

Risk Factors For Oral Cancer in Young Patients Aged 40 Years And Below in Karachi Pakistan

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ABSTRACT: OBJECTIVE: To determine the potential risk factors associated with oral cavity Squamous Cell Carcinoma in young patients aged 40 years and below. **STUDY DESIGN:** Case control study. **PLACE AND DURATION OF STUDY:** Department of ENT and Head & Neck Surgery, Karachi Medical & Dental College and Abbasi Shaheed Hospital, Karachi, from March 2010 to March 2011. **PATIENTS AND METHOD:** One hundred cases and 100 controls were recruited during one year of study. Cases were patients with biopsy proven oral cancer and controls were age and sex matched individuals of same locality with similar life style. Data collection procedure was in the form of interview, clinical examination and high resolution CT/MRI. Demographic data like age and sex were recorded. **RESULTS:** The average age was 33 ± 6.09 . Males were 73%. The ethnicity variable showed that Urdu speaking were 75% followed by Punjabi 9%, Balauchi 8%, Sindhi 4%, and Pathan 2%. Majority of the cases consumed gutka and smoking followed by pan with tobacco. In a comparative study it was found that pan with tobacco was consumed in 85% of case but only 40% of the controls (p-value 0.0001). Gutka alone was consumed in 73% of case but only 26% of the controls (p-value 0.0001).

CONCLUSION: Gutka and pan with tobacco were strong predictors of oral cancer in young population 40 years and below.

Key Words : Oral young patients cancer, risk factors, {STATISTICAL ANALYSIS: SPSS version 15 was used for Data analysis.}

INTRODUCTION : Oral cavity squamous cell carcinoma (SCC) is one of the commonest cancer in the world with approximately, 274,300 new cases and 127,000 deaths occurring each year. The highest incidence rates have been observed in the Indian subcontinent¹. Although oral cavity is located in a part of body that is readily assessable for early detection, still most lesions remain undiagnosed until they reach advance stage. The early diagnosis is crucial for better five year survival rate, yet the majority of the patients seen in the out-patient clinics are in their third or fourth stage. Tumors of oral cavity show varying incidence worldwide, depending on environment and cultural habits. Cancer of the oral cavity account for 2 to 6 % of all cancers, and 30% of all head and neck cancer diagnosed annually in the United States but in South Asia and Indian subcontinent, cancer of the oral cavity is the leading malignancy diagnosed in men, accounting for up to 20% of all cancers. The habit of chewing areca nut with or without tobacco is the principal cause and the most common site is the buccal mucosa². Oral cavity squamous cell carcinoma typically occurs in elderly patients during the fifth through eighth decade of life throughout the world, but there is a recent increase in the incidence of oral cavity squamous cell carcinoma in young patients aged 40 years and below³. Several studies indicate that the incidence of oral cavity squamous cell carcinoma in young adults accounts for 0.4 to 3.6% of all cases of this disease^{3,4}. It is also observed that young patients are considered to have more aggressive disease as compared to the patients in the older age group^{5,6}. Several studies have shown that young patients tend to present a greater loco-regional recurrence and a decreased five year survival rate when compared to older patients^{7,8}.

Chewing of pan tobacco quid is the strongest predictor for oral cavity squamous cell carcinoma with the highest risk estimates observed among female chewers in Indian subcontinent⁹. In a study from India, the males had an adjusted relative risk of 6.14 associated with chewing 10 or more pan tobacco quid per day compared to those who never chewed¹⁰. In a study from Vietnam where betel quid chewing is common, 70% of the patients who had oral cancer took betel nut quid in comparison to controls in whom 30% took betel nut quid¹¹. In other studies from rest of the world smoking cigarettes and drinking alcohol is considered as main predictors for oral cavity SCC^{4,12}. Tobacco is responsible for nearly 1/3rd of all cancer deaths worldwide. The overall risk is related to the amount of tobacco a person smokes each day, the intensity of smoking, the age at which smoking began, the number of years a person has smoked and a smoker's second hand smoke exposure. It exhibits a clear linear dose-response carcinogenic effects in which duration is more important than the intensity of exposure¹³. Tobacco smoke contains approximately 4000 different chemicals including about 60 that are known to be carcinogenic. Chewing of betel quid with tobacco is the most common form of smokeless tobacco in south central Asia (India, Pakistan, Bangladesh, & Srilanka) and Southeast Asia (like Indonesia) and encompasses type such as nass, naswar, khaini, mawa, mishri and ghutka¹⁴. It appears to greatly increase cancer risk for the oral cavity^{15,16}. Regular alcohol consumption, along with combined tobacco and areca nut increases risk of oral cancer and other upper aero digestive tract cancers several folds^{17,18}. Alcohol is the second most important global risk factor for oral and head & neck cancer.

Extensive epidemiological evidence, both from western world and Southeast Asia suggests that it potentiates the carcinogenic effect of tobacco^{5,19}. This interaction appears to be multiplicative rather than additive, with high level of exposure²⁰. Alcohol is also an independent risk factor for Head & Neck cancer. It does not appear that alcohol is a carcinogen on its own but described as a co-carcinogen, or tumor promoter. The chewing of betel quid is an important risk factor for oral cancer throughout the Indian subcontinent and Southeast Asia⁶. It is estimated that there are 600 million betel quid chewers worldwide²¹. Betel quid with tobacco was first designated as a carcinogens by the IARC in 1985 and more recently betel quid without tobacco has also been classified as a human carcinogen²². For oral cavity cancer overall, chewers of pan with tobacco had a more than eight fold higher risk than non-chewers^{17,23,24}. In Karachi, oral cancer is 2nd most common in all malignancies among both males and females with the highest reported incidence in the world. In the absence of alcohol use, chewing of products of betel, areca, and tobacco remain the main etiological risk factors. These products include paan, chaalia, ghutka and naswar²⁵. Although in western developed countries, the oral cancer is mostly found in the sixth and seventh decade but in India and Pakistan the incidence in younger age group is on the rise. Data from Karachi institute of radiation and nuclear medicine shows steep rise in oral cancer in Karachi. In 2005, the total number of new registrations was 593, while in 2007 it had swollen to 818 new cases, a rise of 40%. The 41 % of these were below 45 years of age, while the world literature shows incidence in younger population from 0.4 to 3.6% only^{2,3}. As the statistics from Pakistan are not available and only few studies are found in the world literature regarding oral cancer, this is the reason to choose the study for research and to identify the predictors of oral cavity SCC preferably in younger age group under the age of 40 years.

SUBJECTS AND METHODS: This case control study to determine the predictors of oral cancer in patients 40 years and less in our population was conducted at the ENT department of Karachi Medical & Dental College and Abbasi Shaheed Hospital from March 2010 to March 2011. All the cases of oral cavity squamous cell carcinoma proved by histopathology of either gender were included in this study and were considered as cases. An equal number of controls were recruited. Controls were patients who do not have the disease (oral cancer). Controls were with matching age and sex of attendants living in the same locality and having the same life style and who do not have the disease.. Data collection on variables was derived from interview, physical examination, laboratory tests, and high resolution CT or MRI. Demographic data like age, sex, socio-economic status were recorded. A written consent was taken from cases and controls, who were participating in the study.

Inclusion Criteria:

Cases: All consecutive adult patients but less than 40 years of age, coming to department of ENT and Head and Neck surgery of Abbasi Shaheed Hospital with histopathologically proven carcinoma of oral cavity were included in this study.

Controls: An equal number of age, gender matched

controls living in the same locality, with same life style, and who do not had the disease, were included as controls.

Exclusion Criteria:

1: Patients with simultaneous other lesions like tuberculosis, syphilis

2: Patients with concurrent carcinoma in any other part of the body.

3: Previously treated patients of oral cavity carcinoma.

Data Analysis Technique:

A descriptive analysis of the cases and controls was performed by SPSS version 15. Categorical variables were presented as proportions (%), and continuous variables were presented as mean +/- standard deviation. The characteristics of cases and controls were compared. Chi square was used to compare categorical variables, and t - test to compare continuous variables. p value < 0.05 was considered as statistically significant.

RESULTS: One hundred cases and 100 controls were studied during the study period in the outpatient of ENT, Abbasi Shaheed Hospital. Overall, the data showed that the average age was 33 ± 6.09 , males were 73%. The ethnicity variable showed that Urdu speaking were 75%, followed by Punjabi (9%), Baluchi (8%), Sindhi (4%) and Pathan (2%). Majority of the population consumed ghutka followed by pan with tobacco. Consumption of ghutka and smoking was 51% and smoking alone was 16.5%, respectively. In a comparative analysis between the cases and controls, it was found that pan and tobacco was consumed in 85% cases but only in 40% of the controls (p-value 0.0001). Ghutka alone was consumed in 73% cases and 26% controls (p-value 0.0001). Ghutka and smoking was consumed by 51% of cases and 26% of controls (p-value 0.0001). Characteristics of patients with oral cancer among those who had oral cancer, Urdu speaking were 75%, Punjabi were 9%, Sindhi were 5%, Baluchi were 8% and Pathan were 2%. Among the cases, 16.5% were smokers, while among the controls 10.7% were smokers (p-value=0.236). The characteristics of cases and controls were significantly different regarding consumption of ghutka (alone), the use of paan and tobacco, and gutka plus smoking. The use of paan and tobacco was found to be 85% in cases and only 40% in controls (p-value=0.0001). The consumption of Ghutka (alone) was 73% among cases, and 26% in controls (p-value=0.0001). The smoking and ghutka useage was found in 51% of cases and 24% of controls (p-value 0.0001).

DISCUSSION : Head and neck cancer is becoming a serious health hazard in many Asian countries and it has become one of the leading causes of death in Asian pacific countries. The highest incidence rates have been observed in the Indian sub-continent¹. In this study the male: female ratio was 2.7: 1. It may be because the habits of ghutka, paan with tobacco and smoking were mostly found in males as compared to females. It is in contrast to two case control studies from India where chewers were compared with non-chewers, a much higher risk of oral cancer was found in women chewers of paan with tobacco as compared to men paan chewers with tobacco^{26,27}. Another study on oral cancer from Abbotabad, Pakistan showed 60% males and 40% females²⁵. The other study from different parts of the world show male preponderance as far as oral cancer is concerned. The

Variables	Patients with Oral Ca. (Cases) Mean \pm SD or %	Patients with No. Cancer (Controls) Mean \pm SD or %	p values
Age	33 \pm 5.97	32 \pm 6.2	0.55
Gender:			
Male	73%	73%	0.515
Ethnicity:			
Urdu Speaking	75%	76%	0.850
Punjabi	9%	8%	
Sindhi	5%	2%	
Baluchi	8%	8%	
Pathan	2%	3%	
Smoking	16.5%	10.7%	0.236
Paan and Tobacco	85%	40%	0.0001
Ghutka (alone)	73%	26%	0.0001
Ghutka and smoking	51%	24%	0.0001

Table-1 : Comparison of characteristics of cases versus controls.

Characteristics	Odds Ratio	p values
Age (per year increase)	0.98 (0.94-1.03)	0.62
Gender:		
Male (reference female)	1.05 (0.56-1.99)	0.86
Ethnicity: (Ref Others)	1.30 (0.68-2.5)	0.42
Urdu Speaking		
Others	1.0	
Smoking	1.71 (0.87-3.37)	0.11
Paan and Tobacco	8.5 (4.20-17.0)	0.0001
Ghutka (alone)	8.03 (3.61-17.85)	0.0001
Gutka and smoking	8.41 (4.10-16.7)	0.0001

Table-2 : Binary logistic regression analysis of factors associated with the risk of oral cancer:

incidence of oral cancer in Michigan is 3.3 times in males²⁸ while in our study it is 2.7 times in males.. One study from Indians living in South Africa found a 1: 1.6 male to female ratio among oral cancer patients²⁹. The ethnicity variables showed that Urdu speaking were 75% followed by Punjabi (9%), Baluchi (8%), Sindhi (4%) and Pathan (2%). Rests were from other communities. The justification of this result lies in the fact that this study was conducted in Abbasi Shaheed Hospital, situated in the center of Urdu speaking population. Majority of the patients attending this hospital are from Urdu speaking population. So this variable only shows local statistics and don't represent whole country. The average age was 33 \pm 6.09. The majority of the cases and controls were from poor and lower middle class, 64.38%, and 31.51% respectively. This clearly indicates that the habits of ghutka, smoking and paan with tobacco are rampant in poor population.

This study is different from other studies of the world as the main factors in western world are smoking and drinking, while in this study the main factors belong to smokeless tobacco, that is ghutka and paan with tobacco. Similarly smoking alone was observed only in 16.5% of cases and 10.7% of controls (p-value=0.236), however ghutka and smoking was observed in 51%, followed by paan with tobacco 35.6%. In a comparative analysis between cases and controls, it was found that paan and tobacco was consumed in 85% of cases but only in 40% of the controls (p-value 0.0001). Ghutka was consumed in 73% of cases and 26% of controls (p-value 0.0001). This clearly indicates that pan with tobacco and ghutka are strong predictors of oral cancer in this part of the world. Although cigarette smoking is a known predictor of oral cancer worldwide but in our study only 16.5% of cases and 10.7% of controls were habitual of smoking. The oral cancer is most prevalent in parts of subcontinent and Southeast Asia where the use of betel nut and various forms of oral tobacco are widespread⁵⁴.

A descriptive analysis of 116 cases of oral cancer in patients 45 years and under. It revealed recent increase in young patients with oral cancer. According to this study oral cancer in the young may be a disease distinct from that occurring in older patients with a different etiology and disease progression⁴. Recent evidence from a case series suggests an absence of traditional factors in a significant population of younger patients. Moreover the time span for tobacco and alcohol to exert a detrimental effect in these younger patients is relatively short. The author suggested examining other potential risk factors like genetic, environmental, stress, previous viral infections and other carcinogens. In this study 47% of all cases were SCC of tongue. The mean age in males was 39 years and in females was 38 years⁷. In our study the mean age was 33 years with standard deviation of 6.09. The most common site in our study was cheek followed by tongue and floor of mouth. Majority were either ghutka eaters, paan with tobacco eaters or smokers. According to IARC monogram volume 85, percentage of oral cancer diagnosed in Asia was always higher than the usually found in western countries, where the habit of chewing betel quid with or without tobacco is virtually unknown³⁰. A case control study, India, with 591 cases of oral cancer and equal number of controls showed relative risk of 4.2 in betel quid chewers which increased to 6.1 in betel quid chewers with tobacco smoking³¹. Another study by Znoar et al³² has shown relative risk of 2.2 in betel quid chewers which increased to 5.1 in betel quid chewers along with tobacco smoking. In our study those who consume paan and tobacco, were 8.5 times more likely to have oral cancer (OR 8.5; CI 95%; p-value 0.0001) when compared to nonconsumers. Similarly compared to those who did not consume ghutka, those who did were 8 times more likely to develop oral cancer (OR 8.0; CI 95%; p-value 0.0001). In India, it has been shown that chewing the mixtures containing areca nut and tobacco, which is becoming more and more popular among the youth, is causing an increase in oral cancer at younger age^{33,34}. In another study from India, male bidi smokers who also chewed paan with tobacco regularly, had a 7 fold greater risk of cancer of the tongue or floor of the mouth, a more than 16 fold greater risk of gingival cancer and a more than 21 fold greater risk of cancer of buccal and labial mucosa than men not using any tobacco. (P < 0.05)³⁵. The use of areca nut among the youth is increasing mainly due to availability of packaged, readymade forms of areca nut preparations like ghutka, mawa, paanmasala, etc. Habits ghutka, smoking and paan with tobacco are rampant in poor population. Another factor is their intensive advertising and marketing. Dry products like ghutka, mawa and paanmasala are based on the idea of betel quid containing multiple ingredients minus the betel leaf. Although gutka has been banned in Pakistan but it is freely available on every paan shop all over Pakistan at a very cheap rate.

CONCLUSION : The consumption of paan with tobacco and use of ghutka alone were significantly associated with the risk of developing oral cancer. The other independent variables age, gender ethnicity and smoking did not show a significant association.

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