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Clinicopathological Characteristics and Related Risk Factors of Oral Cancer: A Cross-Sectional Study

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ABSTRACT

Introduction: Oral cancer is the most prevalent and globally fifteenth-most reported cancer worldwide, as per International Agency for Research on Cancer (IARC). Several forms of oral malignancies are recognized clinically and pathologically, although oral squamous cell carcinomas (OSCC) account for 90% of all oral cancers.

Aim: To find out whether socioeconomic factors and clinicopathological traits may play a role in the development of oral squamous cell carcinoma (OSCC).

Methodology: A total of 197 individuals were incorporated in the study who were diagnosed and treated in the ENT department. A systematic questionnaire was used to collect clinicopathological and socioeconomic data. Descriptive analysis was used for socioeconomic status (SES) and demographics, whereas regression analysis was used to establish a link between SES and tobacco chewing practices, tumor size, and stage. Study design: A cross-sectional study. Place and Duration: This study was conducted at Jhalawan Medical College Khuzdar Pakistan from January 2021 to December 2021.

Results: We found a higher prevalence of males, +++++ and the average age of patients with OSCC was 43.6 ± 12.2 years. Most of the individuals had a low SES status, and 76.6% chewed tobacco and related substances regularly. Tobacco chewing behaviors or consumption of Smoke Less Tobacco (SLTs) products were substantially connected with gender (male) and SES ($p < 0.05$). The late-stage presentation of OSCC was strongly linked with middle age, tobacco chewing behaviors, and education ($= 0.05$).

Conclusion: Most OSCC cases were male patients in their forties from low socioeconomic backgrounds who had a long history of tobacco chewing practices. Tobacco chewers' most prevalent tumor site was the buccal mucosa, and the majority had advanced malignancies.

Key Words: Buccal cavity, Chewing Tobacco, Low socioeconomic status, Oral cancer, Tumor site, Smoke Less Tobacco

INTRODUCTION

Oral cancer is the most prevalent and globally fifteenth-most reported cancer worldwide, as per International Agency for Research on Cancer (IARC).¹ Oral cancer is becoming more common worldwide, with significant regional differences in incidence and mortality.² According to the GLOBOCAN 2018, there were 18.1 million new cancer diagnoses and 9.6 million cancer deaths in 2018, up from 14.1 and 8.2 million in 2012. Head and Neck Squamous Cell Carcinoma (HNSCC) accounts for six lac cases worldwide, with a death rate of 40%-50%, and the burden is expected to nearly quadruple in developing nations by 2030.³ Several forms of oral ma-

lignancies are recognized clinically and pathologically, although oral squamous cell carcinomas (OSCC) account for 90% of all oral cancers.⁴ In Southeast Asia, unlike in Western countries, the clinicopathological character of oral cancer differs greatly.⁵ Oral cancer is the second most prevalent cancer in Pakistan, Bangladesh, India, and Sri Lanka. In India, oral cancer is the most prevalent cancer among men, while it is the second most common cancer among Pakistani women.⁶ Western Africa and Eastern Asia have the lowest rates. Incidences are also low in North African countries. Malignant melanomas, salivary gland tumors, and soft tissue or jaw bone sarcomas are among the remaining cancers.

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OSCC can develop spontaneously or as a result of potentially malignant lesions. Males and the elderly are more likely to be affected. Exophytic, ulceroinfiltrative, and verrucous lesions are the most common types.⁴ Oral cancer is a multifactorial disease where genetic and environmental risk factors play a role. There is widespread agreement that patient, tumor, and treatment-related characteristics are predictors of survival. All factors such as gender, race, financial level, education, and family status affect the patient. Aspects to consider are grade, location, stage, and tumor biology for the diagnosis. Collective aetiological variables are tobacco, poor oral hygiene, smokeless tobacco (naswar), alcohol, and the human papillomavirus. Smokeless tobacco, such as naswar, betel leaf (paan), and areca nut, is widely used in Pakistan (gutka).⁷ There are around 28 recognized carcinogens in these chemicals, the most important of which being choline, volatile aldehydes, nitrosamines, nonvolatile alkaloid-derived, flavonoids, and tannins.⁸ All of these chemicals affect the normal shape of cells, resulting in cytogenetic or genetic changes. According to a study in Lahore, lip and oral cavity malignancies were the second most common form, and the most common addictions were naswar, paan, smoking and alcohol.⁹ Low socioeconomic level (SES) is associated with an increased incidence of HNSCC, found in low-income nations. Tobaccochewing habits have also been linked to low socioeconomic status and lack of education and are more widespread in males in the local setting.¹⁰ With such a high prevalence of OSCC in our population, there is scarce data on the prevalence and relationship of these practices with OSCC and poor socioeconomic status in recent years. Together with cigarettes and alcohol, poor oral hygiene is one of several variables that negatively impact oral cancer. Chronic inflammation, such as periodontitis, is caused by poor oral hygiene and can lead to oncogenesis and OSCC. This study aimed to determine the relationship between socioeconomic characteristics and tobaccochewing practices, including frequency of tobaccochewing, smoking, family history, and clinicopathological aspects of OSCC in a subset of high-risk populations.

METHODOLOGY

The present cross-sectional study included only those patients that were registered and treated with OSCC in our hospital. The 'cases' were pathologically confirmed oral cancer patients who were currently registered. Patients with OSCC of all ages were incorporated in the current investigation. Written consent and information with a pre-designed questionnaire were taken. Permission was taken from the ethical review committee of the institute. Patients other than OSCC were excluded, as well as those who declined to provide information or had inadequate contact information were disqualified from the present study.

The initial list from the ENT Department was taken from a hospital in which 205 patients were operated on with OSCC; contact information, medical record numbers, tumor site, and operation date were gathered, and patients were screened according to inclusion criteria. Out of the 8 patients who did not qualify for the inclusion criteria, they were omitted from the study, leaving 197 patients. A standard questionnaire was used to collect data on demographics, oral health conditions, and risk factors, including tobacco/betel nutchewing habits, smoking, occupations, and socioeconomic status were noted. Complete smoking and naswar consumption history were obtained. All forms of chewing substances, including naswar, paan, gutka, mawa and chalia etc. were regarded as tobacco chewing as they contain some form of tobacco. Pathologists studied extensive pathology reports to learn about the tumor stage, grade, and location. The staging was separated into two categories based on the AJCC 8th Edition criteria: early-stage (I, II) and late-stage (III, IV). The SPSS package version 21 was used to analyze age, gender, marital status, educational level, monthly income, type of occupation, patient condition, tobaccochewing habits, chewing frequency, chewing substance, smoking, smoking frequency, family history of cancer, tumor site and stage.

RESULTS

Descriptive analysis was used to estimate SES, and odds ratios (OR) were used to evaluate the association among dependent variables using univariate as well as multivariate logistic regression. The baseline sociodemographic characteristics of the patients are shown in **Table 1**. A total of 197 patients were incorporated in the present study 162 (82.2%) were males, and 35 (17.8%) were females. Out of the 84.8% were alive, and 15.2% were dead. In the present study, 35.1% of cases had completed middle/matric education, 13.2% completed intermediated, 23.8% with graduate or above education level, while 27.9% did not have any qualification. Our study includes 29.4% unemployed and 70.6% of patients were employed in a variety of occupations, including Labors 29.9%, Office workers (18.3%), Businessman (21.8%), Housewife (20.3%), Retired (4.1%) and other (5.6%) occupations were noted. The majority of the 42.6% of patients' monthly income was less than 20,000 PKR, 26.9% of patients' income was between 20,000 to 40,000 PKR, and 18.3% earned more than 60,000 PKR a month. A total of 89.8% of cases were married, and 10.2% were unmarried. Only 23.4% were smokers, with 19.7% being those who smoked more than 20 cigarettes. This study showed that 76.6% of cases were using some tobacco chewing, in 42.6% were using some sort of chalia regularly. Out of the 27.9% were using it more than 20 times a day. A total of 83.5% of patients had no family history of cancer. However, 16.5% of patients have some cancer history in the family. According

to the treatment types, 22.3% of the participants had multimodality treatment, including surgery, chemotherapy, and radiotherapy. Buccal mucosal cancer accounted for 68 % of tumors, whereas Grade II (moderately differentiated) cancers accounted for 68.5% of cases. Furthermore, 79 percent of the individuals were diagnosed with advanced cancer. SES and tobacco chewing habits were linked in a univariate logistic regression study. [As shown in Table 1]

Table 2 indicates the socioeconomic characteristics of patients with OSCC with tobaccochewing habits. Factors were considered significant when the CI was 95 percent, the OR was greater than one, and the p-value was < 0.05. Males were observed to have tobaccochewing habits more than two times higher compared to females (CI: 1.12–4.86). Patients with a low income of less than 20,000-40,000 PKR were more involved in tobacco chewing habits OR 3.4 (CI: 1.21–9.23). Whereas patients who earn >60,000 monthly were less involved in these activities. Patients with education (matric) were more involved in chewing tobacco OR 4.2 (CI: 1.72–10.61) than the educated patients who were less involved in these activities. No significant correlation was observed between tobacco chewing habits, marital status, cancer family history, smoking, and type of profession.

Table 3 shows the substantially linked variables ($p < 0.05$, OR >1) with the tumor site of OSCC patients. Univariate and multivariate logistic regression were used to examine the relationship between psychosocial characteristics and SES and the tumor site (buccal and non-buccal). Males were 2.7 times more prevalent than females to develop a buccal cavity tumor (CI: 1.32–6.54). In contrast, monthly income doesn't correlate with cancer sites. The patients employed were more likely linked with the tumor site of the buccal cavity. Age, occupation, marital status, family history, and chewing materials were not correlated with tumor size.

When the relationship between tumor stage early-stage (I/II) and late-stage (III and IV), psychosocial factors, and SES were examined, age, occupation, chewing substance (areca nut), and tobacco chewing habits with late-stage tumors were found significantly associated (As shown in Table 4). Middle-aged people (43.5 years) were more likely diagnosed with late-stage cancer (CI: 1.02–1.05). Tobacco chewing habits were linked to a 2.1-fold increased risk of acquiring late-stage cancer (CI: 1.9–5.24).

Table 1: Descriptive analysis for clinicopathological features, socioeconomic status, and demographics of OSCC

Characteristic		Frequency (%)
Gender	Male	162 (82.2)
	Female	35 (17.8)

Table 1: (Continued)

Characteristic		Frequency (%)
Current Status	Alive	167 (84.8)
	Dead	30 (15.2)
Occupation	Unemployed	58 (29.4)
	Employed	139 (70.6)
Types of Occupation	Office Worker	36 (18.3)
	Labor	59 (29.9)
	Businessman	43 (21.8)
	Housewife	40 (20.3)
	Retired	8 (4.1)
	Other	11 (5.6)
Marital Status	Married	177 (89.8)
	Unmarried	20 (10.2)
Education	Uneducated	55 (27.9)
	Middle/matric	69 (35.1)
	Intermediate/diploma	26 (13.2)
	Graduate/master	47 (23.8)
Family income (monthly)	< 20,000	84 (42.6)
	20,000- 40,000	53 (26.9)
	40,000- 60,000	24 (12.2)
	> 60,000	36 (18.3)
Smoking Status	Yes	46 (23.4)
	No	151 (76.6)
No. of Cigarettes per day	< 5	64 (32.5)
	6-20	94 (47.8)
	> 20	39 (19.7)
Use of tobacco	Yes	151 (76.6)
	No	46 (23.4)
Types of Tobacco	Paan	84 (42.6)
	Chalia	45 (22.8)
	Gutka	61 (31)
	Mawa	4 (2)
	Naswar	10 (5.1)
	Pure Tambaku	31 (15.7)

Table 1: (Continued)

Characteristic		Frequency (%)
Frequency of tobacco use daily	< 5 times	76 (38.6)
	6-20 times	66 (33.5)
	> 20 times	55 (27.9)
Types of cancer in the family	Lung cancer	23 (11.6)
	Oral cancer	6 (3.04)
	Other cancers	3 (1.52)
	None	165 (83.5)
Patients Treatment	Chemotherapy	4 (2)
	Radiotherapy	9 (4.6)
	Surgery	44 (22.3)
	Surgery + Chemotherapy	10 (5.1)
	Surgery + Radiotherapy	23 (11.7)
	Surgery + Chemotherapy + Radiotherapy	77 (39)
	Chemotherapy + Radiotherapy	30 (15.2)
Tumor site	Buccal Mucosa	134 (68)
	Non-Buccal Mucosa	63 (32)
Tumor Grade	I	39 (31.5)
	II	135 (68.5)
	III	23 (11.7)
Tumor Stage	Early (I, II)	48 (24.4)
	Late (III, IV)	(75.6)

OR 1 is taken as Reference, $p < 0.05$ as significant.

Table 2: In OSCC patients, univariate and multivariate regression analyses were used to examine SES features with tobaccochewing patterns as dependent factors.

Variable	Tobacco Chewing Habits		Odd Ratio (95% CI)-univariate	Odd Ratio Adjusted (95% CI)-multivariate
	(Yes)	(No)		
Age	43.6 ± 12.2	51.8 ± 13.6	1.0 (1.01-1.05)	
Gender				
Male	131 (80.9)	31 (19.1)	2.1 (1.12-4.86)	

Table 2: (Continued)

Variable	Tobacco Chewing Habits		Odd Ratio (95% CI)-univariate	Odd Ratio Adjusted (95% CI)-multivariate
	(Yes)	(No)		
Female	22 (62.8)	13 (37.2)	1 (Reference)	
Monthly income				
<20,000	68 (80.9)	16 (19.1)	2.5 (1.01-6.02)	
20,000-40,000	47 (88.7)	6 (11.3)	3.6 (1.09-10.3)	
>60,000	22 (61.2)	14 (38.8)	1	
Education				
None	42 (76.3)	13 (23.6)	2.2 (1.01-4.78)	6.2 (1.52-24.60)
Middle/Matric	60 (87)	9 (13)	4.2 (1.72-10.61)	5.6 (1.67-20.98)
Intermediate/Diploma	21 (80.8)	5 (19.2)	3.3 (1.02-12.01)	
Graduation and above	18 (38.3)	29 (61.7)	1	

OR 1 is taken as Reference, $p < 0.05$ as significant.

Table 3: Analysis of SES characteristics with tumor sites using univariate and multivariate regression analysis in OSCC patients.

Variable	Oral Cavity n (%)	Non-Oral Cavity n (%)	OR (95% CI)-univariate	Adjusted OR (95% CI)-multivariate
Gender				
Male	119 (73.5)	43 (26.5)	2.7 (1.32-6.54)	
Female	35 (48.5)	18 (51.5)	1 (Reference)	
Monthly income				
20,000	58 (69)	26 (31)	1.6 (0.81-4.13)	4.3 (1.52-12.7)
20,000-40,000	43 (81.1)	10 (18.9)	3.4 (1.21-9.23)	4.8 (1.7-14.6)
60,000	19 (52.8)	17 (47.2)	1	
Education				
Middle/Matric	55 (79.7)	14 (20.3)	3.1 (1.28-7.6)	
Graduation and above	26 (55.3)	21 (44.7)	1	

OR 1 is taken as Reference, $p < 0.05$ as significant.

Table 4: Association of significant correlation of tumor stage of OSCC patients with SES using univariate and multivariate regression analysis.

Factors	Early Stage Tumor	Late Stage Tumor	OR (95% CI)-univariate	Adjusted OR (95% CI)-multivariate
Age	51.8 ± 12.9	43.5 ± 10.6	1.02 (1.02–1.05)	1.03 (1.0–1.06)
Tobacco Chewing Habits				
Yes	27 (17.8)	124 (82.2)	2.1 (1.9–5.24)	
No	16 (34.8)	30 (65.2)	1 (Reference)	

OR 1 is taken as Reference, $P < 0.05$ as significant.

DISCUSSION

OSCC is a major public health issue in areas where tobacco-chewing and smoking of tobacco products is frequent with or without alcohol consumption. Tobacco smoking has increased, posing a multifaceted problem and a hazard to the health of 'Pakistan's youth. Exposure to familial, sibling, and peer group pressure, peer smoking, availability to smoking and nonsmoking forms of tobacco, strong advertising and promotion, and low cost are among a few variables that contribute to teenage tobacco use.¹¹ According to the Global Adult Tobacco Survey (GATS, 2009–2010), one-third of India's 15-year-old population uses tobacco in some manner.¹² People aged 15 to 49 have a habit of using tobacco somehow, with 32.9% of men and 18.4% of women using smokeless tobacco.¹³

In the present study, age was found to have a strong relationship with tobacco chewing habits, similar to findings from Pakistan and India, where patients' average ages ranged from 41 to 50 years.^{6,14} Our study observed that males had more prevalent tobacco chewing habits than females. Similar observations were found in different studies.^{15–17} These chewing tobacco, gutka, betel nut, paan, etc., contain dangerous substances, so education about their use is critically important. OSCC is highly linked with the poor socioeconomic background; because of their limited resources, lack of education, and knowledge, they are mostly unaware of the dangerous substances found in these materials. The use of tobacco is mostly associated with the low socioeconomic class as an entertainment source. As per a recent review, tobacco use was roughly twice as high in low-income and participants of socioeconomic status groups.¹⁸ Tobaccochewers or consumers of SLTs in our cohort had two times the risk of OSCC in the buccal mucosa cavity. It was significantly linked to men and poor socioeconomic status, as evidenced by several regional studies that identified the buccal cavity as the most common location of infection.^{19,20} One reason is that the chewing material stays longer in the mouth and can significantly damage mucosa with harmful substances. Long-term exposure to these compounds generates mechanical friction in the buccal mucosa, which can develop into invasive malignancy or premalignant lesions. The rate of tobacco consumption per

day had no significant relationship with the site of the tumor, and the bulk of users chewed these 1–5 times per day for about 20 years. Similar findings were observed in the study in Bangladesh.²¹ In our study, their age, occupation, marital status, family history, and chewing materials were not correlated with OSCC. Whereas, in an Iran study, OSCC was more common in widowed/divorced (mostly widowed) adults.²²

Tumor stages were divided into two categories in this study: early-stage and late-stage (stages I and II) (stages III and IV), respectively. The findings of this study suggest a link between low SES and chewing behaviors and late-stage presentation, which is corroborated by other research. Agarwal et al. (2011) showed that 62% of patients who reported late-stage disease were from low socioeconomic strata.²³ Patients with a poor socioeconomic status are more likely to develop OSCC, but they are also more likely to be detected at a later stage.²⁴ Unfortunately, most cancer patients in Pakistan present late in their disease for various reasons, lack of awareness, lack of education, poverty, inaccessibility to healthcare, social repercussions, fears, and so on. In our study, only 22% of patients were chronic smokers, and we observed smoking had no significant correlation between tumor stage and site with chewing behaviors.

Some patients chewed multiple products together. This could result in a synergistic effect because the tobaccochewing habits of patients varied, and the duration of chewing and the quantities of materials they used were widely different. Other variables such as family history, cancer type, and marital status didn't affect the results, implying that chewing habits, stage, and tumor site are less likely to be affected.

CONCLUSION

Tobacco chewing or use of other Smoke Less Tobacco (SLTs) products behaviors are the major cause of the OSCC increase in our region, which causes the normal mucosa of the oral cavity to change, resulting in cancer. Males were more prevalent for the use of tobacco than females. Despite recent increases in tobacco product prices, total tobacco consumption has increased, even among the poorest socioeconomic

groups. Low socioeconomic status patients with lower education levels were more involved in using these substances. General awareness should be implicated to the population for using these harmful substances that lead to OSCC.

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Conflict of interest

None

Permission

The ethical review committee approved the study of the institute

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