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Association between Smokeless Tobacco Uses and Oral Cancer

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Abstract

Introduction: *Smokeless tobacco has been linked to oral cancer for decades. The incidence of oral cancer is particularly high in some regions, especially in South and Southeast Asia, including Bangladesh.*

Objective: *The aim of current study was to evaluate the risk of oral cancer among smokeless tobacco users in Bangladesh.*

Methodology: *A case-control study was conducted from July 2017 to June 2018. The case group consisted of patients diagnosed with oral cancer who were receiving treatment at the Department of Oral & Maxillofacial Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bangladesh Multicare Hospital (BMH), Dhaka, Bangladesh. The control group included attendants of various cancer patients visiting the hospital during the study period. Odds ratios (OR) and 95% confidence intervals (CI) were calculated, and all reported p-values were considered significant at a threshold of less than 0.05.*

Results: *The odds ratio (OR) for "smokeless tobacco users" comparing cases to controls was 4.98, with a 95% confidence interval (CI) of 2.76 to 9.01. The OR for snuff users was 4.82, with a 95% CI of 2.37 to 9.80, while the OR for betel leaf users was 4.42, with a 95% CI of 1.66 to 11.91. These results were adjusted for smoking and age.*

Conclusions: *The current study provided strong evidence for smokeless tobacco use to be an independent risk factor for oral cancer.*

Keywords: *Smokeless tobacco, risk, snuff, oral cancer, South Asia, Bangladesh*

1. INTRODUCTION

Oral cancer is one of the most common noncommunicable diseases worldwide, with an estimated 275,000 new cases diagnosed each year [1]. This term refers to cancers that develop in the tissues of the oral cavity (the mouth) or the oropharynx (the part of the throat that is located at the back of the mouth) [2]. Together with other head and neck cancers, oral cancer ranks as the sixth most prevalent type of cancer globally and is among the leading causes of death in developing countries [3, 4, 5]. The countries in the South Asian region—including India, Pakistan, Afghanistan, Bangladesh, Sri Lanka, Bhutan, Nepal, Iran, and the Maldives [6]—are particularly affected by this issue, with oral cancer typically ranking either first or second in terms of cancer prevalence in these nations [7]. Researchers have investigated the reasons for the high prevalence of head and neck cancers in South Asia to some extent, but a lack of research infrastructure in most developing countries has hindered comprehensive studies on the epidemiology of these conditions in the region [8].

One major risk factor contributing to the high incidence of head and neck cancers and oral potentially malignant diseases (OPMD) in South Asia is the use of smokeless tobacco (SLT) [9]. It is estimated that over 90% of the global smokeless tobacco burden occurs in South Asia, with around 100 million people using smokeless tobacco in India and Pakistan alone [10, 11]. SLT is consumed in various forms, ranging from chewing tobacco that is not mixed with any other

ingredients to a mixture of tobacco with other substances, such as in betel quid, areca nut with tobacco, Naswar, paan-masala with tobacco, Gutkha, Khaini, and Mishri [12, 13]. Smokeless tobacco contains approximately 28 known carcinogens. These include nonvolatile alkaloid-derived tobacco-specific N-nitrosamines and N-nitrosamino acids as the primary group, while volatile tobacco-specific nitrosamines, volatile aldehydes, and certain polycyclic aromatic hydrocarbons have also been identified in smokeless tobacco products [14]. Smokeless tobacco (SLT) has a higher rate of nicotine absorption compared to smoke [15, 16]. Tobacco product usage is one of the leading causes of preventable deaths, resulting in over 6 million fatalities globally each year [17]. The objective of this study was to find the relationship between smokeless tobacco use and oral cancer. Ethical clearance and written consent were assured before the study.

2. Objectives

- **General Objective:** The primary aim of this study was to evaluate the reason for oral cancer among non-smoking people.
- **Specific Objective:** This study is targeted to find the association between smokeless tobacco use and oral cancer.

3. Methodology

This cross-sectional study included 250 patients with positive test results for oral cancer who visited the Department of Oral & Maxillofacial Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bangladesh Multicare Hospital (BMH), Dhaka, Bangladesh, from July 2017 to June 2018. The present study included all adult patients of 18 years and above. Patients were divided into cases (who were undergoing oral cancer at BSMMU) consisting of 110 people and controlled (who were primarily detected with oral cancer but did not start treatment) consisting of 140 people.

- **Inclusion Criteria:** The current study included adult patients aged 18 or more than 18.
- **Exclusion Criteria:** Patients who were more than 18 but smokes and non-Bangladeshi were excluded from this study. People with a history of diseases or conditions which could have a causal association with oral cavity cancer were also excluded as well.

Participants completed self-administered surveys, and information about the study's objectives and the confidentiality of the questionnaire was provided. Data analysis involved both descriptive statistics, such as calculating frequencies and percentages, and inferential statistics, including Fisher's exact test. The significance level of $p \leq 0.05$ with a 95% confidence interval for determining statistical significance was applied. IBM SPSS software v.27.0.1 (IBM Corp., Armonk, NY) was used for data analysis. The hospital authority gave ethical clearance and well-informed written consent was ensured before the study.

4. Result

Majority of study participants were in the age group between 51–65 years. The case and controlled were age-matched (P = 0.090). Of the 110 cases, 62.2% were males and 37.8% were females (P < 0.001). Where, out of 140 controlled, the males and females were 88.3% and 11.7%, respectively (P <0.001) as shown in Table 1. Out of 110 cases, 58 (64.4%) had the habit of SLT use, while out of 140 controls, 32 (26.7%) had this habit [Table 1]. The odds ratio (OR) for ever smokeless tobacco (SLT) users was 4.98 (95% CI; 2.76–9.01) with a p-value of <0.0001. After adjusting for age and smoking, the adjusted OR was 4.71 (95% CI; 2.53–8.74), significant at P < 0.001. When accounting for gender, females had an increased risk of oral cavity cancer compared to males, with an OR of 28.29 (95% CI; 9.93–80.52, P < 0.001). The highest adjusted OR was for snuff users at 4.82 (95% CI; 2.37–9.80, P < 0.001). Betel nut users had an OR of 4.67 (95% CI; 1.14–19.12, P = 0.032), and betel leaf users had an OR of 4.42 (95% CI; 1.66–11.91, P = 0.003), as shown in Table 2. The amount of smokeless tobacco users among case and controlled groups is shown in figure 1.

Table 1. *Basic characteristics of study population (n=250).*

Characteristics		Case (n=110)	Controlled (n=140)	P-value
Age (years)	18-35	0	11 (8.3%)	0.09
	36-50	10 (8.9%)	21 (15%)	
	51-65	71 (64.4%)	77 (55%)	
	65+	29 (26.7%)	31 (21.7%)	
Gender	Male	68 (62.2%)	124 (88.3%)	<0.001
	Female	42 (37.8%)	16 (11.7%)	

Literacy	Primary	20 (17.8%)	35 (25.0%)	0.003
	Middle	0	11 (8.3%)	
	High / Intermediate	17 (15.5%)	14 (10.0%)	
	Graduate	5 (4.4%)	1 (1.4%)	
	Illiterate	68 (62.2%)	79 (56.7%)	
Smoking status	Ever smokers	22 (20%)	18 (13%)	0.134
	SLT users	71 (64.4%)	37 (26.7%)	<0.001

Table 2. *Association of oral cancer with smokeless tobacco (SLT) use (n=250)*

Variables		Cases (n = 110)	Controlled (n = 140)	Unadjusted OR	95% Cl	Adjusted OR	95% CF	Adjusted OR	95% Cl
Uses	SLT users	68	42	4.98	2.76-9.01	4.71	2.53-8.74	28.29	9.93-80.52
	Never user	42	98	1.00 (referent)	-	1.00 (referent)	-	1.00 (referent)	-
Type of SLT used	Snuff	46	24	4.95	2.51-9.77	4.82	2.37-9.80	32.65	10.6-100.4
	Betel leaf	16	13	5.5	2.15-14.08	4.42	1.66-11.91	23.18	6.23-86.2
	Betel nut	10	9	4.12	1.09-15.57	4.67	1.14 19.12	21.09	3.59-123.6
	Never users	38	93	1.00 (referent)	-	1.00 (referent)	-	1.00 (referent)	-
Duration of snuff use	< 10 years	15	10	3.7	1.20-11.4	5.45	1.59-18.71	21.44	4.89-94.01
	10—20 years	9	10	1.23	0.33-4.56	1.73	0.43-6.99	5.81	1.23-27.45
	>20 years	27	14	4.52	1.95-10.52	3.25	1.37-7.71	6.45	2.50-16.65
	Never users	59	105	1.00 (referent)	-	1.00 (referent)	-	1.00 (referent)	-
Frequency of snuff use	Daily	-	-	5.22	2.66-10.27	5.22	2.56-10.65	34.5	11.2-106.1
	Frequently in a week	-	-	6.6	2.16-20.2	6.8	2.09-22.1	45.8	9.74-216.1
	Weekly	-	-	5.5	0.961-31.5	4.82	0.76-30.4	32.4	3.64-287.8
	Frequently in a month	-	-	2.2	0.56-8.71	1.43	0.35-5.83	5.48	0.97-31.03
	No	-	-	1.00 (referent)	-	1.00 (referent)	-	1.00 (referent)	-

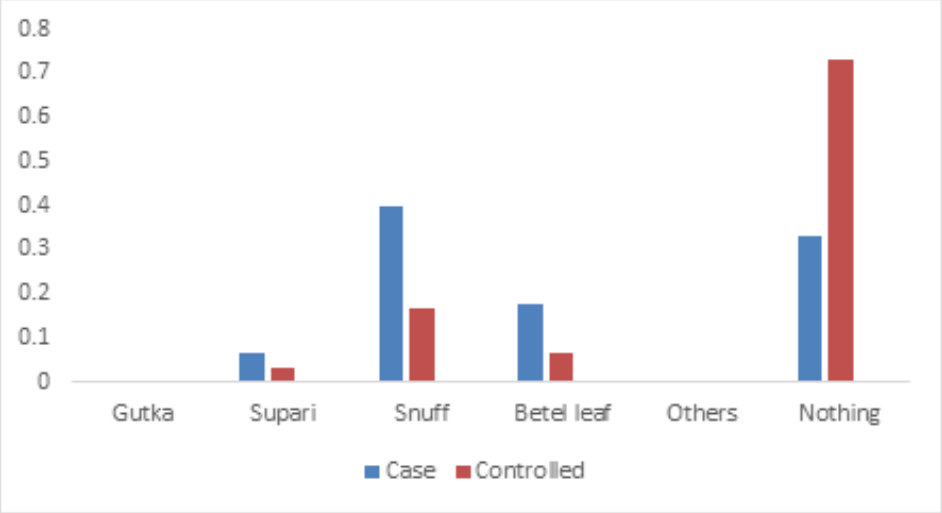

Figure 1. *Smokeless tobacco users among case and controlled groups*

5. Discussion

The use of smokeless tobacco (SLT) is prevalent across various South Asian countries. Commonly available smokeless tobacco products include snuff and betel leaf, while less common products include gutka, betel nut, and certain types of chewing tobacco. This study was conducted as a pilot project to evaluate the risk of oral cancer in the Bangladeshi population related to the use of smokeless tobacco products. Current findings indicate a positive correlation between smokeless tobacco use and oral cavity cancer among participants. The odds ratio (OR) for those who have ever used smokeless tobacco was calculated, showing that participants who consumed such products were approximately five times (OR = 4.98) more likely to develop oral cavity cancer compared to those who had never used smokeless tobacco. This result was statistically significant, with a p-value of 0.0001. Such a substantial and statistically significant increase in the odds ratio emphasises the need for further research with a larger sample size to ensure adequate study power. These findings align with studies conducted in other countries in the region, which report relative risks for oral cavity cancer ranging from 1.2 to 12.9 with smokeless tobacco use. A recent meta-analysis comparing studies in South Asia calculated the pooled OR for chewing tobacco and its associated risk of oral cancer as 4.7 (3.1–7.1) [18-20].

However, some differences in risk estimates were observed among populations primarily using gutka, betel quid, or snuff. The risk of developing oral cancer was particularly high among snuff users, with an estimated OR of 23.7 (6.9–81.0) compared to non-users [19]. Studies from Europe and North America have reported a relative risk of 1.8 (1.1–2.9) for developing oral cancer due to smokeless tobacco use [21]. The regional disparities in relative risk might reflect the different types of smokeless tobacco products used in various locations. In the study region, snuff accounts for about 40% of oral cancer cases. In our study, participants who consumed betel nut had an adjusted OR for cancer of 4.67 (statistically significant with a p-value of 0.032). Betel users showed a likelihood of 4.4 times (OR = 4.42) of developing oral cavity cancer compared to non-users. Additionally, snuff users had 4.82 times greater likelihood of developing oral cavity cancer than non-users ($P < 0.001$). Interestingly, smokeless tobacco use in females significantly increases the likelihood of oral cavity cancer, with an OR of 28.29 (9.93–80.52). This may be due to a lower baseline risk of oral malignancies among women, attributed to the lower prevalence of alcohol consumption and smoking—two other major risk factors for oral cancer. In line with findings from other South Asian studies, the odds ratio among women ranged from 6.5 to 45.8, while for men, it ranged from 1.5 to 10.9. To account for the effect of gender on cancer risk, the odds ratios based on age and smoking were adjusted, both separately and collectively, as shown in the last column of Table 3. The duration and frequency of snuff use also impacted the risk of oral cavity cancer, consistent with findings from other South Asian studies [19]. The current study identified snuff as the most common risk factor for oral cavity cancer, with the buccal mucosa and alveolar ridge (upper/lower) identified as primary affected sites among snuff users. Literature published by the International Agency for Research on Cancer (IARC) indicates that the highest number of cases of buccal mucosa cancer occurs among snuff users, as this area directly contacts the tobacco [22]. Additionally, a meta-analysis focusing on smokeless tobacco use among head and neck cancer cases indicated that snuff use is more frequently associated with buccal mucosa cancer [23].

6. Conclusion

This study demonstrated a statistically significant positive association between the use of smokeless tobacco and the risk of oral cancer in patients, particularly among women. A literature review indicates that these findings align with similar studies conducted in the region and globally. A more comprehensive study that samples from various parts of the country could provide a better understanding of the disease's epidemiology and have a greater impact on public awareness.

Limitations of the Study

A small population and long study duration may affect the overall outcome of the study.

Funding

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Conflicts of Interest

No conflicts of interest were found

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