CLINICO-PATHOPHYSIOLOGICAL DETERMINANTS OF HEALTH AMONG ORAL CANCER PATIENTS IN TERTIARY CARE HOSPITALS OF PAKISTAN

Taqia Fouzia[1], Tariq Ali[2], Attaullah[3], Muhammad Wasif Saleem[4]*, Zainab Abdullah[5], Abdul Samad Gichki[6]

[1]Assistant Professor, Department of Pathology, SMBBMU lyari, Karachi.
[2]*Assistant Professor, Department of Forensic Medicine, Mekran Medical College, Turbat.
[3]Assistant Professor, Department of Community Medicine, Mekran Medical College, Turbat.
[4]Assistant Professor, Department of Pathology, Mekran Medical College, Turbat.
[5]Assistant Professor, Department of Surgery, SMBBMC, Karachi.
[6]Associate Professor, Department of Oral Medicine, Bolan Medical College, Sandeman Provincial Hospital, Quetta.

*Corresponding Author: Muhammad Wasif Saleem
*Department of Pathology, Turbat, Pakistan, drwasifsaleem@outlook.com

ABSTRACT

Objective: To identify clinico-pathophysiological predictors of well-being of oral cancer patients compared in the tertiary care institutions in Pakistan.

Study Design: Cross-sectional study

Setting: Department of Oral and Maxillofacial surgery Jinnah Hospital Karachi, Bolan hospital Quetta and Turbat Hospital Pakistan from Oct 2021 to Nov 2022.

Methodology: Two hundred and seventy-six confirmed cases of oral cancer were recruited in the study and sociodemographic and lifestyle factors were recorded. The mode of clinical presentation at the time of the oral cancer diagnosis was also documented. Results The mean age of the patients was (48.59±14.28) years. The majority of them were males 216 (78.3%) among 276 cases and most of them were of poor socio-economic status 244 (88.4%). Well differentiated squamous cell carcinoma was present in 156(56.5%) patients, moderately differentiated in 118(42.8%) and poorly differentiated oral cancer was found in 2(0.7%) patients only. Oral cancer was found to be the most prevalent among subjects of low socioeconomic status and well-differentiated squamous cell carcinoma was the predominant type. Male sex, smokeless tobacco in the form of chewing and areca nut were also described as risk factors of oral cancer.

Conclusion: Males and low SES people had the highest oral cancer rates, as noted in this study. The majority of cases were well-differentiated carcinoma and reported a history of present and past use of tobacco, alcohol, and betel nut. The most frequent malignancy of the oral cavity was squamous cell carcinoma. There is a need for mass campaigns focusing on the importance of lifestyle practices and risk factors for oral cancer and the need for early help-seeking among the people, particularly low SES.

Key Words: Oral squamous cell carcinoma, tumor, histopathological grading.

INTRODUCTION

Oral cancer constitutes a grave public-health concern, one that commands attention at both national and global levels. The most common oral malignancy in the world is squamous- cell carcinoma, which originated in the squamous epithelial mucosa. Each year, World Health Organization records approximately 10 million newly diagnosed cases with around 4.7 million emerging in the developed countries and 5.5 million in the less developed countries; the total also records over 6 million cancer related deaths. In the latter line, a recent research study by Anjum et al. demonstrated an age standardized incidence rate of 27.03 per 100,000 which is quite high in Pakistan. In that country Karachi is an epicenter of the epidemic. According to the 2019 report issued by the Punjab Authority for Emergency Care, oral cancer occupies the top spot among male patients and ranks third in prevalence among females. Additionally, the upward trend in the incidence witnessed in the country especially among the younger individual's points at the imperativeness of having specific interventions geared towards reducing this preventable morbidity.

Nearly 9 out of every 10 reported cases present evidence of tobacco use which is one of the paramount risk factors that can be prevented by implementing effective primary-prevention programs. Smoking and alcohol intake are the leading factors related to the modifiable behavior that is highly dominant to being diagnosed among people who are under the age 45 years. Multiple researches in Pakistan has confirmed this trend, identifying chewing habits, smoking practices, and alcohol use as principal avoidable contributors to oral cancer.

To have comprehensive health policy emerge we have to first profile adequately sociodemographically as well as clinically the affected individuals, and it has to characterize the tumors as well. This information will inform the decision-makers and teachers who are willing to create awareness in the society and promote the early detection and the adoption of effective prevention measures. In that light, the following study aimed at investigating the clinico-histopathological determinants that exist within the population of oral-cancer patients availed to a tertiary-care facility in Pakistan. These results are a way of initiating further epidemiological research and planning regarding the health of the population.

MATERIALS AND METHODS

The study was cross-sectional study and conducted in the Department of Oral and Maxillofacial Surgery of Pakistan (Jinnah Hospital, Bolan Hospital, Turbat Hospital) from October 2021-November 2022 post Ethical Review. Mekran Medical College board passed ethical permission for the study. The sample size was determined by WHO sample size calculation, assuming a risk of 50% prevalence for oral cancer was estimated as the exact prevalence of risk factors in not known.[11]

Inclusion Criteria:

• Patients of both genders ranging from all age groups with clinical findings indicative of oral cancer: patients with histopathologically confirmed cases oral cancer, both admitted and OPD, to be the included.

Excluding Criteria:

• Patients with a terminal illness and patients with recurrent or residual disease following surgery or chemoradiotherapy were excluded.

Patients who met the inclusion criteria were sought informed consent, and the aim of their confidentiality and to study were explained to them. One-on-one interviews were performed, along with a clinical examination. The principal investigator developed a pretested structured questionnaire, and in-person interviews were carried out to obtain age, history of illness, sex, education, economic status, age of illness, illness severity, and weather. Also form of tobacco use, history of tobacco use, duration of tobacco use, and use of any other addiction, including a household history of any cancer. Details about types, grading, and other parameters of oral cancer was obtained from the medical files.

Analysis was performed with SPSS (Statistical Package for the Social Sciences) version 26.0. Quantitative variables are presented in terms of mean and standard deviation (SD). Categorical variables were described with frequencies and percentages. Chi square test for inferential statistics with level of $p < 0.05$ set as significant.

RESULTS

The mean age of the total enrolled 276 patients was 48.59+14.28. According to Table-I the majority of the patients were males 108(78.3) and 244(88.4%) of them belonged to low socioeconomic status (SES).

TABLE NO.1: Distribution of Socio Demographic Factors & health determinants associated with Oral Cancer (n=276)

VARIABLES	CATEGORIES	N (%)
Age (years) Mean + SD		48.9+14.2
Gender	Male	216 (78.3)
	Female	60 (21.7)
Socioeconomic status	Low class	244 (88.4)
	Middle class	32 (11.6)
Region	Karachi	170 (61.5)
	Turbat	50 (18.1)
	Quetta	18 (6.5)
	Sindh	38 (13.7)
Recurrence of oral cancer	Yes	8 (2.9)
	No	268 (97.1)
Family history of oral cancer	Yes	142 (51.4)
	No	134 (48.6)
Current use of tobacco	Gutka	112 (40.6)
	Naswar	164 (59.4)
History of tobacco use	Gutka	154 (55.8)
	Naswar	122 (44.2)
Current use of alcohol	Yes	18 (6.5)
	No	258 (93.5)
History of alcohol use	Yes	4 (1.4)
	No	272 (98.6)
Current use of areca nut	Yes	152 (55.1)
	No	124 (44.9)
Past use of areca nut	Yes	234 (84.8)
	No	42 (15.2)
Duration of tobacco use	< 1 year	30 (10.9)
	>1 year	246 (89.1)
Duration of alcohol use	< 1 year	16 (5.8)
	>1 year	260 (94.2)
Presence of medical disease	Yes	44 (15.9)
	No	232 (84.1)
Any early sign of oral cancer	Yes	40 (14.5)
	No	236 (85.5)

In our series majority of patients were hailing from central Karachi. It could be the location of Jinnah Hospital in the middle of Karachi's central business district. Only 8(2.9%) had a family history of OSCC and 40(14.5%) had prior OSCC lesions. It also provides information on a history of patients' medical, oral cancer risk aspects, habits of patients, the period of using Tobacco and Areca in the past

years, using average per day, and clinical signs and symptoms about oral cancer. Table-2: Comparison of socioeconomic status with age, sex and other variables.

TABLE NO.2: The association of socioeconomic status with age, gender and tumor characteristics of oral cancer (n=276)

Variables	Lower Socioeconomic Status n (%)	Middle Socioeconomic Status n (%)	p value
Age (years)			0.965*
<35	42 (17.4)	6 (18.8)	
35-45	68 (28.1)	8 (25.0)	
>45	132 (54.5)	18 (56.3)	
Gender			0.025*
Male	184 (75.4)	32 (100)	
Female	60 (24.6)	0 (0)	
Type of oral cancer			0.819*
OSCC	232 (95.1)	30 (93.8)	
Other types	12 (4.9)	2 (6.3)	
Histological grading			0.981
Well differentiated	138 (56.6)	18 (56.3)	
Poorly differentiated	106 (43.4)	14 (43.8)	
Clinical finding			0.149*
White patch	80 (32.8)	18 (56.3)	
Red patch	46 (18.9)	8 (25.0)	
OSF	56 (23.0)	2 (6.3)	
Others	61 (25.4)	4 (12.5)	
Early cancer			0.607*
Yes	34 (13.9)	6 (18.8)	
No	210 (86.1)	26 (81.3)	

*Fisher exact test

Cross tabulation of Histological grading with risk factors was calculated as shown in Table-3 and strong relationship of gutka use was seen with the male gender as shown in Table-4. No correlation of gutka use was found with SES and with any tumor parameters.

TABLE NO.3: Association of Histological Grading of Oral Cancers with Sociodemographic and Lifestyle Related Factors (n=276)

Variables	Well differentiated Oral cancer n (156)	Moderately & Poorly differentiated Oral cancer n (120)	p value
Socioeconomic Status			0.934
Low	138 (88.5)	6 (18.8)	
Middle	18 (11.5)	8 (25.0)	
Current use of Chewable Tobacco			0.306
Gutka	68 (43.6)	42 (37.6)	
Niswar	88 (56.4)	76 (64.4)	
Past use of Chewable Tobacco			0.400
Gutka	92 (59.0)	62 (40.0)	
Niswar	64 (41.0)	56 (47.5)	
Currently use of Alcohol			0.709
Yes	8 (5.1)	10 (8.5)	
No	152 (94.9)	108 (91.5)	

Alcohol use in the past			0.458
Yes	4 (2.6)	0 (0.0)	
No	152 (97.4)	59 (100.0)	
Current use of Areca nut			0.011
Yes	100 (34.1)	50 (42.4)	
No	56 (35.9)	68 (57.6)	
Past use of Areca nut			0.587
Yes	136 (87.2)	96 (81.4)	
No	20 (12.8)	22 (18.6)	
Duration of Tobacco use			0.910
Less than one year	18 (11.5)	12 (10.2)	
More than one year	138 (88.5)	106 (89.8)	
Quantity of Tobacco			0.865
Less than 5 packets per day	8 (5.1)	4 (3.4)	
Less than 5 packets per day	148 (94.9)	114 (96.6)	

Exact test & chi square

TABLE NO. 4: Distribution of factors associated with the type of Chewable Tobacco use among Oral Cancer Patients (n=276)

Variables	Gutka n (%)	Niswar n (%)	p value
Age			0.287
<35	20 (18.2)	28 (17.1)	
35-45	38 (34.5)	38 (23.2)	
>45	52 (47.3)	98 (59.8)	
Gender			0.009
Male	100 (89.3)	116 (70.7)	
Female	12 (10.7)	48 (29.3)	
Socioeconomic status			0.784
Low	98 (87.5)	146 (89.0)	
Middle	14 (12.5)	18 (11.0)	
Types			0.507*
OSCC	108 (96.4)	154 (93.9)	
Others	4 (3.6)	10 (6.1)	
Histological grading			0.412
Well differentiated	68 (60.7)	88 (53.7)	
Moderately & poorly differentiated	44 (39.3)	76 (46.3)	
Clinical finding			0.497
White patch	36 (32.1)	62 (37.8)	
Red patch	22 (19.6)	32 (19.5)	
OSF	20 (17.9)	38 (23.2)	
Other	34 (30.4)	32 (19.5)	
Early sign of cancer			0.663
Yes	18 (16.1)	22 (13.4)	
No	94 (83.9)	142 (86.6)	

Fisher exact test

DISCUSSION

In this study, distribution of sociodemographic characteristics, clinical and tumor variables of Oral Cancer patients as well as the lifestyle related risk factors were reported among tertiary care hospitals'

patients in Pakistan. Mean age in years of patients with oral cancer is 48.59+14.28 which is very young age but contradicts with majority of the previous studies.[12,13]

Men and women with oral cancer in the present study spanned in age from 14 to 90 years of age. The present study showed a higher incidence of oral cancer in the younger patients than in the study of Karachi Cancer Registry 2000 where 30% of patients were found have been affected with the disease at the age of 40 years.[14]

Another research demonstrated a concerning upward trend in the number of young women affected with OSSC.[15] For our study males were more prevalent (78.3%) among oral cancer patients and this prevalence rate is comparable with the Karachi Cancer Registry in which males were found to have a high rate of oral cancer in the Pakistani population.[16] Likewise, a study from Dow University Health Sciences, 2020, also reported cases of oral cavity diseases more in males than females.[17]

In the present series, majority of the cases were from low socioeconomic status. Income, housing, education and family lifestyle but are a few of the many factors that contribute to a person's socioeconomic status. It supports the results of the study in Iran where there is an association of low SES with oral cancer.[18] An investigation based on the British Columbia cancer registry found that the areas with more deprived neighborhoods had increased rate of oral cancer mortality that was associated with a delay in diagnosis.[19] The present study consolidates the earlier studies that advanced the relationship of tobacco, areca nut, and niswar to oral cancer.[11-20] It has been shown in an Indian study that tobacco chewing is the leading etiological factor (41.5%) in the causation of oral cancer followed by smoking and alcohol consumptions (28.1%).[21] As reported in the literature.[22]

Squamous cell carcinoma of buccal mucosa OSSC was the predominant tumor (94.9%), site of OSCC was buccal mucosa and lip and palate. Histopathology features of 44 cases indicated well differentiated squamous cell carcinoma (56.5%) as the most prevalent. Several investigations have tried to determine association of different types of SES with oral cancer and have reported a significant association of lower SES with oral cancer.[18] The most common clinical presentation in the present article was that of a white patch. The diagnosis of an initial white lesion is difficult, ranges from benign reactive lesions and is due to severe dysplastic lesions of etiology, and prognosis. Oral cancer causing addiction is prevalent among young adults in Pakistan. However, early detection of oral mucosal lesions enables early diagnosis of cancer, which is an important step in treatment and leads to a decrease in mortality. It is thus of great public health importance, and public health awareness campaigns should be initiated to promote awareness relating to oral cancer risk factors and about tobacco and betel nut hazards in particular. The confirmation of diagnosis and timely treatment is based on the patient's self-representing, so the public should be educated in order to ensure an early diagnosis and timely treatment, thus making the prognosis of the disease better.

CONCLUSION

The research revealed that oral cancer was predominantly found in males and low SES. Well differentiated carcinoma was seen in majority of the cases and all of them had history of present and past habbit of tabacco, alcohol and Areca nut. The majority of oral cancers were squamous cell carcinoma 262 (94.9%). In the case of low SES districts, mass campaigns will be necessary in order to inform the public, about the benefits of healthy lifestyle habits, the oral cancer risk factors and the necessity of not consulting with a doctor when there is doubt. Affordable cancer control programs targeted at young for oral cancer are needed in Pakistan. General dental practitioners, health visitors, lay organizations, and medical students too, may have a significant role in the early recognition of oral cancer and ensuring a referral for successful management.

LIMITATIONS OF STUDY

The main limitation of this study was its small sample size. Additional studies with larger sample sizes are highly recommended to assess the reasons for using oral cancer-causing factors and prevention strategies for oral cancer control in Pakistan.

ETHICAL APPROVAL:
Ethical approval was taken from the Review Broad of the Mekran Medical College, turbat.

PATIENT'S CONSENT:
Informed written consent was taken from each patients for participating in the study, and publication of study results.

CONFLICT OF INTEREST:
The study has no conflict of interest to declare by any author.

AUTHOR'S CONTRIBUTION:
1. Literature search, conduct of study and editing.
2. Literature search, ethical approval and manuscript writing.
3. Sampling and results writing.
4. Statistics writing.
5. Literature review and discussion editing.
6. Review and editing.

REFERENCES
1. Petersen PE. Oral cancer prevention and control--the approach of the World Health Organization. Oral Oncol 2009 ; 45(4-5): 454-460. https://doi.org/10.1016/j.oraloncology.2008.05.023
2. Conway DI, Purkayastha M, Chestnutt IG. The changing epidemiology of oral cancer: definitions, trends, and risk factors. Br Dent J 2018; 225(9): 867-873. https://doi.org/10.1038/sj.bdj.2018.922
3. Moore SR, Johnson NW, Pierce AM, Wilson DF. The epidemiology of mouth cancer: a review of global incidence. Oral Dis 2000; 6(2): 65-74. https://doi.org/10.1111/j.1601-0825.2000.tb00104.x
4. Ng JH, Iyer NG, Tan MH, Edgren G. Changing epidemiology of oral squamous cell carcinoma of the tongue: A global study. Head Neck 2017; 39(2): 297-304. https://doi.org/10.1002/hed.24589
5. Ren ZH, Hu CY, He HR, Li YJ, Lyu J. Global and regional burdens of oral cancer from 1990 to 2017: Results from the global burden of disease study. Cancer Commun 2020; 40(2-3): 81-92. https://doi.org/10.1002/cac2.12009
6. Bhurgri Y, Bhurgri A, Hussainy AS, Usman A, Faridi N, Malik J, et al. Cancer of the oral cavity and pharynx in Karachi-- identification of potential risk factors. Asian Pac J Cancer Prev 2003; 4(2): 125-130.
7. Sohaib M. Pakistan Atomic Energy Commission Report Nuclear Medicine & Oncology Division Pakistan Atomic Energy Commission, Headquarter, Islamabad, Pakistan: Atomic Energy Cancer Hospitals; 2019.
8. Babu KG. Oral cancers in India. Semin Oncol 2001; 28(2): 169- 173. https://doi.org/10.1016/s0093-7754(01)90088-0
9. Alqahtani WS, Almufareh NA, Al-Johani HA, Alotaibi RK, Juliana CI, Aljarba NH, et al. Oral and Oropharyngeal Cancers and Possible Risk Factors Across Gulf Cooperation Council Countries: A Systematic Review. World J Oncol 2020; 11(4): 173-181. https://doi.org/10.14740/wjon1283
10. Azhar N, Sohail M, Ahmad F, Fareeha S, Jamil S, Mughal N, et al. Risk factors of Oral cancer-A hospital based case control study. J Clin Exp Dent 2018; 10(4): e396-e401. https://doi.org/10.43 17%2Fjced.54618
11. Akhtar A, Hussain I, Talha M, Shakeel M, Faisal M, Ameen M, et al. Prevalence and diagnostic of head and neck cancer in Pakistan. Pak J Pharm Sci 2016; 29(5 Suppl): 1839-1846.
12. Badar F, Mahmood S. Hospital-based cancer profile at the Shaukat Khanum Memorial Cancer

Hospital and Research Centre, Lahore, pakistan. J Coll Physicians Surg Pak 2015; 25(4): 259-263.

13. Coelho KR. Challenges of the oral cancer burden in India. J Cancer Epidemiol 2012; 2012: 701932. https://doi.org/10.1155/2012/701932

14. Amarasinghe A, Usgodaarachchi US, Johnson NW, Warnakulasuriya S. High Prevalence of Lifestyle Factors Attributable for Oral Cancer, and of Oral Potentially Malignant Disorders in Rural Sri Lanka. Asian Pac J Cancer Prev 2018; 19(9): 2485-2492. https://doi.org/10.22034/apjcp.2018.19.9.2485

15. Al-Jamaei AAH, van Dijk BAC, Helder MN, Forouzanfar T, Leemans CR, de Visscher J. A population-based study of the epidemiology of oral squamous cell carcinoma in the Netherlands 1989-2018, with emphasis on young adults. Int J Oral Maxillofac Surg 2022; 51(1): 18-26. https://doi.org/10.1016/j.ijom.2021.03.006

16. Bhurgri Y. Cancer of the oral cavity - trends in Karachi South (1995-2002). Asian Pac J Cancer Prev 2005; 6(1): 22-26.

17. Qureshi MA, Syed SA, Sharafat S. Lip and oral cavity cancers (C00-C06) from a mega city of Pakistan: Ten-year data from the Dow Cancer Registry. J Taibah Univ Med Sci 2021; 16(4): 624-627. https://doi.org/10.1016/j.jtumed.2021.02.001

18. Azimi S, Rafieian N, Manifar S, Ghorbani Z, Tennant M, Kruger E. Socioeconomic determinants as risk factors for squamous cell carcinoma of the head and neck: a case-control study in Iran. Br J Oral Maxillofac Surg 2018; 56(4): 304-309. https://doi.org/10.1016/j.bjoms.2018.02.014.

19. Auluck A, Hislop G, Bajdik C, Hay J, Bottorff JL, Zhang L, et al. Gender- and ethnicity-specific survival trends of oral cavity and oropharyngeal cancers in British Columbia. Cancer Causes Control 2012; 23(12): 1899-909. https://doi.org/10.1007/s10552-012-0065-0

20. Khan Z, Suliankatchi RA, Heise TL, Dreger S. Naswar (Smokeless Tobacco) Use and the Risk of Oral Cancer in Pakistan: A Systematic Review With Meta-Analysis. Nicotine Tob Res 2019; 21(1): 32-40. https://doi.org/10.1093/ntr/ntx281

21. Gupta B, Bray F, Kumar N, Johnson NW. Associations between oral hygiene habits, diet, tobacco and alcohol and risk of oral cancer: A case-control study from India. Cancer Epidemiol 2017; 51: 7-14. https://doi.org/10.1016/j.canep.2017.09.003

22. Mehrotra R, Pandya S, Chaudhary AK, Kumar M, Singh M. Prevalence of oral pre-malignant and malignant lesions at a tertiary level hospital in Allahabad, India. Asian Pac J Cancer Prev 2008; 9(2): 263-265.