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ORIGINAL ARTICLE

CLINICOPATHOLOGICAL SPECTRUM OF ORAL SQUAMOUS CELL CARCINOMA AT A PUBLIC SECTOR HEALTH FACILITY

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ABSTRACT

Background: Oral epithelial cancer is one of the most common malignant diseases in the world. Over 90% of the oral cancers are oral squamous cell carcinomas (OSCC), which arise from epithelial lining of oral cavity. It is the second most frequent cancer in Pakistan. The aim of this study was to assess the demographic and clinicopathological features of oral cancer patients reporting to Department of Pathology at Post Graduate Medical Institute, Lahore, Pakistan.

Methods: This cross – sectional descriptive study was done from January 2013 to December 2013. Demographic, clinical and pathological details of cases diagnosed with oral squamous cell carcinoma were collected. Anneroth et al, multifactorial grading system was used to perform histological grading. SPSS version 19.0 was used to analyze the data.

Results: Of the total 57 cases majority of patients were in their 4th and 5th decades of life with male predilection as male to female ratio was 1.3:1. Major risk factors reported were smoking (n = 33) and chewing tobacco (n = 18). Majority of oral cancer cases were seen in age group 41 – 50 year. Buccal mucosa was the most commonly affected site followed by tongue. The most common clinical complaint was ulceration and well differentiated sqaumous cell carcinoma appeared as the major histopathological type.

Conclusions: Oral cancer is a common malignancy in Pakistan with tendency of developing among males and at an early age. This study lays emphasis on awareness about the role of various risk factors such as tobacco and related products.

Key Words: Oral cancer, Squamous cell carcinoma, Oral pathology, Oral neoplasm, Oral cavity, Pakistan.

INTRODUCTION

Globally oral cancer is amongst the top fifteen most common cancers as reported by International Agency for Research on Cancer.[1] Oral cancer incidence is increasing worldwide with a marked variation in its incidence and mortality across the globe.[2] Unlike developed countries, the clinico-pathological profile of oral cancer varies widely in Southeast Asia.[3] In countries such as Pakistan, Bangladesh, India and Sri Lanka, oral cancer is by far the second most common cancer based on its frequency of occurrence and prognostic implications.[4]

Clinico-pathologically several types of oral cancers are recognized, however oral squamous cell carcinomas (OSCC) make up 90% of all oral cancers. The remainder include malignant melanomas, salivary gland tumors and sarcomas of the soft tissues or jaw bones.[5] OSCC may arise from potentially malignant lesions or de novo. Males and old aged people are more frequently affected.[2,4] Lesions usually present as exophytic, ulceroinfiltrative or verrucous type.[6]

Oral cancer is considered a multi-factorial disease with the involvement of both genetic and environmental risk factors.[7] There is general agreement that factors related to patients, tumor and treatment are predictors of survival.[8] Factors related to patient include gender, race, socioeconomic status, education, and family status. Tumor related factors comprise tumor biology, location, grade and stage at diagnosis.[9]

The epidemiology of oral cancers is well documented in literature for developed and developing countries. However population based data in our country is limited as majority of studies are restricted to institutions or cancer registries. In addition, these instituteions or registries are located in major cities of the country that are accessible to relatively lesser number of patients.[10]

Geographical variation exists in Pakistan for oral

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cancer risk profile.[7] In Pakistan estimated oral cancer incidence is over 12000 persons and among them more than 7000 people constitute estimated mortality for oral cancer.[1] Highest prevalence rates have been documented in South Karachi and Jamshoro (Sindh) followed by Multan (Punjab) and relatively lesser occurrence is noted in Peshawar (Khyber Pakhtunkhwa).[4,10]

The current study was planned to acquire baseline data for oral cancers reporting at Post Graduate Medical Institute, Lahore. The aim of this study was to assess histological patterns of these oral cancer cases with respect to demographic and clinicopathological parameters. In this study, patient related factors such as age, gender, marital status, economic status and location were focused. Tumor related factors such as site, risk factor, clinical presentation and histological grades were also assessed and reported.

METHODS

This descriptive cross sectional study was conducted at Histopathology section of Department of Pathology, Post Graduate Medical Institute (PGMI), Lahore which is a tertiary care referral laboratory in central region of Punjab province. It receives biopsy specimens from hospitals based in Lahore and the adjacent regions of central Punjab.

Inclusion criteria were complete clinico-pathological data (including demographic, clinical and pathological parameters) and availability of sufficient paraffin-embedded tumor material. Biopsy specimens of all primary oral squamous cell carcinoma patients, irrespective of age and gender, reporting to the department from January 2013 to December 2013 were included. Exclusion criteria included patients on radiotherapy or chemotherapy. Demographic, clinical and pathological findings i.e. age, gender, history of smoking, presenting symptoms, clinical features, type of biopsy procedure done etc. were collected in a proforma. Convenient sampling technique was used for sample selection.

All biopsy specimens were received in 10% formalin. After gross examination, these were processed for paraffin embedding, sectioned and finally stained with Haemtoxylin and Eosin. Histological grading was performed according to Anneroth et al, multifactorial grading system.[11] Three parameters, that represent tumor cell features, were assessed in the whole thickness of tumor. These included keratinization, nuclear pleomorphism and mitoses. Similarly three parameters, that denote tumor – host relationship, were evaluated in the most invasive margins. These included pattern of invasion, stage of invasion and lymphoplasmacytic infiltration. Each parameter was presented with four

Table 1: *Relationship of socio-demographic factors with histological grade (n = 57).*

Parameter		*Histological Grade*					*p-value*
		Grade 1	*Grade 2*	*Grade 3*	*Grade 4*	*Total n (%)*	
Age in years	≤30 Years	5	2	1	1	9 (15.79)	0.072
	31 – 40 Years	3	3	1	0	7 (12.28)	
	41 – 50 Years	9	1	6	3	19 (33.33)	
	51 – 60 Years	4	8	0	1	13 (22.81)	
	60+ Years	3	2	2	2	9 (15.79)	
Gender	Male	13	8	6	5	32 (56.14)	0.876
	Female	11	8	3	3	25 (43.86)	
Marital status	Married	21	7	8	5	41 (71.93)	0.012*
	Unmarried	3	9	1	3	16 (28.07)	
Economic Status	Upper	7	4	0	3	14 (24.6)	0.578
	Middle	7	5	5	2	19 (33.3)	
	Lowers	10	7	4	3	24 (42.1)	
Locality	Urban	10	4	3	1	18 (31.58)	0.689
	Semi urban	6	4	1	2	13 (22.81)	
	Rural	8	8	5	5	26 (45.61)	

*p-value 0.05 level = statistically significant.

modalities rated from 1 to 4. Then cumulative score was calculated and cases were grouped as follows: 5 – 10 grade I (well differentiated), 11 – 15 grade II (moderately differentiated), 16 – 20 grade III (poorly differentiated), 20+ grade IV (undifferentiated).

The study protocol was approved by the Ethics Review Committee of PGMI, Lahore. Participants were informed with regard to the research objectives, methods, possible benefits and potential risks and a written voluntary consent was obtained from all participants.

The data were analyzed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics such as frequency distribution and cross-tabulation were used to analyze the data. Categorical variables (gender, site of lesion, histological grades and risk factors) were expressed as frequency and percentages. Age being a quantitative variable was expressed as mean (± standard deviation). Relationship of histological grade with different factors was established using Fisher Exact test. Bivariate analysis was performed using correlation coefficient.

RESULTS

This study included 57 cases of OSCC including 32 males and 25 females with a male to female ratio of 1.3:1. The mean age of participants was 45.77 (± 13.01) years with females showing 45.64 (± 12.74) years and males showing 45.88 (± 13.53) years. Highest frequency of cases occurred in the 5th decade of life in both sexes. Majority of participants were married (71.9%) and nearly two third of total study participants belonged to non-urban areas (including rural and semi urban). Except marital status, no other parameter showed association with respect to histological grade of the tumor (Table 1).

Majority of patients were in the age group of 41 – 60 years (56%). The frequency of OSCC was higher in males of all age groups except for 31 – 40 years where females formed 57% of the cases (Figure 1). Regarding the risk factors, 58% cases reported tobacco usage. All clinic-pathological parameters showed no association with respect to histological grade of the tumor (p-value > 0.05). Buccal mucosa (33%) was the most commonly affected site followed by tongue (Table 2).

Histopathological assessment revealed that well-differentiated squamous cell carcinoma was the most frequent type of oral SCC (n = 24, 42.11%) among the study population, followed by moderately – differentiated OSCC and poorly – differentiated OSCC (28.07% and 15.79%) respectively (Figure 2). Results of bivariate analysis show that site was positively correlated with gender and clinical presentation and all these were statistically significant (Table 3).

Table 2: *Relationship of clinico-pathological parameters with histological grade (n = 57).*

Parameter		*Histological Grade*					*p-value*
		Grade 1	*Grade 2*	*Grade 3*	*Grade 4*	*Total n (%)*	
Clinical Presentation	Ulcer	12	6	2	4	24 (45.6)	0.756
	Exophytic	8	6	4	2	20 (31.6)	
	Swelling	3	2	3	2	10 (17.4)	
	Pain	1	2	0	0	3 (5.3)	
Site	Buccal Mucosa	10	4	5	0	19 (33.33)	0.151
	Tongue	3	5	1	2	11 (19.30)	
	Alveolar Region	6	3	0	1	10 (17.54)	
	Floor of Mouth	3	1	1	2	7 (12.28)	
	Retromolar Region	1	3	1	1	6 (10.53)	
	Gingiva / Palate	1	0	1	2	4 (7.02)	
Risk Factor	Smokers	14	8	7	4	33 (57.9)	0.657
	Alcohol	3	0	0	0	3 (5.2)	
	Chewing Tobacco	6	6	2	4	18 (31.6)	
	Betel Quid	1	2	0	0	3 (5.2)	

*p-value 0.05 level = statistically significant

Table 3: *Correlation matrix of study parameters.*

	Age	*Gender*	*Marital Status*	*Economic Status*	*Locality*	*Clinical Presentation*	*Site*	*Risk Factor*	*Histological Grade*
Age	1.000	-.037	-.040	-.166	.207	-.243	.072	-.177	.070
	.	.787	.766	.218	.123	.068	.594	.189	.603
Gender	-.037	1.000	.077	.078	.257	-.154	.326*	.059	-.073
	.787	.	.568	.563	.054	.253	.013	.665	.591
Marital status	-.040	.077	1.000	-.043	.087	-.037	.156	-.133	.179
	.766	.568	.	.750	.520	.786	.246	.322	.182
Economic Status	-.166	.078	-.043	1.000	.025	.113	-.002	.036	.029
	.218	.563	.750	.	.856	.405	.991	.790	.830
Locality	.207	.257	.087	.025	1.000	-.062	.031	.138	.231
	.123	.054	.520	.856	.	.647	.820	.306	.083
Clinical presentation	-.243	-.154	-.037	.113	-.062	1.000	-.390**	.232	.120
	.068	.253	.786	.405	.647	.	.003	.082	.374
Site	.072	.326*	.156	-.002	.031	-.390**	1.000	-.220	.017
	.594	.013	.246	.991	.820	.003	.	.101	.899
Risk Factor	-.177	.059	-.133	.036	.138	.232	-.220	-.177	.120
	.189	.665	.322	.790	.306	.082	.101	.189	.372
Histological Grade	.070	-.073	.179	.029	.231	.120	.017	.120	1.000
	.603	.591	.182	.830	.083	.374	.899	.372	.

*Significance at 0.05 level (2-tailed). **Significance at the 0.01 level (2-tailed).

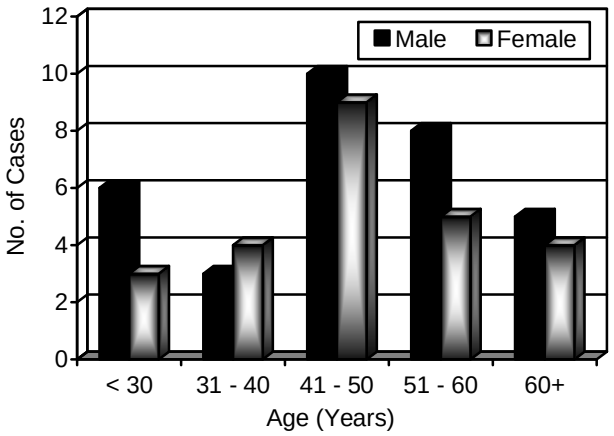

Fig. 1: *Age distribution of study participants.*

DISCUSSION

Our insight of the pathology and etiology of oral cancer has been increased by new breakthroughs in the biomedical field. However, there is still a challenge to counter this lethal disease. With extensively high frequency among oral malignancies, oral squamous cell carcinoma is described as disorganized cellular proliferation in squamous layer of the oral epithelium.[12]

Analysis of the records revealed that data for gender showing male commonness is in agreement with findings from Brazil[12], India [8] and Indonesia.[13] In our study M:F ratio was found to be 1.3:1 which is close to local studies reporting from 1.2:1 to 1.5:1[14-16] and those from Indonesia[13] and Libya[17] (1.6:1 in both studies). However there is difference with other international data where this ratio changes from 3:1 to 4.3:1.[12,18] This could be explained by the fact that risk factors for oral cancer varies across regions.

Finding of most frequent age group (41 – 50 years, 33.3%) differed from the findings from Brazil,[12] US[19] and India[20] where older age groups were more affected. Similar findings have been reported by local studies.[6,21] In recent years, rising tendency of oral cancer in younger people have been noticed in various regions of the world.[8] The proportion of younger patients in our population is extremely high (61% below age 50) when compared with international (15%,[12] 32%,[17] 29%[20]) and

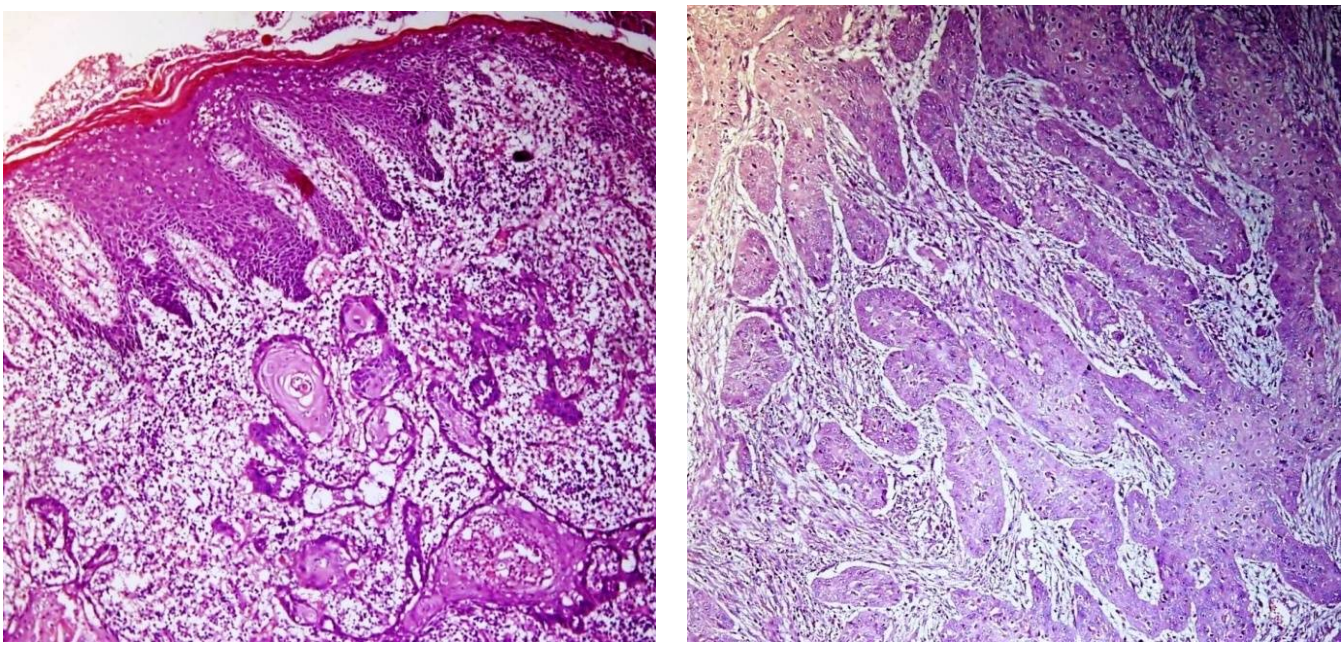

Fig. 2: *Photomicrographs showing well differentiated oral squamous cell carcinoma (left) and moderately differentiated oral squamous cell carcinoma (right).*

local data (38%).[14,16] This trend could be due to increased inclination of younger people towards tobacco and related social habits.

Risk factor distribution in our study showed tobacco as the most common risk factor. In the present study, smoking and chewing tobacco were the most commonly reported risk factors. These findings are consistent with reports from India,[8,20] Indonesia[13] and Pakistan.[6,22] Among the signs of oral cancer ulcer was most common which is favored by other studies.[23] Nevertheless, exophytic appearance was reported to be dominant in some international studies as well.[8]

As for site distribution of OSCC, studies clearly show variations across the country. Two most frequent tumor localizations found in Pakistan are buccal mucosa and tongue.[6,14,24,25] Saliva pool harboring carcinogens and reduced protection due to thinner non-keratinized mucosa are two possible explanations for high risk involving these sites.[17] In Western countries, more than half of OSCC cases affect tongue and floor of the mouth.[2,12] In Asian countries, buccal mucosa is the most common anatomical site for OSCC.[8] Similar findings are documented in current study that is also in agreement with other local reports.[7,24,26] It is further supported by regional studies.[20] Nevertheless, it is in contrast with some local findings [21,25] and studies from Indonesia,[13] Libya[17] and US[19] that reported tongue as the most common site. It is also dissimilar to reports from Sindh[22] and Khyber Pakhtunkhwa[27] provinces that show alveolus as the most commonly affected site. This difference can be explained with different risk factors. In West alcohol and tobacco consumption whereas betel quid chewing and tobacco are the leading risk factors in Asia.

As for histological grade, present study confirmed that there was an overall dominance of well - differentiated OSCC which is in agreement with local data.[6,22] Similar findings were reported by studies conducted in Iran,[23] Libya[17] and India.[20] Contrarily, moderately differentiated OSCC formed majority of OSCC (51%) at another centre from Lahore.[15] Poorly differentiated carcinoma constituted a higher proportion of oral malignancies in yet another Lahore based setup (39%).[25] This variation can be explained on the basis of referral bias, difference in study periods, sample size or study design.

It is worth mentioning that the results of current study may not be the true representation of the population large as it is a single centre study and was carried out on reporting patients only. However it is important with regards to extent of a serious problem like oral cancer. A larger scale study may need to be conducted to get to a definitive conclusion.

It is ***concluded*** that oral cancer has become a serious problem of public health owing to high rates of morbidity and mortality. Within the limitations of this study, it is concluded that OSCC is a common entity in our region with developing tendency among males and at an early age. Of all the studied clinico-pathological parameters, marital status appeared as the only parameter to reveal association with respect to histological grade of the tumor.

This study necessitates primary prevention through awareness, especially among younger group, about

the role of tobacco and related products. Additional epidemiological studies are needed including a larger number and wider spectrum of participants from different hospitals in various areas of the country. Further studies are suggested to explore association of different variables like clinical site and histological grading, gender, age and tobacco (smoking / chewing) in future.

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