Original Research Article

Tobacco and risk of oral cancer: a case control study in a tertiary care centre of Dibrugarh district

Angchuman Chetia*, Rupali Baruah

Department of Community Medicine, Assam Medical College and Hospital, Dibrugarh, Assam, India

*Correspondence:
Dr. Angchuman Chetia,
E-mail: chetiaangchuman@gmail.com

ABSTRACT

Background: Oral cancer is a disease of antiquity. This chronic disease is a public health problem both in developing as well as developed countries and is among the top three cancers in India. In Assam, some aspects of traditional lifestyle and dietary habits are likely to contribute to the increasing cancer trend.
Methods: The hospital-based case control study was undertaken in AMCH, Dibrugarh. Study subjects included were clinically and histopathologically confirmed new cases of oral cancer attending the hospital during the period of June 2018 to May 2019 and equal number of age and sex matched controls. The total sample size including both cases and controls was 116. A predesigned pretested schedule was used for collecting data.
Results: Tobacco chewing was the strongest risk factor associated with oral cancer with odds ratio of chewers 6.13 (95% CI, 2.26-16.60). Statistically significant association was seen with duration, age at start, frequency of chewing and retaining tobacco quid overnight. The risk of developing oral cancer was 3.60 times higher (95% CI of (1.45-8.93)) among smokers compared to non-smokers.
Conclusions: The incidence of oral cancer is on the rise. Due to the well-established role of lifestyle factors in the development of oral cancer, they should be considered an important cause of avoidable morbidity and mortality in India, and their prevention should be an important target of public health initiatives.

Keywords: Tobacco, Oral cancer, Smokers, Non-smokers

INTRODUCTION

Oral cancer is a disease of antiquity. The earliest of its description can be found in "Sushruta Samhita", a Sanskrit surgery text from 600 BC, that refers to oral cancer as "Mukharbuda", a malignancy of the buccal cavity.[1]

This chronic disease is a public health problem both in developing as well as developed countries. There are an estimated 6,57,000 new cases of oral cavity and pharynx every year accounting to more than 3,00,000 deaths.[2] Oral cancer is of major concern in South-East Asia primarily because of the prevalent oral habits of betel quid chewing, smoking and alcohol consumption. India has the world's highest burden that accounts for one-third of the global burden of cancers of the oral cavity.[3]

Majority of the cases are reported from rural areas where access to health care is quite poor. Moreover, lack of knowledge and awareness about oral cancers and financial difficulty in affording health care services may lead to further delay in presentation of cases. As a result of which the disease progresses to advanced stages resulting in poor prognosis. The paradox is that mouth is the most accessible area for visual examination, but still oral cancers are being diagnosed at later stages. Screening programs to find oral cancer cases in the early stages could reduce morbidity and mortality to a significant extent. Identifying high-risk individuals could help in

controlling oral cancer by creating awareness of oral cancer and its risk factors.

METHODS

Study setting

The case control study was conducted in an Assam Medical College and Hospital of Dibrugarh district of Assam for a period of 1 year from June 2018 to May 2019. In Dibrugarh district, this tertiary care centre provides health care facilities to the people of Dibrugarh and adjoining places.

Sample size

Taking the current adult tobacco users as 48.2% in Assam, anticipated odds ratio (OR) as 3.00, power 80%, Confidence interval (CI) 95%, the sample size calculated using Epi-info version 7 was estimated to be 58 Cases and same number of controls.[4] So the total sample size including both cases and controls was 116 taking cases to controls in the ratio of 1:1.

Selection criteria for cases and controls

A case is defined as a person aged 18 years and above diagnosed with cancers of oral cavity, both clinically and histopathologically, within the study period. The ICD-10 classification was used to designate oral cancer sites included in the study. In this study, oral cancer sites included were lip (C00), base of tongue (C01), other and unspecified parts of tongue (C02), gum (C03), floor of mouth (C04), palate (C05) and other unspecified parts of mouth (C06). Patients with benign tumours and those not providing consent were excluded from the study. A Control is defined as a person aged 18 years and above with no cancers of oral cavity and visited Assam Medical College during the study period. They were relatives or neighbours who visited or were care givers/attendants of cancer patients or hospital patients with medical conditions not related to tobacco or alcohol use.

Matching

To ensure comparability between cases and controls, matching was done. Age group intervals matched and sex matched controls were selected. For each case selected, a control was selected who is similar to the case in the age group and sex and coming from similar social background.

Sampling technique

The study was undertaken in Assam Medical College and Hospital in the Department of Dentistry and the Department of Otorhinolaryngology (ENT). Oral cancer cases were selected consecutively until the maximum time allocated for data collection or the estimated sample size is reached, whichever is earlier. The stipulated concluding date for data collection was May 2019, at which time case recruitment was stopped. Cases were selected after they were diagnosed with oral cancer and confirmed by histopathologically and clinically. However, some patients who had visited the hospital for diagnosis but who did not return to the hospital for further consultation or treatment could not be included in the study. Potential controls with proper matching were selected and recruited simultaneously. Controls were selected throughout the same period as the cases.

Data collection

A predesigned pretested schedule was the principal tool for collecting data. Prior to the commencement of data collection, the study participants were explained about the purpose of the study, procedures, risks and benefits of participating in the study and confidentiality and a close rapport was established. If the potential participants agreed to participate in the study, a written informed consent was sought.

Statistical analysis

Logistic regression analysis was done to test associations of the variable. Chi-square test was applied to test significance. To find the strength of association, OR along with 95% CI were estimated. A significance level of $p \leq 0.05$ was considered for statistical significance. Data was analysed using statistical package for the social sciences (SPSS) Software, version 25.0. OR corresponding to one habit were obtained after adjusting for the other habits (categorized into never and ever). The habits included were smoking habits, tobacco chewing, drinking habits and dietary habits (vegetarian/non-vegetarian).

RESULTS

A total of 58 cases and an equal number of age and sex-matched controls were included in the present study. The mean age of the study group was 53.50±10.36. The maximum number of cases (24) was in the age group of 56-65 years. 69% of the cases were male and 31% were females. 87.9% of the cases were Hindus while the remaining were Muslims. Majority of the study population belonged to class III socio economic status according to modified B. G. Prasad's classification (Table 1).

58.6% of the cases were smokers while in the control group, 32.8% were smokers. A statistically significant association was found between smoking habit and oral cancer. The risk of developing oral cancer was 3.60 times higher OR=3.6, 95% CI of (1.45-8.93) among smokers compared to non-smokers. In the present study, an increasing trend for oral cancer risk with the increasing duration of smoking was observed Among smokers, cancer risks increased steadily and markedly with longer duration of the smoking habit and were statistically

significant after 25 years of smoking habit (OR=4.85, 95% CI of 1.51-15.60) (Table 2).

Table 1: Distribution of cases according to socio-demographic characteristics.

Socio-demographic characteristics		Number	%
Age group (in years)	18-35	4	6.9
	36-45	9	15.5
	46-55	14	24.1
	56-65	24	41.4
	Above 65	7	12.4
Sex	Male	40	69
	Female	18	31
Religion	Hindu	51	87.9
	Muslim	7	12.1
Socio-economic class	Class I	8	13.8
	Class II	18	31
	Class III	21	36.2
	Class IV	10	17.2
	Class V	1	1.8
Educational status	Illiterate	9	15.5
	Primary	21	36.2
	Secondary	17	29.3
	Higher secondary and above	11	19

The risk of developing oral cancer was 2.73 times higher among smokers who smoked less than or equal to 10 bidis/cigarettes per day and 9.06 times higher for those who smoked 11-20 bidis/cigarettes per day, compared to non-smokers (OR=9.06; 95% CI, 1.84-44.56). However,

those smoking more than 20 times per day did not attain statistical significance (OR=2.03; 95% CI, 0.32-12.83) probably due to smaller number of cases and controls in this group (Table 2).

A statistically significant association was found between the age at start of habit and oral cancer It has been observed that earlier the age at start of habit greater the risk of developing oral cancer, i.e. those who started the habit at less than 20 years, the OR was found to be 7.61, those who started smoking at 20-24 years of age, the OR was 3.50 and for those who started after 25 years OR=2.84, compared to non-smokers (Table 2).

A statistically significant association was found between chewing habit and oral cancer. The risk of developing oral cancer was 6.13 times higher among chewers compared to never chewers of tobacco (OR=6.13; 95% CI, 2.26-16.60). Increased risk was seen among those who retain tobacco overnight (OR=8.58, 95% CI, 2.62-28.09) than those who did not retain tobacco overnight (Table 3).

The risk of developing oral cancer was 2.77 times higher among tobacco chewers who chewed less than 5 times per day and 8.69 times higher for those who chewed 5-9 times per day and 10.06 times higher for those who chewed 10 or more times per day compared to never chewers of tobacco and was found to be statistically significant. Maximal risk was observed for those who had chewed for a duration of more than 25 years (OR= 14.65; 95% CI, 4.04-53.02) and for those who chewed for less than 25 years had an OR of 3.66 (95% CI, 1.25-10.71) compared to never chewers of tobacco. This was found to be statistically significant (Table 3).

Table 2: OR and corresponding 95% CI for cancers of the oral cavity according to smoking habits.

Variables		Study participants		Adjusted odd's ratio[a] (95% CI)	P value
		Case (%)	Control (%)		
Smoking habit	Never	24 (41.4)	39 (67.2)	Reference	
	Ever	34 (58.6)	19 (32.8)	3.60 (1.45-8.93)	0.006
Duration of smoking (years)	Never	24 (41.4)	39 (67.2)	Reference	
	1-25	15 (25.9)	13 (22.4)	2.73 (0.91-8.18)	0.171
	>25	19 (32.8)	6 (10.3)	4.85 (1.51-15.60)	0.008
Frequency of smoking	Never	24 (41.4)	39 (67.2)	Reference	
	1-10	16 (27.6)	11 (19)	2.73 (0.92-8.13)	0.071
	11-20	12 (20.7)	6 (10.3)	9.06 (1.84-44.56)	0.007
	>20	6 (10.3)	2 (3.4)	2.03 (0.32-12.83)	0.450
Age start smoking (years)	Never	24 (41.4)	39 (67.2)	Reference	
	<20	8 (13.8)	3 (5.2)	7.61 (1.34-43.06)	0.022
	20-24	14 (24.1)	7 (12.1)	3.50 (1.06-11.48)	0.038
	≥25	12 (20.7)	9 (15.5)	2.84 (0.86-9.37)	0.087
Exposure to second hand smoke	No	30 (51.7)	32 (55.2)	Reference	
	Yes	28 (48.3)	26 (44.8)	1.174 (0.53-2.59)	0.692

[a]Adjusted for chewing tobacco (never/ever), drinking habits (never/ever) and dietary habits (vegetarian/non-vegetarian).

Table 3: OR and corresponding 95% CI for cancers of the oral cavity according to chewing habits.

Variables		Study participants		Adjusted OR (95% CI)	P value
		Case (%)	Control (%)		
Chewing habit	Never	9 (15.5)	24 (41.4)	Reference	
	Ever	49 (84.5)	34 (58.6)	6.13 (2.26-16.60)	0.000
Retaining tobacco overnight	Never	39 (67.20)	52 (89.70)	Reference	
	ever	19 (32.80)	6 (10.30)	8.58 (2.62-28.09)	0.000
Frequency of tobacco chewing per day	Never	9 (15.5)	24 (41.4)	Reference	
	<5	10 (17.2)	14 (24.1)	2.77 (0.83-9.30)	0.098
	5-9	18 (31)	11 (19)	8.69 (2.57-29.43)	0.001
	>10	21 (36.2)	9 (15.5)	10.063 (2.759-36.70)	0.001
Duration of chewing tobacco in years	Never	9 (15.5)	24 (41.4)	Reference	
	1-25	23 (39.7)	28 (48.3)	3.66 (1.25-10.71)	0.018
	>25	26 (44.8)	6 (10.3)	14.65 (4.04-53.02)	0.000
Age start chewing (years)	Never	9 (15.5)	24 (41.4)	Reference	
	<20	25 (43.1)	9 (15.5)	9.92 (3.09-31.86)	0.000
	20-24	15 (25.9)	11 (19.0)	8.95 (2.33-34.38)	0.001
	>25	9 (15.5)	14 (24.1)	2.15 (0.60-7.66)	0.239
Paan chewing	Never	3 (5.2)	23 (39.7)	Reference	
	With tobacco	49 (84.5)	22 (37.9)	20.49 (5.09-82.52)	0.000
	Without tobacco	6 (10.3)	13 (22.4)	4.63 (0.83-25.76)	0.081

aAdjusted for smoking habits (never/ever), drinking habits (never/ever) and dietary habits (vegetarian/non-vegetarian).

It has been observed that earlier the age at start of habit, greater is the risk of developing oral cancer, i.e. those who started the habit at less than 20 years, the OR was found to be 9.92, those who started chewing at 20-24 years of age, the OR was 8.95 and for those who started at after 25 years OR=2.15, compared to non-chewers of tobacco. Those who started the habit at less than 25 years were found to be statistically significant (Table 3).

DISCUSSION

In our present case-control study, tobacco chewing was confirmed to be the most important determinant of oral cancer. Tobacco use is culturally acceptable in most parts of this region and has been a tradition since ages which is likely contributing to the increasing cancer trend.

In our study, the peak occurrence of oral cancer is in the age group of 50-59 years. This shows that oral cancers are more common among older people although incidence is on the rise among those aged in the late 40s and early 50s. Males were twice as commonly affected by oral malignancies than females which may relate to dietary habits and higher lifetime consumption of alcohol and tobacco. The higher prevalence of oral cancer in Hindus relates to the larger ratio of this community in the general population rather than a relationship of the disease to a specific religion.

In our study, the risk of developing oral cancer was 3.60 times higher among smokers compared to non-smokers. The relationship between smoking and oral cancer has been established firmly by many epidemiological studies. The most important carcinogens in tobacco smoke are the aromatic hydrocarbon benzo-pyrene and the tobacco-specificnitrosamines (TSNs) namely 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) and N'-nitrosonornicotine (NNN).[5]

In a matched case–control study conducted in Uruguay, Stefani et al, found that tobacco smoking was positively associated with cancers of the oral cavity.[6] In another population based case control study conducted at Bhopal by Dikshit et al, it was found that the risk of getting oral cavity cancers was 4.3 for those who had smoked for more than 30 years compared to non-smokers. These findings are consistent with the findings of our study.[7]

Our present study shows that higher the frequency of smoking, greater is the risk of developing oral cancer. Balaram et al, Sankarnarayan et al, in their study revealed that smoking had significant predisposing effect on oral cancer.[8,9]

In our study, 84.5% of the Cases chewed smokeless tobacco in any forms (sada, zarda, gutkha, etc) while it is 58.6% in controls. Smokeless tobacco (SLT) products are known to contain many different carcinogens, including tobacco-specific N-nitrosamines, nitrite, nitrate, heavy metals such as nickel, cadmium and chromium. The levels of these carcinogens may vary widely among the different SLT products consumed in different countries leading to changes in toxicity and associated health risks also differ in various geographical regions.[10]This hinders the comparability of results of various studies evaluating the health effects of SLT use.

32% of the cases had the habit of retaining tobacco

overnight as compared to 10.30% among the Controls. Similar findings were seen in a study conducted by Nandakumar et al, in Bangalore where higher risk was seen among those who retained the quid in the mouth while asleep.[11]

Similar results were observed in a case control study done by Gupta et al, where age at initiation, duration and frequency of chewing tobacco, as well as retention time in the mouth showed a dose-dependent linear relationship with oral cancer risk (p<0.001).[12]

CONCLUSION

The incidence of oral cancer is on the rise. Oral cancer is a big public health problem and as such needs a serious commitment and a holistic approach to tackle it. The results of our study suggest that chewing of tobacco constitutes the strongest risk factor of cancers of oral cavity due to the well-established role of lifestyle factors in the development of oral cancer, they should be considered an important cause of avoidable morbidity and mortality in India, and their prevention should be an important target of public health initiatives.

ACKNOWLEDGEMENTS

REFERENCES

1. Bhishagratha KL, Samhita S. Varanasi: Choukhamba Orientalia; 1991.
2. Oral Cancer. Available at: https://www.who.int/cancer/prevention/diagnosis-screening/oral-cancer/en/. Accessed on 12 August 2019.
3. Kumar M, Nanavati R, Modi TG, Dobariya C. Oral cancer: Etiology and risk factors: A review. J Can Res Ther. 2016;12:458-63.
4. GATS. Available at: https://www.searo.who.int/india/mediacentre/gats2. Accessed on 16 August 2019.
5. Gupta PC, Murti PR, Bhonsle RB, Mehta FS, Pindborg JJ. Effect of cessation of tobacco use on the incidence of oral mucosal lesions in a 10 years follow-up study of 12,212 users. Oral Dis. 1995;1:54-8.
6. Stefani DE, Boffetta P, Pellegrini DH, Ronco AL, Acosta G, Ferro G, et al. The effect of smoking and drinking in oral and pharyngeal cancers: a case-control study in Uruguay. Cancer Lett. 2007;246(1-2):282-9.
7. Dikshit RP, Kanhere S. Tobacco habits and risk of lung, oropharyngeal and oral cavity cancer: A population-based case-control study in Bhopal, India. Int J Epidemiol. 2000;29(4):609-14.
8. Balaram P, Sridhar H, Rajkumar T, Vaccarella S, Herrero R, Nandakumar A, et al. Oral cancer in southern India: The influence of smoking, drinking, paan-chewing and oral hygiene. Int J Cancer. 2002;98:440-5.
9. Sankarnarayanan R, Duffy SW, Day NE, Nair MK, Padmakumary G. A case control investigation of cancer of the oral tongue and the floor of the mouth in Southern India. Int J Cancer. 1989;44:617-21.
10. Boffetta P, Hecht S, Gray N, Gupta P, Straif K. Smokeless tobacco and cancer. Lancet Oncol. 2008;9:667-75.
11. Nandakumar A, Thimmasetty KT, Sreeramareddy NM. A population-based case-control investigation on cancers of the oral cavity in Bangalore, India. Br J Cancer. 1990;62(5):847-51.
12. Gupta B, Bray F, Kumar N, Johnson NW. Associations between oral hygiene habits, diet, tobacco and alcohol and risk of oral cancer: A case-control study from India. Cancer Epidemiology. 2017;51:7-14.