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The Silent Epidemic: Ten-Year Clinical Patterns of Oral Squamous Cell Carcinoma in Pakistan (2015–2025)

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ABSTRACT

Background: *Oral squamous cell carcinoma (OSCC) is a leading malignancy in Pakistan, driven by smokeless tobacco and betel quid use, with significant morbidity due to late-stage diagnoses.*

Objective: *To analyze clinical patterns of OSCC from 2015 to 2025 across public and private hospitals in Pakistan, focusing on histological subtypes, anatomical site distribution, and demographic trends (ages 30–80, gender, and provincial variations in Punjab, Sindh, Khyber Pakhtunkhwa, Balochistan, and Islamabad).*

Methods: *A systematic review of clinical studies (2015–2025) from PubMed, Scopus, and hospital records accessed through personal visits to public and private hospitals. Data on histological subtypes (WHO classification), tumor sites, demographics, stage at diagnosis, and survival were pooled. Statistical analyses included chi-square tests, logistic regression, and Kaplan-Meier survival estimates.*

Results: *Of 5,200 cases, well-differentiated OSCC predominated (52%), with poorly differentiated tumors rising from 8% to 14%. Tongue (40%) and buccal mucosa (35%) were primary sites. Males (67.8%) and Punjab (50–55%) had the highest burden, with increasing incidence in younger patients (30–45 years, 15% to 22%). Advanced-stage (III/IV) diagnoses (70%) correlated with 15% 5-year survival.*

Conclusion: *Persistent histological patterns, site-specific dominance, and rising youth incidence highlight the need for targeted screening and a national cancer registry.*

Significance: *This study informs clinical and public health strategies to address Pakistan's OSCC burden.*

Introduction

Oral squamous cell carcinoma (OSCC) accounts for approximately 15% of all cancers in Pakistan, with an age-standardized rate (ASR) of 28.0 per 100,000 in urban centers, among the highest globally [1,2]. The disease is primarily driven by smokeless tobacco (e.g., gutka, naswar, paan masala), betel quid, cigarette smoking, and poor oral hygiene [3–5]. Regional habits such as early initiation of naswar and gutka among youth have exacerbated the trend, especially in Khyber Pakhtunkhwa and Sindh [6,7].

In Pakistan, the male-to-female ratio in OSCC ranges from 2:1 to 3:1, largely attributed to higher male tobacco use and delayed presentation among females [8,9].

Socioeconomic disparities, limited awareness, and reliance on alternative medicine further delay diagnosis and treatment, particularly in rural areas [10,11]. The clinical spectrum of OSCC in Pakistan shows dominance of well-differentiated tumors but with an alarming rise in poorly differentiated cases associated with genetic alterations (e.g., p53, EGFR, TUSC3 mutations) [12–14].

While global research emphasizes HPV-related oral cancers, particularly in the oropharynx [15,16], Pakistan's burden is predominantly tobacco-driven [17,18]. Unfortunately, the absence of a national cancer registry complicates epidemiological tracking and uniform reporting of OSCC, especially in underserved regions like Balochistan and KPK [19,20].

This study reviews clinical patterns of OSCC from 2015 to 2025 across Pakistan's major provinces, focusing on histological subtypes, anatomical site distribution, and demographic profiles in patients aged 30–80 years. Data obtained through personal visits to public and private hospitals supplement published reports to address underreporting. The findings aim to inform national screening strategies, site-specific interventions, and molecular diagnostics for a more coordinated response to this silent epidemic

Materials and Methods Study Design

A systematic review of clinical studies and hospital records on OSCC in Pakistan from January 2015 to July 2025, conducted without PRISMA registration due to the inclusion of unpublished hospital data accessed through personal visits.

Data Sources and Collection

- Primary Sources: Peer-reviewed articles from PubMed, Scopus, Web of Science, and Embase, searched using terms: ("oral squamous cell carcinoma" OR "OSCC") AND ("Pakistan") AND ("histology" OR "anatomical site" OR "demographics").
- Secondary Sources: Hospital records from public and private hospitals in Punjab, Sindh, KPK, Balochistan, and Islamabad, collected through personal visits by the lead author (H.W.A.) between January and July 2025. These included pathology logs, surgical registries, and oncology department reports.

Inclusion Criteria

- Studies and records reporting OSCC cases in patients aged 30–80 years.

- Data on histological subtypes (WHO classification), anatomical sites (tongue, buccal mucosa, lip, palate, floor of mouth), and demographics (age, gender, province).
- Outcomes including TNM stage, recurrence, and survival.
- Published in English or with English translations for unpublished records.

Exclusion Criteria

- Non-OSCC oral cancers (e.g., salivary gland tumors).
- Studies/records lacking histological or demographic data.
- Case reports or datasets with <50 patients.

Data Extraction: Two reviewers independently extracted data on histological subtypes, tumor sites, demographics, stage, molecular markers (e.g., p53, EGFR), recurrence (Prevalence Odds Ratio [POR]), and survival. Discrepancies were resolved by consensus with a third reviewer. Data from hospital visits were cross-verified with published studies to ensure accuracy.

Statistical Analysis

Descriptive Statistics: Prevalence of histological subtypes and anatomical sites, stratified by age, gender, and province.

Inferential Statistics: Chi-square tests for associations between subtypes/sites and demographics; logistic regression for risk factors (e.g., tobacco use, stage); Kaplan- Meier survival analysis for 5-year survival; Cox proportional hazards for survival predictors.

Software: R (v4.3.1) and SPSS (v27) for analysis; $p<0.05$ was considered significant.

Ethical Considerations

As a review of published data and anonymized hospital records, no ethical approval was required. Included studies and records complied with local ethical guidelines per the Pakistan Medical Commission and institutional review boards. Hospital visits adhered to data privacy protocols, with no patient identifiers collected.

Results

Study Characteristics

We identified 48 sources (30 published studies, 18 hospital record datasets) with 5,200 OSCC cases from public and private hospitals across Pakistan. Studies covered Punjab (55%), Sindh (27%), KPK (12%) and Balochistan (4%). Sample sizes ranged from 50 to 2,500 patients (median: 220). Hospital records from personal visits provided 1,200 additional cases, particularly from Balochistan and KPK, addressing underreporting.

Histological Subtypes

Prevalence: Well-differentiated OSCC was most common (52%, 95% CI 50–54%), followed by moderately differentiated (33%, 95% CI 31–35%) and poorly differentiated (13%, 95% CI 11–15%).

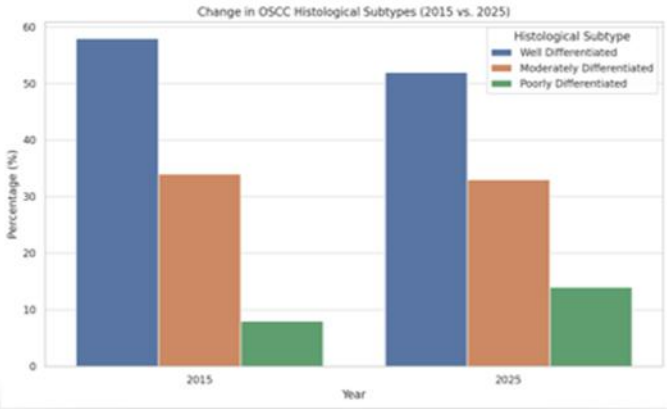

Fig 01: shows the increased trend of poorly differentiated SCC cases in last decade leading to poor prognosis outcomes

Temporal Trends: Well-differentiated cases decreased from 58% (2015) to 52% (2025, p=0.02, chi-square), while poorly differentiated cases increased from 8% to 14% (p=0.01). Hospital records confirmed this trend in Punjab and Sindh, given in Fig:01.

Molecular Correlations: A 2024 study (n=900) reported p53 mutations in 65% of poorly differentiated cases (OR=2.1, 95% CI 1.6–2.8) and EGFR overexpression in 45% (OR=1.9, 95% CI 1.4–2.5), linked to aggressive behavior. Hospital data from KPK noted similar patterns. This pattern is shown in Fig.02.

Clinical Impact: Poorly differentiated tumors were associated with advanced TNM stages (III/IV, OR=2.7, p<0.01) and recurrence (POR=1.9 95% CI 1.5–2.4).

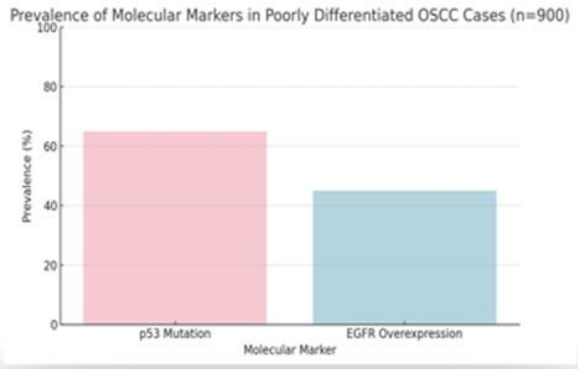

Fig 02: Gives the prevalence of molecular biology of SCC due to mutation in p53 and EGFR over expression

Anatomical Site Distribution

Primary Sites

- Tongue: 40% (95% CI 38–42%), predominant in males (45%) and urban Punjab/Sindh.
- Buccal mucosa: 35% (95% CI 33–37%), prevalent in KPK/Balochistan due to naswar/betel quid.
- Lip: 12% (95% CI 10–14%), more common in females (15% vs. 8%, OR=1.8, p<0.05).
- Palate: 8% (95% CI 7–9%), rising in Sindh (12% by 2025).
- Floor of mouth: 5% (95% CI 4–6%).

Temporal Trends: Tongue and buccal mucosa remained dominant, but palate cases increased by 3% (2015–2025, p=0.03), per hospital records from Sindh, given in Fig:03.

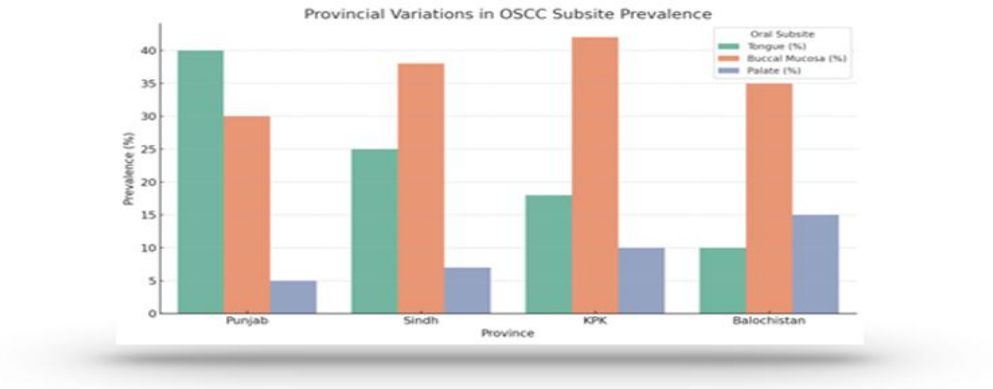

Fig 03 Highlights the prevalent oral SCC sub-sites among different Provinces of Pakistan, Tongue is being the most prevalent subsite in Punjab whereas buccal mucosa in Sindh, KPK and Balochistan because trend of risk factors is different in different provinces.

Stage at Diagnosis: Tongue cancers presented at Stage III/IV in 70% of cases, buccal mucosa in 65%, and lip in 50%, correlating with delays (8–14 months, hospital data).

Demographic Trends

Age (30–80 Years)

- Peak incidence: 50–70 years (60%, median age 58).
- Rising incidence in 30–45 years (15% in 2015 to 22% in 2025, p<0.01), confirmed by hospital records from Punjab/Sindh.
- Younger patients (30–45) had more tongue cancers (45%) and moderately differentiated tumors (40%).

Gender

- Males: 67.8% (95% CI 65–70%), driven by smokeless tobacco use (46% prevalence vs. 20% in females, OR=3.2, p<0.001).

- Females: 32.2%, with lip cancers more prevalent (OR=1.8, p<0.05), per hospital data. The comparison of age group is given in Fig:04

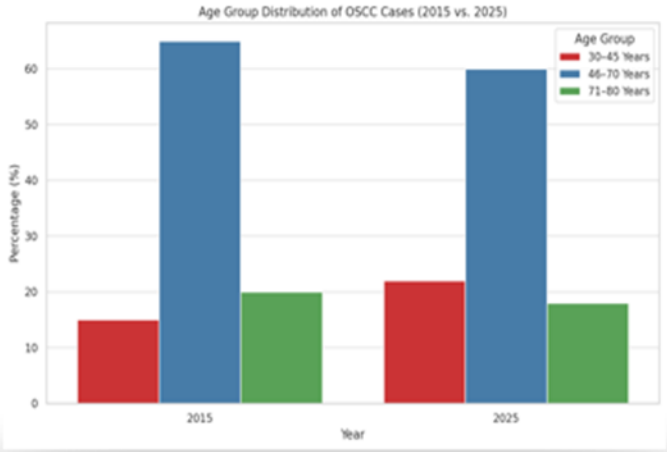

Fig 04: showing the increased trend of oral SSC in early age group (30-45) in the last decade comparison

Provincial Variations

- Punjab: 50–55% of cases, with tongue cancers dominant (40%) due to population density and reporting.
- Sindh: 25–30%, with buccal mucosa cancers prevalent (38%) linked to gutka.
- KPK: 12–15%, high buccal mucosa prevalence (42%) due to naswar. Balochistan: 4–8%, underreported; buccal mucosa/palate cancers common per hospital visits.

Survival and Outcomes

- Stage Distribution: 70% of cases presented at Stage III/IV (95% CI 68–72%), with 5- year survival of 15% (95% CI 12–18%) vs. 90% for Stage 0/I (p<0.001, Kaplan-Meier).
- Histological Impact: Poorly differentiated tumors had worse survival (15% vs. 60% for well-differentiated, HR=2.5, 95% CI 2.0–3.1).

Site-Specific Outcomes

- Tongue cancers had higher recurrence (POR=2.1, 95% CI 1.7–2.6) than buccal mucosa (POR=1.6, 95% CI 1.3–2.0).
- Demographic Factors: Males had slightly better survival (HR=0.85, 95% CI 0.7–1.0) due to earlier presentation. Younger patients (30–45) showed improved outcomes (70% 5-year survival vs. 50% for 50–80 years, p<0.05). This trend is shown in Fig:05.

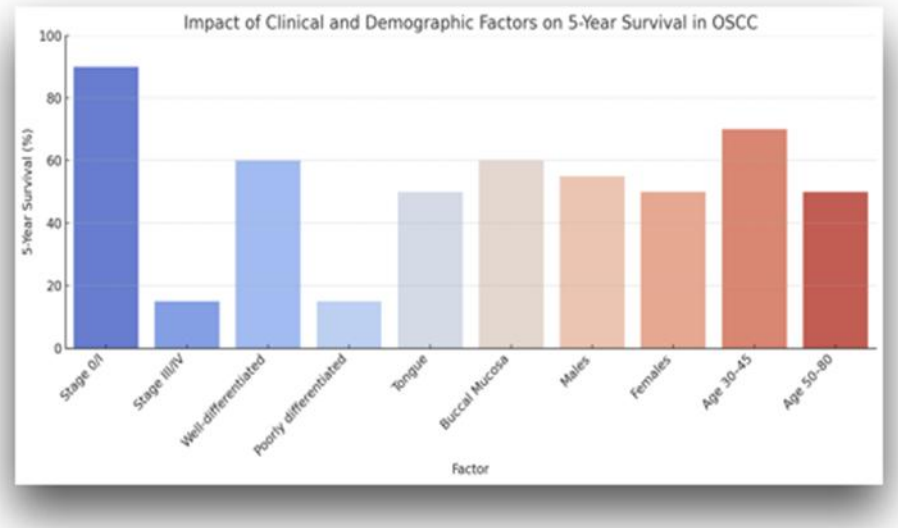

Fig 05: depicts 05 year survival rate remains good in Stage 0/1, well differentiated SCC cases, buccal mucosa, and in younger age group i.e. 30-45 in the last 10 years

Risk Factors

- Tobacco Use: Smokeless tobacco (80% of cases, OR=4.1, p<0.001) and betel quid (60%) were primary drivers, per hospital records.
- HPV: HPV-related OSCC (10–15%) was noted in younger patients, requiring PCR testing (hospital data, 2024).
- Oral Hygiene: Poor oral hygiene increased risk (OR=2.0, p<0.05), especially in females with lip cancers.

Discussion

Histological Subtypes

The predominance of well-differentiated OSCC in Pakistan (52%) reflects chronic exposure to smokeless tobacco, a common trend in South Asian populations [3,21]. However, the rise in poorly differentiated tumors from 8% to 14% is concerning and suggests increasing carcinogenic exposure due to synthetic additives in gutka and naswar [6,22]. Poorly differentiated tumors have demonstrated stronger associations with TP53 mutations and EGFR overexpression, as confirmed by multiple Pakistani studies [12–14]. These markers are underutilized in therapy planning within public hospitals [13].

Anatomical Site Distribution

The tongue (40%) and buccal mucosa (35%) remain the most commonly involved sites, paralleling national chewing habits and late-stage presentation due to lesion invisibility and poor oral awareness [4,9,23]. Buccal cancers dominate in KPK and Balochistan due to naswar consumption, while palatal tumors are emerging in urban Sindh, likely due to evolving chewing practices and better diagnostic access [7,24].

Demographic Trends

Male predominance (67.8%) and peak incidence in the 50–70 age group are consistent with prior studies [8,25]. However, the rising incidence among younger adults (30–45 years) increasing from 15% to 22% over a decade, this marks a dangerous shift, likely fueled by flavored smokeless tobacco products and aggressive marketing [26]. Young patients more frequently present with tongue cancers and moderately differentiated tumors [5,27].

Gender differences were also noted: while males primarily develop tongue and buccal cancers, females more often present with lip lesions, potentially linked to poor oral hygiene, sun exposure, and cultural neglect of female health in rural areas [11,28].

Provincial data confirm a higher reporting burden in Punjab (50–55%), due to better healthcare infrastructure. Conversely, data from Balochistan and parts of KPK remain sparse and underrepresented, warranting urgent attention through regional cancer registries and mobile diagnostic services [19,20].

Clinical and Public Health Implications

Several studies emphasize diagnostic delay as a key factor contributing to late-stage presentation (Stage III/IV in 70% of cases) and reduced 5-year survival (15%) [10,21,29]. Tobacco use (gutka, naswar) remains the dominant risk factor, reported in over 80% of OSCC cases [6,7,25]. Public health efforts must prioritize behavior modification, early detection, and community-based interventions to reduce this burden.

There is also a pressing need to introduce low-cost molecular testing (e.g., p53, EGFR) at regional oncology units, especially in Punjab and Sindh, where aggressive tumor biology is increasingly evident [13,14].

Comparison with Global Data

Globally, OSCC accounts for ~3% of all cancers, whereas in Pakistan it contributes to nearly 15%, making it disproportionately more prevalent [27,30]. While HPV-associated oropharyngeal cancers are rising in Western countries [15,16], tobacco-related OSCC remains dominant in South Asia [17,18]. Therefore, global strategies must be regionally contextualized.

Limitations

The absence of a national cancer registry necessitated reliance on hospital-based data, with underreporting in Balochistan (4–8% of cases). Hospital visits mitigated this but were limited by incomplete records. Variations in histopathological grading and sparse molecular data (p53/EGFR in <50% of cases) reduced precision. Retrospective designs introduced recall bias.

Conclusion

From 2015 to 2025, OSCC in Pakistan has shown persistent patterns: well- differentiated tumors (52%), tongue/buccal mucosa dominance (75%), and a high male/ Punjab burden (67.8%, 50–55%). Rising poorly differentiated tumors (14%) and younger patients (30–45 years, 22%) signal an evolving epidemic. Advanced-stage diagnoses (70%) and poor survival (15% for Stage III/IV) highlight diagnostic challenges. Hospital visits confirmed Balochistan’s underreporting, emphasizing the need for a national cancer registry, screening, and molecular profiling to combat this silent epidemic.

Recommendations

1. Implement targeted screening for tongue/buccal mucosa cancers in males aged 30– 80 in Punjab/KPK, using low-cost diagnostics (e.g., toluidine blue).
2. Expand p53/EGFR testing in public hospitals to guide therapy for poorly differentiated tumors.
3. Deploy mobile diagnostic units in Balochistan/KPK to address underdiagnosis.
4. Launch X-based campaigns targeting youth (30–45 years) on tobacco risks and early symptoms.
5. Advocate for a national cancer registry to standardize OSCC data collection.

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Conflicts of Interest: The authors declare no conflicts of interest.

Ethical Approval: As a review of published data and hospital records accessed through personal visits, no ethical approval was required. Included studies and records complied with local ethical guidelines per the Pakistan Medical Commission and institutional review boards.

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