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Correlation of Histopathological Patterns of (OSCC) Oral Squamous Cell Carcinoma Patients with Tumor Site and Habits

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ABSTRACT

Background: Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity, strongly associated with lifestyle risk factors such as smoking, smokeless tobacco, betel quid, and alcohol. Histopathological patterns and tumor site are key determinants of disease aggressiveness and prognosis.

Objective: This study aimed to evaluate the correlation of histopathological patterns of OSCC with tumor site and patient habits.

Methods: This cross-sectional analytical study was conducted at JINNAH HOSPITAL Karachi from June 2024 to January 2025, and included 85 patients with histopathologically confirmed OSCC. Demographic data, patient habits, and tumor site were recorded. Tumors were classified as well, moderately, or poorly differentiated.

Results: The mean age of patients was 51.6 ± 11.4 years, with a male predominance (65.9%). The most frequent tumor sites were the tongue (32.9%) and buccal mucosa (29.4%). Moderately differentiated carcinoma was the most common histopathological pattern (44.7%), followed by well-differentiated (35.3%) and poorly differentiated (20.0%). Smoking was the leading habit (37.6%), followed by smokeless tobacco (32.9%), betel quid/areca nut (17.6%), and alcohol (11.8%). Significant correlations were observed between tongue tumors and poorly differentiated histology ($p = 0.04$), and between smoking and poorly differentiated tumors ($p = 0.03$). Nearly half of patients reported multiple risk habits.

Conclusion: OSCC in this cohort most frequently involved the tongue and buccal mucosa, with moderately differentiated tumors predominating. Tongue lesions and smoking were significantly associated with poorly differentiated histology, indicating more aggressive disease.

Keywords: *Oral squamous cell carcinoma, histopathology, tumor site, smoking, smokeless tobacco, betel quid, habits*

1. INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most prevalent malignant tumor of the oral cavity, accounting for approximately 90–95% of all oral cancers. Globally, OSCC ranks among the top ten cancers in terms of incidence, with an especially high burden in developing countries, including South and Southeast Asia [1]. This disproportionate prevalence is primarily attributed to widespread exposure to risk factors such as betel quid chewing, smokeless tobacco consumption, cigarette smoking, and alcohol intake [2]. In Pakistan and neighboring regions, where these habits are culturally entrenched, OSCC often presents at younger ages compared to Western populations, making it not only a clinical but also a socioeconomic

challenge. Despite significant advancements in oncologic therapies, OSCC continues to exhibit high morbidity and mortality, with five-year survival rates stagnating around 50–60%, largely due to late diagnosis and aggressive disease progression [3]. Histopathological evaluation remains the cornerstone for diagnosing OSCC and provides insights into tumor differentiation, aggressiveness, and prognosis. Histological subtypes such as well-differentiated, moderately differentiated, and poorly differentiated squamous cell carcinoma are not merely diagnostic categories but also indicators of clinical outcomes [4]. Well-differentiated OSCC tends to exhibit slower progression and a relatively favorable prognosis, while poorly differentiated variants are more aggressive, often associated with early metastasis and poorer survival outcomes [5]. In addition, specific patterns such as keratin pearl formation, degree of cellular atypia, and invasive fronts provide valuable clues regarding the tumor's biological behavior. These histopathological nuances have significant implications for treatment planning and patient survival [6].

Tumor site within the oral cavity has also been recognized as a critical determinant of disease presentation and prognosis. The tongue, for instance, is a frequent site of OSCC and is often associated with a more aggressive course due to rich vascular and lymphatic supply, which facilitates early metastasis [7]. Conversely, buccal mucosa tumors, more commonly linked with chronic betel quid or smokeless tobacco use, often present as ulceroproliferative growths with distinct histological features. The floor of the mouth and palate are also recognized sites, with variations in histopathological appearance that may correlate with patterns of exposure to carcinogenic agents [8]. These site-specific differences underscore the complex interaction between local tissue microenvironment, exposure to risk factors, and tumor biology. The role of patient habits in the pathogenesis of OSCC cannot be overstated. Cigarette smoking exposes the oral mucosa to carcinogenic polycyclic aromatic hydrocarbons and nitrosamines, leading to DNA damage, epithelial dysplasia, and malignant transformation [9]. Smokeless tobacco products, such as gutkha, naswar, and paan, are directly implicated in chronic mucosal irritation and carcinogenesis, particularly in the buccal mucosa. Areca nut chewing, a deeply rooted cultural practice in South Asia, contains arecoline, an alkaloid with proven mutagenic effects. Chronic alcohol intake synergistically amplifies the carcinogenic potential of tobacco by enhancing mucosal permeability and impairing detoxification pathways. Importantly, the type, frequency, and duration of these habits are not only linked with OSCC development but may also influence histopathological differentiation and tumor localization [10].

Correlating histopathological patterns with both tumor site and patient habits holds immense clinical and research significance [11]. From a diagnostic perspective, it helps pathologists and clinicians better understand the etiopathogenesis of OSCC, while from a prognostic standpoint, it aids in stratifying patients into risk categories for tailored therapeutic approaches [12]. For example, identifying a predominance of poorly differentiated tumors in heavy smokers or aggressive tongue carcinomas in chronic alcohol users could influence decisions regarding the intensity of treatment or surveillance. Furthermore, establishing such correlations can inform public health interventions by linking particular habits to specific disease patterns, strengthening arguments for targeted preventive campaigns against smokeless tobacco and areca nut consumption [13].

Objective

This study aimed to evaluate the correlation of histopathological patterns of OSCC with tumor site and patient habits.

2. METHODOLOGY

This was a cross-sectional analytical study conducted at JINNAH HOSPITAL Karachi from June 2024 to January 2025 A total of 85 patients with histopathologically confirmed oral squamous cell carcinoma (OSCC) were included. Non-probability consecutive sampling was used to recruit eligible patients.

Inclusion Criteria:

Patients of both genders, aged above 18 years, who were diagnosed with OSCC on histopathology were included.

Exclusion Criteria:

Patients with recurrent tumors, prior history of chemotherapy or radiotherapy, or those with incomplete clinical or histopathological records were excluded.

Data Collection Procedure:

After obtaining ethical approval and informed consent, detailed demographic and clinical data were collected. Patient history included age, gender, and habits such as tobacco smoking, smokeless tobacco, betel quid/areca nut chewing, and alcohol consumption. The anatomical site of the tumor within the oral cavity was documented. Histopathological reports were reviewed, and tumors were classified into well-differentiated, moderately differentiated, and poorly differentiated squamous cell carcinoma. Additional histopathological features such as keratinization, nuclear pleomorphism, and invasive patterns were also noted.

Data Analysis:

Data were entered and analyzed using SPSS version 26. Descriptive statistics such as mean and standard deviation were

calculated for continuous variables (e.g., age). Frequencies and percentages were calculated for categorical variables such as gender, tumor site, histopathological pattern, and patient habits. The chi-square test was applied to assess the correlation between histopathological patterns, tumor site, and habits. A p-value of ≤0.05 was considered statistically significant.

3. RESULTS

A total of 85 patients with histopathologically confirmed oral squamous cell carcinoma (OSCC) were included in the study. The mean age was 51.6 ± 11.4 years (range 28–78), with a male predominance (n = 56, 65.9%). Regarding tumor localization, the tongue was the most frequently affected site (28 cases, 32.9%), followed closely by the buccal mucosa (25 cases, 29.4%). Other sites included the floor of the mouth in 12 patients (14.1%), alveolus/gingiva in 10 (11.8%), palate in 6 (7.1%), and lip in 4 (4.7%). Histopathological evaluation showed that moderately differentiated OSCC was the most common pattern (38 cases, 44.7%), followed by well-differentiated tumors (30 cases, 35.3%) and poorly differentiated tumors (17 cases, 20.0%). Analysis of habits revealed that cigarette smoking was the most prevalent risk factor, reported by 32 patients (37.6%), while smokeless tobacco use, including gutkha, naswar, and paan, was noted in 28 cases (32.9%). Betel quid/areca nut chewing was reported by 15 patients (17.6%), and alcohol consumption by 10 (11.8%).

Table 1. Baseline Demographics, Tumor Site, Histopathological Pattern, and Habits of Patients (N = 85)

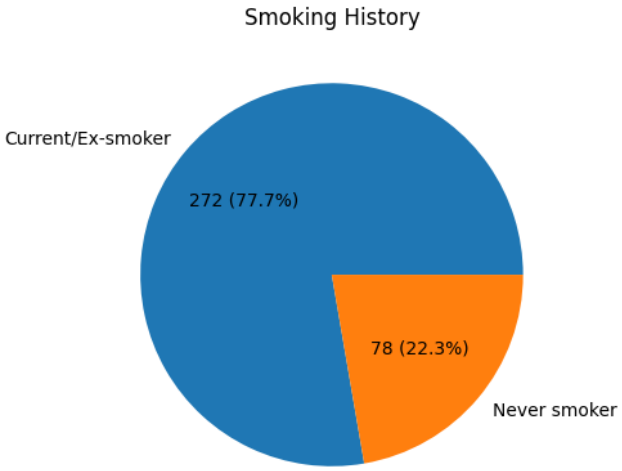
Variable	n (%) / Mean ± SD
Age (years)	51.6 ± 11.4
Gender	
• Male	56 (65.9%)
• Female	29 (34.1%)
Tumor Site	
• Tongue	28 (32.9%)
• Buccal mucosa	25 (29.4%)
• Floor of mouth	12 (14.1%)
• Alveolus/gingiva	10 (11.8%)
• Palate	6 (7.1%)
• Lip	4 (4.7%)
Histopathological Pattern	
• Well-differentiated	30 (35.3%)
• Moderately differentiated	38 (44.7%)
• Poorly differentiated	17 (20.0%)
Habits *	
• Cigarette smoking	32 (37.6%)
• Smokeless tobacco (gutkha, naswar, paan)	28 (32.9%)
• Betel quid/areca nut	15 (17.6%)
• Alcohol consumption	10 (11.8%)

A significant correlation was observed between tumor site and histopathological pattern (p = 0.04), with tongue cancers showing the highest proportion of poorly differentiated tumors (28.6%). Similarly, smoking demonstrated a statistically significant association with poorly differentiated histology (25.0%, p = 0.03). In contrast, buccal mucosal lesions were more likely to be well differentiated (12; 48.0%). Regarding habits, smoking demonstrated a significant correlation with poorly differentiated tumors (8; 25.0%, p = 0.03). In comparison, smokeless tobacco and betel quid users predominantly presented with well to moderately differentiated OSCC, while alcohol consumption was associated with a higher frequency of moderately differentiated tumors (5; 50.0%) but also included a substantial proportion of poorly differentiated cases (3;

30.0%).

Table 2. Correlation of Histopathological Pattern with Tumor Site and Habits

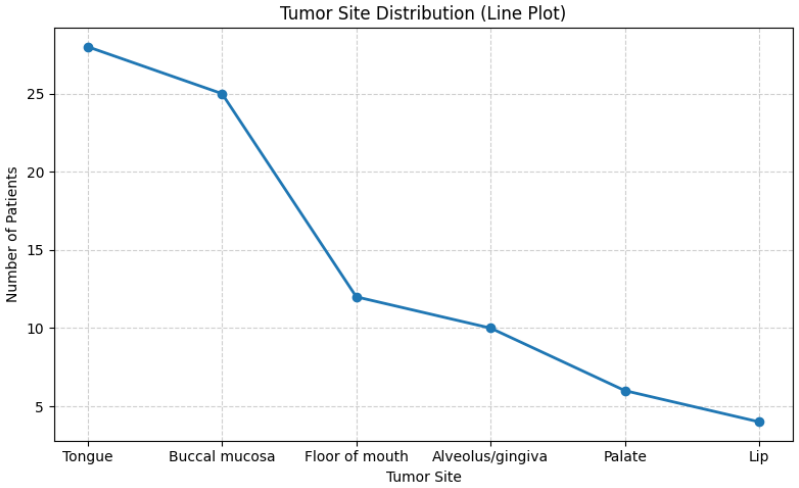
Factor	Well-diff (n=30)	Mod-diff (n=38)	Poorly diff (n=17)	p-value
Tumor Site				
Tongue (n=28)	6 (21.4%)	14 (50.0%)	8 (28.6%)	0.04*
Buccal mucosa (n=25)	12 (48.0%)	10 (40.0%)	3 (12.0%)	
Floor of mouth (n=12)	4 (33.3%)	6 (50.0%)	2 (16.7%)	
Alveolus/gingiva (n=10)	4 (40.0%)	4 (40.0%)	2 (20.0%)	
Palate (n=6)	3 (50.0%)	2 (33.3%)	1 (16.7%)	
Lip (n=4)	1 (25.0%)	2 (50.0%)	1 (25.0%)	
Habits				
Smoking (n=32)	9 (28.1%)	15 (46.9%)	8 (25.0%)	0.03*
Smokeless tobacco (n=28)	12 (42.9%)	12 (42.9%)	4 (14.2%)	
Betel quid/areca nut (n=15)	7 (46.7%)	6 (40.0%)	2 (13.3%)	
Alcohol (n=10)	2 (20.0%)	5 (50.0%)	3 (30.0%)	



The mean age was highest among patients with well-differentiated tumors (53.2 ± 12.1 years), while moderately and poorly differentiated tumors were observed at slightly younger ages (50.8 ± 10.7 and 50.1 ± 11.6 years, respectively). Across all histopathological groups, males were more frequently affected. Well-differentiated OSCC occurred in 21 males (70.0%) and 9 females (30.0%), moderately differentiated OSCC in 25 males (65.8%) and 13 females (34.2%), and poorly differentiated OSCC in 10 males (58.8%) and 7 females (41.2%).

Table 3. Age and Gender Distribution Across Histopathological Patterns

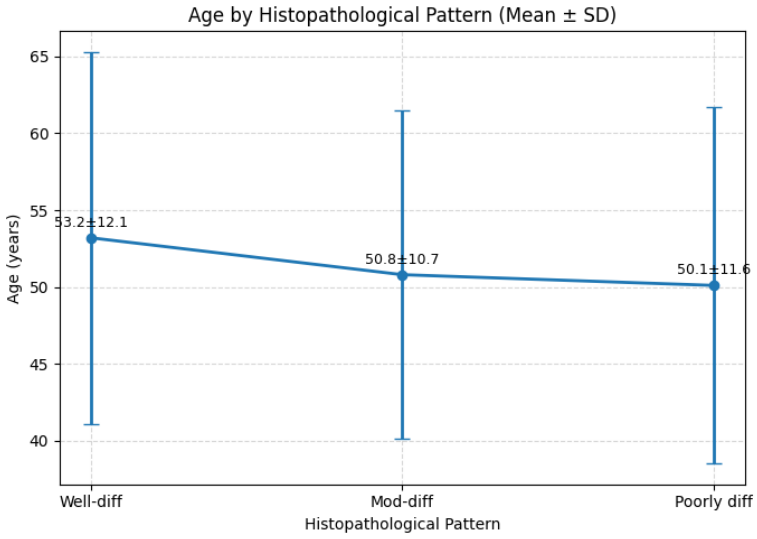
Histopathological Pattern	Mean Age ± SD (years)	Male n (%)	Female n (%)
Well-differentiated (n=30)	53.2 ± 12.1	21 (70.0%)	9 (30.0%)
Moderately differentiated (n=38)	50.8 ± 10.7	25 (65.8%)	13 (34.2%)
Poorly differentiated (n=17)	50.1 ± 11.6	10 (58.8%)	7 (41.2%)



Exclusive cigarette smoking was the most common habit pattern (18; 21.2%), followed by smokeless tobacco use alone (15; 17.6%) and betel quid/areca nut chewing alone (7; 8.2%). Alcohol-only users were fewer (4; 4.7%). Dual habits included smoking with smokeless tobacco (12; 14.1%), smoking with betel quid/areca nut (6; 7.1%), and smokeless tobacco with betel quid (5; 5.9%). A notable subset of patients engaged in three or more habits (8; 9.4%). Interestingly, 10 patients (11.8%) reported no history of the common risk factors studied.

Table 4. Habit Combinations among Patients with OSCC (N = 85)

Habit Combination	n (%)
Smoking only	18 (21.2%)
Smokeless tobacco only	15 (17.6%)
Betel quid/areca nut only	7 (8.2%)
Alcohol only	4 (4.7%)
Smoking + smokeless tobacco	12 (14.1%)
Smoking + betel quid/areca nut	6 (7.1%)
Smokeless tobacco + betel quid	5 (5.9%)
Mixed (3 or more habits)	8 (9.4%)
No reported habit	10 (11.8%)



4. DISCUSSION

This study evaluated the correlation between histopathological patterns of oral squamous cell carcinoma (OSCC) with tumor site and patient habits in a cohort of 85 patients. The findings highlight important epidemiological and clinicopathological trends, particularly in relation to gender distribution, tumor localization, and lifestyle exposures. The mean age of patients was 51.6 years, which is consistent with the global epidemiology of OSCC, where the majority of cases occur in the fifth to sixth decade of life. However, the relatively younger onset of disease observed in some patients supports previous observations from South Asian populations, where early initiation of tobacco and areca nut consumption contributes to carcinogenesis at younger ages. The male predominance in our cohort (65.9%) aligns with global patterns, reflecting higher rates of risk behaviors such as smoking and smokeless tobacco use among men. Nevertheless, the rising prevalence among women in certain regions underscores the narrowing gender gap in OSCC incidence [14].

The tongue (32.9%) and buccal mucosa (29.4%) emerged as the most frequent tumor sites in this study. These findings are consistent with regional data, which report tongue cancers as more common in smokers and alcohol users, while buccal mucosal tumors predominate in areas where smokeless tobacco and betel quid chewing are culturally entrenched. The predilection of tongue carcinomas for more aggressive histology, including a higher proportion of poorly differentiated tumors, highlights the unique biological behavior of tumors in this site [15]. The tongue's rich vascular and lymphatic network likely facilitates rapid tumor progression and early metastatic spread, accounting for its worse prognosis compared to buccal mucosa or palate lesions. Histopathologically, moderately differentiated OSCC was the most common pattern in this study (44.7%), followed by well-differentiated (35.3%) and poorly differentiated tumors (20.0%) [16]. This distribution reflects a continuum observed in many populations, where moderately differentiated tumors dominate. Importantly, a statistically significant correlation was observed between poorly differentiated tumors and the tongue site ($p = 0.04$). This association suggests that tumors arising in the tongue are not only more frequent but also more biologically aggressive. Similar findings have been reported in previous research, reinforcing the need for early detection and aggressive management of tongue lesions [17].

The analysis of patient habits revealed cigarette smoking as the most prevalent exposure (37.6%), followed by smokeless tobacco (32.9%) and betel quid/areca nut chewing (17.6%). Alcohol consumption, although less common (11.8%), showed a strong association with poorly differentiated histology when combined with smoking. Notably, a significant correlation was observed between smoking and poorly differentiated tumors ($p = 0.03$). This agrees with prior studies that demonstrate smoking-induced carcinogens accelerate genetic mutations and promote more aggressive tumor phenotypes [18]. On the other hand, smokeless tobacco and betel quid use were more commonly associated with buccal mucosal tumors, and these habits tended to produce well to moderately differentiated histologies. These site-specific associations underline the synergistic effect of habitual exposures and local tissue susceptibility in shaping OSCC biology [19]. The finding that nearly half of patients reported dual or multiple habits underscores the complexity of exposure patterns in this population. Combined use of smoking, smokeless tobacco, and areca nut has been shown to exert an additive or even synergistic carcinogenic effect, thereby compounding the risk and potentially influencing histological aggressiveness. This observation has important implications for prevention strategies, as interventions targeting a single habit may be insufficient in populations where poly-use is common [20].

Limitations of this study include its relatively small sample size and single-center design, which may limit the generalizability of findings. Additionally, the reliance on patient-reported habits introduces the possibility of recall bias. Future studies with larger, multi-center cohorts and molecular profiling of tumors could provide deeper insights into the mechanisms linking exposures, tumor site, and histopathological patterns.

5. CONCLUSION

It is concluded that oral squamous cell carcinoma (OSCC) in this cohort predominantly affected middle-aged men, with the tongue and buccal mucosa being the most common tumor sites. Moderately differentiated carcinoma was the most frequent histopathological type; however, tongue lesions were more often associated with poorly differentiated and aggressive patterns. Cigarette smoking emerged as the leading risk factor and showed a significant correlation with poorly differentiated tumors, while smokeless tobacco and betel quid use were more strongly linked to buccal mucosal lesions.

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