ORIGINAL ARTICLE

Tobacco smoking and pulmonary tuberculosis

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Background: The prevalence of tuberculosis in adult men in India is 2–4 times higher than in women. Tobacco smoking is prevalent almost exclusively among men, so it is possible that tobacco smoking may be a risk factor for developing pulmonary tuberculosis. A nested case control study was carried out to study the association between tobacco smoking and pulmonary tuberculosis.

Methods: A tuberculosis disease survey was carried out in two Panchayat unions in the Tiruvallur district of Tamil Nadu in India. Eighty five men aged 20–50 years with bacteriological tuberculosis (smear and/or culture positive) were selected as cases and 459 age matched men without tuberculosis were selected randomly as controls. Information on smoking status, type of tobacco smoked, quantity of tobacco smoked, and duration of tobacco smoking was collected from cases and controls using a questionnaire.

Results: The estimated crude odds ratio (OR) of the association between tobacco smoking and bacillary tuberculosis was 2.48 (95% confidence interval (CI) 1.42 to 4.37), p<0.001.The age adjusted OR (Mantel-Hanszel estimate) was 2.24.(95% CI 1.27 to 3.94), p<0.05. The ORs for mild (1–10 cigarettes/day), moderate (11–20/day), and heavy (>20/day) smokers were 1.75, 3.17, and 3.68, respectively (p<0.0001 test for linear trend). The ORs for smokers with <10 years, 11–20 years, and >20 years of smoking were 1.72, 2.45, and 3.23, respectively (p<0.0001 test for linear trend).

Conclusion: There is a positive association between tobacco smoking and pulmonary (bacillary) tuberculosis (OR 2.5). The association also shows a strong dose-response relationship.

It has been consistently shown from various disease surveys in India that the prevalence of pulmonary tuberculosis among men aged 15 years and over is 2–4 times higher than in women of the same age. Interestingly, in the 10–14 age group there is no difference in the prevalence between the two sexes,[1] but the rates for the two sexes diverge above the age of 15. This sex difference could be due to either biological or behavioural (health related) changes occurring at about the age of 15 in one or both the sexes. The tobacco smoking habit starts in men around the age of 15, so it is possible that there is an association between tobacco smoking and the higher rates of tuberculosis in men. A case-control study was carried out to determine whether there is an association between tobacco smoking and pulmonary tuberculosis in cases and controls selected from a nested population surveyed for pulmonary tuberculosis.

METHODS

A survey of tuberculosis was carried out in 30 villages from two areas of the Tiruvallur district of Tamil Nadu in South India during the period 1993–6. All those aged 10 years and above were screened for pulmonary tuberculosis by chest symptoms and chest radiography. Those with chest symptoms and/or positive radiographs were investigated by sputum smear and culture examination. The population surveyed was about 60 000 and was the source for cases and controls for the present study. The disease status of the cases and controls was ascertained during the survey period, and exposure to tobacco smoking was determined for both cases and controls at the time of the study in 1998. Cases were defined as men aged 20–50 years who were sputum smear and/or culture positive for pulmonary tuberculosis. Men aged 20–50 years who were screened and declared not to have tuberculosis formed the control group.

Since the prevalence of tobacco smoking among women in India is very low (<0.4%),[2] women were not included in this study. The study population was restricted to men aged 20–50 years to minimise the confounding effect of other risk factors.

Selection of cases

All the bacillary cases detected from the nested population who satisfied the definition criteria described above for a case were included in the study; 88% were culture positive and 12% were smear positive.

Selection of controls

For each case selected from a village, five controls were selected randomly from among the non-cases from the same village. The controls were neighbourhood controls. The entire village was considered as the neighbourhood for the cases occurring in a village—for example, if there were five cases in a village, 25 controls were selected randomly from the non-cases aged 20–50 from the same village as neighbourhood controls and none of the controls was matched to any of the cases.

Exposure to tobacco

Tobacco smoking is a common habit among men in India. Two types of tobacco smoking are prevalent among the study population—cigarettes and "beedi". "Beedi" consists of flaked tobacco rolled in a rectangular piece of dried Tendu leaf (*Diospyros exsculpta*). The Tendu leaf is odourless and tasteless when smoked. Because of its smaller size, "beedi" may produce less smoke than a cigarette.

The following data on tobacco smoking were collected from the cases and controls at the time of the interview:

- smoking status,
- age at which smoking started,
- duration of smoking,
- type of tobacco smoking,
- quantity of item smoked/day

The interview was carried out by experienced health workers from the Epidemiology Unit of the Tuberculosis Research Centre. The health workers were blinded to the disease status of the individuals interviewed.

Table 1 Distribution of study population by census status

Census status	Cases	Controls	Total
Present	85	459	544
Absent	3	29	32
Left	10	54	64
Dead	13	10	23
Fate unknown	1	1	2
Total	112	553	665

Thus, the study population was selected from the survey records (survey period 1993–6) while information on exposure to tobacco smoking was collected from an interview in 1998.

Statistical analysis

Odds ratios were estimated as the measure of effect. The age distribution of cases and controls was found to be significantly different so the crude odds ratio was adjusted for age by the Mantel-Hanszel technique. The dose-response relationship was studied by the test for linear trend using Epi Info 6 software.

RESULTS

Among the study population, 58% were smokers and 42% were non-smokers. The distribution of smokers by age at which smoking started was as follows: 130 (40.7%) <20 years of age, 263 (82.4%) <25 years of age, 56 smokers (17.6%) >25 years of age; the earliest age was 7 years. 91% were "beedi" smokers and 9% were cigarette smokers.

The status of the study population at the time of the interview in 1998 is shown in table 1. Eighty five of 112 cases (76%) and 459 of 553 controls (83%) were present, giving a total of 544 of the 665 individuals (82%) available for interview; subsequent analysis was confined only to these individuals because exposure data were collected only from them. Since all the study population came from the rural villages which were homogenous with respect to social and demographic characteristics, it is reasonable to assume that the remaining subjects did not differ sociodemographically from the population interviewed.

Among the 85 cases there were 64 smokers and, of the 459 controls, 253 individuals smoked (estimated odds ratio 2.48 (95% confidence interval (CI) 1.42 to 4.37), p<0.001). Table 2 shows the age adjusted crude odds ratio was 2.24 (95% CI 1.27 to 3.94).

Table 3 shows the dose-response relationship between smoking and tuberculosis. Smokers were categorised as mild (1–10 cigarettes/day), moderate (11–20/day), and heavy smokers (>20/day) on the basis of the mean number of cigarettes/beedies smoked per day. The odds ratios for mild, moderate, and heavy smokers were 1.75, 3.17, and 3.68, respectively (p<0.0001).

Table 4 shows the cumulative effect of smoking on the occurrence of pulmonary tuberculosis. Smokers were classified on the basis of duration of smoking into the following three categories: <10 years, 11–20 years, and >20 years. Odds ratios of 1.72, 2.45, and 3.23, respectively, were obtained for the three categories (p<0.0001).

Table 3 Dose-response relationship

	Smokers			
	Mild (1–10/day)	Moderate (11–20/day)	Heavy (>20/day)	Non-smokers
Cases	25	21	18	21
Controls	140	65	48	206
Odds ratio	1.75	3.17	3.68	–

p<0.0001 (χ^2 for linear trend=18.365).

Table 4 Cumulative effect of smoking on occurrence of pulmonary tuberculosis

	Smoking duration (years)			
	<10	11–20	>20	Non-smokers
Cases	14	22	28	21
Controls	80	88	85	206
Odds ratio	1.72	2.45	3.23	–

p<0.0001 (χ^2 for linear trend = 15.867).

DISCUSSION

Tobacco smoking is a common habit among men living in both rural and urban parts of India, being generally more common in urban than in rural areas. In rural areas "beedi" smoking is more common mainly because it is cheaper than cigarettes.

The odds ratio (2.48) and the age adjusted odds ratio (2.24) obtained in this study are statistically significant. This effect may be real or may be due to chance, bias or confounding. It has already been shown that the probability of obtaining this odds ratio by chance is very low (p<0.001, table 1). Since all the eligible cases from the survey were selected for the study, there was no bias in case selection. Similarly, the controls were selected randomly from all the eligible non-cases in the survey, thereby giving equal opportunity to every one of them to be selected as a control. There was thus no bias in the selection of controls. As the cases were selected from the survey records, there was no possibility of misclassification of disease status of the study subjects. Observer bias was minimised by blinding the interviewers to the disease status of the subjects. Generally there was no inhibition or hesitation by the study subjects to discuss their smoking habits as tobacco smoking is common among men. If there was any responder bias in revealing their smoking status, it could only result in a smoker being misclassified as a non-smoker and not vice versa. This misclassification could result in an underestimation of the effect of smoking on tuberculosis—that is, if this bias was present, the actual effect would have been greater than was estimated. Since smoking is a familiar habit, cases and controls would have no difficulty in recalling its presence or

Table 2 Age adjusted crude odds ratio

	20–30 years		31–40 years		41–50 years	
	Smoker	Non-smoker	Smoker	Non-smoker	Smoker	Non-smoker
Cases	13	11	22	3	29	7
Controls	78	110	95	61	79	35

Age adjusted odds ratio 2.24 (95% CI 1.27 to 3.94), p<0.05 (Mantel-Hanszel estimate).

absence so there is little chance of recall bias. As age is a possible confounder, the crude odds ratio was adjusted for age. To minimise the effect of other confounders the study population was restricted to men aged 20–50 years only.

This study has shown that there is a strong dose-response relationship as shown by the highly significant test for trend. The positive dose-response relationship is one of the important criteria for a causal association. Adelstein and Rimingston[3] studied volunteers in a radiographic survey of the association between smoking and pulmonary tuberculosis. Using the criterion "in need of treatment", they reported disease rates of 0.42/1000 for male non-smokers and 2.09/1000 for male current smokers with a rate ratio of 1:5. Brown and Campbell[4] studied the association between tobacco smoking and alcohol consumption with tuberculosis in 100 ex-servicemen with tuberculosis and 100 ex-servicemen undergoing surgery as controls. They concluded that alcohol but not smoking was directly associated with tuberculosis, although the validity of their conclusion is questionable for the following reasons. Firstly, there may have been a strong bias in the selection of cases and controls with respect to alcohol consumption as alcoholics are more likely to be admitted to hospital than non-alcoholics. Secondly, they did not use the appropriate analytical method to reach their conclusion as they used only the χ^2 test of significance to study the difference between the two groups. In case-control studies the odds ratio is the best measure for studying the association between exposure and disease. However, from the published data it was possible to estimate the odds ratios for smoking and alcoholism as 3.02 (95% CI 1.32 to 6.92) and 4.17 (95% CI 1.97 to 8.20) respectively. The alcoholism adjusted odds ratio for smoking cannot be estimated as information on non-smokers among subjects with various levels of alcohol consumption was not available from the published data.

Yu *et al*[5] reported a relative risk for heavy smokers (≥400 cigarettes/year) of 2.17 (95% CI 1.29 to 3.63) compared with non-smokers. Using a binomial regression model they showed that the influence of age and sex on the risk of tuberculosis was largely due to smoking. Alcaide *et al*,[6] using a case-control design and multiple logistic regression model for analysis of variables of interest, reported an odds ratio of 3.8 (95% CI 1.5 to 9.8) for active smokers. They also found a dose-response relationship between the number of cigarettes smoked daily and active pulmonary tuberculosis.

Thus, studies conducted in different parts of the world have used different types of study designs, case definitions, and analytical methods to yield results which suggest that there may be an association between tobacco smoking and pulmonary tuberculosis. Although the exact mechanism is not known, it is possible that the nicotine in tobacco smoke might interfere with the immune response of the host to *Mycobacterium tuberculosis*.

In conclusion, using a case-control design and appropriate analysis, we have shown that there is an association between tobacco smoking and the development of pulmonary tuberculosis which is dose dependent. It is possible that tobacco smoking is a potential risk factor for developing pulmonary tuberculosis. Further studies using different study designs including a follow up period are needed to measure the incidence rate ratios between smokers and non-smokers which will strengthen the evidence for a causal relationship between tobacco smoking and pulmonary tuberculosis.

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