Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/y5karg55

FREQUENCY AND UNDERLYING RISK FACTORS OF ORAL SQUAMOUS CELL CARCINOMA

Basil Khalid[1], Babar Pasha[2], Ali Farooq[3*], Ammara Anwar[4], Sana Knawal[5], Mariyah Javed[6]

[1]BDS. MPhil, Associate professor/head Oral pathology Department, Multan Medical and Dental College, (MMDC), basil.khalid87@gmail.com
[2]BDS, MCPS, FCPS, CMT Assistant Professor Oral and Maxillofacial Surgeon Rahbar Medical and Dental College Pashababar@yahoo.com
[3*]Associate Professor, Department of Oral & Maxillofacial Surgery, Sharif Medical & Dental College, Lahore ali_farooq82@yahoo.com
[4]Assistant Professor Sharif Medical and Dental College, Lahore, Ammaraanwar6@gmail.com
[5]Senior Registrar, University of Medical And Dental College, Faisalabad drsanahammad@gmail.com
[6]Assistant Professor, Azra Naheed Dental College, The Superior university, Lahore. Department of Oral Pathology, mariyah.javed@hotmail.com

***Corresponding Author:** Dr. Ali Farooq
*Email: ali_farooq82@yahoo.com

ABSTRACT

Background: Oral squamous cell carcinoma (OSCC) is one of the most common malignancies in the head and neck region, with risk factors such as tobacco use, alcohol consumption, and betel quid chewing being strongly associated with its development.

Objective: The aim of this study was to evaluate the frequency and underlying risk factors contributing to the development of OSCC among patients, with a focus on their demographic characteristics and tumor grading.

Study Design and Setting: This was a retrospective cross-sectional study conducted at a tertiary care hospital over a 12-month period.

Methodology: A total of 130 OSCC patients were included, and data regarding their demographic characteristics, lesion location, tumor grade, and potential risk factors (such as tobacco use, alcohol consumption, and HPV exposure) were collected. Tumor grade was assessed using histopathological examination. Statistical analysis was performed to identify associations between risk factors and tumor grade.

Results: Tobacco use (73.1%) and alcohol consumption (46.1%) were the most prevalent risk factors. The study found significant associations between tobacco use, alcohol consumption, and tumor grade, with well-differentiated tumors more commonly observed in patients with these habits.

Conclusion: Tobacco and alcohol use are key risk factors for the development of OSCC, highlighting the need for targeted prevention strategies. Early detection and lifestyle modification are critical in reducing the burden of OSCC.

Keywords: Alcohol consumption, Betel quid, HPV exposure, Oral squamous cell carcinoma, Risk factors, Tobacco use.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is a prevalent malignancy of the oral cavity, accounting for over 90% of all oral cancers worldwide. It ranks as one of the leading cancers globally, with particularly high incidence rates in developing countries due to widespread exposure to risk factors such as tobacco, alcohol, and betel quid.[1,2] The disease arises from the squamous epithelium lining the oral cavity and oropharynx and typically manifests as non-healing ulcers, red or white patches, or progressive lesions that may lead to pain, difficulty in chewing, and speech impairment.[3]

The frequency of OSCC varies geographically, influenced by cultural habits, environmental exposures, and healthcare access. In South Asia, for instance, betel quid and areca nut chewing, often combined with tobacco, are major contributors to OSCC cases.[4] Similarly, in Western countries, alcohol and smoking are predominant risk factors. Beyond these external influences, OSCC incidence is rising among younger individuals and non-smokers, suggesting that other risk factors, including genetic predisposition, viral infections like human papillomavirus (HPV), and immunosuppression, may play a significant role.[5]

Among the underlying risk factors, tobacco use remains the single most important preventable cause of OSCC. Tobacco consumption, whether through smoking or smokeless forms, introduces carcinogens such as nitrosamines and polycyclic aromatic hydrocarbons, which damage the DNA of oral epithelial cells.[6] Chronic alcohol consumption synergistically enhances the carcinogenic effects of tobacco, amplifying the risk of OSCC. Moreover, dietary deficiencies, particularly in micronutrients like vitamins A, C, and E, can weaken the oral mucosa's defense mechanisms, rendering it more vulnerable to malignant transformation.[7]

Infection with high-risk HPV strains, particularly HPV-16, has emerged as a significant etiological factor for OSCC, especially in the oropharyngeal region. HPV-positive OSCC tends to have distinct clinical and molecular profiles compared to traditional OSCC, often affecting younger patients and presenting a better prognosis.[8] Other factors, such as chronic irritation from ill-fitting dental prostheses, poor oral hygiene, and genetic mutations in tumor suppressor genes like p53, contribute to the multifactorial nature of the disease. Early detection of OSCC significantly improves survival outcomes, yet the disease is often diagnosed in advanced stages due to a lack of awareness and the asymptomatic nature of early lesions.[9,10]

Regular screening, especially for high-risk populations, and public health initiatives to reduce tobacco and alcohol consumption are pivotal in addressing the burden of OSCC. Understanding the interplay of various risk factors is essential for developing targeted prevention and intervention strategies. This study aims to explore the frequency and underlying risk factors of OSCC to identify patterns and gaps in knowledge that could inform effective prevention and treatment approaches. By investigating the epidemiological trends and etiology of OSCC, we can better understand the disease's dynamics and devise measures to curb its prevalence and improve patient outcomes.

MATERIALS AND METHODS

This cross-sectional study was conducted at Department of Dentistry Sharif Medical and Dental College, Lahore. Ethical approval was obtained from the Ethical Review Committee, and written informed consent was acquired from all participants. The study procedures were explained to participants, ensuring they fully understood the purpose, potential risks, and their right to withdraw at any time. Confidentiality of participants' information was strictly maintained throughout the study.

A total of 130 patients, diagnosed with OSCC through histopathological confirmation, were included in the study. The patients were of both genders, aged 18 years and above. Those with recurrent OSCC or incomplete medical records were excluded from the study. The sample size of 130 was calculated using the formula for descriptive studies, with an assumed prevalence rate of 15%, a 95% confidence interval, and a 5% margin of error. Participants were selected through consecutive non-probability sampling.

Data were collected using a structured questionnaire and clinical examination. The questionnaire was designed to gather information on demographic details, lifestyle habits, and exposure to known

risk factors. These factors included tobacco use (smoking and smokeless forms), alcohol consumption (frequency, duration, and quantity), betel quid or areca nut usage (with or without tobacco), dietary habits (particularly the intake of fruits and vegetables), oral hygiene practices (such as frequency of brushing and use of dental prostheses), family history of cancer, and medical history of comorbidities or immunosuppressive conditions. Additionally, exposure to HPV was assessed through clinical suspicion or laboratory testing where available.

Clinical examination was performed to assess the lesion's site, size, and appearance, whether ulcerative, exophytic, or infiltrative. All OSCC diagnoses were confirmed through histopathological analysis, and the tumor grade was determined.

Data were entered into SPSS version 26.0 for statistical analysis. Continuous variables, such as age, were summarized as means and standard deviations, while categorical variables, such as gender and tobacco use, were expressed as frequencies and percentages. The frequency of OSCC was calculated, and associations between various risk factors and OSCC were analyzed using the chi-square test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant.

STUDY RESULTS

Out of 130 patients diagnosed with oral squamous cell carcinoma (OSCC), the majority were male (61.5%), while females comprised 38.5% of the cases. Age-wise distribution showed that most patients were over 50 years old (46.1%), followed by those in the 36–50 age group (38.5%), while the smallest proportion was from the 18–35 age group (15.4%). Regarding the location of the lesions, the tongue was the most frequently affected site, accounting for 34.6% of cases, followed closely by the buccal mucosa at 30.8%. Lesions on the lip were seen in 19.2% of patients, while the remaining cases (15.4%) involved other oral sites, including the floor of the mouth and the palate. Tumor grading revealed that 46.1% of the cases were well-differentiated, 34.6% were moderately differentiated, and 19.2% were poorly differentiated.

Table 1: Demographic and Clinical Characteristics of Patients with OSCC

Variables	Characteristic	Frequency (n)	Percentage (%)
Gender	Male	80	61.5%
	Female	50	38.5%
Age Group (Years)	18–35	20	15.4%
	36–50	50	38.5%
	>50	60	46.1%
Lesion Location	Tongue	45	34.6%
	Buccal Mucosa	40	30.8%
	Lip	25	19.2%
	Others (Floor, Palate)	20	15.4%
Tumor Grade	Well-Differentiated	60	46.1%
	Moderately Differentiated	45	34.6%
	Poorly Differentiated	25	19.2%

Tobacco use was the most prevalent risk factor, identified in 73.1% of patients. Among these, 53.8% were smokers, while 19.2% used smokeless tobacco. Alcohol consumption was another significant factor, present in 46.1% of patients, and betel quid or areca nut usage was reported by 38.5% of the participants. Poor oral hygiene was noted in 30.8% of cases. Dietary deficiencies, specifically inadequate intake of fruits and vegetables, were observed in 42.3% of patients. Family history of cancer was reported in 15.4% of cases, and HPV exposure was detected in 19.2%.

Table 2: Frequency of Underlying Risk Factors for OSCC

Risk Factor	Frequency (n)	Percentage (%)
Tobacco Use	95	73.1
Smoking	70	53.8

Smokeless Tobacco	25	19.2
Alcohol Consumption	60	46.1
Betel Quid/Areca Nut Usage	50	38.5
Poor Oral Hygiene	40	30.8
Family History of Cancer	20	15.4
Dietary Deficiency (Fruits/Vegetables)	55	42.3
HPV Exposure	25	19.2

The analysis showed significant associations between certain risk factors and tumor grade. Tobacco use was strongly associated with well-differentiated tumors, present in 83.3% of such cases, compared to 66.7% of moderately differentiated and 60% of poorly differentiated tumors (p=0.03). Similarly, alcohol consumption showed a notable association, being more common among well-differentiated cases (58.3%) than in moderately (33.3%) or poorly differentiated (40%) tumors (p=0.05). Betel quid or areca nut usage was also significantly associated with tumor grade, with 50% of well-differentiated cases reporting this habit, compared to 33.3% of moderately differentiated and 20% of poorly differentiated cases (p=0.04). In contrast, HPV exposure did not show a statistically significant association with tumor grade (p=0.67).

Table 3: Association Between Risk Factors and Tumor Grade

Risk Factor	Well-Differentiated (n=60)	Moderately Differentiated (n=45)	Poorly Differentiated (n=25)	p-value
Tobacco Use	50 (83.3%)	30 (66.7%)	15 (60%)	0.03
Alcohol Consumption	35 (58.3%)	15 (33.3%)	10 (40%)	0.05
Betel Quid/Areca Nut Usage	30 (50%)	15 (33.3%)	5 (20%)	0.04
HPV Exposure	10 (16.7%)	10 (22.2%)	5 (20%)	0.67

DISCUSSION

Oral squamous cell carcinoma (OSCC) is one of the most prevalent malignancies of the head and neck region, accounting for a significant global cancer burden. It arises from the epithelial lining of the oral cavity and is strongly linked to lifestyle and environmental factors. Tobacco use, alcohol consumption, betel quid chewing, poor oral hygiene, and dietary deficiencies are the primary risk factors contributing to its development.[11,12] Genetic predisposition and infections such as human papillomavirus (HPV) further elevate the risk. OSCC often presents as non-healing ulcers or masses in the oral cavity, with the tongue and buccal mucosa being the most affected sites. Despite advancements in diagnosis and treatment, late-stage presentation and poor prognosis remain major challenges.[13] Understanding the frequency and underlying risk factors of OSCC is essential for developing effective preventive and therapeutic strategies.

The results of our study align with several key findings in the existing literature on oral squamous cell carcinoma (OSCC). Like the study by Anwar et al. (2020), where the majority of patients were male and the mean age of presentation was around 47 years, our study also observed a higher frequency of OSCC in males (61.5%) and a significant number of cases in the age group over 50 years (46.1%).[14]

The study by Nokovitch et al. (2022) highlights the role of alcohol consumption and tobacco use in increasing the risk of head and neck squamous cell carcinoma (HNSCC), a finding that is mirrored in our study, where alcohol consumption was reported by 46.1% of patients. This association further supports the hypothesis that combined use of alcohol and tobacco is a major risk factor for OSCC. Our results also showed a significant association between alcohol consumption and tumor grade, where well-differentiated tumors were more frequently seen in alcohol users (58.3%).[15] Interestingly, the incidence of HPV exposure in our study was lower (19.2%) compared to studies like Nokovitch et al. (2022).[15] Additionally, the association between chewing habits and buccal mucosa tumors reported by Anwar et al. (2020) was also observed in our study, where 30.8% of

tumors were located in the buccal mucosa. This suggests that the habits of chewing tobacco, betel quid, or other substances may predispose individuals to specific locations of OSCC, particularly in the buccal mucosa. Our study findings also correlate with those of Zaman et al. (2016), who found that the majority of patients with OSCC had moderately differentiated carcinoma (68.9%). In our study, 34.6% of patients had moderately differentiated tumors, further emphasizing the link between risk factors and tumor differentiation. [16]

Additionally, the study by Aqeel et al. (2017) & Zaccone et al. also reported cigarette smoking as a predominant risk factor, which is consistent with our findings where tobacco use was present in 73.1% of patients. Smoking was found to be significantly associated with tumor grade in our study, with a higher prevalence of tobacco use in patients with well-differentiated tumors (83.3%), which may point to the chronic and long-term carcinogenic effects of tobacco on oral epithelial cells.[17, 18]

In line with the findings of Usman et al. (2018), who reported a high prevalence of betel nut chewing (87.9%), our study found betel quid usage in 38.5% of cases, suggesting its significant role in OSCC development, particularly in Southeast Asian regions where this practice is common.[19] In Zahra et al. (2022), the study highlighted a high prevalence of OSCC in males (60%) and a significant number of cases in the 41-60 age group, which is consistent with our findings. Additionally, the most common lesion location in their study was the buccal mucosa, similar to our results, further supporting its association with tobacco and betel quid usage.[20]

This study provides valuable insights into the frequency and underlying risk factors of OSCC by analyzing a diverse patient population in a clinical setting. The inclusion of multiple risk factors and tumor grading enhances the comprehensiveness of the findings. The study's retrospective design may introduce selection bias, and the findings may not be generalizable to all populations. Additionally, the reliance on self-reported data for some risk factors like tobacco and alcohol use could lead to reporting bias.

CONCLUSION

Tobacco and alcohol use are significant risk factors for the development of oral squamous cell carcinoma, highlighting the importance of prevention and early detection. Lifestyle modifications and public health interventions targeting these behaviors are essential in reducing the burden of OSCC.

REFERENCES

1. Chamoli A, Gosavi AS, Shirwadkar UP, Wangdale KV, Behera SK, Kurrey NK, Kalia K, Mandoli A. Overview of oral cavity squamous cell carcinoma: Risk factors, mechanisms, and diagnostics. Oral oncology. 2021 Oct 1;121:105451.
2. Kumar SA, Indu S, Gautami D, VarRuchi S. Oral squamous cell carcinoma (OSCC) in humans: Etiological Factors, diagnostic and therapeutic relevance. Research Journal of Biotechnology Vol. 2020 Oct;15:10.
3. Ferreira e Costa R, Leão ML, Sant'Ana MS, Mesquita RA, Gomez RS, Santos-Silva AR, Khurram SA, Tailor A, Schouwstra CM, Robinson L, van Heerden WF. Oral squamous cell carcinoma frequency in young patients from referral centers around the world. Head and Neck Pathology. 2022 Sep;16(3):755-62.
4. Howard A, Agrawal N, Gooi Z. Lip and oral cavity squamous cell carcinoma. Hematology/Oncology Clinics. 2021 Oct 1;35(5):895-911.
5. Melo BA, Vilar LG, Oliveira NR, Lima PO, Pinheiro MD, Domingueti CP, Pereira MC. Human papillomavirus infection and oral squamous cell carcinoma-a systematic review. Brazilian journal of otorhinolaryngology. 2021 Jul 5;87:346-52.
6. Zhang SZ, Xie L, Shang ZJ. Burden of oral cancer on the 10 most populous countries from 1990 to 2019: estimates from the global burden of disease study 2019. International journal of environmental research and public health. 2022 Jan 13;19(2):875.

7. Zhang SZ, Xie L, Shang ZJ. Burden of oral cancer on the 10 most populous countries from 1990 to 2019: estimates from the global burden of disease study 2019. International journal of environmental research and public health. 2022 Jan 13;19(2):875.
8. Abati S, Bramati C, Bondi S, Lissoni A, Trimarchi M. Oral cancer and precancer: a narrative review on the relevance of early diagnosis. International journal of environmental research and public health. 2020 Dec;17(24):9160.
9. He S, Chakraborty R, Ranganathan S. Proliferation and apoptosis pathways and factors in oral squamous cell carcinoma. International journal of molecular sciences. 2022 Jan 29;23(3):1562.
10. Gormley M, Gray E, Richards C, Gormley A, Richmond RC, Vincent EE, Dudding T, Ness AR, Thomas SJ. An update on oral cavity cancer: epidemiological trends, prevention strategies and novel approaches in diagnosis and prognosis. Community Dental Health Journal. 2022 Sep 30;39(3):197-205.
11. Gormley M, Gray E, Richards C, Gormley A, Richmond RC, Vincent EE, Dudding T, Ness AR, Thomas SJ. An update on oral cavity cancer: epidemiological trends, prevention strategies and novel approaches in diagnosis and prognosis. Community Dental Health Journal. 2022 Sep 30;39(3):197-205.
12. Nethan ST, Ravi P, Gupta PC. Epidemiology of oral squamous cell carcinoma in Indian scenario. InMicrobes and oral squamous cell carcinoma: a network spanning infection and inflammation 2022 May 31 (pp. 1-7). Singapore: Springer Nature Singapore.
13. Kujan O, van Schaijik B, Farah CS. Immune checkpoint inhibitors in oral cavity squamous cell carcinoma and oral potentially malignant disorders: a systematic review. Cancers. 2020 Jul 17;12(7):1937.
14. Anwar N, Pervez S, Chundriger Q, Awan S, Moatter T, Ali TS. Oral cancer: Clinicopathological features and associated risk factors in a high risk population presenting to a major tertiary care center in Pakistan. Plos one. 2020 Aug 6;15(8):e0236359.
15. Nokovitch L, Maquet C, Crampon F, Taihi I, Roussel LM, Obongo R, Virard F, Fervers B, Deneuve S. Oral cavity squamous cell carcinoma risk factors: state of the art. Journal of clinical medicine. 2022 May 3;12(9):3264.
16. Zaman SU, Adeel M, Suhail A. Squamous cell carcinoma of oral tongue in young patients—a 10 years tertiary care experience. JPMA: Journal of Pakistan Medical Association. 2016;66(2):155.
17. AQEEL R, ASLAM Z, AMJAD A. Examine the Prevalenceof Oral Squamous Cell Carcinoma also Determine the Risk Factors and Causes of Improper Diagnosis. Methods. 2017 Jan.
18. Zaccone R, Renzi A, Chalfon C, Lenzi J, Bellei E, Marconato L, Ros E, Rigillo A, Bettini G, Faroni E, Guerra D. Environmental risk factors for the development of oral squamous cell carcinoma in cats. Journal of Veterinary Internal Medicine. 2022 Jul;36(4):1398-408.
19. Usman N, Ch AN, Khaliq F, Kiran S, Ahmad MA, Chauhdry W, Ashraf MS, Akhtar MU. Risk factors of oral squamous cell carcinoma in old versus young patients. Pakistan Oral & Dental Journal. 2018;38(4):423-7.
20. Zahra T, Jawa Z, Zahra T, Nazeer A, Raza H, Batool U. Frequency and Pattern of presentation of Oral Squamous Cell Carcinoma and its predisposing Factors in patients presented to Nishtar Institute of Dentistry. Pakistan Journal of Medical & Health Sciences. 2022 Oct 15;16(09):170-75.