Research Article

A study on the effect of smokeless tobacco on oral cancer done in a Tertiary Care Hospital in Southern India

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ABSTRACT

Background: Oral cancer is a major problem in India. The incidence is 10.1 cases per lac for males and 4.3 per lac in females. The risk factors for the development of oral cancers include smokeless tobacco. **Objectives**: The objectives of this study were to find the association between smokeless tobacco and oral cancer. **Materials and Methods**: A case–control study done at a tertiary care hospital, Bengaluru, India. Study subjects included new cases of oral cancer attending the hospital during the study period and equal number controls. Data collection was done by interview method. **Results**: Tobacco chewing with an odds ratio (OR) of 2.3 was significantly associated with the risk of oral cancer. Paan chewing with tobacco showed greater risk than paan chewing without tobacco. Chewers who started the habit before the age of 25 years showed an higher risk with OR of 4.5. An increasing trend in oral cancer risk with increase in the frequency and duration of paan chewing was found. The risk was 30 times higher for those with quid retention as compared to never chewers. Duration of quid retention for ≤5 h showed 29.6 times higher risk and for more than 5 h showed 33.3 times higher risk, as compared to those without quid retention. **Conclusion**: Smokeless tobacco shows higher risk for oral cancer. There is a great need to augment tobacco control measures and educate the public about harmful effects of smokeless tobacco.

KEY WORDS: Smokeless Tobacco; Case-control Study; Oral Cancer

INTRODUCTION

Modern epidemics are assuming importance among the adult population in both developed and developing countries. In the developing countries, cancer is one among the 10 most common causes of mortality.[1] This cancer epidemic is due to the combined effect of increased life expectancy and the high or increasing levels of prevalence of cancer risk factors.[2] India has one of the highest incidences of oral cancer in the world.[3] The risk factors for the development of oral cancers include tobacco smoking, tobacco chewing, oral snuff, chewing betel quid, consumption of alcohol, the presence of potentially malignant oral lesions, and poor oral hygiene.[4] Oral cancer is any cancerous tissue growth located in the mouth. It may arise as a primary lesion originating in any of the oral tissues, by metastasis from a distant site of origin, or by extension from a neighboring anatomic structure.[5] Tobacco is the most important risk factor for oral cancer. Prevalence of tobacco use has declined in some high income countries but continues to increase in low- and middle-income countries. Tobacco use can be broadly classified as smoking tobacco and smokeless tobacco. The types of smokeless tobacco are chewing tobacco and snuff. Types of chewing tobacco are as follows: Paan, mainpuri tobacco, mawa, mishri, zarda, gudakhu, and gutka. Paan: The most common form of chewing tobacco. Paan means betel leaf.

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Quid contains areca nut which may be used raw, baked, or boiled lime obtained from limestone and may also include aniseed, catechu, cardamom, cinnamon, coconut cloves, sugar, and tobacco. Mainpuri tobacco includes tobacco, slaked lime, finely cut areca nut, camphor, and cloves. People in Uttar Pradesh use this type of tobacco. Mawa: A preparation containing thin shavings of areca nut with the addition of some tobacco and slaked lime. Usually wrapped in cellophane papers and tied in the shape of ball. Most commonly seen in Gujarat. Mishri: Prepared by roasting tobacco on a hot metal plate until it is uniformly black. It is then powdered and used with catechu used commonly in Maharashtra. Zarda: Tobacco leaf is boiled in water along with lime and spices until evaporation. The residual tobacco is then dried and colored with dyes. Gudakhu: It is the paste of powdered tobacco, molasses, and other ingredients primarily used to clean teeth. It is mostly used in Bihar. Gutkha: It is prepared by crushing the betel nut, tobacco, and adding some sweet or savory flavor.[6] In this context, there is need for more in-depth studies of various modifiable risk factors in India. This will help us to evolve effective preventive measures to reduce the burden. Thus, the present study would attempt to find the strength of association between smokeless tobacco and oral cancer.

MATERIALS AND METHODS

The case–control study was conducted at a tertiary care hospital located in Bengaluru for 1 year after obtaining Institutional Ethical Committee Clearance. The proportion of smokers among controls and cases was considered to calculate the sample size. The considered level of probability was 5% (α error) and with the β error of 20% and a permissible error of 0.15. Total sample size was 400.

Newly diagnosed case of oral cancer of all age groups and all stages of the disease confirmed by biopsy and histopathological report were included. For each case, one control was selected. Matching was done for age and gender. Controls included hospital controls and patient attendees. Hospital controls included patients with other cancers, other than tobacco-related cancers. Patient attendees were either their relatives or friends. Among cases, terminally ill patients and cases with oral cancer as secondary carcinoma were excluded. Among hospital controls, patients with tobacco-related cancers such as cancer of esophagus, larynx, lungs, and urinary bladder were excluded. Consent was obtained from all the study subjects. Information regarding the sociodemographic details, the exposure to risk factors such as smokeless tobacco in terms of age at start of habit, type used, dose, and duration of exposure was obtained with the help of pretested semi-structured questionnaire by interviewing the study subjects.

Statistics

Descriptive statistics and inferential statistics were used. Chi-square test of significance was employed. To find the strength of association, odds ratio (OR) along with 95% confidence interval (CI) was estimated. A significance level of $P \leq 0.05$ was considered for statistical significance.

RESULTS

Majority of the study population, 39.0% belonged to the age group of 50–59 years. The average age of oral cancer was 54.8 years with a standard deviation of 10.70 years. The study population consisted of 74.0% males and 26.0% females. Hindus constituted the maximum number followed by Muslims and Christians. A higher proportion of illiterates and unskilled workers were found among cases compared to controls.

It was observed that 94 (47.0%) of the cases were chewers as compared to 56 (28.0%) of the controls and 106 (53.0%) of the cases were non-chewers as compared to 144 (72.0%) of the controls. A statistically significant association was found between chewing habit and oral cancer. The risk of developing oral cancer was 2.3 times higher among chewers compared to non-chewers [Table 1].

Paan chewing with tobacco showed greater risk for oral cancer than paan chewing without tobacco. The risk of developing oral cancer among those who chewed only tobacco was 4.9 times higher and for those who chewed tobacco+betel leaf+areca nut+lime was 2.5 times higher when compared to never chewers. Chewers of betel leaf+areca nut+lime showed a borderline increase in risk with OR 1.7 and betel leaf+areca nut showed non-significant increase in risk for oral cancer OR 1.3 [Table 2].

Table 1: ORs for oral cancer according to chewing habit

Chewing habit	*n* (%)		OR (95% CI)
	Cases	Controls	
Yes	94 (47.0)	56 (28.0)	2.3 (1.50–3.45)
No	106 (53.0)	144 (72.0)	1.0
Total	200 (100)	200 (100)	

(Chi-square value=15.53, df=1, P<0.001). (OR: Odds ratio, 95% CI: 95% confidence interval, df: Degrees of freedom)

Table 2: ORs for oral cancer according to type of paan chewing

Type of paan chewing	*n* (%)		OR (95% CI)
	Cases	Controls	
Tobacco only	11 (5.5)	3 (1.5)	4.9 (1.35–18.18)
Tobacco+betel leaf+areca nut+lime	51 (25.5)	27 (13.5)	2.5 (1.51–4.36)
Betel leaf+areca nut+lime	29 (14.5)	23 (11.5)	1.7 (0.93–3.12)
Betel leaf+areca nut	3 (1.5)	3 (1.5)	1.3 (0.26-6.84)
Never chewers	106 (53.0)	144 (72.0)	1.0
Total	200 (100)	200 (100)	

(Chi-square value=18.85, df=4, P<0.001). OR: Odds ratio, 95% CI: 95% confidence interval

It was observed that earlier the age at start of chewing habit greater the risk of developing oral cancer, i.e. chewers who started the habit before the age of 25 years showed an higher risk with an OR of 4.5 as compared to those who started the habit after 25 years [Table 3].

An increasing trend in oral cancer risk with increase in the frequency of paan chewing was found. The risk of developing oral cancer was 1.7 times higher for ≤5 paans/day, 2.5 times higher for 6–10 paans/day, and 8.8 times higher for >10 paans/day compared to never chewers [Table 4].

A dose-response relationship was observed between duration of chewing habit and oral cancer, i.e., greater the number of years of chewing betel quid, the higher the risk as compared with the non-chewers. Duration of chewing habit for ≤20 years showed an OR of 2.0, 21–30 years showed an OR of 2.1, and more than 30 years showed an OR of 2.5 compared to never chewers [Table 5].

It was observed that among cases 64 (32.0%) had the habit of quid retention as compared to only 3 (1.5%) of the controls. The difference in proportions between cases and controls with respect to quid retention was found to be statistically significant ($P < 0.001$). The risk of developing oral cancer was 30 times higher for those with quid retention as compared to never chewers [Table 6].

There was increase in the risk as the duration of quid retention increased. Duration of quid retention for ≤5 h showed 29.6 times higher risk and for more than 5 h showed 33.3 times higher risk, as compared to those without quid retention [Table 7].

DISCUSSION

The risk of developing oral cancer was 2.3 times higher in chewers with an OR of 2.3 compared to non-chewers. Betel quid with tobacco showed higher risk of developing oral cancer compared to those who chewed betel quid without tobacco. As the frequency and duration of chewing, betel quid increased the risk of developing oral cancer also increased. The risk of developing oral cancer was 30 times more for those with quid retention and chewers with more than 5 h quid retention showed an OR of 33.3 as compared never chewers.

In a similar study done in South India, tobacco chewers had 5-fold risk (95% CI: 4.26–5.97) for oral cancer[7] and significant dose-response relationships were observed for duration of chewing and average daily amount of consumption of smokeless tobacco in the risk of developing oral cancer.[8] In a study among people with chewing habits, those who chewed betel quid with tobacco showed an OR 3.19, 95% CI: 0.48–2.13 and tobacco alone (OR 2.89) showed a greater risk than controls.[9] Chewing tobacco was found to be associated with the occurrence of oral cancer, with highest prevalence observed in people who had a history of chewing for more than 20 years. The use of tobacco both in smoking and smokeless forms had a significant association (OR = 12.14, $P = 0.007$) with the occurrence of oral cancer.[10] The present study findings are in confirmation with findings of other investigators of the above-mentioned studies.

Table 3: ORs for oral cancer according to age at start of the chewing habit

Age at start (years)	*n* (%)		OR (95% CI)
	Cases	Controls	
≤25	63 (31.5)	19 (9.5)	4.5 (2.54–8.0)
>25	31 (15.5)	37 (18.5)	1.1 (0.66–1.95)
Never chewers	106 (53.0)	144 (72.0)	1.0
Total	200 (100)	200 (100)	

(Chi-square value=31.22, df=2, $P<0.001$). OR: Odds ratio, 95% CI: 95% confidence interval

Table 4: ORs for oral cancer according to frequency of paan chewing

Frequency (times per day)	*n* (%)		OR (95% CI)
	Cases	Controls	
≤5	50 (25.0)	38 (19.0)	1.7 (1.08–2.89)
6–10	30 (15.0)	16 (8.0)	2.5 (1.30–4.85)
>10	14 (7.0)	2 (1.0)	8.8 (1.93–40.0)
Never chewers	106 (53.0)	144 (72.0)	1.0
Total	200 (100)	200 (100)	

(Chi-square value=20.45, df=3, $P<0.001$). OR: Odds ratio, 95% CI: 95% confidence interval

Table 5: ORs for oral cancer according to total duration of chewing habit

Total duration of habit (years)	*n* (%)		OR (95% CI)
	Cases	Controls	
≤20	23 (11.5)	15 (7.5)	2.0 (1.03–4.18)
21–30	33 (16.5)	21 (10.5)	2.1 (1.16–3.89)
>30	38 (19.0)	20 (10.0)	2.5 (1.42–4.69)
Never chewers	106 (53.0)	144 (72.0)	1.0
Total	200	200	

(Chi-square value=15.86, df=3, $P<0.005$). OR: Odds ratio, 95% CI: 95% confidence interval

Table 6: ORs for oral cancer according to habit of quid retention among chewers

Quid retention	*n* (%)		OR (95% CI)
	Cases	Controls	
Yes	64 (32.0)	3 (1.5)	28.9 (8.84–90.9)
No	30 (15.0)	53 (26.5)	0.76 (0.46–1.28)
Never chewers	106 (53.0)	144 (72.0)	1.0
Total	200 (100)	200 (100)	

(Chi-square value=80.63, df=2, $P<0.001$). OR: Odds ratio, 95% CI: 95% confidence interval

Table 7: ORs for oral cancer according to duration of quid retention

Duration of quid retention (hours)	*n* (%)		OR (95% CI)
	Cases	Controls	
≤5	41 (20.5)	2 (1.0)	29.6 (7.04–125)
>5	23 (11.5)	1 (0.5)	33.3 (4.44–250)
Non-quid retention	136 (68.0)	196 (98.5)	1.0
Total	200 (100)	200 (100)	

(Chi-square value=79.62, df=2, $P<0.001$). OR: Odds ratio, 95% CI: 95% confidence interval

In a study done by Muwonge *et al*. increased risk was seen in individuals who had chewed more than 5 times a day and those who had chewed more than 20 years or more. An increased risk was also seen among those chewing paan without tobacco significant for females with OR = 5.4 and borderline significance for males with OR = 3.3. Both keeping and not keeping, the quid in the mouth overnight increased the effect of chewing further among both male and female chewers.[11] An increased risk of about 2-fold was observed among chewers without tobacco, whereas among chewers with tobacco, the increase in risk was 5-fold for oral cancers. A significant dose-response relationship was observed between the duration of chewing and cancer up to 40 years of chewing.[12] However, the present study could not analyze the results separately for males and females.

Case–control studies have some important limitations and are subject to bias. Bias due to confounding was removed by matching. Recall bias was minimized by making the subjects to remember certain important local events. The cases and the controls were selected from a single hospital, but the hospital where the study was carried out is a comprehensive and regional center for cancer research and treatment in Karnataka. Control patients hospitalized for cancers related to alcohol and tobacco consumption were excluded from the study, thereby minimizing the selection bias. Interviewer's bias could not be completely eliminated but was minimized by equal duration of interview for both cases and controls. Heterogeneous group of controls was selected, but the analysis could not be done separately because of smaller sample size.

CONCLUSION

Smokeless tobacco shows higher risk for oral cancer. Thus, there is a great need to augment tobacco control measures and educate the public about harmful effects of tobacco consumption.

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