CLINICO-PATHOLOGICAL FEATURES OF ORAL SQUAMOUS CELL CARCINOMA AMONG TOBACCO USERS AND NON-TOBACCO USERS

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Abstract

Objectives: *To assess the clinicopathological features of oral squamous cell carcinoma (OSCC) cases among tobacco users and non -users.*

Materials & Methods: *This cross-sectional study was conducted at various departments of oral and maxillofacial surgery [BKDC, KCD, PDC, KIDS, PIMS] and IRNUM on 140 cases of OSCC from March 2103 to September 2017. OSCC cases were randomly selected by adopting a convenient sampling technique. Histopathologically diagnosed cases of OSCC with and without a history of tobacco products use were included. Data regarding age, gender, primary anatomical site of a tumour and details about the type and pattern of tobacco products use were recorded, evaluated and analyzed by SPSS version 20.*

Results: *The mean age recorded for OSCC patients was 53.03 years with a male to female ratio of 1.5:1. The least commonly affected site was a lip (3%). The most commonly occurring histopathological grades among tobacco users and non-users were well differentiated squamous cell carcinoma (WDSCC) and moderately differentiated squamous cell carcinoma (MDSCC) respectively. Majority of cases presented in stage III (46%), followed by stage IV (25%), stage II (21%) and stage I (8%).*

Conclusion: *The study observes a high frequency of male tobacco user patients, aged 40 years and above. PDSCC was the least commonly observed histopathological grade among tobacco users and non-users. Most commonly affected sites of development for OSCC were cheek mucosa, retromolar area and vestibule of mouth and mostly the patients reported in the late stage (III) of oral malignancy.*

Key Words: *Oral Squamous Cell Carcinoma, Tobacco, Grading and TNM staging.*

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Introduction

Globally, oral cancer represents one of the most commonly occurring malignant neoplasms[1]. In Pakistan, it is the 2nd most prevalent (6.06%) malignancy affecting both adult male and female

population[2,3]. The peak age incidence of occurrence of the disease is 40-60 years. The most commonly occurring histopathological variant of oral cancer is a conventional type of squamous cell carcinoma[4]. Besides tobacco, multiple risk factors (eg., Alcohol, HPV etc.) are proved to be responsible for oral squamous cell carcinoma (OSCC)[5-10]. Tobacco is one of the confirmed risk factors for the development of oral malignancy[11,12]. Tobacco is a product manufactured by curing of leaves of the tobacco plant[13]. It was introduced to the world in 1492[14]. The tobacco products consumed orally include smoked tobacco (ST) and smokeless tobacco (SLT). Both of the forms are consumed in most of the regions of the world, in different forms, numerous presentations and various constituents[15,16]. All forms of tobacco are carcinogenic. According to the International Agency for Research on Cancer (IARC), there are about 70 carcinogens in ST products and 28 carcinogens in SLT products. The most harmful carcinogens are tobacco-specific nitrosamines (TSNA). They include four compounds (N-nitrosonornicotine; NNN, Nicotine-derived nitrosamine ketone or 4-methyl-N-nitrosamino-1-(3-pyridyl) -1-butanone; NNK, n- nitrosoanatabine; NAT and n-nitrosoanabisine; NAB). Among them, two, (NNN and NNK) are considered to be potentially carcinogenic[17,18]. TSNA are present in very low concentration in green tobacco but their concentration increases during curing, when amine alkaloids in tobacco leaf react with either nitrite, which is formed by the reduction of nitrate by bacterial activity or nitrous oxides, which are combustion by-products of firing-curing[19,20]. The carcinogens in the tobacco damages the DNA causing mutation in the genome of oral epithelial tissue. This leads to the development of OSCC[17,21]. The present descriptive cross-sectional study is designed to assess the clinicopathological features of OSCC cases in general and to evaluate these features specifically in tobacco users and non-users. This will add knowledge to the existing literature specifically related to clinicopathological characteristics of tobacco non-tobacco users in our community.

Materials and Methods

This study was conducted on 140 histologically diagnosed cases of OSCC at the department of oral and maxillofacial surgery (Bacha Khan Dental College; Mardan, Khyber College of Dentistry [KCD], Peshawar Dental College [PDC], Pakistan Institute of Medical Sciences (PIMS); Islamabad, and Kohat Institute of Dental Sciences[KIDS]) from March 2016-September 2017; and at IRNUM Peshawar, from March 2013-August 2013 and April 2017 – September 2017. Non-probability, convenient sampling technique was adopted. Histopathologically diagnosed cases of OSCC with and without a history of tobacco use were included in the study that was willing to participate.

The data was recorded on proforma which contained details of patients demography, type of tobacco product being consumed (smoked tobacco[ST] or smokeless tobacco[SLT] or both), present status of tobacco use, frequency of use in days, tobacco consuming habit in years and case of SLT ; association between the site of placement and development of lesion were included. Data was documented, evaluated and analyzed by statistical package for social sciences (SPSS) version 20. Results were analysed using Chi-square test, Fisher's exact test and where appropriate. A p-value of ≤ 0.05) was considered statistically significant.

Results

Results of our study are summarized in table 1,2,3 and 4. The age of study participants ranged from 20-95 years (53.03±14.02). In our study, 83% of subjects presented with age greater than 40 years, among them 34% were exposed to tobacco. A comparison made between the habit of tobacco use and gender revealed a significant difference (0.001) [Table-1]. The most commonly occurring histopathologic grade was moderately differentiated squamous cell carcinoma; however among non-tobacco users well-differentiated squamous cell carcinoma was the common grade [Table-1].

Among the OSCC cases most commonly (N=51) affected sites were cheek mucosa, the vestibule of mouth and retromolar area and the least commonly affected site was a lip (N=5) among both tobacco and non-tobacco users[Table-1].

Regarding the stage of a tumour; most of the non-tobacco users presented in stage III [N=34(24%) and most of the tobacco using patients reported in stage IV [N=19(13%)][Table-1].

Among male and female population of our study who are exposed to tobacco, a non- significant difference was observed for the type of tobacco prod-

uct consumed (p=0.06), present status of tobacco (p=0.12), frequency of tobacco product per day (p=0.15) and total period of tobacco use in years (p=0.67) [Table-2].

Among naswar (a type of SLT) users the relation between the site of placement of the product and development of OSCC lesion revealed a non- significant difference (p=0.88).

A comparison made between histopathological grades of a tumour and site of development of a tumour revealed a significant difference (p=0.01) while comparison made between histological grade and stages of OSCCrevealed non-significant difference (0.57) [Table-4].

Discussion

OSCC is prevalent in most of the regions of Pakistan and is one of the most commonly occurring malignancies in Pakistan[22-25]. Tobacco is consumed in many areas of the country and has been proved to be one of a highly associated risk factor with the development of OSCC in Pakistani population[26-30]. The Present cross-sectional study is planned to assess and report the clinicopathological features of OSCC among tobacco users and non-tobacco users.

Table 1: Study subjects clinicopathological characteristics

Variables		Tobacco history		Total	P value
		Yes	No		
Age	Less than 40 yrs	10 (7%)	14 (10%)	24 (17%)	0.97
	Greater than 40 yrs	48 (34%)	68 (49%)	116(83%)	
Gender	Male	45 (32%)	40 (29%)	85 (61%)	0.001
	Female	13 (9%)	42(30%)	55 (39%)	
Histopathological grade	WDSCC	26(18%)	31(23%)	57 (41%)	0.21
	MDSCC	24(17%)	45(32%)	69 (49%)	
	PDSCC	8(6%)	6 (4%)	14 (10%)	
Stage of tumor	Stage I	3(2%)	9 (6%)	12 (8%)	0.02
	Stage II	6 (4%)	23 (17%)	29 (21%)	
	Stage III	30 (22%)	34 (24%)	64 (46%)	
	Stage IV	19 (13%)	16 (12%)	35 (25%)	
The site of development of OSCC	Lip	2 (1%)	3 (2%)	5 (3%)	0.50
	Tongue	14 (10%)	20 (15%)	34 (15%)	
	Gum	15 (11%)	11 (8%)	26 (19%)	
	Floor of mouth	5 (3%)	8 (6%)	13 (9%)	
	Palate: Soft,hard	5 (4%)	6 (4%)	11 (8%)	
	Cheek mucosa,retromolar area,vestibule of mouth	17 (12%)	34 (24%)	51 (36%)	

Table 2: Pattern of Tobacco usage among OSCC cases with a history of tobacco usage

The pattern of tobacco use	Male (N)	Female (N)	p-value
i) Type of tobacco product consumed			
Smokeless tobacco(SLT)	24	9	0.06
Smoked tobacco (ST)	16	3	
Both forms of tobacco(SLT&ST)	5	1	
ii) Present status of tobacco consumed			
Current snuff user	34	7	0.12
Ex snuff user	11	6	
iii) The frequency of tobacco product consumed			
1-10 times/day	29	11	0.15
>10 times/day	21	3	
iv) Exposure period in years to tobacco product consumed			
1-10 yrs	10	4	0.67
11-20 yrs	20	4	
>20 yrs	19	6	
v) In case of SLT positive association between site of placement of SLT and development of the lesion			
Yes	8	3	0.88
No	21	7	

Table 3: Site of involvement of lesion with Histopathological grades of OSCC among both tobacco users and non-tobacco users

Histopathological grade	The site of OSCC lesion						Total	p-value
	Lip	Tongue	Gum	Floor of Mouth	Palate	Cheek Mucosa, retromolar area, vestibule of mouth		
WDSCC	2	13	13	4	3	22	57 (41%)	0.01
MDSCC	2	17	11	6	7	26	69 (49%)	
PDSCC	1	4	2	3	1	3	14 (10%)	
Total	5 (4%)	34 (24%)	26 (19%)	13 (9%)	11 (8%)	51 (36%)	140 (100%)	

Our study revealed that most of the cases of OSCC reported in the age greater than 40 years. This finding is consistent with the findings observed other authors; locally and internationally published reports[31,32,33]. Our study reported male to female ratio of 1.5:1; which is, in contrast, to study by Khan AS[31] and Khan A et al[36]. (4:1), and in accordance with Nisar W[33], Feller L et al[37]. (1.5:1) and Khan A[32] (1.4:1). This finding is consistent with the view that males are more likely indulged in tobacco using habits than females.

Our study showed that buccal mucosa, retromolar area and vestibule of the mouth are among the most common sites for the development of OSCC.

Table 3: Site of involvement of lesion with Histopathological grades of OSCC among both tobacco users and non-tobacco users

		Stage of Tumor				Total	P value
		Stage I	Stage II	Stage III	Stage IV		
Histopathological Grade	WDSCC	7	11	23	16	57 (41%)	0.57
	MDSCC	4	17	33	15	69 (49%)	
	PDSCC	1	1	8	4	14 (10%)	
Total		12 (8%)	29 (21%)	64 (46%)	35 (25%)	140 (100%)	

This may be due to the habitual carrying of tobacco products, especially SLT by their consumers in such sites. Considering the commonly affected primary site and commonly observed histological grade (MD-SCC) of OSCC our study results are in agreement with other nationally and internationally reported studies[31,32,33,34]. Our study observed that most of the cases of OSCC reported in advance stage of OSCC (stage III, followed by IV, II and I). These findings are comparable with a study conducted by Nisar W et al[33]. and contrary to Alamgir MM et al[38]. (stage II, followed by IV, III and I) and Rikardsen et al[39] (stage II, followed by, III, and IV).

While comparing patterns of tobacco use our results varied, if compared to other studies. Our study reported that among SLT users only 11(28.2%) cases of expressed positive association between site of placement of SLT product and OSCC lesion. These findings are contrary to study by Khan M[40] who observed strong association (N=80(80%) of naswar (an SLT product) placement with the primary site of development of OSCC.

In our study, among OSCC cases SLT products are more frequently used than ST products. These findings are consistent with the study conducted by KM Bile[41].

In our study, a comparison made between the habit of tobacco use and age, gender, histopathological grade revealed a non-significant difference. However, a significant difference was observed with gender (p=0.001) and stage of a tumour (0.02).

By adopting the non-probability convenient sampling technique, the findings in our study may not be a perfect representative of the clinicopathological features of OSCC in our region, which has a high prevalence of the said disease. Besides the addition of knowledge to the existing literature about the characteristics of OSCC subjects; our study may help the researchers of our region to some extent in planning studies related to OSCC and tobacco. The detailed history taking about the risk factors regarding the development of OSCC can always be kept in mind while interviewing the carcinoma patients and should be recorded while sending the biopsy specimen to the oral /histopathologist.

Conclusion

This study revealed that OSCC is more common among male subjects with age 40 or above and mostly presented in the late stage (III & IV) of the disease. Our study concludes that there exist a relationship gender and stage of OSCC with a history of tobacco product used. Also, a relation was observed between the primary site of OSCC and histopathological grade.

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