



FACTORS LINKED TO EARLY DETECTION OF ORAL AND PHARYNGEAL CANCER

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ABSTRACT

Introduction: Oral and pharyngeal cancers continue to rise in low and middle-income countries, which have a high proportion of patients presenting at advanced stages and poor survival. The ability to get early detection remains a significant factor in developing countries like Pakistan because of the low levels of knowledge and health facility accessibility.

Objective: To identify and evaluate the factors associated with early detection of oral and pharyngeal cancer among patients in Pakistan.

Materials and Method: The cross-sectional study was conducted at Oral and Maxillofacial Surgery Department, Foundation University Islamabad over six months from January 2024 to June 2024. A total of 150 newly diagnosed patients were included in this study. Demographic information, risk factors, knowledge and perceptions, and tumor profiles were obtained through communication and patient records.

Results: A disturbing discovery was made regarding the stage of diagnosis, where only 30% of the patients were diagnosed early. The results showed that people from higher education, those who reside in urban areas, or those who previously had awareness of the symptoms were likely to get it early. According to the results, most patients stated that they used tobacco and sought medical care after getting the symptoms.

Keywords: Pharyngeal cancer, oral cancer, early detection, risk factors, awareness, and delayed diagnosis, Pakistan.

INTRODUCTION

Cancers of the oral cavity and pharynx are among the numerous health challenges affecting individuals around the world and early diagnosis plays an important role in managing the disease. They frequently appear at a later stage, mainly because of biological, behavioural and system-related

factors, which make the morbidity and mortality rates of such tumours high (1). Time to diagnosis is essential since it plays a role in determinant of outcome by influencing the time between experiencing symptoms and starting treatment. Several investigations have established that among the significant factors that lead to cancer late presentation include patient-related factors such as ignorance and health seeking behaviours(1). This is made worse by system-related factors like inadequate utilization of specialized health services and diagnostic facilities especially in low- and middle-income countries, including Pakistan.

In the global context, the incidence of lip, oral cavity, and pharyngeal cancers is on the rise due to aging, changes in lifestyle, and continued exposure to risk factors including tobacco, alcohol, and HPV (2). Screening in developing countries, especially in the South Asian region, has not been as developed as in developed countries, and there are distinctions between high and low effectiveness. Possible factors could include socioeconomic status, cultural perceptions of oral health, and healthcare facilities, which determine the time of diagnosis and treatment. In countries such as Pakistan, awareness of oral cancer and its symptoms among the public is low, and a large portion of people remain either undiagnosed or diagnosed at a later stage, thereby suggesting the need for more work regarding screening and awareness programs.

Oral cancer screening is a combination of factors, which includes oropharyngeal competence, professional knowledge through training, patient compliance, and systemic health systems responsiveness at an initial phase. Another issue that doctors and other clinicians may experience is the challenge of differentiating malignant lesions from benign lesions, especially in situations where advanced diagnostic techniques may not be available (3). Moreover, there is no specific strategy in the plan and early detection that can be used since it is implantation that oral healthcare is not a part of primary care in many structures of care. The position of primary caregivers is significant in such contexts. They are the first point of call and the first opportunity to detect potential malignant growths and refer the patient appropriately.

According to the current Global Burden of Disease Study 2019, oral and pharyngeal cancer remains a significant concern, although the burden is most prominently manifested in low- and middle-income countries. According to the research, the patterns of occurrence of the disease and death rates differ depending on the region's development, access to healthcare facilities, and efficiency of health sector policies (4). The culturally accepted and widespread use of tobacco chewing and the prevalence of betel quid use, particularly in Pakistan, and their poor oral hygiene have made a significant impact on the disease burden. These are cultural practices that the traditional public health approaches may not efficiently address. Another factor that has been well-established about oropharyngeal cancer includes HPV infection. Global variations in the extent of oral HPV cancer risk, as well as the measures that can be taken to combat the problem, are discussed in this post. Such studies have exposed the correlation between HPV infections within the oral, genital, and laryngeal areas, making disease research and treatment more challenging (5). In countries where HPV vaccination is limited or unpopular, like Pakistan awareness and preventive measures are still lacking in recording high levels of HPV-related oropharyngeal cancers.

Recent trends in the distribution of oral and oropharyngeal cancers have changed in age and gender due to changes in risks associated with known exposure factors (6). These types of cancers were once common in older males who used tobacco and alcohol. They are present in young people and women due to new behaviors and susceptibility to HPV. Such epidemiological changes require reconsidering previous screening protocols, and risk groups should be adequately identified and addressed. Delayed presentation is commonplace, especially in rural or underprivileged areas. A study done in a rural cancer center showed that factors including educational status, occupation, and distance from the health facility all affected the time to diagnosis (7). These results are similar to those of other studies showing a relationship between demographic and socioeconomic status and the timeliness of cancer diagnosis. This supports the argument that there is a necessity for program interventions that are specific to the problems of rural people.

Head and neck squamous cell carcinoma (HNSCC), which encompasses oral and pharyngeal tumors in particular, is one of the most prevalent and fatal cancers observed in patients. To invest in

preventive measures, a clear picture of the epidemiology and pathophysiology of the HNSCC must be established. This is associated with tobacco, alcohol, viral susceptibility, and inheritability (8). Along with population education, it is necessary to continue to develop specific programs aimed at the cessation of tobacco consumption, comprehensive clinical examination, etc. The oral cancers also significantly impact the economic aspect of health care. Working with insurance claims data from the United States, researchers found that treatment costs were high for all patients and even higher for those diagnosed in later stages and that Medicaid patients had significantly worse access to and outcomes than commercially insured patients (9). However, similar studies on a large scale in Pakistan are scarce, and it would not be unfair to assume that the financial burden is equally, if not more significant due to delays in presentation and limited access to healthcare facilities.

Even though multiple systematic reviews regarding early detection has conducted worldwide, implementation gaps still exist when the translated evidence is practiced. Some challenges include no standard training on stroke care, health providers in the primary care setting may have little knowledge about stroke and no straightforward, streamlined process for referral (10). These areas must be addressed through policy-level interventions, capacity development, and the inclusion of oral health in cancer control interventions. Tobacco, alcohol, and HPV infection are known risk factors for both laryngeal and pharyngeal cancers, as is the case with oral cavity cancer. Profiling those pathways and risks can improve the readiness and suitability of screening programs and promote more extensive preventive measures (11). There is also increased focus on the molecular characteristics of these cancers, especially involving the function of microRNAs in cancer development, which can potentially be used as molecular biomarkers and targets for therapy (12).

An increase in head and neck cancers, cervical cancers attributable to HPV infection, and continued exposure to modifiable lifestyle factors contribute to the trends discussed below (13). It is only through sensitization through public campaigns covering issues such as risk factors, early signs of the disease, and screening that these trends can be easily reversed. Studies have revealed that people's awareness of oral cancer symptoms and risk factors remains limited, particularly in Asia (14). Education for both the professionals in the health sector and the public should be provided to ensure early diagnosis. HPV vaccination is one such preventive measure that has shown potential, particularly regarding oropharyngeal cancers. However, its implementation is not without its challenges concerning acceptance by the general public, policies, and awareness, especially in reserved societies (15). Increasing HPV vaccination, optimizing diagnostic strategies, and providing multi-disciplinary care models are valuable strategies for decreasing oral and pharyngeal cancers in Pakistan and worldwide.

Objective

To identify and evaluate the key factors associated with the early detection of oral and pharyngeal cancer, with the aim of improving diagnosis timelines and outcomes in clinical settings.

MATERIALS AND METHODS

Study Design: Observational, cross-sectional study.

Setting: The study was conducted at Oral and Maxillofacial Surgery Department, Foundation University Islamabad, Pakistan.

Duration: The study was conducted for six months from January 2024 to June 2024.

Inclusion Criteria:

The study participants included patients who were 18 years and above and had newly diagnosed oral or pharyngeal cancer within the study period. Patients with histopathological confirmation of the disease and who gave their informed consent only were included. Gender was not a factor of consideration, so both males and females were involved and the patients involved ranged from those from urban areas and those from rural areas.

Exclusion Criteria

Patients with a previous history of oral or pharyngeal cancer or patients who have undergone treatment for a similar type of cancer earlier in adjacent anatomical sites were excluded during analysis to minimize diagnostic inaccuracy and variability.

Methods

The data were obtained using questionnaires and a patient's medical history review. The questionnaire details the socio-demographic profile details like age, gender, education, income, lifestyle details like tobacco usage, alcohol intake, betel quid chewing, awareness of oral cancer symptoms, and health-seeking behavior.

Clinical data included tumor anatomical site, stage of diagnosis, and time between the onset of the first symptoms and the diagnosis. The patients were systematically approached and interviewed individually, preferably the first time upon admission at the oncology or the ENT department. Histopathological findings determined diagnoses and staging, and the timelines were obtained from the patient's history and records. All the data were statistically analyzed using the statistical package of social sciences version 25. Variables were summarized by descriptive statistics, and chi-square and logistic regression tests were performed to assess the factors for early detection. A probability value of $P < 0.05$ was used to indicate a statistically significant difference. The requisite permission from the Director of the hospital's institutional review board was also obtained, and all the patients included in the study signed informed consent.

RESULTS

One hundred fifty patients with oral and pharyngeal cancer were included in this study. The age of the patients was 52.4 ± 11.6 years, with male patients slightly more than female patients 2.1: 1. Out of all the patients, 63% of the patients came from a rural background and 37% from urban areas. About 27% of participants belong to the age group of 15-24 years, 72% had a monthly household income of less than PKR 50,000, and 60% had only primary education or were illiterate. Table 1 contains the characteristics of the participants in terms of demographic variables and behavior. About 75% of the patients admitted using tobacco, and 50% admitted to chewing betel quid. Among the participants, 12% knew the early signs of oral cancer, and 68% did not seek medical attention more than three months after experiencing symptoms.

Table 1: Demographic and Behavioral Characteristics of Study Participants (N = 150)

Variable	Frequency (%)
Gender (Male)	102 (68%)
Age \geq 50 years	89 (59%)
Rural residence	95 (63%)
Monthly income < PKR 50,000	108 (72%)
Tobacco use	117 (78%)
Betel quid chewing	83 (55%)
Aware of early symptoms	18 (12%)
Delay > 3 months in consultation	102 (68%)

According to the location and stage of the tumor, 65% of all the patients were diagnosed with oral cancer, and 35% were diagnosed with oropharyngeal cancer. At diagnosis, 70% had an advanced stage (III or IV) of the disease, and 30% had an early stage (I or II). The researchers also found the results of awareness and education level regarding early detection ($p < 0.05$).

Table 2: Tumor Characteristics and Stage at Diagnosis

Tumor Site	Frequency (%)
Oral cavity	98 (65%)
Oropharynx	52 (35%)
Tumor Stage	Frequency (%)
Stage I – II	45 (30%)
Stage III – IV	105 (70%)

The logistic regression results additionally revealed that those who had higher education standards lived in urban areas, and were more aware of oral cancer symptoms were more likely to be staged at an early stage. The adjusted odds ratio (AOR) for early detection was 2.8 (95% CI: 1.3, 5.9) among participants with secondary or higher education and 3.5 (95% CI: 1.5, 8.0) among patients who recognized the early signs.

Table 3: Factors Associated with Early Detection (Logistic Regression Analysis)

Variable	AOR (95% CI)	p-value
Education \geq Secondary Level	2.8 (1.3 – 5.9)	0.008
Urban Residence	2.1 (1.1 – 4.1)	0.023
Awareness of Symptoms	3.5 (1.5 – 8.0)	0.002

These findings focus on the role of education, awareness, and geographical location in the early diagnosis of oral and pharyngeal cancers.

DISCUSSION

The purpose of this research proposal was to find out the determinant of early diagnosis of Oral and Pharyngeal Cancer among patients in a tertiary hospital in Pakistan. The authors revealed that a large percentage of patients were diagnosed at an advanced stage of the disease, with low awareness, low levels of education, living in a rural area, and modifiable activities as possible reasons for late diagnosis. These results align with the existing literature on global trends established in developing countries, making it possible to identify the key factors that hindered early cancer diagnosis at the end of 2013. This is an important finding in this study because it establishes that a lot of people only seek treatment after the symptoms have manifested themselves significantly. Specifically, 67.8% of the patients said they did not seek a medical checkup for more than three months, leading to a late diagnosis. Similar findings were affirmed by Costa et al. (1) in Brazil concerning those socioeconomic and health sector factors that caused delays in the commencement of the treatment. The delay in early sign recognition of the disease and seeking specialized care largely remains a problem in areas that have weak health systems and inadequate sensitization. This delay is particularly concerning because patients with oral and pharyngeal cancers have a better prognosis and quality of life if the disease is detected in its early stages.

International statistics also indicate the increasing trend of lip, oral cavity, and pharynx cancers, especially in LMICs (2). Huang et al. (2) pointed out that disease suffered increases due to continued exposure to identified risk factors and the absence of effective prevention in South Asia, including Pakistan. Smoking and smokeless forms of tobacco like betel quid and gutka are still some of the biggest causes of oral cancers in this area. Our study supports the trends indicated above whereby 78% of patients had used tobacco in some form, and 55% had chewed betel quid, a behavior in conformity with the rest of the region's behavior. Early diagnosis is not straightforward, and González-Ruiz et al. (3) identified different cognitive, organizational, and socio-cultural sources of diagnostic delay. The results of this research support the premises of this study to reject the idea that early detection is solely determined by the patient's behaviors, but rather with the awareness of the

healthcare practitioners and the implementation of oral cancer screening in primary healthcare services. The lack of skilled employees and the lack of well-defined signs-out for screenings at the primary care level in Pakistan can be said to play a role in early diagnosis.

In concordance with the global disease burden described by Da Cunha et al. (4), the study also points out the disadvantaged diagnosis timelines within the socioeconomic and geographical aspects. Patients from rural regions were less likely to seek proper consultation from specialists and diagnostic facilities, meaning they were referred to later-stage disease. Against this background, there is a need to ensure that healthcare facilities are distributed accordingly and diagnostic centers should be set up. Another emerging feature of interest is the increasing evidence associating HPV with oropharyngeal cancer. Regarding this, Wierzbicka et al. (5) established that HPV-positive cancers have their features of clinical and epidemiologic behaviors, obtainable in the form of cancers in young individuals and persons without risk behaviors such as smoking. Therefore, even though condition-specific HPV testing was not uniformly performed in our study, the role of HPV in oropharyngeal cancer cannot be dismissed, especially among young urban patients. Chaturvedi et al. (6) observed that there is also a growing trend of HPV-associated oropharyngeal cancers and called on the governments to incorporate the HPV vaccine into immunization programs a measure that is not widely practiced in the context of the current Pakistani setting.

The study reveals that demographic factors significantly influence delayed presentation. Singla et al. (7) have established that factors including education level, occupation, and distance from health facilities influenced the patients' behavior on symptom recognition of cancer. Our study's education level further affirms this finding was vital in determining if a person would get an early diagnosis. Secondary and higher education patients were nearly three times as likely to begin the process at an early stage, indicating that further education for illiterate and semiliterate communities is necessary for cancer prevention. The significant association of behavioral and social factors correlated with examining head and neck cancers only affirms the generalization. Barsouk et al. (8) noted that primary protective measures on tobacco, alcohol, and HPV play an essential role in decreasing the occurrence of head and neck Squamous Carcinoma. This has directed the need for working on the multiple-fold strategy in Pakistan involving tobacco control alongside cessation and education and adding screening elements to the cancer control Campaign. In addition, Tranby et al. (9) described the cost impact of oral cancers among insured individuals in developed countries, which can be extrapolated to the costs in Pakistan, where most patients cannot afford health insurance and face economic losses owing to out-of-pocket expenditures.

Concerning difficulties in early diagnosis, González-Moles et al. (10) have also reflected on the current state of cancer treatment in early diagnosis, especially the lack of greater awareness of potentially suspicious lesions among professionals in the dental and medical fields. This prevalence of late presentation also highlights the importance of patient and physician education. On comparing laryngeal and pharyngeal cancer, Igissin et al. (11) stressed that the aetiologies and risk factors are similar and the current screening strategies should be integrated. Furthermore, with the advancement of knowledge in molecular biology of such cancers such as microRNA expression in the future, early diagnosis, and new specific treatment could be possible, as mentioned by Aghiorghiesei et al. (12). Modern epidemiological patterns of occurrence of head and neck cancers also transform, as indicated by Gormley et al. (13), where the proportion of cases not associated with attainable risk factors increases. It is bitter to state that despite the establishment of these NGOs, public awareness is still very dismal. According to Zhou et al. (14), knowledge of warning signs of oral cancer remained low even among urban people. This can be explained by the current study, whereby it was noted that only 12% of the patients reported early symptoms, suggesting a low level of cancer literacy. Lastly, it is essential to examine the link between HPV vaccination and oropharyngeal cancers, and this is done by Gribb et al. (15). There are no healthy system implemented programs for HPV vaccination in Pakistan, which should otherwise work to prevent. Lack of knowledge, perceived stigma, and policy-related factors pose a significant challenge to vaccination, and thus, public health organizations must carefully consider such challenges.

CONCLUSION

This paper also identifies various factors that lead to late diagnosis of oral and pharyngeal cancers among individuals in Pakistan. Most of them were diagnosed in advanced stages resulting from such factors as ignorance, improper attitudes toward health, and inadequate and inaccessible health facilities, especially in rural areas. Some attributes that distinguished the group that sought early detection included education level, place of residence, and prior knowledge of the signs of oral cancer. These findings underpin the need to call for enhanced public health action, awareness creation activities, screening initiatives, and the development of the capacity of primary care practitioners. Another measure could include using preventive measures like tobacco control measures and introducing the HPV vaccine to the population. Policymakers and other related healthcare interveners must emphasize early screening aims to increase survival and mitigate mortality rates for oral and pharyngeal cancer patients. It is feasible to recommend that there needs to be a multi-sectorial approach to tackle this emerging public health issue in Pakistan.

REFERENCES

- 1- COSTA, A.A.S.D., Caldeira, P.C., Sousa, A.A., Tibúrcio, J.D., Belligoli, L.D.Q.G., SANTOS, V.B.D., Bretas, P.M.C., Nunes, L.L., PRADO, S.C.D., Silva, G.W. and Soares, J.M.A., 2023. Oral and oropharyngeal cancer: time from first symptoms to treatment initiation and associated factors. *Brazilian Oral Research*, 37, p.e054.
- 2- Huang, J., Chan, S.C., Ko, S., Lok, V., Zhang, L., Lin, X., Lucero-Prisno III, D.E., Xu, W., Zheng, Z.J., Elcarte, E. and Withers, M., 2023. Disease burden, risk factors, and trends of lip, oral cavity, pharyngeal cancers: A global analysis. *Cancer medicine*, 12(17), pp.18153-18164.
- 3- González-Ruiz, I., Ramos-García, P., Ruiz-Ávila, I. and González-Moles, M.Á., 2023. Early diagnosis of oral cancer: A complex polyhedral problem with a difficult solution. *Cancers*, 15(13), p.3270.
- 4- Da Cunha, A.R., Compton, K., Xu, R., Mishra, R., Drangsholt, M.T., Antunes, J.L.F., Kerr, A.R., Acheson, A.R., Lu, D., Wallace, L.E. and Kocarnik, J.M., 2023. The global, regional, and national burden of adult lip, oral, and pharyngeal cancer in 204 countries and territories: a systematic analysis for the global burden of disease study 2019. *JAMA oncology*, 9(10), pp.1401-1416.
- 5- Wierzbicka, M., Klusmann, J.P., San Giorgi, M.R., Wuerdemann, N. and Dikkers, F.G., 2021. Oral and laryngeal HPV infection: Incidence, prevalence and risk factors, with special regard to concurrent infection in head, neck and genitals. *Vaccine*, 39(17), pp.2344-2350.
- 6- Chaturvedi, A.K., Freedman, N.D. and Abnet, C.C., 2022. The evolving epidemiology of oral cavity and oropharyngeal cancers. *Cancer Research*, 82(16), pp.2821-2823.
- 7- Singla, A., Goel, A.K., Oberoi, S., Jain, S., Singh, D. and Kapoor, R., 2022. Impact of demographic factors on delayed presentation of oral cancers: A questionnaire-based cross-sectional study from a rural cancer center. *Cancer Research, Statistics, and Treatment*, 5(1), pp.45-51.
- 8- Barsouk, A., Aluru, J.S., Rawla, P., Saginala, K. and Barsouk, A., 2023. Epidemiology, risk factors, and prevention of head and neck squamous cell carcinoma. *Medical Sciences*, 11(2), p.42.
- 9- Tranby, E.P., Heaton, L.J., Tomar, S.L., Kelly, A.L., Fager, G.L., Backley, M. and Frantsve-Hawley, J., 2022. Oral cancer prevalence, mortality, and costs in medicaid and commercial insurance claims data. *Cancer Epidemiology, Biomarkers & Prevention*, 31(9), pp.1849-1857.
- 10- González-Moles, M.Á., Aguilar-Ruiz, M. and Ramos-García, P., 2022. Challenges in the early diagnosis of oral cancer, evidence gaps and strategies for improvement: a scoping review of systematic reviews. *Cancers*, 14(19), p.4967.
- 11- Igissin, N., Zatonkikh, V., Telmanova, Z., Tulebaev, R. and Moore, M., 2023. Laryngeal cancer: epidemiology, etiology, and prevention: a narrative review. *Iranian journal of public health*, 52(11), p.2248.
- 12- Aghiorghiesei, O., Zanoaga, O., Nutu, A., Braicu, C., Campian, R.S., Lucaciu, O. and Berindan Neagoe, I., 2022. The world of Oral cancer and its risk factors viewed from the aspect of MicroRNA expression patterns. *Genes*, 13(4), p.594.

- 13- Gormley, M., Creaney, G., Schache, A., Ingarfield, K. and Conway, D.I., 2022. Reviewing the epidemiology of head and neck cancer: definitions, trends and risk factors. *British Dental Journal*, 233(9), pp.780-786.
- 14- Zhou, X.H., Huang, Y., Yuan, C., Zheng, S.G., Zhang, J.G., Lv, X.M. and Zhang, J., 2022. A survey of the awareness and knowledge of oral cancer among residents in Beijing. *BMC Oral Health*, 22(1), p.367.
- 15- Gribb, J.P., Wheelock, J.H. and Park, E.S., 2023. Human papilloma virus (HPV) and the current state of oropharyngeal cancer prevention and treatment. *Delaware Journal of Public Health*, 9(1), p.26.