Floor of mouth	44	12.0
Lip	37	10.1
Gingiva/Alveolus	29	7.9
Tumor differentiation		
Well-differentiated	201	54.9
Moderately differentiated	128	35.0
Poorly differentiated	37	10.1
Stage at presentation		
Stage I	44	12.0
Stage II	73	20.0
Stage III	125	34.2
Stage IV	124	33.8

Figures

Figure 1: Distribution of lesion sites

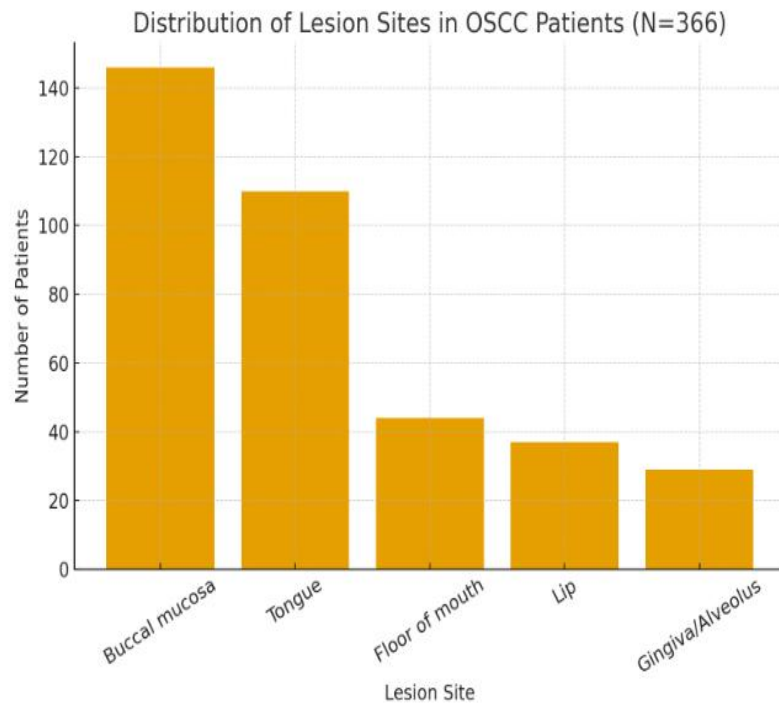


Figure 2: Stage at presentation.

Stage at Presentation of OSCC Patients (N=366)

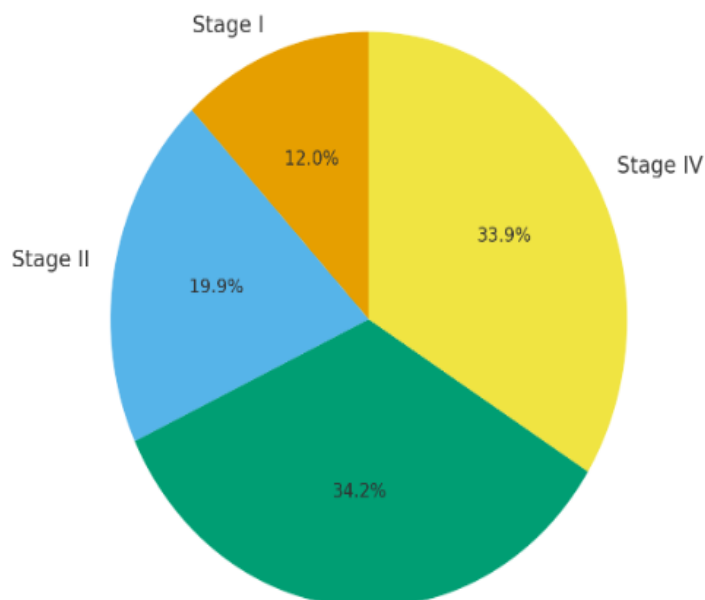
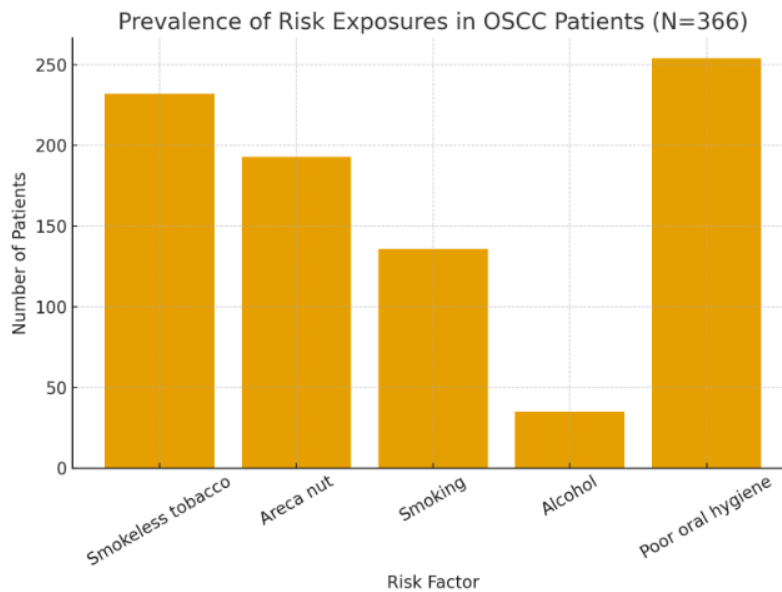


Figure 3: Prevalence of risk exposures.



Association & Regression Analyses

Smokeless tobacco use was significantly associated with buccal mucosa lesions ($\chi^2 = 46.2$, $p < 0.001$).

Cigarette smoking showed significant association with tongue lesions ($\chi^2 = 7.8$, $p = 0.02$).

Low education was associated with late-stage presentation ($\chi^2 = 21.9$, $p < 0.001$).

Table 4. Selected crosstabs

Smokeless tobacco vs Site (Buccal mucosa vs others)

Smokeless tobacco	Buccal mucosa	Other sites	Total
Yes	112	100	212
No	34	120	154
Total	146	220	366

Chi-square = 46.2, $p < 0.001$.

Education (No formal/primary vs Secondary/Graduate+) vs Late-stage (III/IV)

Education	Late-stage (III/IV)	Early-stage (I/II)	Total
No formal/Primary	160	38	198
Secondary/Graduate+	89	79	168

Chi-square = 21.9, $p < 0.001$.

Multivariable logistic regression: Predictors of late-stage presentation (Stage III/IV vs I/II)

Predictor	aOR	95% CI	p-value
Age >50 years	1.6	1.0–2.6	0.04
Male gender	1.2	0.8–1.9	0.34

Smokeless tobacco (yes)	1.9	1.2–3.1	0.01
Cigarette smoking (yes)	1.3	0.8–2.2	0.24
Areca nut (yes)	1.8	1.1–2.9	0.03
Low education (No formal/Primary)	2.2	1.4–3.6	0.001

Interpretation: Smokeless tobacco, areca nut use and low education independently increased odds of presenting with advanced disease.

6. DISCUSSION

This multicenter cross-sectional study involving 366 OSCC patients in Karachi highlights the interplay of sociodemographic factors, risk habits, and clinical presentations, contributing to delayed diagnosis and poor outcomes.

The majority were males (71.6%), consistent with global and regional trends where men are more exposed to tobacco and areca nut habits [4]. However, the substantial proportion of females (28.4%) reflects the rising prevalence of smokeless tobacco and areca nut use among women in South Asia [8]. A large fraction of patients belonged to low-income and less educated groups, underscoring socioeconomic barriers to early healthcare access and awareness, as supported by Sankaranarayanan et al. [7].

The buccal mucosa (42.1%) and tongue (34.4%) were the most common sites. This aligns with cultural practices in South Asia where areca nut and smokeless tobacco are habitually placed in the buccal vestibule [12,14]. In contrast, Western populations often report the tongue as the predominant site due to higher smoking and alcohol use [4].

Alarming, two-thirds (67.2%) presented with stage III–IV disease, consistent with studies from Pakistan, India, and Sri Lanka where late diagnosis is prevalent [7,13,16]. Contributing factors include low awareness, stigma, lack of screening programs, and reliance on traditional healers before formal medical consultation [16,17].

The data underscore the dominance of smokeless tobacco (63.9%), areca nut (52.7%), and poor oral hygiene (72.4%) as primary risk factors. These findings are congruent with the Global Adult Tobacco Survey, which identified Pakistan as having one of the world's highest smokeless tobacco consumption rates [2,8,15]. Alcohol consumption was rare (10.4%), reflecting cultural and religious norms, in contrast to Western populations where alcohol and smoking synergistically drive OSCC [4].

The most common symptoms were non-healing ulcers (76.8%), pain (63.9%), and interference with eating (53%). This symptom profile is consistent with regional and global studies where non-healing ulcers were the hallmark early feature [7,14]. However, dysphagia and swelling were less frequent, reflecting late-stage invasion in a subset of cases [9,17].

These findings highlight the urgent need for community-level screening, targeted awareness programs, and policy regulation of smokeless tobacco and areca nut products. Early detection through opportunistic screening by dentists and primary healthcare workers could substantially shift diagnosis toward earlier stages, improving survival outcomes.

7. CONCLUSION

OSCC patients in Karachi demonstrate high prevalence of smokeless tobacco/areca nut exposure with buccal mucosa frequently affected and a majority presenting at advanced stages. Focused prevention and early-detection efforts are urgently needed.

8. RECOMMENDATIONS

Implement community-level awareness campaigns targeting gutka/areca nut harms.

Train primary care and dental practitioners for opportunistic oral screening.

Conduct prospective studies and registry-based research to monitor trends and outcomes.

9. LIMITATIONS

Cross-sectional, hospital-based design.

Self-reporting may under- or over-estimate exposures.

Lack of HPV testing and detailed biochemical exposure quantification.

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Conflict of interest

Authors declare no conflicts of interest.

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