ORIGINAL ARTICLE

# Epidemiological and Clinico-pathological spectrum of oral squamous cell carcinoma in patients presenting to a major tertiary care hospital in Lahore Pakistan.

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**ABSTRACT… Objective:** To establish demographics of OSCC patients presenting to a major tertiary care hospital and identify different potential risk factors. **Study Design:** Descriptive Cross Sectional study. **Setting:** Department of Oral and Maxillofacial Surgery Mayo Hospital Lahore. **Period:** July 2021 to July 2022. **Material & Methods:** A total of 86 patients were included in the study. The diagnosis of OSCC was histo-pathologically confirmed. Patients of both gender and all ages were included in the study and a standard questionnaire was developed to collect data including bio-data, demographics and history of illicit habits. **Results:** Out of 86 patients 75.58% (n=65) were males and 24.41% (n=21) patients were females. The mean age of the patients was 47.02 years. Male to female ratio was 3.6:1. Well differentiated squamous cell carcinoma was most common (53.48%), Majority presented with stage 4 disease. Highest proportion of the patients (29.6%) was having no obvious predisposing factor. Most commonly involved site was tongue followed by buccal mucosa. **Conclusion:** The disease trends are changing in our population, as the disease is increasingly affecting younger age group, tongue is now increasing being involved more commonly as in majority of the previous studies the incidence of OSCC of buccal mucosa was much higher, the incidence of OSCC without any obvious risk factor is increasing which needs further investigation.

**Key words:**   Head and Neck Cancers, Oral Squamous Cell Carcinoma, Oral Cancer, Oro-Pharyngeal Squamous Cell Carcinoma, Tongue Cancers.

## INTRODUCTION

Squamous cell carcinoma is ranked as the sixth most common cancer worldwide and it counts for 90% of head and neck cancers, known as head and neck squamous cell carcinoma (HNSCC).[1] 90% of these carcinomas arise from oral mucosal epithelium thus known as Oral squamous cell carcinoma (OSCC).[2] Approximately 630000 new patients are diagnosed with squamous cell carcinoma every year which results in 350000 mortalities annually worldwide.[3,4] There is a wide variation in geographic distribution and incidence of oral squamous cell carcinoma this indicates an association with socioeconomic and cultural values and variation of different habits in different parts of the world. The incidence of OSCC is markedly higher in some developing countries of South East Asia including India and Pakistan. In these countries OSCC is most common cancer in males and third most common cancer in females.[2] In Pakistan squamous cell carcinoma is the second most common cancer.[1] The burden of OSCC is expected to double in the developing countries by 2030.[5] Among the European countries the incidence of squamous cell carcinoma is highest in France, Hungary, Slovakia, and Slovenia. The decrease in incidence of OSCC in developed countries is attributed to a decrease in tobacco use, while there is an upsurge in the incidence of oropharyngeal carcinoma which is attributed to the high risk subtypes of Human Papilloma virus.[2] There are various risk factors for developing OSCC which includes genetics, ethnicity, life styles, exposures and geographic location. The common etiologic factors are smoked tobacco, smokeless tobacco, alcohol, poor oral hygiene

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and human papilloma virus.[6,7] In Pakistan smokeless tobacco is available in the form of betel leaf (paan), niswar, areca nut (Gutka).[6] According to a study poor oral hygiene has an additive effect with alcohol and tobacco and may be a sole cause of OSCC.[8] Poor oral hygiene causes chronic inflammation like periodontitis which may lead to oncogenes is and has an additive adverse outcome on OSCC.[6] The 5 year survival late of OSCC has not improved much in the last 20 years despite evolution in management. The prognosis of SCC depends on various factors like extension of disease at the time of presentation, loco-regional spread, involvement of adjacent structures, general physical status of the patient, histologic type and chosen therapy.[9]

The aim of this study was to establish the clinic-pathological and demographic profile of OSCC in patients presenting to a major tertiary care hospital in Pakistan. This may help to identify and control the modifiable risk factors leading to OSCC through effective preventive programs and increasing awareness. As ever prevention remains the ideal.

## MATERIAL & METHODS
This descriptive cross sectional study was carried out at the Department of Oral and Maxillofacial surgery Mayo Hospital Lahore Pakistan for a period of twelve months from July 2021 to July 2022. A total of 86 patients admitted for surgical management were included in the study. The diagnosis of OSCC was histo-pathologically confirmed. Data was collected after taking informed consent from the patients and after taking approval from ethical committee of the institute (518/RC/KEMU). Patients of both gender and all ages were included in the study and a standard questionnaire was developed to collect data including bio-data, demographics and history of illicit habits.

Data was analysed and entered using SPSS version 20.0. The difference in significance was detected through Chi-square test (p<0.05). Odds ratios (OR) and confidence interval (CI) were calculated to evaluate different risk factors. A stepwise logistic regression model was adopted in stepwise manner to evaluate combined effect of independent variables.

## RESULTS
A total number of 86 patients were included in the study, 75.58% (n=65) of the patients were males and 24.41% (n=21) patients were females (Figure-1). The mean age of the patients was 47.02 years with age range from 25 to 79 years (Table-I). Male to female ratio was 3.6:1.

Hisopathological grading of OSCC showed that n=46 (53.48%) patients were diagnosed with well differentiated, n=35 (40.69%) patients with moderately differentiated, n=4 (4.65%) patients with poorly differentiated and n=1 (1.16%) was carcino-sarcoma (Table-II). 33% (n=29) patients were having different comorbid states, diabetes being most common followed by hepatitis C.

Majority of patients i.e. n=52 (60.46%) presented at an advanced stage of disease i.e. TNM stage IV, n=28 (32.55%) patients presented at stage III, n=4 (4.65%) patients presented at stage II and only n=2 (2.32%) presented at stage I of oral squamous cell carcinoma.

Frequency of involvement of different sub-sites was as follows; n=30 patients (34.88%) were having OSCC of buccal mucosa, n= 31 patients tongue (36.04%), n=1 floor of mouth (1.16%), n=12 mandibular alveolar mucosa(13.95%), n=3 maxillary alveolar mucosa(3.48%), n=3 hard palate (3.48%), n=2 lower lip (2.32%), n=1 commissure of mouth (1.16%), n=3 retromolar trigone (3.48%). Body side distribution showed that n=46 (53.48%) of the lesions were on left side, n=37 (43.04%) on the right side and n=3 (3.48%) were present in the midline. The most commonly involved site in males was buccal mucosa while in females it was the lateral border of tongue (Table-III).

Risk assessment of the present study showed that the greatest number of cases n=25 (29.06%) were having no predisposing factor, n=20 (23.25%) were having a combination of habits (Smoking, Paan, Cchaliya, Niswar), n=14 (16.27%) smoking, n=13 (15.11%) Paan, n=7

(8.13%) Niswar, n=3 (3.48%) Cchaliya, sharp tooth n=2 (2.32%), Xeroderma pigmentosum n=1 (1.16%), and white lesion n=1 (1.16%). The predominant predisposing factor in males was a "combination of habits" while in females it was an "unknown etiology" (Figure-2).

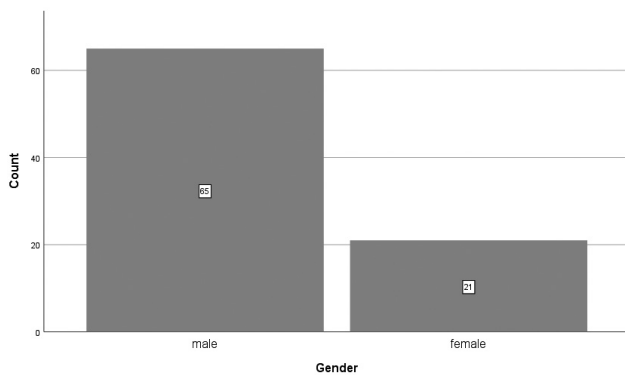| | Number | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Age | 86 | 25 | 79 | 47.02 | 12.008 |

**Table-I. Age range of the patients**



**Figure-1. Gender distribution of the patients**

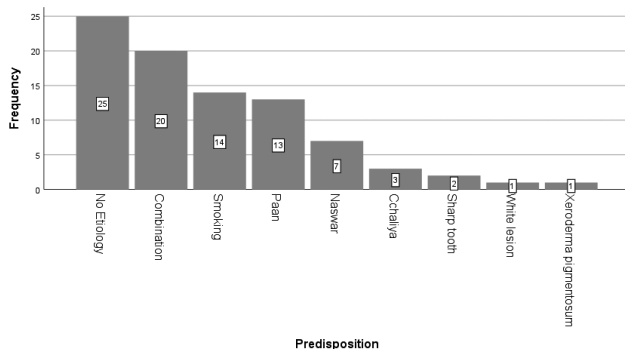| | Frequency (%) |
|---|---|
| Well differentiated oral squamous cell carcinoma (WDOSCC) | 46 (53.5%) |
| Moderately differentiated oral squamous cell carcinoma (MDOSCC) | 35 (40.7%) |
| Poorly differentiated oral squamous cell carcinoma (PDOSCC) | 4 (4.7%) |
| Carcinosarcoma | 1 (1.2%) |
| Total | 86 (100.0%) |

**Table-II. Histo-pathological grading**



**Figure-2. Predisposing factors**

| | Frequency (%) |
|---|---|
| Sub-site | |
| Tongue | 31 (36.0%) |
| Buccal mucosa | 30 (34.9%) |
| Mand. alveolous | 12 (13.95%) |
| Max. alveolous | 3 (3.5%) |
| Hard palate | 3 (3.5%) |
| Retromolar | 3 (2.3%) |
| Lower lip | 2 (2.3%) |
| Floor of mouth | 1 (1.2%) |
| Oral Commisure | 1 (1.2%) |
| Total | 86 (100.0%) |

**Table-III. Frequency of involvement of different sub-sites**

## DISCUSSION

The incidence of OSCC varies widely in different regions of the world regarding age, gender, predisposing factors and site distribution helps in making different therapeutic decisions.[10] In the present study the mean age of the patients was 47.2 years at the time of presentation with age range from 25 years to 79 years. Age range of female patients was 35 years to 70 years and age range of the male patients was 25 years to 79 years. These findings are consistent with a study carried out at Karachi where age range of the patients was from 20-78 years and mean age of the patients was 47.1±12.22 years. The most common age of presentation of the patients was between 41 to 50 years.[11] In another study conducted in Lahore mean age of the patients was 53.13 ± 14.82 years, the age of the male patients ranged from 25 to 80 years and of female patients it ranged from 25 to 75 years.[10]

For years the predominantly affected gender by OSCC has been males, the ratio is now narrowed down to two men for every women. A quarter of yearly diagnosed cancers in men in Sri Lanka, Bangladesh, Pakistan and India are located in head and neck region.[12] Many European studies also report male predominance in OSCC. Majority of the studies conducted on patients of OSCC in Pakistan show male predominance as in the present study. The reason behind this trend may be that the males are more involved in illicit habits of snuff dipping and smoking as compared to females. In our society females are less likely

to be involved in these addictive habits.[13] This male predominance is also explained in terms of being more exposed to the occupational, environmental and outdoor carcinogens and they are more likely to become addictive.[6] The same trend was observed in our study where 75.58% (n=65) of the patients were males and 24.42% (n=21) were females. Another study conducted in India also reported a male predominance in OSCC where 61.25% of the 80 cases were males.[14] However these results are in contrast to another study conducted in Lahore which showed female predominance with a male to female ratio of 1:1.5.[15]

The different sites involved by OSCC varies in different geographical areas and populations depending on ethnicity, age of exposure, nature of exposure to predisposing factor and genetic factors.[6] In the present study the predominantly involved sites were tongue n=31 (36.04%) and buccal mucosa n=31 (34.88%) and both involved in approximately equal number of cases, followed by the mandibular alveolar mucosa n=12 (13.95%), maxillary alveolar mucosa n=3 (3.48%), hard palate n=3 (3.48%), retromolar trigone n=3(3.48%), lower lip n=2 (2.32%), floor of mouth n=1 (1.16%) and commissure of mouth n=1 (1.16%). Majority of the cancers (53.48%) n=46 were present on the left side, 43.04% of the cases n=37 were present on right side and 3.48% n=3 being in the midline.

A study conducted by Akram S et al in Karachi Pakistan showed that buccal mucosa was affected in 54% of the cases followed by tongue 24%, alveolus 9%, lip 7%, and floor of the mouth was affected in 6% of the cases. These findings are inconsistent with the findings of the present study.[16]

According to a study conducted in Eastman Dental Hospital London; tongue was predominantly affected site (46.9%) followed by floor of the mouth (20.9%), buccal mucosa (9.6%) and alveolus (10.4%). In European and American populations tongue remains the predominantly involved site (40-50%). In Asian populations buccal mucosa is the predominantly affected site due to betel nut or tobacco chewing habits. In Sri Lankan population OSCC of buccal mucosa comprises 40% of cases. The more posteriorly located cancers show poor prognosis in terms of five year survival as the sites influences nodal metastasis of the disease. Furthermore the surgeons accessibility is compromised which leads to difficulty in achieving clear margins needing adjuvant therapy postoperatively (i.e. radiotherapy).[9]

The grading of OSCC on the basis of histology into well, moderate and poorly differentiated is based on the degree of keratinization and cytological maturation. This grading is of a limited prognostic value. However it shows a trend towards regional lymph node metastasis and higher grade tumors show increased nodal metastasis.[2]

In contrast to this in another study conducted on 215 patients the grade of OSCC was found having a significant predictive value in loco-regional failure and recurrence.[17]

Majority of the patients included in this study were having well differentiated OSCC ie: 53.48% (n=46), followed by moderately differentiated 40.69% (n=35), 4.65% (n=4) of the patients were having poorly differentiated OSCC and one patient was diagnosed with carcino-sarcoma which constitutes 1.16% (n=1) of the total number of patients according to Anneroth's histological grading system.

These findings are in accordance to a study conducted in a tertiary care hospital of south Punjab Pakistan where 42.5% of the patients presented with moderately differentiated OSCC, 37.5% with moderately differentiated and 20% of the patients were having poorly differentiated OSCC.[13] The percentage of the patients having poorly differentiated OSCC was much higher (20%) in this study when compared to the present study i.e. 4.65%.

While according to another study conducted in north-west Pakistan majority of the patients presented with moderately differentiated OSCC (52%) followed by well differentiated OSCC (42%).[6]

TNM staging of squamous cell carcinoma reflects the tumor growth in whole body, according to 'T' tumor size, 'N' lymph node involvement and 'M' distant metastasis. This staging is important for treatment planning, assessing the risk for recurrence and overall survival of the patient. However this staging only takes into account the anatomical aspects of the disease and other prognostic factors like treatment and comorbidities are not included in it.[18]

The results of our study are quite similar to another study in which 61.61% patients presented at stage IV and only 6.53% patients presented at stage I, 8.53% presented at stage II and 25.23% at stage III.[19] Same results were observed in our study where only 2.32% patients presented at stage I and majority (60.46%) presented at stage IV, 4.65% presented at stage II and 32.55 at stage III.

While according to another study 34.7% of the Asian patients presented at TNM stage I, 16.8% presented at Stage II, 14.9% at stage III and 33.7% presented at stage IV.[20] These results vary from the results in our study where only 2.32% patients presented at stage I and majority (60.46%) presented at stage IV.

Betel quid (Paan) and areca nut (Chaliya) chewing habits has been a tradition in some parts of south-east Asia especially in Pakistan, India and Bangladesh. This practice is entrenched in the culture of these populations and dates back to several thousand years. The betel quid or Paan consists of a mixture of catechu( acacia catechu), areca nut (areca catechu), slaked lime (Calcium oxide and calcium hydroxide) along with some spices and sweeteners all wrapped in a betel leaf. Most of the chewers of betel quid also add smoking to their habit which is implicated in oral and pharyngeal carcinomas.[21]

Chewing betel quid (Paan) is an independent predisposing factor for OSCC but when it is combined with smoking and alcohol the risk increases 11 fold.[22]

This risk of developing OSCC increases with age due to prolonged exposure to the predisposing factors. The other mutagenic and epigenetic changes also tends to accumulate with increasing age.[6] The chewing habits of areca nut (Cchaliya), Niswar and gutka has not only been associated with OSCC but also with some system complications like diabetes mellitus, vascular diseases and hypertension.[21]

Risk assessment in the present study showed that the greatest number of cases n=25 (29.06%) were having no predisposing factor, n=19 (22.09%) were having a combination of habits (Smoking, Paan, Cchaliya, Niswar), n=14 (16.27%) smoking, n=13 (15.11%) Paan, n=7 (8.13%) Naswar, n=3 (3.48%) Cchalia, sharp tooth n=2 (2.32%), Xeroderma pigmentosum n=1 (1.16%), and White lesion n=1 (1.16%).

A study conducted in Karachi Pakistan showed that the Gutka was the most common predisposing factor 30%, followed by Paan 12.9%, Tobacco 21.2%, Niswar 9% and chaliya 6.5%(21). The Unknown etiology and effect of combination of habits which are the most common predisposing factors in our study were not studied here.

According to a study conducted in Pakistan in year 2015 tobacco smoking was associated with 58% of the OSCC but in our study Smoking counts only for 15.11% of the cases.[23]

According to another study conducted in Thailand majority of the patients with OSCC were smokers 64.4%, drinkers 49.6% and betel quid chewers 50.2%. These results are also in contrast to the present study where none of the patients was alcohol abuser.[24]

In the cases where no obvious predisposing factor for OSSC is present the effect of environmental tobacco smoke, occupational exposure and family history of cancer needs to be further investigated with larger sample size.[1]

## CONCLUSION
The disease trends are changing in our population, as the disease is increasingly affecting younger age group, tongue is now increasing being

involved more commonly as in majority of the previous studies the incidence of OSCC of buccal mucosa was much higher, the incidence of OSCC without any obvious risk factor is increasing which needs further investigation. The patients tend to present at an advanced stage of the disease which may be a result of misdiagnosis. Different oral cancer awareness activities need to be devised for disease prevention and making early diagnosis possible.

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## REFERENCES

1.  Kanwal M, Haider G, Zareef U, Saleem S. **Addiction of tobacco chewing and smoking in the patients of head and neck squamous cell carcinoma: A descriptive epidemiological study in Pakistan.** Pakistan J Med Sci. 2019; 35(6):1712–7.

2.  Vigneswaran N, Williams MD. **Epidemiologic trends in head and neck cancer and aids in diagnosis.** Oral Maxillofac Surg Clin North Am [Internet]. 2014; 26(2):123–41. Available from: http://dx.doi.org/10.1016/j.coms.2014.01.001

3.  Upreti D, Pathak A, Kung SKP. **Lentiviral vector-based therapy in head and neck cancer (Review).** Oncol Lett. 2014; 7(1):3–9.

4.  Ma J, Liu Y, Yang X, Zhang C ping, Zhang Z yuan, Zhong L ping. **Induction chemotherapy in patients with resectable head and neck squamous cell carcinoma: A meta-analysis.** World J Surg Oncol. 2013; 11:67.

5.  Anwar N, Pervez S, Chundriger Q, Awan S, Moatter T, Ali TS. **Oral cancer: Clinicopathological features and associated risk factors in a high risk population presenting to a major tertiary care center in Pakistan.** PLoS One [Internet]. 2020;15(8 August):1–15. Available from: http://dx.doi.org/10.1371/journal.pone.0236359

6.  Ahmed R, Malik S, Khan MF, Khattak MR. **Epidemiological and clinical correlates of oral squamous cell carcinoma in patients from north-west Pakistan.** J Pak Med Assoc. 2019; 69(8):1074–8.

7.  Gandini S, Negri E, Boffetta P, La Vecchia C, Boyle P. **Mouthwash and oral cancer risk - Quantitative meta-analysis of epidemiologic studies.** Ann Agric Environ Med. 2012; 19(2):173–80.

8.  Oji C, Chukwuneke F. **Poor oral hygiene may be the sole cause of oral cancer.** J Maxillofac Oral Surg. 2012; 11(4):379–83.

9.  Jerjes W, Upile T, Petrie A, Riskalla A, Hamdoon Z, Vourvachis M, et al. **Clinicopathological parameters, recurrence, locoregional and distant metastasis in 115 T1-T2 oral squamous cell carcinoma patients.** Head Neck Oncol. 2010; 2(1):1–21.

10. Sahaf R, Naseem N, Rehman A ur, Anjum R, Nagi AH. **A study of 89 cases of oral squamous cell carcinoma presenting at Teaching Hospitals of Lahore, Pakistan.** J Pakistan Dent Assoc. 2017; 26(1):26–31.

11. Alam J, Siddiqui AA, Mian RI, Mirza AJ, Khan S, Alam MK, et al. **Conventional clinical and prognostic variables in 150 oral squamous cell carcinoma cases from the indigenous population of Karachi.** Int J Cancer [Internet]. 2016; 15(2):1118. Available from: http://dx.doi.org/10.1016/j.coms.2014.01.001

12. Maxwell Parkin D, Bray F, Ferlay J, Pisani P. **Estimating the world cancer burden: Globocan 2000.** Int J Cancer. 2001; 94(2):153–6.

13. Gul H, Asif F, Ghaffar I, Anwar MA, Tayyab MA, Kashif M. **Epidemiology and pathological trends in oral squamous cell carcinoma in a local tertiary care hospital.** Int J Community Med Public Heal. 2017; 4(12):4440.

14. Khandekar SP, Bagdey PS, Tiwari RR. **Oral cancer and some epidemiological factors : A hospital based study.** 2006; 31(3):157-9.

15. Jamal S, Mamoon N, Mushtaq S, Luqman M. **Oral cancer: A clinicopathological analysis of 723 cases.** PAFMJ [Internet]. 2006 Sep 30; 56(3 SE-Original Articles). Available from: https://www.pafmj.org/index.php/PAFMJ/article/view/1479

16. Akram S, Mirza T, Aamir Mirza M, Qureshi M. **Emerging patterns in clinico-pathological spectrum of oral cancers.** Pakistan J Med Sci. 2013; 29(3):783–7.

17. Kademani D, Bell RB, Bagheri S, Holmgren E, Dierks E, Potter B, et al. **Prognostic factors in intraoral squamous cell carcinoma: The influence of histologic grade.** J Oral Maxillofac Surg. 2005; 63(11):1599–605.

18. Almangush A, Mäkitie AA, Triantafyllou A, de Bree R, Strojan P, Rinaldo A, et al. **Staging and grading of oral squamous cell carcinoma: An update.** Oral Oncol [Internet]. 2020; 107(January):104799. Available from: https://doi.org/10.1016/j.oraloncology.2020.104799

19. Ahmad P, Nawaz R, Qurban M, Shaikh GM, Mohamed RN, Nagarajappa AK, et al. **Risk factors associated with the mortality rate of oral squamous cell carcinoma patients.** 2021; 0(April 2020).

20. Yu AJ, Choi JS, Swanson MS, Kokot NC, Brown TN, Yan G, et al. **Association of Race/Ethnicity, Stage, and Survival in Oral Cavity Squamous Cell Carcinoma: A seer study. O**TO Open. 2019; 3(4):1-10.

21. Saleem S, Shahid SM, Hameed A, Abbasi Z, Khan MA, Qureshi NR, et al. **Prevalence of oral squamous cell carcinoma (OSCC) in relation to different chewing habits in Infectious diseases View project Gemonic Epidemiology of MRSA View project Prevalence of oral squamous cell carcinoma (OSCC) in relation to different chewing habi.** J Biochem Mol Biol [Internet]. 2012; 45(2):59–63. Available from: https://www.researchgate.net/publication/272183368

22. Auluck A, Hislop G, Poh C, Zhang L, Rosin MP. **Areca nut and betel quid chewing among South Asian immigrants to Western countries and its implications for oral cancer screening.** Rural Remote Health. 2009; 9(2):1118.

23. Raza A. **Clinicopathological spectrum of oral squamous cell carcinoma at a public sector health facility carcinoma at a public sector health facility.** Biomedica. 2015; 31(March):21–6.

24. Iamaroon A, Pattanaporn K, Pongsiriwet S, Wanachantararak S, Prapayasatok S, Jittidecharaks S, et al. **Analysis of 587 cases of oral squamous cell carcinoma in northern Thailand with a focus on young people.** Int J Oral Maxillofac Surg. 2004; 33(1):84–8.

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