Original Article

SMOKELESS TOBACCO CONSUMPTION AND ORAL CANCER: A CASE-CONTROL STUDY

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ABSTRACT

Background: Smokeless tobacco consumption leads to oral cancer, which is a substantial source of morbidity and mortality in Bangladesh. This study was conducted to determine the association between smokeless tobacco consumption and the risk of oral cancer.

Methods: It was a case-control study. Participants with oral cancer were considered cases, while those without oral cancer were regarded as controls. Data were collected through face-to-face interviews and reviews of the medical records through a pretested semi-structured questionnaire and checklist.

Results: Tobacco consumption was significantly ($p<0.05$) higher among the cases (93.3%) than in the controls (30.7%). Oral cancer was found 31.6 times (OR=31.6, 95% CI 15.26- 65.64) more likely to develop among the cases than the controls. Smokeless tobacco was 18 times (OR = 18.00, 95% CI 7.18- 45.10) more likely to develop oral cancer than smoked tobacco. On the other hand, consumption of Sadapata and Gul were 15.4 times (OR=15.4, 95% CI 2.02-118.47) more likely to develop oral cancer than betel quid with Zarda consumption. Consumption of Betel Quid with Zarda more than 7 times per day was found 5.3 times (OR=5.3, 95% CI 0.52–35.9) more likely to develop oral cancer among the cases than the controls.

Conclusion: Smokeless tobacco consumption was significantly associated with the occurrence of oral cancer. The study recommends specific strategic actions to reduce tobacco consumption for the prevention of oral cancer.

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Key word: Smokeless tobacco consumption, Oral cancer, Smokeless tobacco, Smoked tobacco

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INTRODUCTION

Oral cancer is a broad term used to describe a variety of neoplasms occurring in different anatomical structures including oral cavity, oropharynx, hypopharynx and the larynx. More than 90% of these malignancies are squamous cell carcinoma.[1] Incidence rate of oral cancer was elevated in France, Slovakia, Germany and Brazil where males were more prevalent with the maximum rates found in India/Chennai, the U.K. and Japan.[2] Globally, the highest incidence existed in South-Central Asia and parts of Oceania, with the highest estimated incidence rates in Papua New Guinea, Pakistan and India. The worldwide estimate was 354,864 new cases of lip and oral cavity cancers and 177,384 deaths in 2018 and more than 70% of these cancer deaths occur in Asia.[3] The prevalence and mortality of oral cancer are higher in developing countries than in developed countries and two-thirds of oral cancer patients are diagnosed in developing countries4. World Bank conveyed that lip and oral cavity cancer is the fourth most common cancer and the sixth cause of cancer deaths in low and middle-income countries.[4] Accounting for nearly one-third of all cancers, oral cancer is one of the leading cause of mortality in countries like India, the Taiwanese region, Sri Lanka, Pakistan and Bangladesh.[5] In South-Central Asia, it is the second most common cancer among men, with an age-standardized incidence of 9.9 and a 5- year prevalence of 129,057 (12.1%).[6]

Cancer is one of the leading causes of death in Bangladesh which accounts for 10% of total deaths in Bangladesh and may reach unto 13% by 2030.[7] Approximately 13,500 people are diagnosed with oral cancer of which nearby 8,500 die every year in Bangladesh. This is the second most-common type of cancer among men and women where man is considered third most and female is fifth most-common accordingly in Bangladesh.[8] The etiology of oral cancers appears to be multifactorial which include tobacco smoking, tobacco chewing, oral snuff, chewing betel quid, consumption of alcohol and the presence of potentially malignant oral

lesions.[9] Recent evidence also suggests virally-mediated carcinogenesis, dental health status and the chronic irritation by prosthetic or dental elements.[10] India, Egypt, and Indonesia had the largest unconditional increases in number of young male smokers.[11] Bangladesh, Nepal and Bhutan had a very high prevalence of chewing tobacco use.[12] On the other hand, Bangladesh is one of the top ten countries in the world with high tobacco use in both smoking and smokeless forms with a prevalence of 43.3% among adults.[13] Tobacco is being chewed in multiple forms and modes in South Asia such as betel leaf with areca nut, betel leaf alone, with Zarda and Gul.[14] Although Bangladesh taxes tobacco, the tax structure is complex and base price is still very low. Smokeless tobacco (SLT), which is more prevalent to cause oral cancer.[15] Smokeless tobacco is used in numerous forms including Zarda, Gul, Khaini. Sada Pata and their stumpy price make it affordable to everyone. Bangladesh has traditionally experienced huge production and consumption of tobacco products, resulting in a substantial burden of tobacco-related illnesse.[16]

The high incidence rates among the Bangladeshi and Indian populations reflect the ongoing prevalence of Paan and tobacco chewing, as well as tobacco smoking habits, which are equally common among both genders.[12] Several studies on oral health status regarding smokeless tobacco has been done in India, Pakistan and Asian residents of UK and USA, but very scanty has been done in Bangladesh. As oral lesions are very common and a preventable one, the study aimed to conduct elaborately on the status of smokeless tobacco consumption in selected oral cancer patients with a view to prevent these conditions.

METHODS

Study design, period, and settings

This was an age and gender-matched case-control study. The study took place from July 2021 to June 2022. The study was conducted at Dhaka Dental College & Hospital and National Institute of Cancer Research & Hospital, Bangladesh.

Study population, ample size, and sampling technique

The study population were both the cases and the controls attending the inpatient (IPD) and outpatient department (OPD) of selected hospitals. Cases were oral cancer patients, previously diagnosed by the Maxillofacial Surgeons or Oncologists / specialist physician based on biopsy and histopathology complaining for a lesion in the oral cavity and reported as malignancy. Severely ill patients and who were suffering from any other cancer were excluded from the study. Controls were the individuals without having oral cancer diagnosed by specialized physician, matched for age and sex attending in the inpatient and outpatient department of selected hospitals.

Sample size had been determined with the help of given formula- $n = \left(\frac{r+1}{r}\right) \frac{(\bar{p})(1-\bar{p})\left(Z_{\beta}+Z_{\alpha/2}\right)^2}{(p_1-p_2)^2}$

Where, n = sample size in the case & control group; r = ratio of control to cases = 1 , $Z_{\alpha/2}$ = percentage point of the normal distribution corresponding to the (two side) significance level. e.g., if significance level is 95%, Zα = 1.96

Z_{β} = one-sided percentage point of the normal distribution corresponding to 100% the power e.g. if power is 80%, Z_{β}= 0.842, OR= 2. The proportion exposed in the control group p_2 is 40% which was taken from previous study. With 10% nonresponsive rate it was 148.5. And by rounding it was 150 case and 150 control. Convenience sampling was used according to the availability of the participants who accomplished the inclusion criteria.

Data collection

A pretested semi-structured questionnaire was developed in English and in Bengali using the variables in respect of specific objectives to collect data from the cases and controls by face to-face interview. The questionnaire comprised of socio-demographic characteristics, tobacco consumption behavior and the other risk factors associated with oral cancer. A checklist was used to collect information regarding type of oral cancer and BMI.

Data were collected by observation and review of medical records. Written permission was obtained from Hospital authority prior to data collection and Informed written consent was obtained from them. At first data of cases were collected by face-to-face interview and privacy was maintained in case of sensitive questions regarding information about alcohol consumption, history of cancer of family members. Relevant medical records of the cases of oral cancer were reviewed to collect information of checklist. After collecting information of cases, at first controls were matched for age and sex with the cases and then data were collected by face-to-face interview. Relevant medical records of the controls were reviewed to collect information of checklist.

Data analysis

Data management was done by data processing which included editing, coding, data cleaning, categorization of data. Then making template for input of data, summarizing the data and entry of data into the SPSS software (v.26.0). Collected data had been checked for consistency, had been compiled, coded, categorized and edited according to objectives and variables.

Ethical Clearance

Ethical clearance was obtained from the Institutional Review Board of National Institute of Preventive and Social Medicine. The Memo number was NIPSOM/IRB/2021/18, dated 13 th December 2021.

RESULTS

Among the participants, majority (54.7%) were male in both the cases and controls and this difference of sex between cases and controls was not statistically significant ($\chi 2$ =0.000, df=1, p=1.000). In both cases and controls, majority (50.0%) were in the age group 45 – 59 years and their mean age ±SD was 54.19±10.65 years. Regarding education level, 49.3% cases and 17.3% controls were illiterate, and this difference was statistically significant (p<0.05). In respect of occupation, majority of cases (53.3%) were home maker compared to controls (46.7%) and this difference was statistically significant (p<0.05). Average monthly family income of cases and controls were 13813.33±9070.48 TK and 33700.00±15317.55 TK respectively and this difference was statistically significant (p<0.05) as shown in Table 1

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Table-1: Comparison of selected socio-demographic characteristics between cases and controls

Characteristics	Case f (%)	Control f (%)	Significance p<0.05
Gender			
Male	82 (54.7)	82 (54.7)	χ^2=0.000 df=1 p-value= 1.000
Female	68 (45.3)	68 (45.3)	
Total f (%)	150 (100)	150 (100)	
Age in years			
30-44	19 (12.7)	19 (12.7.7)	χ^2=0.000 df=2 p-value= 1.000
45-59	75 (50.0)	75 (50.0)	
60-75	56 (37.3)	56 (37.3)	
Total f (%)	150 (100)	150 (100)	
Mean ± SD	54.19±10.65	54.19±10.65	t=0.000; df=298 p= 1.000
Education			
Illiterate	74 (49.3)	26 (17.3)	χ^2=87.81; df=4 p= 0.000
Primary	49 (32.7)	24 (16.0)	
Secondary	21 (14.0)	32 (21.3)	
S.S.C.	5 (3.3)	21 (14.0)	
Higher Secondary	1 (0.7)	47 (31.3)	
Total f (%)	150 (100)	150 (100)	
Occupation			
Unemployed	0 (.0)	11 (7.3)	χ2=65.436; df=7 p= 0.000
Service	6 (4.0)	23 (15.3)	
Student	0 (0.0)	1 (0.7)	
Business	12 (8.0)	24 (16.0)	
Farmer	32 (21.3)	2 (1.3)	
Day Laborer	20 (13.3)	10 (6.7)	
Retired	0 (0.0)	9 (6.0)	
Home maker	80 (53.3)	70 (46.7)	
Total f (%)	150 (100)	150 (100)	
Monthly family income (TK)			
5000-10000	77 (51.3)	10 (6.7)	χ^2=139.48; df=3 p= 0.000
11000-20000	61 (40.7)	31 (20.7)	
21000-40000	9 (6.0)	66 (44.0)	
41000-60000	3 (2.0)	43 (28.7)	
Total f (%)	150 (100)	150 (100)	
Mean ± SD	13813.33±9070.48	33700.00±15317.55	t=-13.68; df=298 p= 0.000

The majority (93.3 %) of the cases had consumed tobacco product ever in life in comparison controls (30.7%) and this difference was statistically significant (p<0.05). On the contrary, 72.1% cases

consumed smokeless tobacco ever in life compared 43.5% controls and this difference was statistically significant ($p<0.05$). The majority (55.0%) of cases compared to 36.4% controls started using smokeless tobacco daily in the age group of 10-20 years and this difference was statistically significant ($p<0.05$). The mean duration of using smokeless tobacco of the cases and controls was 29.93±12.67 and 25.82±10.74 years respectively but this difference was not statistically significant ($p>0.05$). Among all of the former smokeless tobacco users, 58.0% cases all (100.0%) controls had consumed betel quid with Zarda daily. On the other hand, 38.9% and 3.1% cases had consumed Sadapata and Gul respectively but control group didn't consume it. It was found that the mean frequency of Betel quid with Zarda consumption daily was 6.8±3.55 in cases and 3.64±1.62 in controls and this difference was statistically significant ($p<0.05$). The mean frequency of Sadapata and Gul consumption was 7.77±3 and 3.75±2.87, which was statistically significant ($p<0.05$) as shown in Table 2.

Table-2: Comparison of tobacco consumption and former smokeless tobacco consumption between cases and controls

Characteristics	**Case f (%)**	**Control f (%)**	**Significance p<0.05**
Consuming tobacco product in life			
Yes	140 (93.3)	46 (30.7)	$\chi2=122.36$ df=1; p= 0.000
No	10 (6.7)	104 (69.3)	
Total f (%)	150 (100)	150 (100)	
Type of tobacco product consumed ever in life			
Smoked tobacco	8 (5.7)	24 (52.2)	$\chi2=53.99$ df=2; p= 0.000
Smokeless tobacco	101 (72.1)	20 (43.5)	
Both	31 (22.1)	2 (4.3)	
Total f (%)	140 (100)	46 (100)	
Age of starting smokeless tobacco (in years)			
10-20	72 (55.0)	4 (36.4)	Fisher's Exact Test =9.862; df=2; p= 0.004
21-35	42 (32.1)	1 (9.1)	
36-55	17 (13.0)	6 (54.5)	
Total f (%)	131 (100)	11 (100)	
Mean ± SD	23.73±9.86	33.64±12.06	t=-3.142, df=140; p-value=0.002
Duration of using smokeless tobacco (Years)			
1-20	37 (28.2)	6 (54.5)	Fisher's Exact Test =3.955; df=2, p= 0.103
21-40	70 (53.4)	5 (45.5)	
41-60	24 (18.3)	0 (0.0)	
Total f (%)	131 (100)	11 (100)	
Mean ± SD	29.93±12.67	25.82±10.74	t=1.044; df=140; p-value= 0.298
Type of using different smokeless tobacco products			
Betel quid with Zarda or, Zarda only	76 (58.0)	11 (100.0)	$\chi^2=7.53$; df=2; p= 0.039
Sada pata	51 (38.9)	0 (0.0)	
Gul	4 (3.1)	0 (0.0)	
Total f (%)	131 (100)	11 (100)	
Frequency of taking of different smokeless tobacco			
Betel quid with zarda			
1-8	55 (72.4)	11 (100.0)	$\chi2=4.007$ df=1; p= 0.045
9-20	21 (27.6)	0 (0.0)	
Total f (%)	76 (100)	11 (100)	
Mean ± SD	6.8±3.55	3.64±1.629	t=2.896, df=85; p= 0.005
Sada pata			
1-8	32 (62.7)	0 (0.0)	
9-20	19 (37.3)	0 (0.0)	
Total f (%)	51 (100)		
Mean ± SD	7.77±3		

Frequency of taking of different smokeless tobacco			
Gul			
2	2 (50.0)	0 (0.0)	
3	1 (25.0)	0 (0.0)	
8	1 (25.0)	0 (0.0)	
Total f (%)	4 (100)		
Mean ± SD	3.75±2.87		

Regarding using of materials for cleaning teeth, 46.0% cases had used tooth powder for cleaning their teeth compared to 27.3% controls. Majority (84.0%) of cases had cleaned their teeth 1 time daily compared to 89.3% controls. Most of the cases (97.3%) did not drink liquor or alcohol compared to 98.7% controls. Among all, 92.7% cases did not have a family history of oral cancer in comparison to 98.0% controls and this difference was statistically significant ($p<0.05$). Off all, 45.5% cases reported that their fathers had the history of oral cancer during their life period compared to 66.7% controls. Off all, majority (50.7%) of the cases had the history of radiation in comparison to 67.3% controls but it was not statistically significant ($p>0.05$), which is shown in the table 3.

Table-3: Comparison of other risk factors related to oral cancer between cases and controls

Characteristics	**Case f (%)**	**Control f (%)**	**Significance p<0.05**
Having a long-term wound in the mouth			
Yes	0 (0.0)	0 (0.0)	
No	150 (100.0)	150 (100.0)	
Total f (%)	150 (100)	150 (100)	
Material using for cleaning teeth			
Tooth brushing	27 (18.0)	93 (62.0)	χ^2=64.05 df=2 p-value= 0.000
Tooth powder	69 (46.0)	41 (27.3)	
Chhai/ koila	54 (36.0)	16 (10.7)	
Total f (%)	150 (100)	150 (100)	
Frequency of cleaning teeth in a day			
1	126 (84.0)	134 (89.3)	χ^2=3.194 df=2 p-value= 0.203
2	22 (14.7)	16 (10.7)	
3	2 (1.3)	0 (0.0)	
Total f (%)	150 (100)	150 (100)	
Mean ± SD	1.17±.414	1.11±.310	t=1.580 df=298 p-value= 0.115
Alcohol consumption			
Yes	4 (2.7)	2 (1.3)	χ^2=0.680 df=1 p-value= 0.409
No	146 (97.3)	148 (98.7)	
Total f (%)	150 (100)	150 (100)	
Family history of oral cancer			
Yes	11 (7.3)	3 (2.0)	χ^2=4.795 df=1 p-value= 0.029
No	139 (92.7)	147 (98.0)	
Total f (%)	150 (100)	150 (100)	
Family person having oral cancer			
Father	5 (45.5)	2 (66.7)	Fisher's Exact Test =1.378 df=3 p-value= 1.000
Mother	3 (27.3)	1 (33.3)	
Brother	1 (9.1)	0 (0.0)	
Sister	2 (18.2)	0 (0.0)	
Total f (%)	11 (100)	3 (100)	
Family history of other cancer			
Yes	8 (5.3)	7 (4.7)	χ^2=0.070 df=1 p-value= 0.791
No	142 (94.7)	143 (95.3)	
Total f (%)	150 (100)	150 (100)	
Family person having other cancer			

Father	2 (25.0)	4 (57.1)	
Mother	1 (12.5)	3 (42.9)	Fisher's Exact Test =5.706 df=4 p-value= 0.157
Brother	2 (25.0)	0 (0.0)	
Sister	2 (25.0)	0 (0.0)	
Offspring	1 (12.5)	0 (0.0)	
Total f (%)	8 (100)	7 (100)	
History of radiation			
Yes	76 (50.7)	101 (67.3)	χ^2=7.937 df=1 p-value= 0.005
No	74 (49.3)	49 (32.7)	
Total f (%)	150 (100)	150 (100)	
Duration of radiation			
1-10	66 (86.8)	87 (86.1)	Fisher's Exact Test =0.541 df=2 p-value= 0.866
11-20	9 (11.8)	11 (10.9)	
21-30	1 (1.3)	3 (3.0)	
Total f (%)	76 (100)	101 (100)	
Mean ± SD	5.51±5.88	6.92±6.65	t=-1.463 df=175 p-value= 0.145
History of taking any medicine for a long time			
Yes	1 (.7)	0 (0.0)	
No	149 (99.3)	0 (0.0)	
Total f (%)	150 (100)		

Among the total participants, 121 (80.7%) cases had normal BMI compared to 89 (59.3%) controls and was also statistically significant (t=-4.400, p<0.05), which is shown in the table 4.

Table-4: Comparison of other risk factors related to oral cancer between cases and controls

Characteristics	Case f (%)	Control f (%)	Significance p<0.05
BMI			
Underweight	11 (7.3)	4 (2.7)	Fisher's Exact Test =29.063; df=3 p= 0.000
Normal	121 (80.7)	89 (59.3)	
Over weight	18 (12.0)	55 (36.7)	
Obese	0 (0.0)	2 (1.3)	
Total f (%)	150 (100)	150 (100)	
Mean ± SD	22.45±2.55	23.89±3.10	t=-4.400 df=298; p= 0.000
Name of cancers having the participants			
Squamous cell carcinoma	140 (93.3)	0 (0.0)	
Adenocarcinoma	10 (6.7)	0 (0.0)	
Total f (%)	150 (100)	0.0	

Participants who earned between 5000-20000 TK per month were about 7.3 times (OR = 7.3, 95% CI 3.18- 17.07) more likely to suffer from oral cancer than the participants whose income was more. And the participants who were illiterate and completed their primary level of education were about 2.9 times (OR = 2.9, 95% CI 1.40- 6.23) more likely to suffer from oral cancer, which is shown in the table 5.

Table 5: Comparison of selected socio-demographic characteristics related to oral cancer between cases and controls (logistic regression)

Attributes	Co-efficient (B)	S.E.	OR	95% CI for OR		p-value
				Upper	Lower	
Education						
Secondary and higher secondary*						
Illiterate and up-to primary level	1.08	0.38	2.9	6.23	1.40	0.004

Income (TK)						
21000-60000*						
5000-20000	1.99	0.42	7.3	17.07	3.18	0.000
Occupation						
Service holder and retired*						
Home maker	0.31	0.38	1.3	2.93	0.64	0.416

On the contrary, the participants who earned between 5000-20000 TK per month were about 9.6 times (OR = 9.6, 95% CI 5.62- 16.57) more likely to consume tobacco than the participants whose income was more. The participants being illiterate and completed education up to primary level consumed tobacco 6.9 times more (OR = 6.9, 95% CI 4.13– 11.7) likely than those who had completed secondary and higher secondary level of education which is shown in the table 6.

Table 6: Comparison of selected socio-demographic characteristics related to tobacco consumption between cases and controls (logistic regression)

Attributes	Co-efficient (B)	S.E.	OR	95% CI for OR		p-value
				Upper	Lower	
Education						
Secondary and higher secondary*						
Illiterate and up-to primary level	1.94	0.26	6.9	11.7	4.13	0.000
Income						
21000-60000*						
5000-20000	2.26	0.27	9.6	16.57	5.62	0.000

The odds ratio for 'family history of oral cancer' indicated that participants who had a family history of oral cancer were about 4.1 times (OR = 4.1, 95% CI 1.01- 16.90) more likely to suffer from oral cancer and the participants who used koila/chai for cleaning their mouth were about 4.7 times (OR = 4.7, 95% CI 2.54- 8.72) more likely to occur oral cancer than using tooth paste or tooth powder. The odds ratio for BMI indicated that participants who had underweight or normal weight were about 4.4 times (OR = 4.4, 95% CI 2.48- 8.13) more likely to suffer from oral cancer than over weight, which is shown in the table 7

Table 7: Comparison of selected risk factors related to oral cancer between cases and controls (logistic regression)

Attributes	Co-efficient (B)	S.E.	OR	95% CI for OR		p-value
				Upper	Lower	
Cleaning of the mouth						
Tooth paste or powder*						
Chai/Koila	1.55	0.31	4.7	8.72	2.54	0.000
BMI						
Over weight *						
Underweight and Normal weight	1.50	0.30	4.4	8.13	2.48	0.000
Family history of oral cancer						
No*						
Yes	1.42	0.71	4.1	16.90	1.01	0.048
History of radiation						
No*						
Yes	-0.59	0.26	0.55	0.91	0.33	0.022

On the other hand, odds ratio for 'family history of oral cancer' indicated that participants who had a family history of oral cancer were about 8.4 times (OR = 8.4, 95% CI 1.09- 65.8) more likely involved in tobacco consumption and the participants who used koila/chai for cleaning their mouth were about 6.6 times (OR = 6.6, 95% CI 3.03- 14.46) more likely to consume tobacco. The odds ratio for BMI indicated that participants who had underweight or normal weight were about 2.7 times (OR = 2.7, 95% CI 1.58- 4.61) more likely involved in tobacco consumption, which is shown in the table 8.

Table 8: Comparison of selected risk factors related to tobacco consumption between cases and controls (logistic regression)

Attributes	Co-efficient (B)	S.E.	OR	95% CI for OR		p-value
				Upper	Lower	
Cleaning of the mouth						
Tooth paste or powder*						
Chai/Koila	1.89	0.39	6.6	14.46	3.03	0.000
BMI						
Over weight *						
Underweight and Normal weight	0.99	0.27	2.7	4.61	1.58	0.000
Family history of oral cancer						
No*						
Yes	2.13	1.04	8.4	65.8	1.09	0.041
History of radiation						
No*						
Yes	-0.70	0.25	.49	0.80	0.30	0.05

As shown in Table 9, the odds ratio for tobacco consumption indicated that participants who consumed tobacco were about 31.6 times (OR = 31.6, 95% CI 15.26- 65.64) more likely to have oral cancer than non-tobacco users. The odds ratio for 'type of tobacco' indicated that participants who consumed smokeless tobacco were about 18.0 times (OR = 18.00, 95% CI 7.18- 45.10) more likely to have oral cancer than smoked tobacco. The odds ratio for type of smokeless tobacco consumption indicated that participants who consumed sadapata and gul were about 15.4 times (OR = 15.4, 95% CI 2.02-118.47) more likely to have oral cancer than betel quid with zarda consumption. The odds ratio for frequency of betel quid with zarda consumption was 5.3, indicating that participants who consumed more than 7 numbers of betel quid with zarda per day were 5.3 times (OR = 5.3, 95% CI 0.52–35.9) more likely to occur oral cancer.

Table 9: Comparison of tobacco consumption related to oral cancer between cases and controls (logistic regression)

Attributes	Co-efficient (B)	S.E.	OR	95% CI for OR		p-value
				Upper	Lower	
Tobacco consumption						
No*						
Yes	3.45	0.37	31.65	65.64	15.26	0.000
Type of tobacco						
Smoked tobacco*						
Smokeless tobacco	2.89	0.46	18.00	45.10	7.18	0.000
Type of smokeless tobacco						
Betelquid with Zarda *						
Sadapata and gul	2.73	1.03	15.47	118.47	2.02	0.008
Frequency of betel quid with Zarda (numbers of consuming)						
1-7*						
>7	1.66	0.34	5.3	35.9	0.52	0.000

DISCUSSION

This present case-control study examined the association between smokeless tobacco consumption and oral cancer. A study conducted in Saudi Arabia, in 2022 demonstrated that the risk of developing oral cancer increased with age, as concluded that the mean age of oral cancer patients was 53.64 years, which is similar to this study.[17] Participants being illiterate and completed education up to primary level were about 2.9 times (OR = 2.9, 95% CI 1.40- 6.23) more likely to suffer from oral cancer and their tobacco consumption was 6.9 times (OR = 6.9, 95% CI 4.13– 11.7) more. Jabeen *et al* conducted a study in Bangladesh in 2014 in which about the educational status of the respondents, majority (35.8%) were illiterate, only 6.6% had education of higher secondary and above level.[18] On the other hand, in another study conducted by Elsy-Britt *et al* in 1998 revealed the inverse association between low education and oral cancer was

particularly found in women in Europe[19] and which is not similar to this study. This difference was probably due to the geographical variations or may be due to limited count of low educated people. In India, the occupational data reveals that majority of the cases belonged to agriculture sector followed by laborers and housewives; 34.09% vs. 18.94%, 28.78% vs. 16.67% and 25% vs.19.7% as compared to controls (p=0.001 for all). The self-employed and other numbers were higher for controls than cases while there was significant difference in professional and unemployed percentages between the two groups.[20] But some other studies established no association of occupational exposure with oral cancers. A study conducted by Yina Hu in Hunan province, China from January 2014 to September 2015 demonstrated that farmers accounted for 56.6% and 55.6% for oral carcinoma cases and controls, respectively and there was no association of occupational exposure with oral cancers which was not similar to the current study.[4] This difference was probably because of a large number of females as housewives participated in the study and they enjoyed their spare time by gossiping with tobacco consumption. In India, according to modified B. G. Prasad's socio-economic classification, almost 88.64% and 86.37% subjects showed monthly income in the range of Rs. 500 to 4999 /- in case and control group respectively.[20] And Amarasinghe *et al* conducted a study in 2019 in Sri Lanka where oral cancer was highly prevalent and found very high out-of- pocket costs for all patients, most of whom were from low socioeconomic backgrounds.[21] There was statistically significant association between monthly income and oral cancer which is similar to this study due to indistinguishable geographical structure and susceptibility of oral cancer in low socio-economic situation.

The odds ratio for tobacco consumption indicated that participants who consumed tobacco were about 31.6 times (OR = 31.6, 95% CI 15.26- 65.64) more likely to have oral cancer. About 72.1% cases consumed smokeless tobacco compared to 43.5% controls. Al Agili and Park in 2013 found that smokeless tobacco (SLT) is reported to be used among adolescents in Saudi Arabia and the youngest patient was 18 years old. The study conducted in Jeddah, Saudi Arabia, which targeted middle school males in a low socioeconomic area, showed that the mean age of users was 15.7 years. These young males reported starting the habit as young as 12.9 years old and an association was found with the frequency of SLT use.[22] Young users chewed tobacco about five times daily, leaving it for ten minutes each time where 47.4% of the patients chewed SLT one to six times daily with a mean duration of 12.2 years. The mean duration of SLT use reported by Amer *et al*. was 27.1 years.[23] In our study, however, an association was found with the frequency of SLT use which is similar to Al Agili and Park's study due to conduct the study in males in a low socioeconomic area where SLT especially betel quid with is very common. Duration of SLT use was not statistically significant and this result might be affected by biasness of some patients. In other studies, have proved that dose dependency of that time, contact, and frequency of use would increase the risk of developing oral cancer.[24-26] Boffetta *et al* conducted a study in which they found that betel quid with tobacco had a seven-fold higher risk for developing oral cancer as compared to no chewers, OR 7.1 [4.5–11.1].[27] A case-control study of the MENA region was conducted in Yemen by Nasher *et al* with 60 squamous cell carcinoma cases and 120 controls. It revealed that the subjects using SLT demonstrated higher odds (OR=149.5; 95% CI: 12.3–1817.25) of oral cancer than non-users.[28] Later, Quadri *et al* reported that SLT users had nearly 37 times (OR=37.24; 95% CI: 12.25–113.21) higher odds of developing oral cancer in comparison to non-users.[26] A study conducted by Ariyawardana in Sri Lanka in 2006, demonstrated that SLT chewing habit was the commonest both more likely to have oral cancer in cases and controls. Furthermore, it was revealed that 63% of oral cancer patients used to smoke tobacco and 55% had both SLT and smoking habits. A small proportion of oral cancer patients (9.4%) had both betel chewing and smoking habits. Also reported betel quid with tobacco was the most common habit (84%) among Sri Lankan patients with oral cancer. Logistic regression has shown that the betel chewing has the highest risk in developing oral cancer with OR ¼ 171.83 (95% CI: 36.35–812.25).[29] In another study, the relative risk for oral cancer with chewing types of SLT products (n = 46) was higher with an OR of 4.37 (95% CI = 3.27 to 5.83). The individual products that showed the highest association of OR with 8.67 (95% CI = 3.59 to 20.95) were Gutkha followed by 7.18 (95% CI = 5.48 to 9.41) pan tobacco/areca nut + lime + tobacco, 4.18 (95% CI = 2.37 to 7.38) for oral snuff.[30] A study conducted in Hunan province, China from January 2014 to September 2015, demonstrated that the OR was significantly elevated for high levels of betel quid intake and a long duration of consumption. The adjusted OR (AOR) was 8.40 and 8.07 for those who had been chewing for more than 20 years and for those who chewed more than 20 Quids per day (p<.001) respectively. Subjects with the habit of chewing betel quid with Zarda at an early age (<30 years) tended to have a higher OR than those who started chewing at a later age (>30 years) (a OR ¼ 15.32, 95% CI: 3.44-68.26, p<.001). There was a linear relationship between oral cancer and betel quid with Zarda consumption and duration. The risk of oral cancer increased with an increase in the number of betel Quids chewed with Zarda (p<.001).4 In the present study, 37.3% cases had consumed Sadapata 9-20 times and 25.0% cases had

kept Gul in their buccal mucosa 8 times per day daily with no consumption by the control group. Gupta and Ray found in their study that 69.4% patients having habit of chewing betel leaf and highest multiple ulcers, 47.1% reported for patients taking Gul inside mouth. In the South Asian region over one third of tobacco consumed was smokeless. More than 90% cases reported using tobacco products in Asian countries. Betel quid chewing was the most common form of chewing in Asia-Pacific regions. The incidence of oral cancer was 123 times higher in those who smoked, drank alcohol and chewed betel quid than in avoiders.[31]

Some of the limitations are inherent to this case-control study design, such as recall and selection bias, under-/over reporting of exposure status, retrospective exposure assessment and uncontrolled confounding. Moreover, the potential for selection bias existed may trend to mitigate the true association and lead to null results. Even though the association might be underestimated due to such selection bias, a significant association between smokeless tobacco consumption and the risk of oral cancer evident in this study. The present age and gender matched case control study suggested smokeless tobacco related essential risk factors associated with oral cancer. It had also provided the information about the hazardous effect of smokeless tobacco consumption by the rural, illiterate and low income people. Study findings preserve crucial policy inferences in arranging effective interventions and health programs to prevent risk factors of oral cancer in diverse population groups of the country.

CONCLUSION

Consumption of tobacco was significantly higher among cases than in controls. Tobacco consumption had a significant risk of developing oral cancer. Smokeless tobacco consumption had significantly higher risk of developing oral cancer than tobacco smoking. Sadapata and Gul use had a significant risk of developing oral cancer. Participants, being illiterate and completed education up to primary level with low income category were more likely to consume smokeless tobacco associated with developing oral cancer. To reduce oral cancer, the rural, illiterate and low income people should be motivated to create awareness about the high risks of smokeless tobacco and its hazards. To prevent oral cancer, necessary steps should be taken for preventing the availability of SLT products for any age group from all small and local producers across the states, the country should prepare proper national policy guidelines about the availability of smokeless tobacco products.

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