Tobacco Habits and Risk of Lung, Oropharyngeal and Oral Cavity Cancer: A Population-Based Case - Control Study in Jharkhand, India

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Abstract

Background: Tobacco habits in India are unique and vary in different regions. Few studies, and none from North Eastern part India, have reported on type of tobacco used and risk of the most common cancer types in India. We conducted a population-based case- control study to evaluate the risk of tobacco particularly *bidi* smoking and tobacco *quid* chewing on the most common cancer sites among males in Jharkhand.

Methods: In all, 163 lung, 247 oropharyngeal and 148 oral cavity cancer cases from the Population-Based Cancer Registry records and 260 controls randomly selected from a tobacco survey conducted in the Jharkhand population formed the study population.

Results: A significant risk of *bidi* and cigarette smoking with a dose-response relationship was observed for lung and oropharyngeal cancer. Tobacco *quid* chewing showed no risk for lung, marginally increased risk for oropharyngeal and about a sixfold increased risk for oral cavity cancer. Population-attributable risk per cent (PARP) was observed to be 82.7% and 71.6% for smokers for the development of lung and oropharyngeal cancer, while the same was found to be 66.1% for tobacco chewers for the development of oral cavity cancer.

Conclusions: These data provide strong evidence that smoking *bidi* is even more hazardous than cigarette smoking in the development of lung and oropharyngeal cancer. An intervention study to prevent the use of tobacco will be useful in this population as it also coal mine workers.

Keywords: Bidi smoking, tobacco quid chewing, coal mines.

INTRODUCTION

Lung, oropharyngeal and oral cavity cancer are the most common cancer sites observed by Indian registries.[1] These cancer sites are causally related to the use of tobacco in different forms.[2] In India, the use of tobacco is common in the form of chewing and smoking of bidis and cigarettes.3Two studies are available from India on the role of bidi smoking in the development of lung cancer.[4,5] A few studies, mainly from West Maharashtra and South India, have reported the risk of oropharyngeal and oral cavity cancer and smoking and oral use of tobacco,[6,7,8] but no study has been reported from north eastern India.

In the present study three cancer sites (lung, oropharynx and oral cavity) were investigated using a common protocol and data from the Jharkhand Cancer Registry. The risk of tobacco use, particularly bidi smoking and chewing, was estimated for these three sites. A study on tobacco use in this population is particularly important as it suffered exposure to coal and thus is different from other parts of the world.

MATERIALS AND METHODS

The present study examines data for the three most common cancer sites in males (lung, oropharynx and oral cavity), collected by the Jharkhand Population-Based Cancer Registry during the years 2014-2021.The cancer cases were coded by four-digit International Classification of Diseases for Oncology (ICD-O) code.9 The cancer sites included under oropharynx were posterior third of tongue (141.0 and 141.6), soft palate (145.3), uvula (145.4),oropharynx (146.0–146.9), nasopharynx (147.0–147.9), and hypopharynx (148.0–149.0). The cancer sites included under oral cavity were lip (140.0–140.9), anterior two-thirds of tongue. (141.1–141.5), gingiva (143.0–143.9), floor of mouth (144.0–144.9), cheek mucosa (145.0–145.2), hard-palate and retromolar area (145.5–145.9). A total of 260 controls were randomly sampled from a total of about 2500 males surveyed for tobacco habits in the Jharkhand population. This tobacco survey was based on random samples from the voter list of the all the municipal corporation area. The survey was conducted by the Jharkhand cancer registry during2014-2021. The controls were not matched for age with the cases, however, they were age-stratified and then randomly selected to follow the age distribution of cases. The cases and controls were interviewed according to a pre- coded questionnaire. The subjects were asked about identifi- cation particulars, socioeconomic parameters, tobacco habits, and clinical history. The interview was conducted by three qualified social workers of the Cancer Registry staff. The cases for which detailed information about smoking or chewing history were not available were excluded from the study. Cases registered from death certificates were excluded. Similarly, the tongue not otherwise specified cases (141.9) were not included in the analysis. After exclusion, a total of 163 lung, 247 oropharyngeal and 148 oral cavity cancer cases were available for the analysis.

The data collected were compiled and quality checks were carried out. Age-adjusted odds ratio (OR) and 95% CI for the sites under study according to religion, educational status, smoking and chewing habits were estimated using unconditional multiple logistic regression models. The models were compared using the differences in deviance and in degrees of freedom. The result of variable of interest with and without confounding variable was tabulated. The effect of interaction between variable of interest and confounder were also obtained to understand the validity of adjustment. The dummy variable and linear dose-response model was compared for testing the extent to which the linear trend adequately explains the variation between the dose level.[10] The population attributable risk and attributable risk of individuals exposed to exposure of interest were also estimated. For model fitting, the statistical program SPSS was used.[11]

RESULTS

Table 1 presents the distribution of socio-demographic, smoking and chewing habits for lung, oropharyngeal and oral cavity cancer cases and controls. Most of the cases and controls were Hindu. Of the controls, 51.5% never had formal education, while 53.4% of lung, 64% of oropharyngeal and 70.9% of oral cavity cancer cases had never attended the school. The habit of

smoking and tobacco chewing was more common among cases than the controls.

Religion and educational status did not appear to increase the risk of lung, oropharyngeal and oral cavity cancer after con- trolling for smoking and chewing habits (Table 2). As shown in Table 2, tobacco smokers showed increased risk for lung and oropharyngeal cancer but marginally increased risk for oral cavity cancer. Tobacco chewing showed about a six fold increase in risk for oral cavity, marginally increased risk for cancer of the oropharynx and no increase in risk for lung cancer in com- parison to non-tobacco chewers. There were only 16 subjects who had a history of chewing regularly without using tobacco. The estimates for relative risk, based on small numbers, showed increased risk for oral cavity cancer in comparison to non- chewers even after controlling for smoking habits.

The risk of lung and oropharyngeal cancer according to the number of *bidi* and cigarettes smoked per day. The risk estimates for oral cavity cancer could not be estimated separately for *bidi* and cigarette smoking, as there were only six cigarette smokers among the oral cavity cancer cases. The risk of lung and oropharyngeal cancer increased with number of *bidi* as well as cigarettes smoked. This relationship seemed to be linear as observed departure from linear trend was not statistically significant at the 5% level. The multiplicative interaction between *bidi* and cigarette smoking was significant at the 5% level: the risk of *bidi* and cigarette smoking combined was observed to be 24.1 and 6.2 for lung and oropharyngeal cancer, respectively, in comparison to non-smokers of *bidi* and cigarettes. The risk of developing lung cancer (11.6/7.7 = 1.5) and oropharyngeal cancer (7.9/4.1 = 1.9) was higher for *bidi* smokers in comparison to cigarette smokers.

The risk of lung and oropharyngeal cancer increased approximately more than four and three times, respectively, within three levels of grouping done for duration of smoking of *bidi*/cigarettes. The risk of getting oral cavity cancer was 4.3 for those who had smoked for >30 years compared to non-smokers. The risk of >500 cumulative years of tobacco smoked compared to non-smokers was 67.6 for lung cancer, 23.0 for oropharyngeal cancer and 6.0 for oral cavity cancer. The lung cancer risk according to histological types among smokers compared to non-smokers shows that the risk is higher for squamous cell carcinoma. The OR estimates for small cell and oat cell carcinoma were based on small numbers and no convergence was obtained for this type. The risk among smokers by histological types was not estimated for oropharyngeal and oral cavity cancer as only one case of adenocarcinoma was reported for oropharyngeal cancer while for the oral cavity only squamous cell carcinomas were reported during the study period.

DISCUSSION

The motivation for examining the carcinogenic effects of tobacco smoking and chewing in this population was that smoking habits differ in India and in this region from other parts of the world. The habit of *bidi* smoking and '*zarda*', a form of tobacco chewing, is peculiar to this region. Case ascertainment in the present study is based on Cancer Registry data and thus entailed high-quality diagnostic confirmation. The controls were randomly selected from a tobacco survey conducted in the same population. Although the controls were not selected concurrently with the cases, it seems unlikely that this will alter the risk estimates as the period of survey (2014-2021) was almost same as the recruitment of cases (2014-2021) for the study. Further, no anti-tobacco activities were organized during the study period to alter the prevalence of tobacco habits in this population.

Religion and educational status were not observed to be risk factors in the present study. A study of the association of religion and smoking habits with lung cancer likewise did not observe any excess risk for different religion.[5] Both *bidis* and Cigarettes were found to be independently associated with increased risk of lung and oropharynx cancer. Two previous studies on the risk of lung cancer among *bidi* smokers have shown conflicting results. Notani and Sanghavi,[4] taking hospital controls, found a relative risk of 2.6, while Jussawalla and Jain,[5] taking community controls, found a relative risk of 19.3 in com-

parison to non-smokers. Similar to the present study increased risk for oropharyngeal cancer among *bidi* smokers was observed in a previous study.[6]

The observed OR for *bidi* and cigarette smoking combined (OR = 24.1 for lung and OR = 6.2 for oropharynx) in com- parison to non-smokers of both was much lower than expected, indicating that either mode of action is not multiplicative or those smoking both *bidis* and cigarettes are light smokers of each. The risk estimates further revealed that smoking *bidi* is even more hazardous than cigarette smoking in the development of lung and oropharyngeal cancer (Table 4).The Indian *bidi* contains only a small amount of tobacco dust rolled in a dried leaf of tendu (*Diospyrous malanoxylon*) or Temburni tree (*Diospyrous ebenum*).[12] In comparison to US cigarettes, the mainstream smoke of *bidi* contains a much higher concen- tration of several toxic agents such as hydrogen cyanide, carbon monoxide, ammonia, other volatile phenols, and carcinogenic hydrocarbons such as benz (a) anthracene and benzopyrene. *Bidi* also delivers more nicotine than Indian cigarettes. The nitro-sonornicotine (NNN) and 4 (methyl-nitrosoamino)-1-(3-pyridol) (NNK) level of *bidi* tobacco ranged from 6.2 to 12 µg/g com- pared with 1.3 to 58.0 µg/g in cigarette tobacco.[13] Further, *bidi* smokers were found to take almost five puffs per minute com- pared to the cigarette smokers who smoked two puffs per minute.[12] Thus, higher yields of tobacco-specific nitrosamines (TSNA) and higher puffing frequency among *bidi* smokers suggest that the finding of the present study, that the risk for development of lung and oropharyngeal cancer is higher among *bidi* smokers, is biologically plausible. The effect of smoking differed according to cell type of lung cancer. The risk was highest for squamous cell carcinoma. While the risk of smoking was lowest for developing adenocarcinoma, it was still high (OR = 3.9). These results are consistent with the result of other workers.[14,15]

Chewing tobacco contains a high level of TSNA.13 Of these for NNK and its reduction product 4-(methyal nitrosoamino)- 1-1(3-pyridyl)-1-butanol) (NNAL) the major target organ is the lung, especially the peripheral part of the lung. This is independent of the route of admission, whether these procarcinogens are applied topically to the skin, taken orally or by intraperitoneal injection.[16,17] These experimental studies suggest that tobacco chewing may also enhance the risk of lung cancer. The present study, however, did not observe any increased risk of tobacco chewing for lung cancer. The increased risk for oral cavity cancer among tobacco chewers is in accordance to that observed by other workers.[7,8,18] These risk estimates in the present study could not be adjusted for the use of alcohol as history of alcohol use was not taken in the Cancer Registry proforma. However, this does not seem to alter the risk of tobacco chewing to a great extent. In India the prevalence of alcohol consumption particularly relative to tobacco chewing is low. Studies from India have not observed excess risk for oral cancer among alcohol users.[7,8] The interaction model presented in Table 2 gave an indication that the mode of action of tobacco *quid* chewing and smoking may not be multiplicative. It further indicated a decline in risk of chewing of tobacco with increased amount of tobacco smoked, this may be because heavy smokers chew less than light smokers.

In India cross-sectional surveys have shown that the percentage of people who chew betel *quid* without tobacco is small. In the present study also, based on small numbers, elevated risk was observed for oral cavity cancer among chewers not using tobacco, a finding similar to another study from south India.[8]

Tobacco consumption has decreased in many developed countries while in most developing countries it is still increasing. This may largely be due to the fact that relatively fewer studies have been reported from developing countries, including India, on the risk of cancer at different cancer sites due to the use of various forms of tobacco.[19] In the present study it was estimated that the population attributable risk per cent (PARP) for smoking was quite high for lung (82.7%) and oropharyngeal cancer (71.6%). Similarly, the PARP was found to be 66.1% for tobacco chewers for development of oral cavity cancer. The attributable risk among smokers was observed to be 92% and 85% for lung

and oropharyngeal cancer, respectively. The attributable risk for those who chewed tobacco was 84.4% for development of oral cavity cancer. This suggests that the high percentage of lung, oropharyngeal and oral cavity cancers in Jharkhand could be prevented if tobacco habits were not started. Intervention studies encouraging quitting tobacco use have much relevance in Jharkhand as in this population lungs are already damaged to some extent due to exposure to coal.

BIBLIOGRAPHY

1. National Cancer Registry Programme. Biannual Report 1987–1989. New Delhi: Indian Council of Medical Research, 1992.
2. International Agency for Research on Cancer. Tobacco Smoking. Monographs on the evaluation of carcinogenic risk of chemicals to humans, Vol. 38. Lyon: IARC, 1985.
3. Bhonsle RB, Murti PR, Gupta PC. Tobacco habits in India. In: Gupta PC, Hamner JE, III, Murti PR(eds). Tobacco Related Cancer and Other Diseases. Bombay: Oxford University Press, 1992, pp.25–46.
4. Notani PN, Sanghavi LD. A retrospective study of lung cancer in Bombay. Br J Cancer 1974;29:477–82.
5. Jussawalla DJ, Jain DK. Lung cancer in greater Bombay: correlation with religion and smoking habits. Br J Cancer 1979;40:437–48.
6. Jussawalla DJ, Deshpande VA. Evaluation of cancer risk in tobacco chewers and smokers: an epidemiologic assessment. Cancer 1971; 28:244–52.
7. Sankaranarayanan R, Duffy SW, Day NE, Nair MK, Padmakumary GA. Case-control investigation of cancer of the oral, tongue and the floor of mouth in Southern India. Int J Cancer 1989;44:617–21.
8. Nandakumar A, Thimmasetty KT, Sreeramareddy NM et al. A popu- lation based case control investigation on cancers of the oral cavity in Bangalore, India. Br J Cancer 1990;62:847–51.
9. World Health Organization. International Classification of Diseases for Oncology. Geneva: WHO, 1976.
10. Breslow NE, Day NE. Statistical Methods in Cancer Research. Vol. 1: The Analysis of Case-Control Studies. IARC Scientific Publications No. 32. Lyon: International Agency for Research on Cancer, 1980.
11. Backer RJ, Nelder JA. The GLIM system, Rev. 3.77. Oxford: Numerical Algorithms Group, 1985.
12. Jayant K, Pakhale SS. Toxic constituents in bidi smoke. In: Sanghavi LD, Notani P (eds). Tobacco and Health: The Indian Scence. Bombay:Tata Memorial Centre, 1989, pp.101–10.
13. Gupta Prakash C, Murti PR, Bhonsle RB. Epidemiology of cancer by tobacco products and the significance of TSNA. Crit Rev Toxicol 1996; 26:183–98.
14. Lubin JH, Blot WJ. Assessment of lung cancer risk factors by histologic category. J Natl Cancer Inst 1984;73:383–89.
15. Siemiatycki J, Krewski D, Franco E, Kaiserman M. Associations between cigarette smoking and each of 21 types of cancer: a multisite case control study. Int J Epidemiol 1995;24:504–514.
16. Rivenson A, Hecht SS, Hoffmann D. Carcinogenecity of tobacco- specific N-nitrosoamines (TSNA): the role of vascular network in the selection of target organs. Crit Rev Toxicol 1991;21:255.
17. Hoffmann D, Rivenson A, Hecht SS. The biological significance of tobacco specific N nitrosamines: smoking and adenocarcinoma of the lung. Crit Rev Toxicol 1996;26:199–211.
18. Hirayama T. An epidemiological study of oral and pharyngeal cancers in Central and South East Asia. Bull World Health Organ 1966; 34:41–69.
19. Derman U, Demir G, Akan P. Is awarness of its risk enough to stop people from smoking? J Cancer Educ 1995;10:68–70.

Table 1: Distribution of socio-demographical, smoking and chewing variables studied among lung, oropharyngeal and oral cavity cancer cases and controls

VARIABLE	CANCER SITES							
	Lung		Oropharynx		Oral cavity		Controls	
	No.	%	No.	%	No.	%	No.	%
Religion								
Hindu	104	63.8	174	70.4	107	72.3	201	77.3
Muslim	56	34.4	73	29.6	40	27.0	57	21.9
Others	3	1.8	–	–	1	0.7	2	0.8
Education								
Ever had schooling	76	46.6	89	36.0	43	29.1	126	48.5
Never had schooling	87	53.4	158	64.0	105	70.9	134	51.5
Smoking								
Smokersa	146	89.6	209	84.6	72	48.6	114	43.8
Bidi smokers only	100	68.5	167	79.9	50	69.4	81	71.1
Cigarette smokers only	15	10.3	21	10.0	6	8.3	20	17.5
Bidi and cigarette smokers	31	21.2	21	10.0	16	22.2	13	11.4
Non-smokers	17	10.4	38	15.4	76	51.4	146	56.2
Chewing								
Chewersb	56	34.4	108	43.7	120	81.1	120	46.2
Without tobacco	4	7.1	4	3.7	4	3.3	12	10.0
With tobacco	52	92.9	104	96.3	116	96.7	108	90.0
Non-chewers	107	65.6	139	56.3	28	18.9	140	53.8
Smoking + tobacco chewing	45	27.6	81	33.0	49	33.0	43	16.5
No tobacco habits	10	6.1	15	6.1	9	6.0	81	31.2

a. Smokers with tobacco chewing habits included.

b. Chewers with smoking habits included.

Table 2 Risk of lung, oropharyngeal and oral cavity cancer by religion, education, smoking and chewing habits

VARIABLE	CANCER SITES					
	Lung		Oropharynx		Oral Cavity	
	ORa (95% CI)	ORb,c (95% CI)	ORa (95% CI)	ORb,c (95% CI)	ORa (95% CI)	ORb,c (95% CI)
Religion						
Hindu and others	1.0	1.0	1.0	1.0	1.0	1.0
Muslims	1.8 (1.2–2.9)	1.0b (0.6–1.7)	1.5 (0.9–2.2)	1.1b (0.7–1.8)	1.4 (0.9–2.2)	1.2c (0.7–2.0)

Education Status						
Never had schooling	1.0	1.0	1.0	1.0	1.0	1.0
Ever had schooling	1.1 (0.7–1.6)	0.7b (0.4–1.1)	1.7 (1.2–2.4)	1.4b (0.9–2.0)	2.4 (1.5–3.7)	1.5c (0.9–2.5)
Smoking Status						
No	1.0	1.0	1.0	1.0	1.0	1.0
Yes	12.3 (6.9–22.0)	12.1c (6.7–21.6)	7.1 (4.6–10.7)	7.3c (4.7–11.2)	1.3 (0.8–1.9)	1.5c (0.9–2.4)
Tobacco quid chewing						
No	1.0	1.0	1.0	1.0	1.0	1.0
Yes	0.6 (0.4–0.9)	0.7b (0.4–1.2)	1.1 (0.7–1.5)	1.2b (0.8–1.8)	5.5 (3.4–8.9)	5.8b (3.6–9.5)

a. Odds ratios adjusted for age.

b. Odds ratios adjusted for age and smoking.

c. Odds ratios adjusted for age and tobacco *quid* chewing