RISK FACTORS OF ORAL SQUAMOUS CELL CARCINOMA IN OLD VERSUS YOUNG PATIENTS

¹NEHA USMAN, ²ASIF NAZIR, ³FAHAD KHALIQ, ⁴SAMERA KIRAN, ⁵MUHAMMAD ABRAR AHMAD, ⁶WAJEEHA CHAUHDRY, ⁷MUHAMMAD SHAFIQUE ASHRAF, ⁸MUHAMMAD USMAN AKHTAR

ABSTRACT

Approximately 94% of all oral malignancies are squamous cell carcinoma and numerous risk factors have been determined for its pathogenesis e.g. smoking, betel nut chewing and alcoholism. Traditionally oral squamous cell carcinoma is thought to be disease of males in their 6th or 7th decade of life but in younger people increased incidence has been noticed in recent years. The current study is a contribution to literature to compare risk factors of oral squamous cell carcinoma in younger and older patients.

The patients meeting inclusion criteria from Out Patient Departments of Oral and Maxillofacial Surgery Units of de'Montmorency College of Dentistry Lahore and Nishtar Institute of Dentistry Multan were selected. A structured questionnaire was used to record patient's demographic data and risk factors. Patients were selected after being confirmed for disease clinically and histopathologically. Of the total 232 patients, smoking was positive in 54.3% patients while drinking alcohol and betel nut chewing was in 10.3% and 87.9% respectively. No statistical significance was present in risk factors on comparison of old and young patients. On comparison of risk factors between male and female, difference was significant for betel nut chewing and smoking but not for alcoholism. Smoking was more prevalent in male patients while betel nut chewing was more common in female patients.

Key Words: Squamous cell carcinoma, Old patients, Young patients, Risk factors, Smoking, Betel nut, Alcoholism.

INTRODUCTION

Oral cancer represents 5-10% of all human malignancies and 94% of all oral malignancies is squamous cell carcinoma (OSCC).^{1,2} It is one of the top ten most frequent cancers present around the globe with an incidence of 10-15/100,000 with male to female ratio of 2.5:1. OSCC involves cervical lymph nodes that drain

areas of oral cavity directly or indirectly.^{2,3,4} Most common risk factors include smoked and smokeless tobacco e.g. cigarette smoking, snuff dipping, betel nut chewing and alcoholism.³⁻⁵

About 65 to 75% of OSCC patients are linked to smoking, 30% with alcoholism and 26% with betel nut chewing. Association between genetic factors, poor nutritional status, chronic viral and fungal infections, pre-existing oral disease and bad oral hygiene is also observed in other studies. Linically lesion may be ulcerative, exophytic or verrucous. Site of involvement is typical for particular risk factor and area exposed to risk factor.

Traditionally OSCC is a disease of males in their 6th or 7th decade of life. A number of OSCC cases are noticed in patients of 40 years or younger in recent years. ^{14,15} No local studies are available regarding risk factors of OSCC in young patients. In young patients its incidence and risk factors should be evaluated in Pakistan where a large number of patients remain undocumented. This study will be a contribution to literature to know the risk factors of OSCC and their comparison in old and young patients and consequently it will be helpful in raising the campaigns for awareness in young and older population.

- ¹ Dr Neha Usman, BDS, RDS, Research Student, Oral and Maxillofacial Surgery, de, Montmorency College of Dentistry, Lahore.
- ² Dr Asif Nazir Ch, Corresponding author: BDS, FCPS (Oral & Maxillofacial Surgery), Associate Professor/Head of Department, Oral & Maxillofacial Surgery Unit, Nishtar Institute of Dentistry, Multan. e-mail address: zimalasif@gmail.com
- ³ Dr Fahad Khaliq, BDS, FCPS (Oral & Maxillofacial Surgery), Demonstrator, Oral and Maxillofacial Surgery Department, Nishtar Institute of Dentistry, Multan.
- ⁴ Dr Samera Kiran, BDS, RDS, Demonstrator, Department of Orthodontics, Nishtar Institute of Dentistry
- Muhammad Abrar Ahmad, BDS, RDS, Postgraduate Resident, Oral and Maxillofacial Surgery, Nishtar Institute of Dentistry
- ⁶ Wajeeha Chauhdry, BDS, RDS, Postgraduate Resident, Oral and Maxillofacial Surgery
- Muhammad Shafique Ashraf, BDS, RDS, Postgraduate Resident, Oral and Maxillofacial Surgery
- Professor Dr Muhammad Usman Akhtar, BDS, MCPS, MDS, Principal, Nishtar Institute of Dentistry, Multan and Head of Oral and Maxillofacial Surgery Department, de, Montmorency College of Dentistry, Lahore.

Received for Publication: Dec 8, 2018 **Revised:** Dec 26, 2018 **Approved:** Dec 30, 2018

METHODOLOGY

This descriptive cross sectional study was conducted at the Department of Oral and Maxillofacial Surgery, de'Montmorency College of Dentistry Lahore and Nishtar Institute of Dentistry Multan from March 2017 to February 2018. Ethical approval was taken from ethical committees of the institutions. Patients of both genders, age range from 15 to 75 years with ulcerative lesion in oral cavity with or without cervical lymphadenopathy were taken from Out Patient Departments of Oral and maxillofacial Surgery Units of these institutions. The assessment of patients was done by detailed relevant history, clinical and radiographic examination. The status of ulcerated lesion was assessed by intra-oral and extra oral clinical evaluation and panoramic or occipitomental radiograph. A written informed consent from every patient was taken and every lesion was further confirmed by biopsy report for including the patients in the study. The patients where biopsy report was not conclusive for OSCC were excluded from the study. A structured questionnaire was used to record all the data e.g. patient's demographics like patient's name, age and gender, risk factors (smoking, alcohol, betal nut) occupation, educational and medical status. Clinical characteristics of lesion were also analyzed, including size, site and duration of lesion.

A total of 232 subjects were recruited randomly from OPD and divided into two groups on the basis of age after stratification. Group-I (old patients) consisted of individuals with age above 40 years while Group-II (young patients) consisted of individual ≤ 40 years of age. All records of patients were kept confidential and entered in SPSS version 17 to analyze and find out distribution of different variables in terms of proportions and percentages. The variables were presented in graphs and tables. Mean and standard deviation (mean±SD) were calculated for age of OSCC patients. Frequency and percentages were calculated for gender, monthly family income, educational status and risk factors (smoking, alcohol and betel nut). Chi-square test was applied to compare responsible factors in old and young age group as well as in male and female patients. P value ≤ 0.05 was considered significant.

RESULTS

The current study comprised of a total of 232 patients of oral squamous cell carcinoma. The age range was from 15 to 75 years. Most of the patients were from fifth and sixth decade of life with mean (±SD) age of 46.83±6.93 years. There was a male predilection in current study including 168 (72.4%) male and 64 (27.6%) female patients. Frequencies and percentages of stratified age of patients with OSCC are given in Figure 1.

Paan chewing (88%) was the most common risk factor among all patients followed by smoking (54.3%) and alcohol consumption (10.3%). Frequencies and percentages of age, gender and risk factors of smoking, drinking alcohol and betel nut chewing in old versus young patients are given in Table 1.

Male to female ratio was 2.8:1 in old patients of OSCC and 2.12:1 in young patients. Similarly, comparison was done between frequency of smoking, alcohol drinking and betel nut chewing in old and young patients of OSCC and difference was not statistically significant for all three risk factors (p=0.24, 0.76, 0.99 respectively).

Mean (\pm SD) age of female patients (47.03 \pm 7.16years) was almost comparable to male patients (46.75 \pm 6.93years) and it was not statistically significant (p=0.84). Smoking was more prevalent in male as compare to female patients and no statistical significance was shown by chi-square test statistics due to less than 5 samples of female smokers in OSCC patient (p=0.00) (Table 2).

Similarly, comparison was done between frequency of alcohol drinking in male and female patients and difference was not statistically significant (p=0.11). On comparison, frequency of paan chewing was high in female patients as compared to male patients and difference was statistically significant (p=0.01).

DISCUSSION

Symptoms associated with oral squamous cell carcinoma are common complaints of patients which compel them to present to oral and maxillofacial surgeons for treatment. Oral and Maxillofacial Surgery Departments of de'Montmorency College of Dentistry Lahore and Nishtar Institute of Dentistry Multan are very well renowned Oral and Maxillofacial units in Pakistan and cater the patients from all over the Punjab and adjacent areas of Sindh, Baluchistan and KPK provinces. Being tertiary care centres, most of the patients operated are referred from remote areas and are usually presented with massive disease as well as different educational, social, cultural and financial status.

In recent years, increasing number of OSCC cases in younger individuals have been documented ranging from 6% to 11.7%. 16,17,18,19 In current study, mean (\pm SD) age of OSCC patients was 46.83 ± 6.93 years. These results indicate that OSCC patients of current study presented in late 5^{th} decade or in early 6^{th} decade of life. These results were in accordance with other Asian studies. 20,21 These results were not in accordance with North American and American populations. In North American populations OSCC patients presented in 7^{th} or 8^{th} decade of life while USA oral cancer statistics

TABLE 1: COMPARISON OF RISK FACTORS OSCC IN OLD VERSUS YOUNG PATIENTS

| Risk factor | Old patients (41-75years) | Young patients (15-40years) | p-value |
|----------------------------|---------------------------|-----------------------------|---------|
| Number of patients N, (%) | 182 (78.88%) | 50(21.12%) | |
| Age (Mean ±SD) | 49.81±3.88 | 35.96 ± 4.37 | |
| Male/female, n (ratio) | 134/48 (2.8: 1) | 34/16 (2.12: 1) | |
| Smoking (yes/no) | 104/78 | 22/28 | 0.24 |
| Drinking alcohol (yes/no) | 18/164 | 6/44 | 0.76 |
| Betal nut chewing (yes/no) | 160/22 | 44/6 | 0.99 |

N=total numbers of subjects, SD=standard deviation, $p \le 0.05$ = statistically significant

TABLE 2: GENDER BASED COMPARISON OF RISK FACTORS IN OSCC PATIENTS

| Risk factor | Male patients | female patients | p-value |
|----------------------------|------------------|-----------------|---------|
| Number of patients N, (%) | 168 (72.4%) | 64 (27.6%) | |
| Age (mean±SD) | 46.75 ± 6.93 | 47.03±7.16 | 0.84 |
| Smoking (Yes/no) | 124/44 | 2/62 | 0.00* |
| Drinking alcohol (yes/no) | 22/146 | 2/62 | 0.11 |
| Betal nut chewing (yes/no) | 140/28 | 64/0 | 0.01* |

N=total number of subjects, SD=standard deviation,*p≤0.05= statistically significant

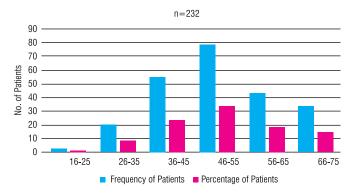


Fig. 1: Age Distribution in Oral Squamous Cell Carcinoma

found that median age of OSCC patients was 62 years. ²² Most probable reason for contradictory result is early exposure of chewing habits to individuals in Asian populations.

In current study, 54.3% of OSCC patients were smoker that was in agreement with results found by Iype *et al* where they found that 56.4% patients associated with smoking of tobacco.²³ Rodriquez *et al* found 77% and Khalili J 90% association of smoking with OSCC that was not in accordance with current study.^{24,25} These differences might be due to social trends of Asian subcontinent.

In present study, alcohol drinking was positive in 10.3% OSCC patient that was not in accordance with study of Rodriquez *et al* who found 52% association between alcohol drinking and OSCC.²⁴ Social disparity and trends might be reason of this difference. In current

study, 87.9% of OSCC patients chewed areca nuts. Results of current study were in accordance with study of Akhtar *et al* who found similar association between paan chewing and OSCC in south Asian populations. There was a slight difference between results of current study and study conducted on Thai population where areca nut chewing was in 50.2% of individuals. ²⁶

In this study, it was revealed that paan chewing (87.9%) is highly associated with OSCC as compared to smoking (54.3%) and alcohol drinking (10.3%). On comparison with other studies of subcontinent, it was in accordance with results of Iype $et\ al$ and Akhtar $et\ al$. While results compiled by Iamaroon $et\ al$ was not in agreement with current study. Contradiction in results might be due to ethnic back ground and socioeconomic status of study population.

Current study determined that percentage of older OSCC patients (78.88%) was higher as compared to younger people (21.12%). These results were not in agreement with study of Iamaroon et al who determined incidence up to 12.4% in Thai individuals and incidence was 10.7% in Brazilian OSCC patients. ^{16,26} In current study, higher occurrence of OSCC in younger patients seems to be due to longer and earlier exposure to smoking and paan chewing. In current study, mean (±SD) age was 49.81±3.88 years in old patients and 35.96±4.37 in young patients. These results are in accordance with Iamaroon et al where median age of young patients was 39 years. In present study, male to female ratio was almost equal in both groups (2.8:1 in old patients and 2.12:1 in young patients). These results were also

comparable to Iamaroon *et al* who found it as $2.3:1.^{26}$

In current study, risk factors were also compared between old and young patients. Smoking was positive factor in 57% of old patients and 44% young patients. Similarly, percentages of paan chewing and alcohol consumption in both groups did not show statistical significance (Table 1). In Pakistan, tobacco is used in both smoked as well as in smokeless form. Smoking cigarette is common throughout the country. Pan a type of smokeless tobacco is popular in Karachi and some cities of Punjab. Snuff (Niswar) is powdered tobacco mixed with ash or lime and some flavoring or chemical agents. It is place between gums and upper or lower lip. This type of smokeless tobacco is popular in Baluchistan and Khyber Pakhtunkhwa.^{27,28}

Results of current study are in accordance with the study of Hirota $et~al.^{29}$ According to current study, OSCC was more prevalent in male gender (72.4%) as compared to females (27.6%) and male to female ratio was 2.63:1. Results of current study were in agreement with previous studies of subcontinent where Iype et~al reported male to female ratio of 2.3:1. 9,23 These slight differences might be due to Islamic and social trends in Pakistan or different ethnic groups.

Risk factors were also compared between both genders in current study. Smoking was almost exclusively present in male patients (p=0.00) and drinking alcohol was also more prevalent in male patients but there was not any statistical difference. Difference between both genders was statistically significant for paan chewing habit (p=0.01) and it was more common in female patients (Table 2). Results of current study are similar to study of Iamaaroon $et\ al$ and Llewellyn $et\ al$ but contradict with study of Hirota $et\ al$. 26,29,30 This difference might be due to social trend of Indo-Pak subcontinent and Europe.

CONCLUSION AND RECOMMENDATIONS

In present study, there was no difference of risk factors of oral squamous cell carcinoma in old and young patients. Smoking was more prevalent in male patients while betel nut chewing was more common in female patients. Continuous campaigns regarding different risk factors and their consequences should be arranged to create awareness in general public. Heavy taxes should be imposed on snuff and paan manufacturing making these products more expensive thereby decreasing their use. Moreover, import of cigarettes and alcohol should be banned in Pakistan. The issue should also be raised at mass level to sort out the reasons for more consumption of tobacco by males and betel nut by female population and strict legislation should be implemented to check these risk factors so as to decrease overall incidence of OSCC in general population.

REFERENCES

- 1 Alves AM, Correa MB, Silva KDD, Araújo LMA, Vasconcelos ACU, Gomes APN, et al. Demographic and Clinical Profile of Oral Squamous Cell Carcinoma from a Service-Based Population. Braz Dent J 2017; 28: 301-6.
- Neville BW, Damm DD, Allen CM, Chi AC. Oral and Maxillofacial Pathology. Epithelial Pathology. 1st ed (South Asian). New Delhi, India: Elsevier Publishers, 2016: 374-91.
- 3 Malcolm AM, Yasantha A, Farhana B, YasminB, Aleyamma M, Paleth G et al. Cancer Epidemiology in South Asia - Past, Present and Future. Asian Pac J Cancer Prev 2010; 10: 49-67.
- 4 de Camargo CM, Voti L, Guerra-Yi M, Chapuis F, Mazuir M, Curado MP. Oral cavity cancer in developed and in developing countries: population-based incidence. Head Neck 2010; 32:357-67
- 5 Kohn CS, Tsoh JY, Weisner CM. Changes in smoking status among substance abusers: baseline characteristics and abstinence from alcohol and drugs at 12-month follow-up. Drug Alcohol Depend 2003; 69:61-71.
- 6 Parkin DM. Tobacco-attributable cancer burden in UK in 2010. Br J Cancer 2011; 105:6-13.
- 7 Parkin DM. Cancers attributable to consumption of alcohol in UK in 2010. Br J Cancer 2011; 105:14-8.
- 8 Shiu MN, Chen TH, Chang SH, Hahn LJ. Risk factors for leukoplakia and malignant transformation to oral carcinoma: a leukoplakia cohort in Taiwan. Br J Cancer 2000; 82:1871-4.
- 9 Akhtar S, Sheikh AA, Qureshi HU. Chewing areca nut, betel quid, oral snuff, cigarette smoking and the risk of oesophageal squamous-cell carcinoma in South Asians: a multicentre case control study. Eur J Oncol 2012; 48:655–61.
- 10 Rosenquist K, Wennerberg J, Schildt EB, Bladstorm A, Hansson BG, Anderson G. Oral status, oral infections and some life style factors as risk factors for oral and oro-pharyngeal squamous cell carcinoma: A population-based study case-control study in southern Sweden. Acta Otolaryngol 2005; 125:1327-36.
- 11 Markopoulos AK. Current Aspects on Oral Squamous Cell Carcinoma. Open Dent J 2012; 6: 126-30.
- Madani AH, Dikshit M, Bhaduri D, Jahromi AS and Aghamolaei T. Relationship between Selected Socio-Demographic Factors and Cancer of Oral Cavity - A Case Control Study. Cancer Inform 2010; 9: 163–8.
- 13 Shafique S, Haider SM, Ali Z. Histological patterns and clinical presentation of oral squmous cell carcinoma. J Pak Dent Assoc 2010; 9:171-6.
- 14 Jovanovic A, Schulten EB, Kostense PJ, Snow GB, Isaac V. Tobacco and alcohol related to the anatomical of oral squamous cell carcinoma. J Oral Pathol Med 1993; 22:459-62.
- 15 Kapila1 SN, Natarajan S, Boaz K. A Comparison of Clinicopathological Differences in Oral Squamous Cell Carcinoma in Patients Below and Above 40 Years of Age. J Clin Diagn Res 2017; 11: 46-50.
- 16 Udeabor SE, Rana M, Wegener G, Gellrich NC, Eckardt AM. Squamous cell carcinoma of the oral cavity and the oropharynx in patients less than 40 years of age: a 20-year analysis. Head Neck Oncol. 2012; 4: 28-34.
- 17 Ramachandra NB. The hierarchy of oral cancer in India. Int J Head Neck Surg 2012; 3: 143-46.
- 18 Kiran G, Shyam NDVN, Rao J, Krishna A, Reddy BS, Prasad N. Demographics and histological patterns of oral squamous cell carcinoma at a tertiary level referral hospital in Hyderabad, India: A 5-year retrospective study. J Orofac Res 2012; 2: 198-201

- 19 Agrawal KH, Rajderkar SS. Clinico-epidemiological profile of oral cancer: A hospital based study. Indian J Commun Health 2012; 24: 80-85.
- 20 Padma R, Paulraj S, Sundaresan S. Squamous cell carcinoma of buccal mucosa: Prevalence of Clinicopathological pattern and its implications for treatment. SRM J Res Dent Sci 2017; 8: 9-13.
- 21 Ahmed SQ, Junaid M, Awan S, Choudhary MM, Kazi M, Masoom A, et al. Relationship of Tumor Thickness with Neck Node Metastasis in Buccal Squamous Cell Carcinoma: An Experience at a Tertiary Care Hospital. Int Arch Otorhinolaryngol 2017; 21: 265-69.
- 22 Sieczka E, Datta R, Singh A, Loree T, Rigual N, Orner J, et al. Cancer of the buccal mucosa: are margins and T-stage accurate predictors of local control. Am J Otolaryngol 2001; 22:395-9.
- 23 Iype EM, Pandey P, Mathew A, Thomas G, Sebastian P, Nair MK. Oral cancer among patients under the age of 35 years. J Postgrad Med 2001; 47: 171-6.
- 24 Rodriguez T, Altieri A, Chatenoud L, Gallus S, Bosetti C, Negri E, et al. Risk factors for oral and pharyngeal cancer in young adults. Oral Oncol 2004; 40:207-13.
- 25 Khalili J. Oral Cancer: Risk Factors, Prevention and Diagnostic. Exp Oncol. 2008; 30: 259-64.

- 26 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; 33:84–8.
- 27 Khan A, Iqbal A, Haleem M, Khan M, Rehman AU, Din QU. Different Histopathological Grades of Oral Squamous Cell Carcinoma in Patients with History of Snuff Dipping. J Khyber Col Dent 2016; 6: 2-6.
- 28 Khan AS, Ahmad S, Zahoorullah, Khattak MR, Khan MM. Association Between Oral Squamous Cell Carcinoma and Serum Vitamin E in Snuff Users and Non Snuff Users in Khyber Pakhtunkhwa Province of Pakistan. J Khyber Col Dent 2017; 7: 9-15.
- 29 Hirota SK, Braga FB, Penha SS, Sugaya NN, Migliari DA. Risk factors for oral squamous cell carcinoma in young and older Brazilian patients: a comparative analysis. Med Oral Patol Oral Cir Bucal 2008; 13:227-31.
- 30 Llewellyn CD, Linklaterb K, Bell J, Johnson NW, Warnakulasuriya S. An analysis of risk factors for oral cancer in young people: a case control study. Oral Oncol 2004; 40: 304-13.

CONTRIBUTIONS BY AUTHORS

Neha Usman:
Asif Nazir Ch:
Tahad Khaliq:
Data collection, Literature search, Conducted the research work.
Literature search, Data analysis, Designed and compiled the Manuscript.
Data collection, Literature search, Results compilation/Conclusion.

4 Samera Kiran: Literature search, Introduction/Discussion.

5 Muhammad Abrar Ahmad: Data collection, Literature search, Results compilation.

6 Wajeeha Chauhdry: Data collection, Literature search, Introduction/Results compilation.
7 M. Shafique Ashraf: Data collection, Literature search, Introduction/Results compilation.
8 Muhammad Usman Akhtar: Supervised the whole research work, Data analysis, Final proof reading

and review of manuscript.