***Original Research Article***

# Oral Squamous Cell Carcinoma; ~~A Multicausal Disease~~

Comment [B1]: and tobacco use


## Abstract:

**Aims:**To ~~find out the risk factors and~~determine the habits of tobacco use in patients with OSCC, as well as localization,~~of OSCC and also the prevalence of different stages and grades~~ staging and grading of OSCC at the time of diagnosis.

**Study Design:** This is a case-control study.

**Place and duration of study:** The study was conducted at Ziauddin dental hospital KDLB and Clifton Campus, Karachifrom October 2017 to April 2018.

**Methodology**:Variables like age, gender, ethnicity, socioeconomic status, detail history of different types of tobacco used, oral hygiene habits, family history of cancer were noted. The stage and grade of oral cancer were interpreted from the biopsy and CT scan reports according to the CAP protocol.Quantitative variables were presented as mean and standard deviation. For categorical data frequency and percentages was calculated.

**Results:**The oral cancer cases comprised of 38(81%) males and 9(19%) females with mean age of 49 years. The most common location of oral cancer in this study was the buccal mucosa, followed bytongue and lips.The majorly consumed type of tobacco was gutka in55% of patients, followed by pan in 30%, naswarin 15%, betel nut in 11% and smoking in 11% among OSCC cases.Histological reports showed that there were equal number of moderately and poorly

differentiated OSCC (n=16; 34%). According to TNM staging, in our study stage II was 34%, followed by stage I that was 32%.

**Conclusion:**

It can be concluded that the major etiological factors of OSCC among Pakistani population are chewing tobacco habits including gutka, pan, naswar, betel nut and smoking with male predominance. So the incidence of OSCC can be reduced by raising oral cancer awareness among general population about carcinogenic effect of tobacco chewing and smoking and also by encouraging dental and medical professionals to conduct free oral cancer screenings.

**Keywords:**Oral squamous cell carcinoma, Risk factors, Stages of OSCC, Grades of OSCC.

**Introduction:**

Oral squamous cell carcinoma (OSCC) is an epithelial lesion and is the most common neoplasm of oral cavity. It is actually the sequel of cellular changes, starting from cellular atypia which is the alterations in the cell epithelium, followed by dysplasia, leading to multiple cell involvement, then carcinoma in situ and finally cell invasion and metastasis(1).It is the cancer affecting any part of the oral cavity including lips, tongue, upper or lower gingiva,buccal mucosa, floor of mouth, hard palate, vestibule of mouth, retromolartrigone or major salivary glands (2).The oral cavity is that part of the body which is easily accessible for direct visual examination but still the mortality from oral cancer remains high because in early stages the patient has no symptoms(3).

The global mortality rate due to oral cancer is about 3-10% (4). In South Asia OSCC is one of the major health problem and is considered as the 5$^{th}$ most frequently occurring carcinoma (4).

Pakistan and India have higher prevalence of OSCC as compared to the western countries, ~~this~~ which can be attributed to the same cultural practices and habits.In Pakistan, the prevalence of oral cancer is 10%, standing second to bronchogenic cancer in males and breast carcinoma in females(5). Karachi is the home to oral cancer, which is the second most common malignancy in both ~~the~~ genders(6).

The risk factors that are significantly associated with oral cancer are tobacco(7) , alcohol(8), viral infection like EBV and HPV(9) and genetic susceptibility(10). There is a significant geographical variation in the incidence of OSCC due to area specific etiological factors.~~like i~~In the developed world ~~the smoked~~ tobacco smoking and alcohol consumption are the main etiological factors. On the other hand, in developing countries the major etiological factors are betel quid chewing, bidi, smoking and alcohol (4, 11, 12). So the objectives of the current study ~~are to find out the risk factors~~was to determine the prevalence of tobacco chewing and smoking in patients diagnosed with OSCC, as well as to observe~~and~~ the localization of OSCC,~~and also the prevalence of different~~ stages and grades of OSCC in the time of diagnosis.

**Methods:**

A Case control study was conducted from October 2017 to April 2018. Approval of the Ethics Review Committee (ERC) of Ziauddin University was obtained according to institutional guidelines. The sample size was calculated by using Openepi calculator version 3 using confidence level of 99%.Inclusion criteria was preoperativelyhistopathologically proven OSCC diagnosis in patients older than 18 years who signed informed consent to participate in the research.~~The samples included inthe study were the histopathologically proven preoperative OSCC patients of age 18 years and above.~~Patients who did not give consent or were diagnosed

**Comment [B2]:** no other risk factor was examined.

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**Comment [B3]:** what about the control group?? why was the sample size calculated? there is no mention of the control group later in the text. Explain or change these sentences in the text.

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with other type of cancer were excluded from the study. ~~Those patients were excluded from the study who either refused to give consent or werediagnosed with other type of cancer.~~ The samples were collected from the OPD of Ziauddin dental hospital KDLB and Clifton Campus, Karachi.Consecutive sampling technique was used.

Comment [B4]: is this oral pathology department? first the full word should be written, then the abbreviation

Variables like age, gender, ethnicity, socioeconomic status, detail history of different types of tobacco used, oral hygiene habits, family history of cancer were noted. The stage and grade of oral cancer were interpreted from the biopsy and CT scan reports according to the CAP protocol. OSCC were graded as well-differentiated when it resembled closely to normal squamous epithelium, moderately-differentiated if consisting of nuclear pleomorphism, atypical mitosis and with less keratinization and poorly differentiated when consisting predominantly of immature cells, typical or atypical mitosis with very minimal keratinization and rarely necrosis.The criteria given by American Joint Committee on cancer (AJCC) for staging of oral cavity cancer was used (13).

Data was entered on statistical package of social science(SPSS) version 20. Quantitative variables were presented as mean and standard deviation. For categorical data frequency and percentages was calculated.

**Results:**

There were 47 oral cancer samples. The histological tumor type of all 47 patients was squamous cell carcinoma. The oral cancer cases comprised of 38(81%) males and 9(19%) females with mean age of 49. The urdu speaking ethnic group was the most common.The most common location of oral cancer in this study was the buccal mucosa (n=39; 83%) followed bytongue and lips as mentioned in Table.

The frequency and distribution of different types of tobacco consummation among oral cancer patients are shown in Table. In our research, the majorly consumed type of tobacco was gutka (n=26; 55%), followed by pan (n=14; 30%),naswar (n=7; 15%), betel nut (n=5; 11%) and smoking (n=5; 11%) ~~in cases~~.

Grade and stage of OSCC were also evaluated in the oral cancer patients. The histological reports showed that there were equal number of moderately and poorly differentiated OSCC (n=16; 34%). The patients withwell differentiated OSCC were 32% (n=15). According to TNM staging, in our study stage I was 15(32%), stage II was 16 (34%), stage III and stage IV were 12 (26%) and4(9%) respectively.

Table 1 Demographic and Clinicopathological features of OSCC cases

| Variables | | Cases | |
|---|---|---|---|
| | | n | % |
| Gender | Female | 9 | 19% |
| | Male | 38 | 81% |
| | | | |
| Ethnicity | Balochi | 0 | 0% |
| | Others | 3 | 6% |
| | Pukhtoon | 3 | 6% |
| | Punjabi | 2 | 4% |
| | Sindhi | 7 | 15% |

| | | | |
|---|---|---|---|
| | Urdu Speaking | 30 | 64% |
| | (blank) | 2 | 4% |
| | | | |
| Tobacco Use | Naswar | 7 | 15% |
| | Gutka | 26 | 55% |
| | Areca Nut | 5 | 11% |
| | Betel quid | 14 | 30% |
| | Smoking | 5 | 11% |
| | | | |
| Location of OSCC | Buccal | 39 | 83% |
| | Lips | 1 | 2% |
| | Tongue | 6 | 13% |
| | Not Available | 1 | 2% |
| | | | |
| Stages of OSCC | Stage I | 15 | 32% |
| | Stage II | 16 | 34% |
| | Stage III | 12 | 26% |
| | Stage IV | 4 | 9% |
| | | | |
| Grades of OSCC | Well Differentiated | 15 | 32% |
| | Moderately Differentiated | 16 | 34% |
| | Poorly Differentiated | 16 | 34% |

**Discussion:**

Different geographic areas host a wide variation in the incidence of oral cancer, this could be due to differences in lifestyles, culture and developmental status(14). Approximately 77% of 145,000 number of deaths were mostly reported from lesser developed countries (15).About 30,000 new cases of oral cancer are diagnosed per year and majority of them are at critical stage of III or IV (4).Literature reported that males are predominantly affected as compare to females(15) and the current study favored this finding. The reason behind this male predominance in current study is might be that males are more prone to OSCC developing risk factors including naswar, gutka, areca nut, betel quid and smoking.

The most commonly diagnosed age group is between 50-69 years of age (16) and the current study reported mean age of 49. OSCC can appear in all anatomical sites of oral cavity including lips, tongue, upper or lower gingiva,buccal mucosa, floor of mouth, hard palate, vestibule of mouth, retromolartrigone or major salivary glands (2).In the current study, the most common location of oral cancer was the buccal mucosa followed bytongue and lips.

**Comment [B5]:** could this be attributed to habits of tobacco chewing in younger persons?? is there some possible explanation for this finding?

**Comment [B6]:** could this be explained by habits of tobacco chewing? try to explain it, because in tobacco smokers the most frequent localization is the floor of the mouth

Looking over the risk factors for oral cancer, literature review revealed that risk of OSCC among smokers is 1.4 to 1.7 times higher than non-smokers and it can even further increase with the increase in frequencyand duration of smoking (17-19).Globally 20-30% of OSCC ~~are~~ developdue to tobacco use. Looking at the alcohol consumption the risk of developing OSCC rises up to 18%, depends upon the quantity and duration of drinking. Combined tobacco and alcohol consumption multiplies the risk of OSCC ~~and is~~to about 40% (20). The current study also reported incidence of OSCC among smokers but none of the patient having history of

alcohol consumption. ~~t~~This might be due to the hesitation of patient regarding confession about alcohol consumption as it is banned in Pakistan.

On the other hand, chewing tobacco also shows a strong correlation with the development of the risk of OSCC (21)**.**In our research, the majorly consumed type of chewing tobacco was gutka followed by pan, naswar and betel nut among OSCC cases.Dental risk factors including poor oral health like missing or damaged teeth, periodontal diseases, decrease frequency of checkups and chronic dental trauma also significantly increases the risk of OSCC (22) but the current study couldn't assess these dental risk factors.

The global statistics report showed that majority of newly diagnosed cases of OSCC are at critical stage of III or IV (4) while the current study reported that majority of OSCC cases in Pakistan are diagnosed at stage II while very few reached up to the stage IV. ~~OSCC originate as epithelial dysplasia in which there is altered proliferation of squamous cells on the layer of epithelium, resulting in degradation of subepithelial basement membrane. Due to this ruptured basement membrane, the surrounded area gets degraded. The local invasion of OSCC occur by the islets and cords of epithelial cell. Histopathological appearance of OSCC invasion occur in sequel as initiated as pushing border, followed by finger like pattern and finally islands of small cell (23).~~

**Comment [B7]:** Is there some possible explanation for this?

**Comment [B8]:** this is not relevant for the subject of the manuscript

**Conclusion:**

It can be concluded that the major etiological factors of OSCC among Pakistani population are chewing ~~tobacco~~ tobacco habits including gutka, pan, naswar, betel nut and smoking with male predominance. ~~So t~~The incidence of OSCC can be reduced by raising oral cancer awareness

among general population about carcinogenic effect of tobacco chewing and smoking and also by encouraging dental and medical professionals to conduct free oral cancer screenings.

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