

# DISTRIBUTION AND DETERMINANTS OF ORAL SQUAMOUS CELL CARCINOMA: A RETROSPECTIVE OBSERVATIONAL STUDY AT ORAL & MAXILLOFACIAL DEPARTMENT OF AYUB TEACHING HOSPITAL ABBOTTABAD

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## ABSTRACT

*Oral cancer has emerged as one of the most rapidly growing cancer types in south East Asia in recent years. In a developing country like Pakistan, oral cancer is associated with significant financial burden on healthcare system. It is a potentially fatal disease and may be associated with high morbidity even after cure. The aim of this study was to assess the characteristics of Oral Squamous Cell Carcinoma (OSSC) in relation to age, gender, predisposing factor, histopathological grading and site of involvement and relationship of these factors with each other. A retrospective study was carried out in department of Oral and Maxillofacial Surgery at Ayub Teaching Hospital, Abbottabad from March 2018 to March 2020. A total of 102 patients with biopsy proven OSCC were included in the study. Data regarding patient's age, gender, site of involvement, habit, histopathological grading and patients address were collected on a structured proforma. Among 102 patients, 52 were females (51 %) and 50 were males (49 %). Mean age of patients was 57.22±13.87. Snuff dipping was found as the most common predisposing habit which was especially common among female patients (84.61 %). Equal number of patients presented with well differentiated and moderately differentiated histopathologic grading of squamous cell carcinoma (44 % each). Buccal mucosa was the most commonly involved site (35.3 %) followed by mandibular alveolus.*

**Key Words:** Oral Squamous Cell Carcinoma, Snuff Dipping, Smoking, alcohol.

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## INTRODUCTION

Cancer constitutes a major cause of mortality and morbidity worldwide. The global cancer burden is

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estimated to have risen to 18.1 million new cases and 9.6 million deaths in 2018.<sup>1</sup>

Oral cancer represents the most common form of neoplasm in head and neck with squamous cell carcinoma being the most common histotype.<sup>2</sup> Oral squamous cell carcinoma (OSCC) arises from the mucosal lining of anterior two third of tongue, gingiva, buccal mucosa, floor of mouth, hard palate, maxillary and mandibular alveolus, retro molar trigone and maxillary sinus.<sup>3</sup> Combined with lip and pharyngeal cancers, OSCC ranks as seventh most common worldwide and accounts for approximately 300,000 deaths every year.<sup>4</sup> The incidence of oral cancer varies in different parts of world. Southeast Asia is considered a common location for cancer but its incidence in north America and European union countries is comparatively low<sup>5,6</sup> Pakistan is considered to have one of the highest prevalence of oral cancer worldwide.<sup>7</sup> It has been reported that oral cancer is the most common cancer in males and second

most frequent cancer in both genders in Pakistan.<sup>8</sup>

Although the exact etiology of OSCC is not completely understood but a number of factors are known to be associated with increased disease occurrence. Some of these are preventable e.g. tobacco use, alcohol consumption, snuff dipping, betel quid and betel nut chewing while inherited genetic mutations and immune conditions are among non-modifiable factors. These risk factors may act simultaneously or in sequence to initiate or promote cancer growth.

Tobacco and chewing of areca nut have been widely researched and are considered as main predisposing factors for OSCC.<sup>9,10</sup> Apart from tobacco, alcohol consumption, human papilloma virus, dietary deficiencies and poor oral hygiene are some of the predisposing factors.<sup>11-13</sup> High consumption of tobacco in Southeast Asia may explain the greater incidence of OSSC in these countries. Tobacco is used in various forms in these countries such as smokeless form like betel quid, tobacco with lime, snuff or it is used as smoking cigarettes, bidi, hookah, cigar etc. Snuff dipping is especially common in Northwest part of Pakistan whereas betel quid is common in Southern areas. The aim of this study was to investigate the distribution of OSCC according to age, gender, site of involvement, habits of the patient and histopathological grading so that preventive programmes can be developed for the community to detect OSSC at an early stage which improves the prognosis of disease.

## MATERIALS & METHODS

A retrospective observational study was carried out including patients who visited Oral & Maxillofacial Surgery department of Ayub Teaching Hospital, Abbottabad from March, 2018 to March, 2020. A total of 102 patients with biopsy proven Oral squamous cell carcinoma were included in the study. Data regarding patient's age, gender, site of involvement, side of involvement, habits regarding tobacco usage, grading of tumor (Broder's classification) and patient's address was collected on a structured proforma. All biopsy specimens were submitted at local laboratory of Shaukat Khanum Memorial Cancer Hospital & Research Centre. Data were retrieved from the biopsy reports. Continuous data were presented as mean  $\pm$  SD (standard deviation) while discrete variables were presented as percentage. Analyses were performed on SPSS version 25. Continuous groups were compared by applying independent t- test while categorical groups were compared by applying chi-square test. P value of  $\leq 0.05$  was considered significant.

## RESULTS

A total of 102 patients with biopsy proven squamous cell carcinoma were included with an age range of 83

where minimum age of patients was 23 years and maximum age was 106 years. Among 102 patients, 50 were males i.e. 49 % and 52 were females i.e. 51%. Mean age of patients was  $57.22 \pm 13.87$  years. Mean age of males was  $58.94 \pm 14.39$  years including youngest patient to be 23 years old while oldest was of 106 years. Mean age of females was  $55.57 \pm 13.28$  years with minimum age of 28 years and maximum age of 90 years. There was no significant difference between mean age of males and females ( $t = 1.22, p \geq 0.05$ ).

Prevalence of OSCC in males was maximum at age of 41-50 and 51-60 years each having 26 % of disease burden. While, in females maximum number of patients were found in age range 51-60 years having 38.4% of total female patients. There was no significant difference between frequencies of OSCC among genders i.e.  $\chi^2 = 5.25, p \geq 0.05$ .

Frequency of OSCC varies with the habits of patients. Frequency was highest in patients with smokeless tobacco use i.e. 68.62%. Second most common habit was snuff and smoking in combination responsible for 12.7% of cases. Betel quid and betel nut chewing comprised 6.9% of patients. Betel quid, betel nut and smoking in combination comprised 2% whereas 2% of patients were not indulged in any predisposing habit. We have found highly significant relationship between age and habits of patients and distribution of disease.  $\chi^2 = 111.45, p \leq 0.001$  Table 2

Frequency of OSCC according to habits of patients and gender distribution varies as shown in Table 3. Maximum number of males was found to be snuff dippers (a form of smokeless tobacco) with 52% of cases while 24% were snuff users as well as smokers. In females, maximum frequency of OSCC was found to be in snuff dippers again resulting in 84.61% cases. Second common cause was found to be use of betel quid and betel nut chewing resulting in 7.69% cases. There was statistically significant difference between habits of patient and gender i.e.  $\chi^2 = 22.54$  and  $p \leq 0.001$

Out of total 102 patients, histopathological picture of 45 presented to be well differentiated comprising 44% of the total while 45 (44%) presented to be moderately differentiated OSSC.

Poorly differentiated presented to be 6.9% , undifferentiated 2.9% and carcinoma in situ 2%. Gender wise distribution of grading shows 42% females and 46.1% presented with well differentiated OSSC while 48% females and 40.3% males presented with moderately differentiated OSSC. There was no statistically significant relationship between habits and grading of disease i.e.  $\chi^2 = 16.04, p \geq 0.5$

Distribution of OSCC according to the site of involvement showed buccal mucosa to be the most

TABLE 1: AGE GENDER CROSSTABULATION

		Gender		Total
		Male	Female	
Age	21-30yrs	1(2%)	2(3.8%)	3(2.94%)
	31-40	2(4%)	4(7.6%)	6(5.88%)
	41-50years	13(26%)	13(25%)	26(25.4%)
	51-60 years	13(26%)	20(38.4%)	33(32.3%)
	61-70 years	12(24%)	6(11.53%)	18(17.6%)
	71-80 years	7(14%)	6(11.53%)	13(12.7%)
	81-90 years	1(2%)	1(1.92%)	2(1.96%)
	More than 100	1(2%)	0	1(0.98%)
Total		50	52	102

TABLE 2: HABITS & AGE CROSSTABULATION

		Habits					Total	
		Snuff dipping	Smoking	Snuff & smoking	Betel quid & betel nut	Betel quid, betel nut & smoking		Nil
Age	21-30yrs	0	0	0	0	1	2	3 (2.9%)
	31-40	2	0	1	2	1	0	6 (5.8%)
	41-50years	16	3	6	1	0	0	26(25.5%)
	51-60 years	22	4	4	3	0	0	33(32.3%)
	61-70 years	14	1	2	1	0	0	18(17.6%)
	71-80 years	13	0	0	0	0	0	13(12.7%)
	81-90 years	2	0	0	0	0	0	2 (1.96%)
	More than 100	1	0	0	0	0	0	1 (0.98%)
Total		70 (68.6%)	8 (7.8%)	13 (12.7%)	7 (6.86)	2 (1.96%)	2 (1.96%)	102

TABLE 3: HABITS & GENDER CROSSTABULATION

		Gender		Total
		Male	Female	
Habits	Snuff dipping	26 (52%)	44 (84.61%)	70 (68.62%)
	Smoking	7 (14%)	1 (1.92%)	8 (7.84%)
	Snuff & smoking	12 (24%)	1 (1.92%)	13 (12.7%)
	Betel quid, Betel nut chewing	3 (6%)	4 (7.69%)	7 (6.8%)
	Betel quid, Betel nut & smoking	2 (4%)	0	2 (1.96%)
	Nil	0	2 (3.84%)	2 (1.96%)
Total		50 (49%)	52 (51%)	102

commonly involved site i.e. 35.3% following mandibular and maxillary alveolus involving 19.6% and 14.7% patients respectively. Lower lip involvement was seen in 13.7%. Lateral border of tongue was involved in 10.8% of patients. Oral commissure and retromolar trigone constituted 2% each. Floor of the mouth and

maxillary sinus was the least involved site presenting 1% patients each. There was highly significant relationship between site of involvement and the habit of patients i.e.  $\chi^2 = 91.52, p \leq 0.001$  (Table 4). There was statistically significant relationship between site of involvement and grading of disease i.e.  $\chi^2 = 47.98, p \leq$

TABLE 4: SITE &amp; HABIT CROSS TABULATION

		Site								Total	
		Buc- cal Muco- sa	Lat- eral tongue	Man- dib- ular alveo- lus	Max- illary alveo- lus	Lower lip	Com- mis- sure	Floor of mouth	Retro- molar trigone		max- illary sinus
H A B I T S	Snuff dip- ping	22	10	15	8	11	2	0	2	0	70 (68.6%)
	Smoking	3	0	3	1	1	0	0	0	0	8 (7.84%)
	Snuff & smoking	7	1	2	3	0	0	0	0	0	13 (12.7%)
	Betel quid & betel nut	4	0	0	1	1	0	1	0	0	7 (6.8%)
	Betel quid, Betel nut & smok- ing	0	0	0	0	1	0	0	0	1	2 (1.96%)
	Nil	0	0	0	2	0	0	0	0	0	2 (1.96%)
Total		36 (35.2%)	11 (10.7%)	20 (19.6%)	15 (14.7%)	14 (13.7%)	2 (1.96%)	1 (0.98%)	2 (1.96%)	1 (0.98%)	102

TABLE 5: SITE GRADING CROSS TABULATION

		Grading					Total
		Well dif- ferentiat- ed	Moderate- ly differ- entiated	Poorly differenti- ated	Undiffer- entiated	Carcino- ma in situ	
Site	Buccal Mucosa	20	15	1	0	0	36 (35.2%)
	Lateral tongue	2	8	0	0	1	11 (10.7%)
	Mandibular alveolus	12	4	4	0	0	20 (19.6%)
	Maxillary alve- olus	3	7	2	3	0	15 (14.7%)
	Lower lip	7	6	0	0	1	14 (13.7%)
	Commissure	1	1	0	0	0	2 (1.96%)
	Floor of mouth	0	1	0	0	0	1 (0.98%)
	Retromolar trigone	0	2	0	0	0	2 (1.96%)
	Maxillary sinus	0	1	0	0	0	1 (0.98%)
Total		45 (44.1%)	45 (44.1%)	7 (6.9%)	3 (2.9%)	2 (2%)	102

0.05 (Table 5)

## DISCUSSION

Oral cancer is a global health problem but is especially common in South East Asia. Because of greater indulgence in the risk factors, oral cancer constitutes

about 15 % of new cancer cases each year in Pakistan.<sup>8</sup> Use of tobacco is considered as one of the main predisposing factors in the etiology of oral cancer, but the form in which it is consumed also influences the epidemiologic variables of this disease. Unlike western countries, where tobacco is consumed in the form

of smoking, smokeless tobacco use is more prevalent northern part of Pakistan where this study was conducted.

OSSC was once considered as a disease of old age affecting predominantly males in their sixth, seventh and eighth decade of life and same predicted by the results of this study in which it was found that most of the patients presented in their sixth decade of life (33%). Tandon P and colleagues also concluded in their study that most of the patients suffering from OSSC were above 50 years of age.<sup>14</sup> In the present study the second most common age range was fifth decade of life constituting 26 % of total cases. Younas and colleagues in their study conducted in the southern part of Pakistan found the fifth decade as the most common age range for presentation of OSSC cases.<sup>15</sup> Similarly, Singh showed that most of the patients in his study conducted in north India also presented in fifth decade.<sup>9</sup> The shift in the age range may be attributed to the indulgence of younger age group in the risk factors of OSSC in South East Asia. Lack of awareness about the consequences and easy availability of tobacco may be the reasons for involvement of youngsters in the use of tobacco. This is an alarming situation and while the sale of cigarettes to minors is prohibited by law, the smokeless form is readily available to them. Strict legislations and law implementation may help this age group falling victim to this habit and disease.

The results of the current study showed more than half of the patients to be females (51 %). This is in contradiction to results of other studies conducted in the country as well as internationally. The literature suggests a definite male predilection for OSSC which is rendered to more common participation of males in the predisposing factors for OSSC like smoking, drinking etc. Tandon in his study conducted in India showed that 79 % of the patients were males.<sup>14</sup> Similarly, Mirza D identified that 71 % of the patients presenting in his study were males.<sup>10</sup> Hernandez-Guerrero and colleagues in their study conducted in Mexico found out a male to female ratio of 1.4:1 in the population of patients suffering from OSSC.<sup>16</sup> In Pakistan, smoking by females is considered against the social norms of society. However, the consumption of smokeless form of tobacco i.e. snuff is common among females of north region. Using snuff is comparatively easy for them because of easy availability as well as the way it is placed in buccal sulcus; it's not visible to others. In this study, the high proportion of females presenting with disease is associated with over indulgence of females in snuff dipping in this region.

Tobacco, betel quid and alcohol are strong risk factors for both oral cavity as well as oropharyngeal cancers.<sup>17</sup> The synergistic effect of tobacco use, alcohol

consumption and betel quid chewing in the carcinogenesis of oral cavity mucosa has already been established and well understood by a number of studies.<sup>18,19</sup>

The results of the present study showed that the most common predisposing factor in our sample of patients was snuff dipping. This is a smokeless form of tobacco use in which a chunk of finely ground tobacco product i.e. snuff is placed in the buccal pouches of upper or lower alveolus. This snuff is retained at the place for a considerable period of time as it is dispersed slowly into the saliva. This leads to exposure of tissues in the immediate vicinity of tobacco product for a longer period of time and with greater intensity due to close proximity. Therefore, there is increased involvement of gingivo-buccal and gingiva-labial complex in the population of patients who indulge in snuff dipping, as is evident in the results of this present study where the most common site of involvement of OSSC was buccal mucosa (35.3 %) followed by mandibular gingiva (19.6 %). In South East Asia, where the smokeless form of tobacco is commonly used, the buccal mucosa forms the most common site of involvement of OSSC. Tandon and colleagues, in a large study conducted in India, found out that the most common site of involvement was buccal mucosa (31.47%) followed by mandibular alveolus (21.5 %).<sup>14</sup> Similarly Mirza D reported that the most common site of involvement of OSSC in Karachi Pakistan is buccal mucosa (50 %) followed by mandibular gingiva (22.1 %).<sup>10</sup> On the other hand, studies conducted in western countries like America where smoking and alcohol consumption is more common suggested different results. Pires NR conducted a study and concluded that the most common site of involvement of OSSC in Brazilian population is lateral border of tongue (34.9 %) and buccal mucosa constituted only 5.7 % of the total cases.<sup>20</sup> Similarly, Olaleya O revealed that the most common site of involvement of OSSC in south east England is lateral border of tongue (33.1 %). Thus, in our experience, there's a change in the site of involvement of OSSC with the change in the risk factor and the way the risk factor is applied.

We studied the relationship between predisposing habit of the patient and site of involvement of OSSC in our study population and found it highly significant (p value  $\leq 0.001$ ). It was found out that buccal mucosa was the most commonly involved site constituting 35.2 % of total cases and 31.42 % of these patients were snuff dippers. Mandibular alveolus (21.4 %) and lower lip (15.7 %) were the next common sites of involvement respectively among the snuff dippers because of the immediate proximity to the site of placement of snuff.

In the current study, we analyzed the histopathologic grading of patients suffering from OSSC. We found equal number of patients representing the well

differentiated and moderately differentiated groups each comprising 44.1 % whereas 6.9 % of patients were suffering from poorly differentiated tumors. Sahaf R in their study also found that the leading histological subgroup was well differentiated OSSC comprising 68.4 % of their study population whereas only 22.8 % were from moderately differentiated group.<sup>21</sup> Similarly, Bunget AM, too, concluded that the most common histological type of OSSC was well differentiated (53.3 %) followed by moderately differentiated (31.3 %) in a population of patients in Romania.<sup>1</sup> In this study, it was concluded that the relationship of histological grading with gender and habit were statistically insignificant.

Further studies reporting the distribution of disease should be carried out with larger sample size and those etiological factors should be researched in future which are not being studied widely. Moreover, there is a dire need of such studies reporting the incidence and prevalence of disease all around Pakistan which can help to develop a national database regarding cancer statistics and may lead maxillofacial fraternity to take initiative for development of preventive programmes for community taking an account of the alarming situation this disease has created.

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| 4 Amber Farooq:            | Data Interpretation, Results write up            |
| 5 Adil Shah Nawaz:         | Referencing, Review                              |
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