



ASSOCIATION OF TOBACCO SMOKING AND PULMONARY TUBERCULOSIS IN WEST DISTRICT OF TRIPURA: A CASE CONTROL STUDY

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ABSTRACT

BACKGROUND: India is the highest TB burden country in the world and accounts for nearly one fifth (20%) of global burden of TB. Every year approximately 1.80 million persons develop TB of which 0.82 million are infectious. India is also the second largest consumer of tobacco products & the third largest producer of tobacco in the world. India is home to the largest population of patients with TB & tobacco users in the world. **OBJECTIVES:** To assess the risk of developing pulmonary tuberculosis among tobacco smokers. **METHODOLOGY:** A community based Case-Control study was conducted Between Nov 2014 to October 2016 in an area covered by all the ten (10) designated microscopy centers under West Tripura District. A total of 90 cat I pulmonary tuberculosis patients and 270 neighbourhood controls matched for age and sex were interviewed according to a predesigned interview schedule. **RESULT:** Exposure rates among cases are 68.90% whereas exposure rate among controls are 37.80%. The odds of developing pulmonary tuberculosis among smokers was 3.6 times more than that among non smokers [OR= 3.647 (P<0.0001)]. **CONCLUSION:** Tobacco smokers have higher chances of developing PTB.

KEYWORDS : Smoked Tobacco, PTB, Pack Year, Misclassification Error

INTRODUCTION

Tuberculosis, commonly known as TB, is an infectious disease caused by various strains of Mycobacteria, especially Mycobacterium tuberculosis. TB most commonly affects the lung. It can spread through the lymph nodes and blood stream to any organ in the body. The risk factors for TB consists of epidemiological triad of agent, host and environment. The agent being the tubercle bacilli, a susceptible person as a host and an environment, which allows the bacilli to survive and transfer from one host to another. Smoking can act as a risk factor by increasing the susceptibility of human host. Smoking causes cough in the patient which allows the transit of tubercle bacilli into environment from infectious host. The bacilli are then inhaled by another susceptible host leading to pulmonary tuberculosis.² The reason for the increased risk of developing pulmonary TB among smokers may be explained by the effects of smoking on pulmonary host defenses. Chronic exposure to tobacco impairs the normal clearance of secretions on the tracheo bronchial mucosal surface and thus allows the causative organism to escape the first level of host defenses, which prevent bacilli from reaching the alveoli.³ Smoke also impairs the function of pulmonary alveolar macrophages. Alveolar macrophages isolated from the lungs of smokers have reduced phagocytic ability and a lower level of secreted pro inflammatory cytokines than do those from the lungs of nonsmokers.⁴ Recent work has suggested a novel mechanism for the effect: nicotine is hypothesized to act directly on nicotine acetylcholine receptors on macrophages to decrease the production of intracellular tumor necrosis factor and thus impair killing of M. tuberculosis.⁵ India has the highest TB burden country in the world and accounts for nearly one fifth (20%) of global burden of TB. India is also the second largest consumer of tobacco products & the third largest producer of tobacco in the world. India is home to the largest population of patients with TB & tobacco users in the world.⁶ In India, 14% per cent of the population above age 15 smoke tobacco (24% for men and 3% for women). Several studies have reported that there is an extreme of association between tobacco smoking and tuberculosis.^{7,8,9} A meta analysis conducted by Lin et al on 38 studies showed an association between tuberculosis and tobacco use.⁸

Prevalence of smoking among men & women (15 years & above) were reported in Tripura 32.2% & 4.3% respectively¹⁰ and in West Tripura District 27.5% & 1.7% respectively¹¹, which is quite high again the burden of Tuberculosis in Tripura is quite alarming. However, there is a paucity of information regarding tobacco use and tuberculosis risk among the Tuberculosis patients of the North Eastern part of India. Hence, the present study was conducted with the aim to study the

association between tuberculosis and tobacco use among Pulmonary tuberculosis patients of West Tripura District.

METHODOLOGY

The Study is community based case control study conducted at West Tripura district for a period of 2 years. Study population was cases of Pulmonary Tuberculosis patients who were ≥ 18 years of age diagnosed either bacteriologically or clinically as Pulmonary Tuberculosis, registered as Category I Pulmonary Tuberculosis. The state has eight districts, out of which the West Tripura District is the most populous district of the state. In Tripura, RNTCP has been operational in all the districts since 2005. Currently, the state has 10 tuberculosis unit and 52 designated microscopic centers and the West Tripura district has one tuberculosis unit and 10 designated microscopic centers and 131 DOTS centers. A list of the entire Category I pulmonary tuberculosis patients of age ≥ 18 years, registered under each DOTS center and DMCs were prepared after collecting the names from all the DMCs separately. This list was verified with the list available in District Tuberculosis Office of West District of Tripura. A sampling frame was prepared for the registered Category I pulmonary tuberculosis patients of ≥ 18 years in the DOTS centers under all the DMC in West Tripura District within the period of November' 2014 up to April' 2015 initiated on treatment with DOTS therapy under RNTCP. There were total 241 Category I pulmonary tuberculosis patients registered under RNTCP in West District of Tripura. A sample size of 90 cases was calculated based on formula, $n = \frac{(2a+2z)^2 (p_1q_1 + p_2q_2)}{(p_1 - p_2)^2}$, where p_1 = Proportion of exposed subjects in cases = 33.3%, p_2 = Proportion of exposed subjects in control = 13.8%, including 10% non response. From this list 90 (ninety) Category I pulmonary tuberculosis patients were chosen, as per inclusion criteria, by simple random sampling using random number table. Randomly selected PTB patients were the cases in the present study and were interviewed at their home. Controls were selected simultaneously with the cases. Controls were healthy individuals in the community without the disease and also without any history of tuberculosis in the past. They were selected in a ratio of 1:3 with the cases. As 3 (three) controls were selected for each case, so a total of 270 controls were selected. Controls were selected from the same locality from where the specific case was selected. During the selection of controls matching was done individually by age (± 2 years), sex and place of residence (neighbourhood control) with the cases. All the controls were interviewed in the same way as the cases were interviewed. Data analysis was done manually as well as in SPSS version 15 and EPI info version 7.0. Data were expressed in frequency, percentage and statistical analysis was performed using Pearson's chi square test and

Odds ratio was calculated by multiple logistic regression analysis. P value of < 0.05 was considered as statistically significant. The study protocol was approved by the institutional ethics committee of Agartala Government Medical College.

RESULTS

Table: 1 Socio-demographic profile of the study participants

Variables		Cases N(%)	Controls N(%)
Age(mean±SD)		45.79 + 16.19	45.88 + 16.14
Age groups	< 40 yrs	32(35.60)	89(33.00)
	40 – 60 yrs	49(54.40)	145(53.70)
	>60 years	9(10.00)	36(13.30)
Sex	Male	70(77.80)	210(77.80)
	Female	49(22.20)	60(22.20)
Caste/Community	General	26(28.90)	81(33.00)
	ST	11(12.20)	36(53.70)
	SC	30(33.30)	76(13.30)
	OBC	23(25.60)	77(28.50)
Marital Status	Married	54(60.00)	158(58.50)
	Single	36(40.00)	112(41.50)
Education status	Illiterate	28(31.10)	51(18.90)
	Primary	53(58.90)	143(53.00)
	Secondary and above	9(10.00)	76(28.10)
Occupation	Employee	5(5.60)	54(20.00)
	Skilled Labour	9(10.00)	16(5.90)
	Unskilled labour	34(37.80)	59(21.90)
	Business	9(10.00)	48(17.80)
	Unemployed	19(21.10)	70(25.90)
	Nuclear	51(56.70)	182(67.40)
Type of family	Joint	39(43.30)	88(32.60)
	Per capita income		
	< 3000 rs	59(65.60)	73(27.00)
	3000 – 6000 rs	26(28.90)	123(45.60)
	>6000 rs	5(5.60)	74(27.40)

As the case & controls were age and sex matched, hence the mean age of the cases were (45.79 + 16.19) years and this was similar to the mean age of controls (45.88 + 16.14)(Table 1). Median age for case 45.50 IQR (31.75 – 56.25) & for control 45.50 IQR (32.75 – 56.25). According to the age groups, majority (53.89%) of the study participants were in the age group of 40-60 years for both cases (54.40%) and controls (53.70%). Majority of the participants (60.00%) among cases and majority of the participants (58.50%) among controls were married. Only 10.00% of the participants among cases had secondary and above education whereas 28.10% of the participants among controls had secondary and above education. Majority of the participants (37.80%) among cases were unskilled labour.

Table 2. Association of Tobacco smoking and pulmonary tuberculosis:

Tobacco Consumption	Case N (%)	Control N (%)	Significance
Habit of Smoking	Yes	62(68.90)	$\chi^2=26.341$; $df=1$; $P<0.0001$
	No	28 (31.10)	
Type of Smoker	Ex – smoker	17(18.90)	$\chi^2=28.705$; $df=2$ $P<0.0001$
	Current smoker	45 (50.00)	
	Non smoker	28 (31.10)	
Duration of Smoking	<10 yrs	6(6.70%)	$\chi^2=32.046$; $df=3$ $P<0.0001$
	10-20 yrs	21(23.30%)	
	>20 yrs	33(36.70%)	
	Non-Smokers	28 (31.10)	
Type of tobacco smoking	Bidi	54(60.00)	$\chi^2=27.764$; $df=3$ $P<0.0001$
	Others	8 (8.90)	
	Non Smokers	28 (31.10)	
Total pack year	<10 yrs	17(18.90)	$\chi^2=29.091$; $df=3$ $P<0.0001$
	10-20 yrs	20(22.20)	
	>20 yrs	25(27.80)	
	Non Smokers	28(31.10)	

The study revealed that majority of the participants (68.90%) among cases had a habit of smoking tobacco. About 37.80% of the participants among controls had a habit of smoking tobacco. So exposure rates among cases are 68.90% whereas exposure rate among controls are 37.80%.

The Present study showed a significant association between tobacco smoking habit of participants and Pulmonary Tuberculosis $\chi^2 = 26.34$, $df = 2$, $p < 0.0001$. The current smoker & Ex smoker also showed strong significant association $\chi^2 = 28.71$, $df = 2$, $p < 0.0001$.

Duration of smoking was also another attribute for pulmonary Tuberculosis. The present study showed that duration of smoking more than 20 years had a strong significant association $\chi^2 = 32.046$, $df = 3$, $p < 0.0001$. Analysis also revealed that majority of participants among the cases had a pack year of more than 20. Strong and significant association was also observed for 20 or more pack years $\chi^2 = 29.09$, $df = 3$, $p < 0.0001$. But present study failed to prove any association with chewing tobacco which is consistent with other study reports from elsewhere.

Table 3: Multivariable logistic regression model examining the association between tobacco smoking and pulmonary tuberculosis.

Tobacco Consumption		Odds ratio(OR)	95% Confidence interval for OR	P value
Habit of Smoking	Yes	3.647	(2.191-8.071)	$P<0.0001$
	No	1		
Type of Smoker	Ex – smoker	2.390	(1.442-7.649)	$P=0.020$
	Current smoker	5.415	(2.810-11.589)	
	Non smoker	1	(Reference)	
Duration of Smoking	<10 yrs	1.154	(1.013-3.714)	$P=0.048$
	10-20 yrs	2.394	(1.195-7.648)	
	>20 yrs	3.237	(1.759-8.428)	
	Non-Smokers	1	(Reference)	
Type of tobacco smoking	Bidi	2.059	(0.778-3.327)	$P=0.233$
	Others	1.316	(0.997-2.059)	
	Non Smokers	1	(Reference)	
Total pack year	<10 yrs	1.578	(1.205-5.892)	$P=0.043$
	10-20 yrs	2.656	(1.384-7.112)	
	>20 yrs	5.648	(1.297-13.660)	
	Non Smokers	1	(Reference)	

Multivariable logistic regression analyses revealed that participants who were habituated to tobacco smoking had 3.6 times higher chance of developing pulmonary tuberculosis and this association was statistically significant [OR= 3.647 CI (2.19 – 8.07) ($p < 0.0001$)]. Current smoker had 5.4 times higher chance of developing pulmonary tuberculosis than that among non smokers and this association was also statistically significant [OR= 5.415 CI (2.81 – 11.58) ($p < 0.0001$)]. Participants those were ex-smoker had 2.4 times higher chance [OR= 2.390 CI (1.44 – 7.64) ($P = 0.020$)] of developing pulmonary tuberculosis than that among non smokers and association was statistically significant. Who smoked tobacco for >20 years had 3.2 times higher chance of developing pulmonary tuberculosis than that among non smokers and this association was statistically significant [OR= 3.237 CI (1.75 - 8.42) ($P = 0.003$)], who smoked tobacco in the form of bidi had 2 times higher chance [OR= 2.059 CI (0.77 - 3.32) ($P = 0.233$)], who were smoking >20 pack years had 5.6 times higher chance of developing pulmonary tuberculosis than that among non smokers and this association was also statistically significant [OR= 5.648 CI (1.29 – 13.66) ($P < 0.0001$)].

DISCUSSION

The present study revealed that majority of the participants (68.90%) among cases and about 37.80% of the participants among controls had a habit of smoking tobacco. 31.10% of the participants among cases did not have a habit of smoking tobacco. So exposure rates smoked tobacco cases were 68.90%. After controlling for effects of other variables in the model the odds of developing Pulmonary Tuberculosis among the smoker was 3.6 times more than that of non smokers¹². Similar result was obtained from another study where the odds of developing pulmonary Tuberculosis among the smoker 3.8 times more than non smokers (OR 3.895% CI 2.0 to 7.0) $P < 0.0001$. Other study also reported similar results of association of smoking with Pulmonary Tuberculosis OR 3.53 $p < 0.0001$ is consistent with present study.¹³ The present study also revealed that the current smokers are at most risk than compare to Ex smoker & non smoker. The risk of Pulmonary Tuberculosis among the current smokers in the present study OR = 5.415 $p < 0.0001$, the risk ex smoker OR = 2.390 $P = 0.020$. Duration of smoking had also role of developing Pulmonary Tuberculosis. The present study revealed that those smoked for 20 years and above had the OR of 3.237 $p = 0.003$, and these smoking 10 to 20 years had OR = 2.39 ($p = 0.017$) compared to less than 10 years. (OR = 0.154 $p = 0.048$). Study by Dhangaye T. M also reported those who smoked more than 20

years had higher chance of developing Tuberculosis (OR .07 95% CI 1.37 to 6.86)¹⁴. The present study could not establish any association with pulmonary Tuberculosis tobacco chewing. Similar result reported of non association from different studies^{12,15}

CONCLUSION

The present study revealed smoked tobacco is important and independent risk factors of Pulmonary Tuberculosis. Most of the study subjects belonged to low socioeconomic class, in which bidi smoking was the prevalent mode of smoking. Stronger association was found to be present between tobacco smoking and development of pulmonary tuberculosis. There was a strong dose-response relationship -both in terms of quantity and duration of smoking.

LIMITATION

Recall bias is always present in case-control studies. Memories about exposure of smoking and duration of smoking are not always reliable. Moreover, cases may have a better recall of relevant past events (exclusive smoking habits) than controls-over the years, their illness may provide more easily remembered exposure and they have a better motive for remembering to get better. This is not always true with the controls. This leads to misclassification error in exposure measurement. As the present study is consistent with other study it seems misclassification error was minimized. The higher Odds ratio of present study reveals a bias away from null means that data is indicating a stronger association.

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