Original Research Article

Oral Squamous Cell Carcinoma; A Multicausal Disease

Abstract:

Aims: To find out the risk factors and location of OSCC and also the prevalence of different stages and grades of OSCC.

Study Design: This is a case-control study.

Place and duration of study: The study was conducted Ziauddin dental hospital KDLB and Clifton Campus, Karachi from 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. The most common location of oral cancer in this study was the buccal mucosa followed by tongue and lips. The majorly consumed type of tobacco was gutka 55% followed by pan 30%, naswar 15%, betel nut 11% and smoking 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 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 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, retromolar trigone 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 (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 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

44 females(5). Karachi is the home to oral cancer, which is the second most common malignancy in
45 both the genders(6).

46 The risk factors that are significantly associated with oral cancer are tobacco(7) , alcohol(8), viral
47 infection like EBV and HPV(9) and genetic susceptibility(10). There is a significant
48 geographical variation in the incidence of OSCC due to area specific etiological factors like in
49 the developed world the smoked tobacco and alcohol consumption are the main etiological
50 factors. On the other hand, in developing countries the major etiological factors are betel quid
51 chewing, bidi, smoking and alcohol (4, 11, 12). So the objectives of the current study are to find
52 out the risk factors and location of OSCC and also the prevalence of different stages and grades
53 of OSCC.

54 **Methods:**

55 A Case control study was conducted from October 2017 to April 2018. Approval of the Ethics
56 Review Committee (ERC) of Ziauddin University was obtained according to institutional
57 guidelines. The sample size was calculated by using Openepi calculator version 3 using
58 confidence level of 99%. The samples included in the study were the histopathologically proven
59 preoperative OSCC patients of age 18 years and above. Those patients were excluded from the
60 study who either refused to give consent or were diagnosed with other type of cancer. The
61 samples were collected from the OPD of Ziauddin dental hospital KDLB and Clifton Campus,
62 Karachi. Consecutive sampling technique was used.

63 Variables like age, gender, ethnicity, socioeconomic status, detail history of different types of
64 tobacco used, oral hygiene habits, family history of cancer were noted. The stage and grade of
65 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 by tongue and lips as mentioned in Table.

The frequency and distribution of different types of tobacco 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 with well 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%) and 4 (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, retromolar trigone or major salivary glands (2). In the current study, the most common location of oral cancer was the buccal mucosa followed by tongue and lips.

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 frequency and duration of smoking (17-19). Globally 20-30% of OSCC are due 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 about 40% (20). The current study also reported incidence of OSCC among smokers but none of the patient having history of alcohol consumption 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 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).

Conclusion:

It can be concluded that the major etiological factors of OSCC among Pakistani population are chewing tobacco 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 and also by encouraging dental and medical professionals to conduct free oral cancer screenings.

References:

1. Warnakulasuriya S, Johnson NW, Van der Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. Journal of oral pathology & medicine. 2007;36(10):575-80.
2. Humans IWGotEoCRt, Organization WH, Cancer IAfRo. Betel-quid and areca-nut chewing and some areca-nut-derived nitrosamines: IARC; 2004.
3. McCullough M, Prasad G, Farah C. Oral mucosal malignancy and potentially malignant lesions: an update on the epidemiology, risk factors, diagnosis and management. Australian dental journal. 2010;55:61-5.
4. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral oncology. 2009;45(4-5):309-16.
5. Siddiqui IA, Farooq MU, Siddiqui RA, Rafi ST. Role of toluidine blue in early detection of oral cancer. Pakistan Journal of Medical Sciences. 2006;22(2):184.
6. Bhurgri Y. Cancer of the oral cavity-trends in Karachi South (1995-2002). Asian Pac J Cancer Prev. 2005;6(1):22-6.
7. Warnakulasuriya S, Sutherland G, Scully C. Tobacco, oral cancer, and treatment of dependence. Oral oncology. 2005;41(3):244-60.
8. Ogden GR. Alcohol and oral cancer. Alcohol. 2005;35(3):169-73.
9. Syrjänen S. Human papillomavirus (HPV) in head and neck cancer. Journal of clinical virology. 2005;32:59-66.
10. Bau D-T, Mau Y-C, Ding S-l, Wu P-E, Shen C-Y. DNA double-strand break repair capacity and risk of breast cancer. Carcinogenesis. 2007;28(8):1726-30.
11. Lee CH, Ko AMS, Warnakulasuriya S, Yin BL, Zain RB, Ibrahim SO, et al. Intercountry prevalences and practices of betel-quid use in south, southeast and eastern asia regions and associated oral preneoplastic disorders: An international collaborative study by asian betel-quid consortium of south and east Asia. International journal of cancer. 2011;129(7):1741-51.
12. Stewart BW, Kleihues P. World cancer report: IARC press Lyon; 2003.
13. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Annals of surgical oncology. 2010;17(6):1471-4.
14. Zini A, Czerninski R, Sgan-Cohen HD. Oral cancer over four decades: epidemiology, trends, histology, and survival by anatomical sites. Journal of oral pathology & medicine. 2010;39(4):299-305.
15. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International journal of cancer. 2015;136(5):E359-E86.
16. Mignogna M, Fedele S, Russo LL. The World Cancer Report and the burden of oral cancer. European journal of cancer prevention. 2004;13(2):139-42.
17. Hashibe M, Brennan P, Benhamou S, Castellsague X, Chen C, Curado MP, et al. Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. Journal of the National Cancer Institute. 2007;99(10):777-89.
18. Petti S. Lifestyle risk factors for oral cancer. Oral oncology. 2009;45(4-5):340-50.
19. Castellsagué X, Quintana MJ, Martínez MC, Nieto A, Sanchez MJ, Juan A, et al. The role of type of tobacco and type of alcoholic beverage in oral carcinogenesis. International journal of cancer. 2004;108(5):741-9.
20. Vargas-Ferreira F, Nedel F, Etges A, Gomes APN, Furuse C, Tarquinio SBC. Etiologic factors associated with oral squamous cell carcinoma in non-smokers and non-alcoholic drinkers: a brief approach. Brazilian dental journal. 2012;23(5):586-90.

21. Jayalekshmi P, Gangadharan P, Akiba S, Nair R, Tsuji M, Rajan B. Tobacco chewing and female oral cavity cancer risk in Karunagappally cohort, India. British journal of cancer. 2009;100(5):848.
22. Radoï L, Luce D. A review of risk factors for oral cavity cancer: the importance of a standardized case definition. Community dentistry and oral epidemiology. 2013;41(2):97-109.
23. Fuentes B, Duaso J, Droguett D, Castillo C, Donoso W, Rivera C, et al. Progressive extracellular matrix disorganization in chemically induced murine oral squamous cell carcinoma. ISRN Pathology. 2012;2012.