Original Research Article

Oral cancer and tobacco: a case control study in southern India

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ABSTRACT

Background: Cancer is one of the major threats to public health in the developed world and increasingly in the developing world. In India, oral cancer is the leading cancer in males and ranking third in females. The risk factors for the development of oral cancers include tobacco smoking.

Methods: A Case control study done at Kidwai Memorial Institute of Oncology, Bangalore, India. Study subjects included histological confirmed new cases of oral cancer attending the hospital during the period of April 2014- May 2015 and equal number of age and sex matched controls. Data collection was done by interview method.

Results: Tobacco smoking with an odds ratio (OR) of 3.5 was significantly associated with the risk of oral cancer. The OR was 4.1 for combined bidi plus cigarette smokers and 3.7 for bidi smokers compared to non smokers. The OR was 2.3 for those who smoked less than or equal to 20 bidis/cigarettes per day and 8.3 for those who smoked more than 20 bidis/cigarettes per day, compared to non smokers. Smokers with pack years less than or equal to 20 showed 2.3 times, those with pack years 21- 29 showed 5.9 times and those with pack years more than 30 years showed 9.4 times higher risk for oral cancer compared to non smokers.

Conclusions: Tobacco smoking shows higher risk for oral cancer. There is a great need to augment tobacco control measures and educate the public about harmful effects of tobacco consumption.

Keywords: Oral cancer, Tobacco, Case control study

INTRODUCTION

Non communicable diseases also known as modern epidemics are assuming importance among the adult population in both developed and developing countries. In the developing countries, cancer is one among the ten commonest 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] Approximately 10 million people are diagnosed with cancer and more than 7 million die of this disease every year.[3] Oral cancer is the 8th most common cancer in the world.[4] In South East Asian Region, the great majority of cancers include oral cancers in men and cancer cervix in women.[1] India has one of the highest incidences of oral cancer in the world.[5] 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.[6] In this context, more focused evidence needs to be accumulated in the arena of Indian scenario. Oral cancers are highly amenable for primary and secondary prevention. There is need for more in-depth studies of various modifiable risk

factors in India. This would enable us to evolve appropriate interventions and effective preventive measures to reduce the burden of morbidity and mortality due to this disease, in the subcontinent. Thus, the present study would attempt to find the strength of association between tobacco smoking and oral cancer.

METHODS

The case control study was conducted at Kidwai Memorial Institute of Oncology (KMIO), located in Bangalore for one year from April 2014 to May 2015. The study was conducted after obtaining Institutional ethical committee clearance. The sample size was estimated based on the pilot study conducted at KMIO, Bangalore with a sample size consisting of 30 cases and 30 controls. In this study, the proportion of smokers among controls (0.4) and cases (0.73) 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. So number of cases were 200 and number of controls were 200. Total sample size was 400.

Selection of cases and controls

Definition of a case

Newly diagnosed case of oral cancer of all age groups and all stages of the disease confirmed by biopsy and histopathological report at KMIO. The biopsy and the histopathological report was verified from the hospital records. Sources of cases include the hospital, KMIO, Bangalore. For each case, one control was selected (1: 1). Five year age group matched and sex matched controls were selected. Sources of controls include hospital controls and Patient attendees. Hospital controls included patients with other cancers, other than tobacco related cancers, attending the hospital during the study period. Patient attendees included healthy attendants of cases either their relatives or friends attending the hospital.

Exclusion criteria

Cases

Terminally ill patients and cases with oral cancer as secondary carcinoma were excluded.

Controls

Among hospital controls, patients with Tobacco related cancers such as cancer of esophagus, larynx, lung and urinary bladder were excluded.

Matching

Matching was done to ensure comparability between cases and controls. Five year age group matched and sex matched controls were selected i.e., for each case

selected, a control was selected who is similar to the case in the five year age group and sex.

Preparation of questionnaire

Keeping the objectives as the guidelines, a precoded questionnaire based on pilot study was prepared for data collection.

Data collection

Before the collection of data from the subjects, a close rapport was established by explaining the objectives and the importance of the study. Consent was obtained from all the study subjects. Information regarding the socio demographic details, the exposure to risk factors such as tobacco smoking in terms of age at start of habit, type used, dose and duration of exposure were obtained with the help of pretested semi structured questionnaire by interviewing the study subjects.

Statistical analysis

The data was entered onto a computerized excel spread sheet. Quality control checks such as range, duplicate check before the analysis of data was carried out. Subsequently it was analyzed using SPSS version 11. The following statistical methods were employed to analyze the data. Descriptive statistics, in order to summarize the data where the results were tabulated with necessary percentages, means and standard deviation wherever necessary. Inferential statistics i.e., to evaluate the association between risk factors with the development of oral cancer, Chi square test of significance was employed. To find the strength of association, odds ratio (OR) along with 95% CI (confidence interval) were estimated. A significance level of p$\leq$0.05 was considered for statistical significance.

RESULTS

Majority of the study population, 156 (39.0%) belonged to the age group of 50-59 years followed by 110 (27.5%) in the age group of 60-69 years. The average age of oral cancer was 54.8 years with a standard deviation of 10.70 years. The study population consisted of 296 (74.0%) males and 104 (26.0%) females out of a total of 400. Hindus constituted the maximum number 375 (93.8%), followed by Muslims 14 (3.5%) and Christians 11 (2.8%). A higher proportion of Illiterates and unskilled workers were found among cases compared to controls. Majority of the study population belonged to Class III socio economic status according to modified B. G. Prasad's classification.

It was observed that 120 (60%) of the cases were smokers as compared to 59 (29.5%) of the controls and 80 (40.0%) of the cases were non smokers as compared to 141(70.5%) of the controls. The difference of exposure to smoking among cases and controls was observed to be

statistically significant (p<0.001). A statistically significant association was found between smoking habit and oral cancer. The risk of developing oral cancer was 3.5 times higher (OR=3.5, 95% CI of 2.36–5.43) among smokers compared to non smokers (Table 1).

Among cases and controls, bidi smokers constituted maximum number, compared to cigarette smokers and combined bidi plus cigarette smokers. The difference in exposure to various types of smoking between cases and controls was found to be statistically significant (p<0.001). The risk of developing oral cancer was 4.1 times higher among combined bidi plus cigarette smokers and 3.7 times higher among bidi smokers compared to non smokers. However the increased risk for developing oral cancer with cigarette smoking was not statistically significant with OR=2.3 95% CI, 0.78-7.01 (Table 2).

Table 1: Odds ratios and 95% confidence intervals for oral cancer according to the smoking habit.

Smoking habit	Cases No. (%)	Controls No. (%)	OR (95% CI)
Smokers	120 (60.0)	59 (29.5)	3.5 (2.36-5.43)
Non smokers	80 (40.0)	141 (70.5)	1.0
Total	200 (100)	200 (100)	

Chi square value=38.26, df=1, p<0.001; OR=Odds ratio, 95% CI=95% confidence interval, df=degrees of freedom.

Table 2: Odds ratios and 95% confidence intervals for oral cancer according to type of smoking.

Type of smoking	Cases No. (%)	Controls No. (%)	OR (95% CI)
Cigarettes	8 (4.0)	6 (3.0)	2.3 (0.78-7.01)
Bidis	105 (52.5)	50 (25.0)	3.7 (2.39-5.71)
Both	7 (3.5)	3 (1.5)	4.1 (1.03-16.33)
Non Smokers	80 (40.0)	141 (70.5)	1.0
Total	200 (100)	200 (100)	

Chi square value=38.93, df =3, p<0.001; OR = Odds Ratio, 95% CI=95% confidence interval, df=degrees of freedom.

Table 3: Odds ratios and 95% confidence intervals for oral cancer according to age at start of the smoking habit.

Age at start of the smoking habit (years)	Cases No. (%)	Controls No. (%)	OR (95% CI)
≤25	87 (43.5)	34 (17.0)	4.5 (2.78-7.29)
>25	33 (16.5)	25 (12.5)	2.3 (1.29-4.18)
Non smokers	80 (40.0)	141(70.5)	1.0
Total	200 (100)	200 (100)	

Chi square value=42.18, df =2, p<0.001; OR=Odds ratio, 95% CI=95% confidence interval, df=degrees of freedom.

Table 4: Odds ratios and 95% confidence intervals for oral cancer according to frequency of smoking.

Frequency of smoking (number per day)	Cases No. (%)	Controls No. (%)	OR (95% CI)
≤20	63 (31.5)	47 (23.5)	2.3 (1.48-3.77)
>20	57 (28.5)	12 (6.0)	8.3 (4.23-16.3)
Non smokers	80 (40.0)	141 (70.5)	1.0
Total	200 (100)	200 (100)	

Chi square value=51.28, df=2, p< 0.001; OR=Odds ratio, 95% CI=95% confidence interval, df=degrees of freedom.

Table 5: Odds ratios and 95% confidence intervals for oral cancer according to duration of smoking habit.

Duration of smoking habit (years)	Cases No. (%)	Controls No. (%)	OR (95% CI)
≤20	15 (7.5)	12 (6.0)	2.2 (0.98-4.95)
21-29	51 (25.5)	25 (12.5)	3.5 (2.07-6.25)
>30	54 (27.0)	22 (11.0)	4.3 (2.45-7.63)
Non smokers	80 (40.0)	141 (70.5)	1.0
Total	200 (100)	200 (100)	

Chi square value=40.37, df =3, p<0.001; OR=Odds ratio, 95% CI=95% confidence interval, df=degrees of freedom.

Table 6: Odds ratios and 95% confidence intervals for oral cancer according to pack years of smoking.

Pack years of smoking (years)	Cases No. (%)	Controls No. (%)	OR (95% CI)
<=20	61 (30.5)	45 (22.5)	2.3 (1.48-3.83)
21-29	27 (13.5)	8 (4.0)	5.9 (2.57-13.69)
>30	32 (16.0)	6 (3.0)	9.4 (3.77-23.25)
Non smokers	80 (40.0)	141 (70.5)	1.0
Total	200 (100)	200 (100)	

Chi square value =49.90, df =3, p< 0.001; OR = Odds ratio, 95% CI = 95% confidence interval, df = degrees of freedom.

A statistically significant association was found between the age at start of habit and oral cancer. Among smokers, it was 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 or equal to 25 years, the OR was found to be 4.5 and for those who started after 25 years OR=2.3, compared to non smokers (Table 3).

It was observed that, higher the frequency of smoking, greater the risk of developing oral cancer. The risk of developing oral cancer was 2.3 times higher among smokers who smoked less than or equal to 20 bidis/ cigarettes per day and 8.3 times higher for those who smoked more than 20 bidis/cigarettes per day, compared to non smokers (Table 4).

An increasing trend for oral cancer risk with the increase in 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 20 years of smoking habit. However those smoking <20 years did not attain statistical significance at 5% level probably due to smaller number of cases and controls in this group (Table 5).

A trend of increase in Oral cancer risk with increase in the number of pack years was found. Smokers with pack years less than or equal to 20 showed 2.3 times, those with pack years 21- 29 showed 5.9 times and those with pack years more than 30 years showed 9.4 times higher risk for oral cancer compared to non smokers (Table 6).

DISCUSSION

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, such as the nasal cavity or the maxillary sinus. Oral cancers may originate in any of the tissues of the mouth, and may be of varied histological types: teratoma, adenocarcinoma derived from a major or minor salivary gland, lymphoma from tonsillar or other lymphoid tissue, or melanoma from the pigment producing cells of the oral mucosa. The most common oral cancer is squamous cell carcinoma, originating in the tissues that line the mouth and lips. Oral cancer most commonly involves the tissue

of the lips or the tongue. It may also occur on the floor of the mouth, cheek lining, gingival (gums), or palate (roof of the mouth). These are malignant and tend to spread rapidly.[7]

Oral cancer and tobacco

Tobacco is by far 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, especially among young people and women.[8]

Tobacco use can be broadly classified as,

1. Smoking tobacco
2. Smokeless tobacco

Smoking tobacco: Smoking tobacco is in the form of cigarettes, bidis, cigars, pipes, and sticks.

Manufactured cigarettes: These consist of shredded or reconstituted tobacco processed with chemicals. They are the predominant form of tobacco used worldwide.

Bidis: These consist of small amount of tobacco, hand wrapped in dried temburni leaf and tied with string. Bidis are found throughout South East Asia, and are India's most used type of tobacco.

Cigars: These are made of air cured and fermented tobacco with a tobacco wrapper, and come in many shapes and sizes. In reverse smoking, the ignited end of the cigar is placed inside the mouth. Use of this form is commonly seen in coastal areas.

Pipes: These are made of briar, slate, clay or other substance- tobacco is placed in bowl and inhaled through water. The water pipe is also known as shisha. In South East Asia clay pipes are widely used.

Sticks: These are made from sun-cured tobacco known as brus and wrapped in cigarette paper.[8]

A case control study of oral cancer done in Cuba by Garrote et al, with 200 cases and 200 age and sex matched controls showed that, heavy smoking was very

common among cases. The OR for smoking 30 cigarettes per day or more, compared to never smokers, was 20.8 among current smokers. Former smokers showed an OR of 6.3. Smoking of only cigars was associated with an OR of 4.3 for 3 or less than 3 cigars and OR 20.5 for 4 cigars or more per day. Long-duration smoking and early age of starting smoking were associated with especially increased risks.[9]

In a nested case control study of oral cancer in Trivandrum, India, it was found that the adjusted OR for the past and the current smokers was 1.0 and 1.2 respectively. There was a significant increased risk of oral cancers for smokers of bidi alone, OR=1.9 compared to never smokers. A dose response relationship was observed in duration of smoking for bidi smokers.[10]

In a study done in southern India, it was found that tobacco smoking was associated with oral cancer risk among men (OR=1.8) and women (OR=3.2). Fifty three percent of cases and 39% of controls were current smokers. The majority of them smoked bidi, alone or in combination with cigarettes or cigars (OR for ≥20 bidis v/s never smokers was 2.5. Age at starting among current smokers was relatively late (median age=20 yrs among both cases and controls) and it was not related to oral cancer risk.[11]

Sankarnarayan et al, in their study revealed that, bidi smoking, bidi plus cigarette smoking had significant predisposing effect on oral cancer in males. Paan tobacco chewing had significant predisposing effect in females. Among males, those smoking bidi >20 per day had an OR 4.62 and those smoking bidi >21yrs had an OR 2.72 when compared to never smokers. Those smoking both bidis and cigarettes >20 per day showed an OR 3.19 and those smoking both bidis and cigarettes for >21yrs had an OR 2.36 when compared to never smokers.[12]

A study done on tobacco use and risk of oral cancer in Chennai and Trivandrum, South India by Gajalakshmi et al, showed that current smokers had about 2-fold risk for oral cancer. The risk associated with bidi smoking was higher (OR: 2.2) than cigarette (OR: 0.9) smoking. Former smokers had decreased risk compared to current smokers. Significant dose-response relationships were observed for duration of smoking and average daily consumption of smoking tobacco in the risk of developing oral cancer. Decreased risk was observed even after 2-4 years of stopping smoking.[13]

CONCLUSION

The risk factors such as smoking tobacco in the form of bidis and cigarettes were associated with the risk of development of oral cancer. The risk of developing oral cancer increases as the dose and the duration of smoking tobacco increased.

Recommendations

Tobacco habits show higher risk for oral cancer. The risk factor is highly amenable for primary and secondary prevention. 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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