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ORIGINAL ARTICLE

Impact Of Different Types Of Addiction On Oral Squamous Cell Carcinoma In Pakistani Population

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ABSTRACT

OBJECTIVE: To determine the frequency of different types of oral cavity malignancies in relation to smokeless tobacco addiction.

METHODS: This was a retrospective Cohort Study. Conducted in Department of Otolaryngology, Patel Hospital Karachi.

METHODOLOGY: All biopsy proven cases of oral squamous cell carcinoma (SCC) were included and files from January 2015 to 2020 were retrieved by ICD coding system and total number of files included were 600. A brief history of patient demographics including their eating, chewing, and drinking habits and clinical characteristics were included.

RESULTS: Among the study population most of the patients had history of addiction. These were 492 patients out of which 233 had addiction with chewable tobacco and 259 were smokers only however 65 patients were addicted to both kinds of tobacco. The highest incidence of diagnosis of SCC was seen in group who were addicted to all forms of tobacco followed by patients addicted with chewable tobacco and least incidence was seen in patients with smoking addiction, with a significant p-value.

CONCLUSION: This study concludes that there is a strong association between smokeless tobacco use and squamous cell carcinoma of the oral cavity, the strongest association being with multiple addictions.

Abbreviations: Oral cavity Squamous cell carcinoma (OCSCC), squamous cell carcinoma (SCC), World Health Organization (WHO), Ethical review committee (ERC).

Keywords: Oral cavity cancer, smoking, tobacco, Squamous cell carcinoma

INTRODUCTION: Oral squamous cell carcinoma is one of the most commonly occurring carcinomas in the world. Regarding its prevalence, Pakistan has the highest rates of this carcinoma in the world after Papua New Guinea.[1] As far as the local registry of Karachi is concerned, the oral cavity squamous cell carcinoma is the commonest cancer in the male population, and in females, it is the third most malignant tumour. [2] Chewable tobacco usage in the sub-continent dates to hundreds of years. [3]

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Squamous cell carcinoma (SCC) of the oral cavity represents a substantial health burden in Pakistan with a high incidence and associated mortality rates. Oral cancer is a multifactorial disease, and tobacco consumption is recognized as a significant risk factor contributing to its development. Oral Cancer can affect the lips, gums, tongue, inner surface of the cheeks, and the lining of the mouth. [4] In Asia, smoking and smokeless tobacco are the main reasons for oral cavity squamous cell carcinoma but alcohol, sun exposure of the lips, and weakened immune system are also among the causes. [5] In Pakistan, both oral and smoked forms of tobacco are prevalent, and understanding their respective roles in the ethology of SCC is crucial for devising effective prevention and control strategies.

According to a report by the United Nations World Health Organization (WHO), Pakistan is one of the countries where a large number of people die from diseases caused by addiction of smokeless tobacco. (6) Tobacco use is deeply ingrained in the social fabric of Pakistan, with widespread prevalence across various age groups and socioeconomic backgrounds. The two primary forms of tobacco consumption in the country are oral tobacco, in the form of betel quid and gutka, and smoked tobacco, predominantly in the form of cigarettes and hookahs. Each of these methods exposes the oral cavity to carcinogenic agents, initiating a cascade of events leading to malignant transformation. The tobacco industry has a long history of employing sophisticated marketing strategies to promote their products and attract new consumers. In recent years, Pakistan has witnessed a surge in advertising campaigns promoting various tobacco-related products, including cigarettes, smokeless tobacco, and electronic cigarettes. These campaigns utilize persuasive techniques, appealing to emotions, aspirations, and social acceptance, to entice individuals, particularly the youth, into tobacco consumption. (7) There is a positive association between exposure to tobacco advertisements and increased smoking prevalence among Pakistani adolescents. (8) It is well established that a significantly increased risk of oral cancer is present among individuals using smokeless tobacco products in Pakistan. (9) Moreover, there is an elevated risk of oesophageal cancer associated with smokeless tobacco use in the country. (10)

Since there have been no significant previous epidemiological studies on smokeless tobacco as the main risk factor for head and neck carcinogenesis in Karachi, we here carried out a hospital based retrospective cohort study in a tertiary care hospital.

This research paper seeks to undertake a comparative analysis of the association between oral and smoked tobacco consumption and the development of SCC and other malignancies in the oral cavity among the Pakistani population. By elucidating the specific risks posed by each form of tobacco use, we aim to identify potential differences in the malignant transformation of SCC patients and public health implications, which can pave the way for targeted and evidence-based interventions. Understanding the frequency of incidence and malignant transformation among oral and smoked tobacco products will provide valuable insights into the differential risks associated with each form of tobacco use.

STUDY METHOD: This was a retrospective Cohort Study. Conducted in Department of Otolaryngology, Patel Hospital Karachi, Pakistan after getting the approval from Ethical review committee (ERC). All patients underwent biopsy of oral cavity lesions for histopathology of both genders, age ranged from 25-70 years were included and excluded if there are any psychiatric or mental disorder or non-consenting patient. File from Jan 2015 to 2020 were retrieved by ICD 9 coding system and total number of files included were 600, the patients were divided in two groups smokers and addiction with chewable tobacco. Nonprobability Consecutive Sampling technique was used.

Confidentiality was assured and medical record numbers was represented by a special tag number and only the primary investigator had access to them. Informed consent was taken from the patients or their families, for all the patients included in study. A brief history of patient demographics including their eating, chewing, and drinking habits and clinical characteristics was used in this study to test the hypothesis.

Patients had been asked about their addiction history. Data collected with pre- designed structured questionnaire (provided in annexure A). Informed consent (provided in annexure B) was by all patients before enrolling them in the study.

Data Analysis: Demographic characteristics of the patients was summarized in terms of mean ± standard deviation for quantitative variables like age and weight. While Qualitative variables like gender and different categories of chewing and eating habits was summarized in terms of percentages. Normality distribution was seen by Shapiro Kolmogorov test. Chi-square test for two proportions was performed to obtain the relationship between different qualitative variable with 95% confidence interval (6). Data will be analysed by using SPSS version 21 and a P-value less than 5% will be taken as statistically significant.

RESULTS: Using ICD coding system 679 files were retrieved during the specified period out of these 600 were included. The study population consists of 458 men and 142 women clearly showing a male predominance. The age varies from 22 years to 72 years with mean of 47.2 $\pm$ 12.14. Most common pathology was squamous cell carcinoma seen in 486 patient comprises of 81% of population. Seventy-six patients which is 12.7% were the benign tumours and 38 patients (6.3%) were of other malignancy other than squamous cell carcinoma. Rest of the demographic's variable were shown in Table 1.

Table – 1: Demographics

Baseline Characteristics		**F (%)**
Age	Mean ± Sd	47.2 ± 12.14
Gender	Male	458(76.3%)
	Female	142(23.7%)
Addiction	None	43(7.2%)
	Smoking	65(10.8%)
	Pan	108(18%)
	Supari/Chalia	41(6.8%)
	Gutka	50(8.3%)
	Multiple	252(42%)
	Others	35(5.8%)
	Niswar	6(1%)
Addition	Smoker	65(10.8%)
Chewing	TobaccoTobacco/ Smoker	233(38.8%)
	Both	259(43.2%)
	None	43(7.2%)
Chewable		
Tobacco	Yes	492(82%)
History	No	108(18%)
Smoking	Yes	324(54%)
History	No	276(46%)
Biopsy Finding	Squamous Cell Carcinoma	486(81%)
	Benign Tumour	76(12.7%)
	Other Malignancy	38(6.3%)
Site of lesion	Multiple	28(4.7%)
in Oral Cavity	Soft Palate	4(0.7%)
	Hard Palate	9(1.5%)
	Lips	58(9.7%)
	Floor Of Mouth	5(0.8%)
	Cheek	279(46.5%)
	Upper Alveolar Ridge	9(1.5%)
	Lower Alveolar Ridge	40(6.7%)
	Mandible-Body	18(3%)
	Retromolar Area	17(2.8%)
	Tongue	133(22.2%)
Nature Of	Primary	483(80.5%)
Lesion	Second Primary	8(1.3%)
	Synchronous	3(0.5%)
	Recurrence	18(3%)
	Residual	12(2%)
	None	76(12.7%)

Among the study population most of the patients had history of addiction. These were 492 patients out of which 233 had addiction with chewable tobacco and 259 were smokers only however 65 patients were addicted to both kinds of tobacco. There were only 43 patients which comprises of 15.2% of study population that were non addicted, as shown in Table 2.

Table-2: Comparison of Chewable Tobacco and Smoking History

	Smoking History	
Chew Tobacco History	No	Yes
No	43(15.6%)	65(20.1%)
Yes	233(84.4%)	259(79.9%)
Total	276(100%)	324(100)

According to table 3, most of the patients diagnosed with squamous cell carcinoma of the oral cavity were addicted. The highest incidence was seen in group who were addicted to all forms of tobacco followed by patients addicted with chewable tobacco and least incidence was seen in patients with smoking addiction. The p value is also significant for this association.

Table-3: Comparison of different oral cavity pathologies and different types of addiction

Biopsy Finding	Addiction					
	Smoker	Chewing Tobacco	Both	None	Total	P-value
Squamous Cell Carcinoma	22(4.5%)	195(40.1%)	236(48.6%)	33(6.8%)	486(100%)	<0.0001*
Benign Tumour	39(51.3%)	24(31.6%)	11(14.5%)	2(2.6%)	76(100%)	
Other Malignancy	4(10.5%)	14(36.8%)	12(31.6%)	8(21.1%)	38(100%)	

DISCUSSION: Squamous cell carcinoma was the most common pathology in most among all the lesions of oral cavity this has been shown by our study and by the regional and western literature. (11,12,13) Males was the predominant gender as shown in study conducted by Zhang et all. (11) The most common site of lesion was buccal mucosa in our study, like the results presented in the studies of Noggle and Wolfer et all. (14,15) Most of our patients were addicted to both kinds of tobacco and this was also consistent with a study conducted by Khan and Hasan et all. [16,17]

Our results are consistent with previous studies that have identified smokeless tobacco as a primary risk factor for oral malignancies. Qureshi et al. (2) reported a high incidence of oral cavity cancers (C00-C06) in Pakistan, particularly among individuals with a history of gutka and betel nut consumption. Basu et al. (4) similarly identified tobacco use as a leading risk factor for head and neck squamous cell carcinoma in an Indian population. Awan et al. (7) emphasized the heightened risk of oral cancer in individuals using gutka and other smokeless tobacco products, reinforcing our findings. Additionally, Ali et al. (5) observed a greater burden of oral malignancies in smokeless tobacco users compared to smokers, supporting our study's conclusion that exclusive smokers had a lower prevalence of SCC than those using smokeless tobacco. However, contrasting findings by Malik et al. (8) indicate that tobacco advertisements have contributed to a growing prevalence of smoking among adolescents, which may alter future trends in smoking-related malignancies. These discrepancies highlight the evolving patterns of tobacco use and the necessity of continued research in this area.

The high prevalence of SCC among smokeless tobacco users can be attributed to the carcinogenic effects of arecoline, nitrosamines, and heavy metals, which induce DNA damage, promote cell proliferation, and enhance inflammatory responses. The frequent placement of these substances in the buccal mucosa (cheek region) likely explains the high frequency of lesions in this anatomical site.

From a public health perspective, our findings underscore the urgent need for regulatory policies on the sale and advertisement of smokeless tobacco products. Raising awareness about the increased risk of oral cancers associated with chewing tobacco is crucial, particularly in South Asian populations where its use is deeply rooted in cultural practices. Public health campaigns should aim to educate individuals on the risks and promote tobacco cessation programs to mitigate the rising incidence of oral malignancies.

As it was retrospective study hence there is a possibility of recall bias along and the cross-sectional design prevents the establishment of casualty. Potential confounding factors such as alcohol consumption, genetic predisposition, and dietary habits were not assessed In future to obtain more meaning full information we should try to conduct longitudinal research to establish causality between different forms of tobacco use and oral malignancies. Investigate the molecular mechanisms underlying tobacco-induced carcinogenesis in South Asian populations. Evaluate the impact of tobacco cessation programs and public health interventions in reducing oral cancer incidence.

CONCLUSION: This study highlights the strong association between smokeless tobacco use and squamous cell carcinoma of the oral cavity. Given the high burden of oral malignancies in South Asia, urgent public health efforts are needed to reduce the consumption of smokeless tobacco. Strengthening preventive measures, public awareness, and policy regulations will be crucial in addressing this growing health crisis.

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