

Histopathological spectrum of oral squamous cell carcinoma in Naswar users: Correlation with duration, age and site

Fatima Iqbal¹, Nasiha Bashir², Hoor Maryam³, Sajjad Ahmad⁴

Abstract

Objective: To investigate the relationship of clinico- pathological parameters with the histopathological spectrum of oral squamous cell carcinoma in a high-risk population.

Method: The prospective, cross-sectional study was conducted from January 2019 to September 2022 in the Khyber Pakhtunkhwa province of Pakistan, and comprised histologically confirmed cases of oral squamous cell carcinoma with a history of consumption of Naswar from different hospitals. The duration of use, age, site and histopathological features were recorded, and their association was explored. Data was analysed using SPSS 19.

Results: Of the 80 patients with mean age 56.98 ± 12.94 years at diagnosis, 59(73%) were males and 21(26%) were females. Buccal mucosa was the predominant site of involvement 28(35%). Histologically, the most common presentation was well-differentiated squamous cell carcinoma 63(78.7%). The association of age and duration of use is more appropriate with the histopathological pattern of oral squamous cell carcinoma was statistically non-significant ($p > 0.05$).

Conclusion: There was no significant association of age and prolonged Naswar use with histopathological patterns of oral squamous cell carcinoma.

Keywords: Histopathology, Oral squamous cell carcinoma, Risk factors, Smokeless tobacco. (JPMA 76: 387; 2026) DOI: <https://doi.org/10.47391/JPMA.23254>

Introduction

Globally, lip and oral cavity cancer is ranked 18th, while in Pakistan it is the second most common cancer in both genders with incidence rate of 9.5%.¹ Among tumours of oral cavity, oral squamous cell carcinoma (OSCC) is the frequently occurring histological type (90%).² It is a highly prevalent cancer in males compared to females, and accounts for about 9.1% deaths in Pakistan.³ Concerning the aetiology of the disease, tobacco (burned and unburned) is considered an established risk factor for the development of OSCC.⁴

Smokeless tobacco (SLT) is consumed in different forms, which have been recognised as carcinogenic by the International Agency for Research on Cancer (IARC).⁵ One survey revealed 90% of the consumers in 11 countries, with Pakistan alone having 10.1 million SLT users.⁶ In Pakistan, SLT is chiefly used in the form of gutka, paan, snuff and snus.⁷ Naswar, also used as snuff, is a form of SLT that is linked to the Pashtun tribes of Pakistan. Being a cheaper product, it is easily available in the market,

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¹⁻³Department of Oral Pathology, Riphah International University, Peshawar Campus, Pakistan. ⁴Department of Histopathology, Riphah International University, Peshawar Campus, Pakistan.

Correspondence: Fatima Iqbal. Email: khanfatima319@gmail.com

ORCID ID: 0000-0002-2181-4156

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making it an attractive option. It is composed of powdered tobacco, lime and flavouring agents, and is commonly kept in the buccal sulcus where active constituents are absorbed through oral mucosa. In Khyber Pakhtunkhwa (KP), a strong association between Naswar users and OSCC has been documented.⁸

A number of prognostic factors, such as age, gender, anatomical location, habits, grades and many more have an impact on OSCC.^{9,10} The prognosis of OSCC reported among young and female subjects is encouraging.¹¹ Likewise, higher the grade, worse is the prognosis of the disease.¹² Therefore, these factors should be taken into consideration while planning treatment and management of OSCC.

Keeping in view all these and the fact that, to our knowledge, there is not sufficient research on Naswar users, a high-risk population with different clinicopathological parameters, the current study was planned to investigate the correlation of variables, particularly focusing on the duration of use, age and site with the histopathological spectrum of OSCC in Naswar consumers.

Patients and Methods

The prospective, cross-sectional study was conducted from January 2019 to September 2022 in the KP province of Pakistan after approval from the ethics review board of

Prime Foundation Pakistan (PFP), Peshawar, the capital of KP. A sample size of total of 80 patients was calculated using the World Health Organization (WHO) sample size calculator to ensure the study had sufficient statistical power and precision. The calculation was based on the expected prevalence of OSCC, a 95% confidence level and an acceptable margin of error.¹³ Non probability convenient sampling technique was employed. Written, informed consent was obtained from all the participants before data collection. Data was collected using a predesigned proforma.

The biopsies of the patients who had a history of Naswar use and were clinically diagnosed as OSCC cases were sent to the histopathology laboratory of Peshawar Medical College (PMC), Peshawar, from the maxillofacial departments of different hospitals. Patients undergoing any treatment, such as radiotherapy and chemotherapy, were excluded, and so were recurrent OSCC cases.

The tissue samples were placed in 10% buffered formalin for 16 hours after excision. Sections stained with haematoxylin and eosin (H&E) were prepared, and the diagnosis was confirmed as OSCC with the help of pathology report as per the WHO grading system.¹⁴ Variables, such as age group, duration of Naswar use, and site of the lesion, were compared with histological findings. For this purpose, age was divided into four groups; 20-40 years, 41-50 years, 51-60 years, and >60 years. The duration of Naswar use was divided into three groups; 1-10 years, 11-20 years, and >20 years.

Data was analysed using SPSS 19. Data was expressed as either frequencies and percentages or as mean ± standard deviation. Pearson’s chi-square test was used to compare categorical variables. Fisher’s exact test was applied where values were <5. P≤0.05 was considered statistically significant.

Results

Of the 80 patients with mean age 56.98±12.94 years at diagnosis, 59(73%) were males and 21(26%) were females. The patients consuming only snuff were 75(93%), while the remaining 5(6.3%) were using Naswar with other forms of tobacco, such as cigarette and betel nut. Most of the cases 45(56%) had a history of snuff dipping for >20 years (Table 1).

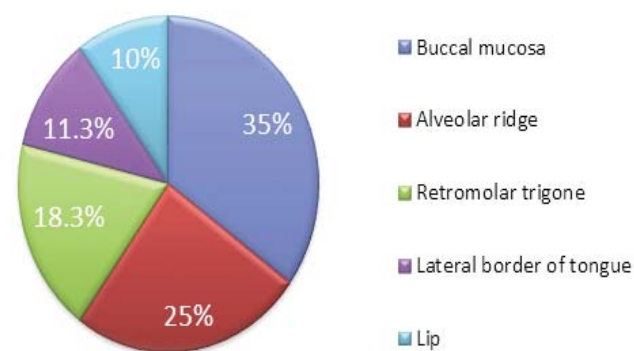


Figure-1: Distribution of the site of lesion.

Table-1: Baseline characteristics of the patients (n=80)

Age	Gender N (%)	Snuff users only N (%)	Snuff with other forms of tobacco N (%)	Duration of use in years	Total (N)
Age range (30-85 years)	Male 59 (73%)	75 (93%)	5 (6.3%)	1-10 n (%)	80
Mean (56.98±12.94)	Female 21 (26%)			11-20 n (%)	
				>20n (%)	
			09 (11%)	26 (32%)	
				45 (56%)	

SD; Standard deviation.

Table 2: Distribution of histopathological variables according to the duration of Naswar use.

Duration of use	Degree of Differentiation and Variants						P value
	Well Differentiated SCC n (%)	Moderately Differentiated SCC n (%)	Adenoid SCC n (%)	Basaloid SCC n (%)	Papillary SCC n (%)	Verrucous SCC n (%)	
1-10 years	7 (77.7)	2 (22.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.10
11-20 years	23 (88.4)	3 (11.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
>20 years	33 (73.3)	8 (17.7)	1 (2.2)	1 (2.2)	1 (2.2)	1 (2.2)	
Total (80)	63 (78.7)	13 (16.2)	1 (1.25)	1 (1.25)	1 (1.25)	1 (1.25)	

SCC: Squamous cell carcinoma.

Table-3: Correlation of degree of differentiation and subtypes of OSCC with age and site

Factors	Degree of Differentiation and Variants						P value
	Well-differentiated SCC n (%)	Moderately-differentiated SCC n (%)	Adenoid SCC n (%)	Basaloid SCC n (%)	Papillary SCC n (%)	Verrucous SCC n (%)	
Age (Years)							
20-40	7 (70)	2 (20)	1 (10)	0 (0.0)	0 (0.0)	0 (0.0)	0.23
41-50	17 (89.4)	2 (10.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
51-60	16 (76.1)	5 (23.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
>60	23 (76.6)	4 (13.3)	0 (0.0)	1 (3.3)	1 (3.3)	1 (3.3)	
Site							
Alveolar ridge	16 (80)	2 (10)	1 (5)	1 (5)	0 (0.0)	0 (0.0)	0.19
Buccal Mucosa	22 (78.5)	6 (21.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Lat Border of Tongue	6 (66.6)	3 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Lip	6 (75)	2 (25)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Retro molar trigone	13 (86.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (6.6)	1 (6.6)	

SCC: Squamous cell carcinoma.

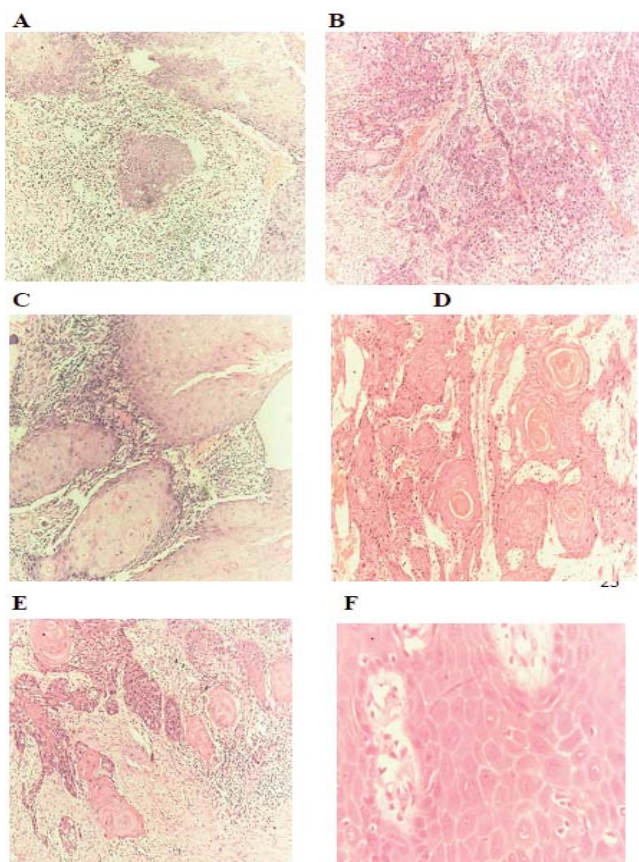


Figure-2: Haematoxylin and eosin (H&E)-stained photomicrographs of the histopathological spectrum of OSCC in Naswar users. (A) An island of pleomorphic epithelial cells surrounded by inflammatory infiltrate predominantly lymphocytes. (B) Sheets of malignant epithelial cells with focal areas of haemorrhage. (C) Keratin pearl formation within the island. (D) Well-formed numerous keratin pearls. (E) Invading sheets containing abnormally large cells into connective tissue. (F) Prominent desmosomes..

The buccal mucosa 28(35%) was the most frequent OSCC site, followed by alveolar ridge 20(25%), retro molar trigone 15(18.7%), lateral border of tongue 9(11.3%) and lip 8(10%) (Figure 1).

The most common histopathological presentation was well-differentiated SCC (WDSKC) 63(78.7%), followed by moderately-differentiated SCC (MDSKC) 13(16.2%), and 1(1.25%) case of adenoid SCC (ASKC), basaloid SCC (BSKC), papillary SCC (PSKC) and verrucous SCC (VSKC). Of the 45(56%) case with a usage history of >20 years, 33(73.3 %) had WDSKC, 8(17.7 %) had MDSKC and 1(2.2%) each had ASKC, BSKC, PSKC and VSKC (Table 2). The relation of histopathological pattern with duration of use was statistically non-significant ($p=0.10$). Microscopic features of OSCC patients consuming Naswar were also noted (Figure 2).

OSCC subtype had no significant association with age ($p=0.23$) and the site of lesion ($p=0.19$) (Table 3).

Discussion

In the current study, the age range for Naswar dippers developing cancer of oral cavity was 30-85 years, with maximum number of cases diagnosed in the 6th decade of life. The overall mean age of the sample was 56.98, which are comparable to other studies¹⁵⁻¹⁷, while some studies have reported mean age different from the current result.^{18,19}

Regarding gender, males were more affected than females, and this was in line with several studies worldwide.²⁰⁻²³ This is due to the fact that males consume Naswar more than females do.

The anatomical sites of OSCC reported from different regions exhibit variation, which could be explained on the basis of exposure to different risk factors. Bai et al.²⁴ and Fukumoto et al.²⁵ showed that the tongue was the frequently involved site, while the floor of the mouth was common in another study.¹⁹ The study reported buccal mucosa as the most common site of involvement for OSCC in snuff dippers. This might be due to the typical use of Naswar by placing it in the buccal sulcus where active ingredients are absorbed through mucosa, making the location high-risk for OSCC. The results are in line with earlier studies.^{26, 27}

Concerning the grades of OSCC, WDSCC (78.7%) was the most commonly occurring grade, which is similar to other studies.^{28,29} The present study identified 1(1.25%) case each of BSCC, ASCC, PSCC and VSCC variants of OSCC. Yasin et al. reported conflicting results, with 52% of spindle cell carcinoma³⁰, while another study concluded almost the same occurrence as 1% of BSCC and PSCC.³¹

The correlation of variables, such as duration of the use of snuff, age and site of tumour, was assessed with grades and variants of OSCC in the current study, and no statistically significant association was found between patient age and the histopathological differentiation or variant of OSCC. Although a predominance of WDSCC was observed across all age groups, occasional appearances of non-conventional subtypes, such as ASCC, in younger patients and VSCC, BSCC and PSCC in older individuals were noted. Lin et al. concluded a contrary relationship³², while Rahaman et al. and Abdulla et al. reported similar findings.^{33,34} The higher percentage of patients (56%) were in the group that consumed Naswar for >20 years, but it had no significant correlation with the histological pattern. While WDSCC remained the most common among all duration groups, patients with >20 years of use uniquely exhibited non-conventional SCC, indicating a possible link between prolonged exposure and more aggressive tumour histology. One study correlated different variants of OSCC with combined risk factors, showing a significant difference ($p=0.046$).³⁰ According to Sarfaraz et al., the same relationship was not significant in both Naswar users and non-users.³⁵ In the current study, the association of site of tumour with grades and variants was not significant, which is in contrast to earlier findings^{32,30}

The current study has a few limitations. Firstly, it was conducted at a single institution, which may restrict the generalisability of the findings. Secondly, the sample had only five participants who used Naswar alongside other tobacco products. The combined carcinogenic exposure may potentially amplify or mask the specific effects

attributable to Naswar alone.

Given the presence of conflicting findings in the existing literature, further research is warranted to explore the association between histopathological patterns of OSCC and various forms of SLT along with other relevant clinical parameters.

Conclusion

WDSCC was the most common OSCC variant among Naswar users, but long-term users uniquely exhibited non-conventional subtypes. Although age and site showed no significant associations, the findings raise concern about the potential histological impact of prolonged SLT use, reinforcing the need for targeted public health interventions in high-risk populations.

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Conflict of Interest: None.

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AUTHOR'S CONTRIBUTION:

FI: Design, literature search, data collection, analysis and drafting.

NB: Drafting and final approval.

HM: Literature search and data collection.

SA: Final approval.