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Original Article

Smokeless Tobacco Use and Its Association with Head and Neck Tumors and its relationship with Ethnicity; A Hospital Based Study

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ABSTRACT

Objective: To identify smokeless tobacco as a risk factor in the development of head and neck cancers and to assess the role of ethnicity in the use of smokeless tobacco in developing head and neck cancers.

Study Design: Case-control study.

Place and Duration of Study: Department of Medical Oncology, Jinnah Postgraduate Medical Center, Karachi Pakistan, from Dec 2018 to Jun 2019.

Methodology: Three hundred patients, aged 18-85 years of either gender was included in the study. Cases were the patients visiting Oncology OPD with biopsy-proven head and neck cancers (HNCs). Controls were patients presenting at the same hospital for a routine checkup. We interviewed participants by using a pre-designed proforma.

Results: The mean age of the cases and controls were reported as 49.26±13.51 years and 40.12±14.89 years, respectively. Majority of the participants were consuming pan (37.0%), gutka (22.6%), tobacco (21.3%), betel nut (19.6%), naswar (12.0%) and mainpuri (9.0%). The participants who consumed tobacco (OR:2.95), gutka (OR:2.39), mainpuri (OR:4.89), pan (OR:2.06) and betel nut (OR:2.28) were times more likely to develop HNCs than those who did not consume tobacco, gutka, mainpuri, pan and betel nut (p<0.05). Among Urdu speaking, the participants who consumed tobacco (OR: 2.49), pan (OR:10.35), and betel nut (OR:3.34), had times more likely to develop HNCs than those who did not consume tobacco, pan and betel nut.

Conclusion: Mainpuri, naswar, betel quid, and betel nut significantly affect the oral health of people and are potential risk factors for the development of risk factors.

Keywords: Head and neck cancers, Mainpuri, Naswar, Smokeless tobacco, Smoking, Tobacco.

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INTRODUCTION

Globally, head and neck cancers (HNCs) are the sixth leading malignancy. Yearly, 650,000 individuals are diagnosed with HNCs, and 330,000 die.[1,2]

HNCs are frequent in South Asian developing countries (40%), especially in Pakistan, India, Afghanistan, Srilanka, Bangladesh, Bhutan, Iran, Nepal, and Maldives.[3] In these countries, HNCs ranked either first or second among different types of cancer. Pakistan has the highest incidence rates of HNCs in the world with potential dominancy of the male gender,[4] whereas, in India, the incidence is higher among females.[5]

One of the potential risk factors of HNCs in South Asian countries is the consumption of smokeless tobacco. Smokeless tobacco products are consumed orally or nasally without being burnt and are accessible in many different forms. Approximately 90% of the global burden of consumption of smokeless tobacco is found in South East Asia, where one-third of the tobacco use is in the form of smokeless tobacco. One hundred million individuals consume smokeless tobacco in Pakistan and India alone,[6] and almost up to 90% of head and neck squamous cell carcinoma (HNSCC) is due to tobacco use.[7]

The consumption of smokeless tobacco is very frequent amongst Pakistanis due to its easy availability, low cost, peer pressure and misconception that it relieves headaches, toothaches and stomach pain, and most of them believe that its use is a safe alternative to cigarette smoking.[8] The forms of smokeless tobacco used by the Pakistani population are chewing tobacco with and without other ingredients such as areca nut, betel quid (containing tobacco, lime, areca nut and other flavourings), gutkha, paan-masala, khaini, naswar (tobacco flavoured with cardamom and menthol), and mishri.[9,10]

Pakistan is a developing country with a huge burden of HNCs with high morbidity. Important factors to consider in this regard are lack of awareness, limited diagnostic tools, low socioeconomic conditions and late presentation. The proportion of smokeless tobacco consumption is also high in Pakistan, and the majority of the people consume smokeless tobacco due

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lack of education and awareness. As a result, they are unaware of its harmful health events. Therefore, there is a dire need for research in this area. The objective of the present study was to identify smokeless tobacco as a risk factor for HNCs. This study would help change the behaviour and habits of consuming smokeless tobacco and thus prevent head and neck cancers.

METHODOLOGY

It was a case-control study conducted at the Department of Medical Oncology of Jinnah Postgraduate Medical Center from December 2018 to June 2019. The Ethical Review Committee Approval (NO.F. 21-81/2018-GENL/Q131/JPMC) was obtained before the study. The sample size was estimated using the Open Epi sample size calculator by taking the frequency of smokeless tobacco as 63%,[11] among cases and 37%,[11] among healthy controls, power of test 80%and 95% confidence level. The estimated sample size came out as 76 cases and 76 in controls, but we have included 150 cases and 150 controls for the adequacy of results. The ratio of cases to controls was kept as 1:1; hence, there was one control for every case.

Inclusion Criteria: All the patients, aged 18-85 years, of either gender were included in the study. Cases were the patients admitted to the hospital with biopsy-proven HNCs. Controls were patients presenting at the same hospital coming for a routine checkup.

Exclusion Criteria: Patients with comorbidities, other malignancies and memory issues were excluded from the study.

The verbal or written informed consent was taken from all the participants before data collection. We interviewed participants using a pre-designed proforma. The proforma included the information regarding demographics, medical history, diagnosis and type of smokeless tobacco like pan, tobacco, gutka, mainpuri and betel nut consumption which was assessed on history. Data related to ethnicity was also reported.

Statistical Package for Social Sciences (SPSS) version 23:00 was used for the data analysis. Mean and SD were calculated for quantitative variables, whereas frequencies and percentages were calculated for qualitative variables. The Chi-square test was applied between cases and controls for smoking and smokeless tobacco habits. The *p*-value less than and equal to 0.05 was taken as statistically significant. The measure of association, i.e. odd ratio, and confidence interval were also calculated.

RESULTS

A total of 150 cases and 150 controls were included in the study. The mean age of the cases and controls were reported as 49.26±13.51 years and 40.12±14.89 years. In cases, 101 patients were males (67.3%), and in controls, 131 were males (87.3%). In addition, about 137 patients were Urdu speaking (45.7%). Besides, 139(48.1%) cases and 150(51.9%) controls had no history of cancer in the family. However, the comparison of HNCs with age (p=0.001), gender (*p*=0.001) and ethnicity (*p*=0.001) showed a statistically significant difference between the stratified groups (Table-I).

Table-I: Descriptive Statistics (n=300)

Variables	Case (n=150)	Control (n=150)	*p*-value
Age in Years (Mean±SD)	49.26±13.51	40.12±14.89	0.001
Gender			
Male	101(67.3)	131(87.3)	0.001
Female	49(32.7)	19(12.7)	
Ethnicity			
Sindhi	38(25.3)	23(15.3)	0.001
Balochi	16(10.7)	21(14.0)	
Pashto	9(6.0)	23(15.3)	
Punjabi	14(9.3)	0	
Urdu	72(48.0)	65(43.3)	
Others	1(0.7)	18(12.0)	
Family History of Cancer			
Yes	11(7.3)	0	-
No	139(92.6)	150(100.0)	

The buccal mucosa was the most common site in 55 patients (18.3%). About 67 of the tumours were moderately differentiated, and according to the stage of cancer, 98 patients were identified in stage-4, as shown in Table-II.

Table-II: Clinico-pathological Characteristics (n=300)

Variables	Frequency (%)
Primary Diagnosis (n=300)	
Buccal Mucosa	55 (18.3)
CA Cheek	47 (15.7)
CA Larynx	8 (2.7)
CA Tongue	38 (12.7)
Floor of mouth	1 (0.3)
Hard palate Carcinoma	1 (0.3)
Stage (n=150)	
2	7 (4.7)
3	45 (30.0)
4	98 (65.3)
Histology (n=150)	
Well differentiated	67 (44.7)
Moderately differentiated	57 (38.0)
Poorly differentiated	26 (17.3)

Majority of the participants were consuming pan (n=111; 37%), followed by cigarette smoking (n=75; 25%), gutka (n=68; 22.7%), tobacco (n=64; 21.3%), betel nut (n=59; 19.6%), naswar (n=27; 9%) and mainpuri (n=12; 4%).

The participants who consumed tobacco (p= 0.001), gutka (p=0.001), mainpuri(p=0.003), pan (p= 0.003) and betel nut (p=0.006) had 2.95, 2.80, 11.79, 2.06 and 2.28 times more likely to develop HNCs as compared to people who donot consume tobacco, gutka, mainpuri, pan and betel nut (Table-III).

Table-III: Association of Smokeless Tobacco with Head and Neck Cancers (n=300)

Variables	Case (n=150) n (%)	Control (n=150) n (%)	*p*-value	Odds Ratio (95% CI)
Tobacco Consumer				
Yes	45(70.3)	19(29.7)	0.001	2.95(1.63-5.35)
No	105(44.5)	131(55.5)		
Gutka				
Yes	47(69.1)	21(30.9)	0.001	2.80(1.57-4.89)
No	103(44.4)	129(55.6)		
Mainpuri				
Yes	11(91.7)	1(8.3)	0.003	11.79(1.50-92.52)
No	139(48.3)	149(51.7)		
Naswar				
Yes	17(63)	10(37)	0.158	1.78(0.79-4.04)
No	133(48.7)	140(51.3)		
Pan				
Yes	68(61.3)	43(38.7)	0.003	2.06(1.27-3.32)
No	82(43.4)	107(56.6)		
Betel nut				
Yes	39(66.1)	20(33.9)	0.006	2.28(1.25-4.14)
No	111(46.1%)	130(53.9%)		

Subgroup analysis was for participants who had never smoked. The participants who consumed tobacco (p=0.001), gutka (p=0.001), mainpuri(p=0.02) and betel nut (p=0.007) had 4.60, 5.68, 8 and 2.69 times more likely to develop HNCs as compared to people who do not consume tobacco, gutka, mainpuri and betel nut (Table-IV).

Association for ethnicity was done for smokeless tobacco type. Among Sindhis, Balochis and Urdu speaking, most participants were consuming pan. Among Pashto speaking, most of the participants were consuming tobacco. Among Punjabis, the majority of the participants were consuming gutka.

Among Urdu speaking, the participants who consumed tobacco, pan and betel nut had 2.49, 10.35 and 3.34 times more likely to develop HNCs than those who did not consume tobacco, pan and betel nut (Table-V).

Table-IV: Association of Smokeless Tobacco with Head and Neck Cancers among Individuals who Have Never Smoked (n=225)

Tobacco	Case (n=116) n(%)	Control (n=109) n(%)	*p*-value	Odds Ratio (95% CI)
Yes	34 (29.3)	9 (8.2)	0.001	4.60(2.08-10.15)
No	82 (70.7)	100 (91.8)		
Gutka				
Yes	36 (31.1)	8 (7.3)	0.001	5.68(2.50-12.90)
No	80 (68.9)	101 (92.7)		
Mainpuri				
Yes	8 (6.9)	1 (0.9)	0.02	8.00(0.98-65.06)
No	108 (93.1)	108 (99.1)		
Pan				
Yes	53 (45.7)	42 (38.5)	0.277	1.34(0.78-2.28)
No	63 (54.3)	67 (61.5)		
Betel Nut				
Yes	29 (25.0)	12 (11.0)	0.007	2.69(1.29-5.60)
No	87 (75.0)	97 (89.0)		

DISCUSSION

In the current research, we have found out whether smokeless tobacco is a risk factor in developing head and neck cancers or not. A survey in India reported that almost 20% of adults aged ≥15 years sniff smokeless tobacco. Whereas current study results stated that the majority was more than 40 years old, which explains that Smokeless tobacco users frequently develop premalignant lesions at the site where the tobacco quid rests, and gradually these lesions may progress to invasive carcinomas.[12] The present study results explain that majority of the patients that were exposed to cancer were males that is self-explanatory that gender plays a significant role in developing cancer. The investigation of carcinogenic factors by the International Agency for Research on Cancer (IARC) reports smokeless tobacco as a risk factor for HNC, the main target organ being the oral cavity.[13,14] Smokeless tobacco is also associated with an increased incidence of head and neck cancer, especially in the oral cavity. In the journal of oncology, it is reported that men are more prone to HNC and out of ten, three males are diagnosed with oral cancer compared to females.[15] In a reported case, around three-quarters of males with HNCs had ever used different types of smokeless tobacco.[16]

Table-V: Association of Ethnicity with Smokeless Tobacco Type (n=300)

Smokeless Tobacco Type	Groups	Sindhi	Balochi	Pashto	Punjabi	Urdu Speaking	Others
Tobacco	Case	7(4.6)	5(3.3)	3(2)	4(2.6)	26(17.3)	0
	Control	0	2(1.3)	3(2)	0	12(8)	2(1.3)
	OR(95% CI)	-	4.31(0.71-26.12)	3.33(0.52-21.03)	-	2.49(1.13-5.49)	-
	p-value	0.029	0.095	0.186	-	0.021	0.725
Gutka	Case	9(6)	3(2)	3(2)	8(5.3)	24(16)	0
	Control	0	0	2(1.3)	0	17(11.3)	2(1.3)
	OR(95% CI)	-	-	5.25(0.70-39.03)	-	1.41(0.67-2.95)	-
	p-value	0.01	0.038	0.084	-	0.395	0.725
Mainpuri	Case	3(2)	1(0.6)	0	1(0.6)	6(4)	0
	Control	0	0	1(0.6)	0	0	0
	OR(95% CI)	-	-	-	-	-	-
	p-value	0.167	0.245	-	-	0.017	-
Pan	Case	16(10.6)	7(4.6)	1(0.6)	3(2)	40(26.6)	1(0.6)
	Control	10(6.6)	16(10.6)	2(1.3)	0	7(4.6)	8(5.3)
	OR(95% CI)	0.94(0.33-2.64)	0.24(0.05-0.99)	1.31(0.10-16.55)	-	10.35(4.16-25.77)	-
	p-value	0.916	0.044	0.833	-	0.001	0.279
Betel Nut	Case	6(4)	3(2)	2(1.3)	4(2.6)	23(15.3)	1(0.6)
	Control	8(5.3)	2(1.3)	0	0	8(5.3)	2(1.3)
	OR(95% CI)	0.35(0.10-1.19)	2.19(0.32-15)	-	-	3.34(1.37-8.14)	-
	p-value	0.087	0.416	0.02	-	0.006	0.018

A large epidemiological study by Guha *et al*. in 2014,[17] reported an adjusted relative risk of 6.19 (CI) 4.16-9.21] for chewing betel quid with tobacco that there was a 66% risk of developing HNCs in patients consuming smokeless tobacco. In an ecological study conducted in India, it was reported that smokeless tobacco is correlated with HNCs. The findings of this study reported that betel quid and tobacco correlate (r =0.53) with oropharynx cancer whereas Gutka was correlated with mouth cancer (r = 0.54).[18] It was also reported that increased smokeless tobacco consumption has a higher risk of developing HNCs (odds ratio = 11.25, 95% CI) (16) . In another study, the association between the usage of smokeless tobacco products (gutka, paan, naswar) and oral inflammation was significant.[19]

Few Pakistani studies,[20-22] also support our finding. In one study by Abbas *et al*. in 2014, it was reported that almost 34% of tobacco users were not educated, and more than 80% were diagnosed with HNCs. Pakistan is a multicultural country.[23] There is also an ethnic variation in Pakistan, and the difference in various ethnic groups is quite noticeable.

In a case-control study, approximately 40% of patients had smokeless tobacco, and less than 10% had smoked cigarettes.[11] Another study showed an association of pan with oral cancer at 95% CI with an odds ratio of 1.291.[21] According to the ethnic groups, the results of the present study showed that most of the participants who were consuming pan belonged to Sindhi, Balochi and Urdu-speaking populations, whereas participants who consumed tobacco belonged to the Pashto speaking population. On the other hand, the participants who were consuming gutka belonged to the Punjabi ethnic group. The Balochi participants had 0.24 times less likely to develop HNCs as compared to people who do not consume pan, and Urdu-speaking participants who consumed tobacco, pan and betel nut had 2.49, 10.35 and 3.34 times more likely to develop HNCs as compared to people who do not consume tobacco, pan and betel nut.

On the other hand, a study showed that smokeless tobacco usage was higher in the Pashtun population (38%), followed by Sindhi Population (22.4%).[23] Because of the above literature and our study, smokeless tobacco is a significant risk factor, and there was a positive association among different ethnic groups. Therefore, within the limitation of this study, we recommend conducting larger sample size cohort studies among different ethnic populations and establishing more local data so that strict actions for smokeless tobacco cessation can be executed.

CONCLUSION

Mainpuri, naswar, betel quid, and betel nut have a significant effect on the oral health of people and are potential risk factors for the development of risk factors.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MN: Study design, data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

GH & SB: Data acquisition, critical review, approval of the final version to be published.

AS & SMAN: Conception, drafting the manuscript, approval of the final version to be published.

RN: Drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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