

A STUDY OF ASSOCIATION OF SMOKING WITH PULMONARY TBLokendra Dave¹, Nishant Shrivastava², Ozair Ahmad Ansari³, Ravi Dohre⁴**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: OBJECTIVES: To determine the association between pulmonary tuberculosis and cigarette smoking. **METHODOLOGY:** This retrospective study was carried out in Hamidia hospital, a tertiary care centre in Bhopal. Medical charts of tuberculosis patients presenting in year 2011 to 2013 were reviewed. Three hundred eleven patients aged 18–60 years with confirm diagnosis of pulmonary tuberculosis (smear positive) were selected as cases and 540 age matched persons without tuberculosis (patients hospitalized in other wards) were selected randomly as controls. Data on smoking status, quantity of cigarette smoked, and duration of smoking was collected from medical charts. Statistical analysis was done to see the correlation. **RESULTS:** Out of total 311 case, 150 (48.3%) were smoker, while, of total 640 controls 143 (22.3%) were smoker. The estimated odds ratio (OR) of the relation between smoking and tuberculosis was 3.58. The mean pack –years of smoking (considering 20 cigarette/packet) in cases and controls were 15.9±13.7 and 13.5±9.1, respectively. The ORs for mild (1–10 cigarettes/day), moderate (11–20/day), and heavy (>20/day) smokers were 2.6, 2.94, and 3.25, respectively. The ORs for smokers with <10 years duration, 11–20 years, and >20 years of smoking were 1.68, 2.51, and 4.10, respectively. **CONCLUSION:** This study showed that pulmonary tuberculosis is associated to cigarette smoking habit. The association is dose-dependent and time related. Smoking may be a risk factor for TB acquisition.

KEYWORDS: Tuberculosis, Cigarette smoking.

INTRODUCTION: TB with 84 per 100000 population incidence rate is the most important endemic infectious disease in India.¹ Although directly observed treatment (DOT) strategy has decreased TB transmission and its prevalence, but, in India, TB is still a major public health problem. Smoking during exposure to tubercle bacilli is likely to produce tuberculosis (TB) disease.² Chronic exposure to tobacco impairs the normal clearance of secretions on the trachea-bronchial mucosal surface and may thus allow the causative organism, Mycobacterium tuberculosis, to escape the first level of host defenses, which normally, prevent bacilli from reaching the alveoli.³

Smoke also impairs the function of pulmonary alveolar macrophages, which are not only the cellular target of M. tuberculosis bacilli, but also constitute an important early defense mechanism against the bacteria.⁴ Cigarette smoke activates alveolar macrophages to produce a local inflammatory response, but nicotine suppresses the antigen presenting function, to develop a specific immune response and induces T cell anergy.^{5,6,7,8}

Recent work has suggested a novel mechanism for this effect; nicotine is hypothesized to act directly on nicotinic acetylcholine receptors on macrophages to decrease intracellular tumor necrosis factor- α production and thus impair intracellular killing of M. tuberculosis.¹⁰ Smoking damages the lung's defense mechanism against infections including M.TB and other infections.^{6,7}

Natural killer cell activity is also less and significantly suppressed in smokers. Interleukin-18 is reduced in induced sputum from smokers.⁶⁻⁹ Therefore chronic exposure to cigarette smoke

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reduces T cell mediated immunity. Since there is such immunodeficiency pattern in smokers, clinical manifestation, imaging test results and response to treatment can be different compared with non-smokers. Smoking predisposes to complication such as cancer, cardiovascular and infection, risk is related to amount of cigarette smoked, which is expressed in pack year. These complications are more prevalent in heavy smokers (>25 pack-years) than light smokers (<25 pack-years).¹¹

Previous studies on the association between smoking and clinical TB disease showed that there was a significantly increased risk of clinical TB among smokers regardless of AFB positivity, adjustment for ages and socioeconomic status, type of study, or choice of controls.¹³⁻²⁰ Cigarette smoking is increasing in India where TB is already a problem.²⁻⁴ It is important for Indian health policy makers to further develop strategies for controlling cigarette use in order to reduce the impact of TB in India. There is no consensus whether smoking increase risk of TB.¹²

Since limited studies have evaluated the impact of smoking on TB and the lack of studies supporting the association between smoking and TB in the region of study, we conducted this retrospective study in Bhopal, a city in central India. This study has answered the question whether cigarette smoking has influence on tuberculosis in our population or not. Possible role of smoking as a risk factor, may guide us for increasing efforts to decrease TB morbidity and mortality, by reducing smoking rate.

METHODOLOGY: This retrospective study based on existing patient data, was carried out from Bhopal city in Central India. Medical record of documented tuberculosis cases hospitalized in infectious diseases ward (cases) and hospitalized patients in medicine, orthopedic, surgery and other OPD - without TB (controls), during two years period from Nov 2011 to Oct 2013 were reviewed.

Demographic characteristics, medical history, smoking status, age at which smoking started, history regarding duration and number of bidi/cigarette per day, imprisonment, HIV serology status, drug addiction, underlying diseases, and other medical problems were taken from their medical file records(as much information as was possible was gathered). Three hundred eleven TB patients as cases and six hundred thirty age and sex matched person without TB as control, were enrolled into the study.

- Inclusion criteria for cases, Indian male adults, who had documented TB, diagnosis based on Revised National Tuberculosis Control Program (RNTCP) criteria.: new pulmonary tuberculosis cases, with at least two sputum smear positive for acid fast bacillus (SSP-AFB) or, a chest radiography (C-X ray) suggestive of tuberculosis plus one SSP-AFB were defined as pulmonary tuberculosis (PTB) patient.
- Exclusion criteria were: age less than 18 years, female gender, cases associated with immune-compromised conditions, including: diabetes, hepatitis, cancer, malignant disease and HIV/AIDS and records with incomplete data.
- The amount of cigarette smoked by studied patients were expressed in pack – year. We retrieved information from the individual records on smoking status (never, current, and former) at baseline. For current smokers, data were available on cigarettes smoked per day, years of smoking, and age of smoking onset.

The chi square test was used to compare the frequency of cigarette smoking in two groups. Odd's ratio calculated. Ninety-five percent confidence intervals were calculated where appropriate. Differences with P value of <0.05 were considered significant

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RESULTS: Three hundred eleven cases with the mean age of 36 ± 18 years, and 640 controls with the mean age of 40 ± 20 years, were studied. Of total 311 case 150 (48.3%) were cigarette smoker.

Whereas, of total 640 control non-TB patients, 143(22.3%) were cigarette smoker.

The estimated odds ratio (OR) of the association between smoking and tuberculosis was 3.2 [(95% confidence interval (CI) 4.3 to 23.5), $p < 0.001$]. The mean cigarette smoked per day in cases and control was 10.6 ± 5.3 and 7.5 ± 2.8 , respectively ($P=0.5$). The distribution of smokers by age at which smoking started was as follows: 5 smokers (3%) <20 years of age, 78 smokers (52%) 20-30 years of age, 49 (32.6%) smokers 30-40 years of age, 18(12%) smokers were > 40 yrs age; the earliest age was 18 years. 91% were “beedi” smokers and 9% were cigarette smokers.

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. Among the 311 cases there were 150 smokers and, of the 640 controls, 143 individuals smoked estimated odds ratio 3.4 (95% confidence interval (CI) 1.42 to 4.37), $p < 0.001$).

	Mild (1-10/day)	Mod (11-20/day)	Heavy (>20/day)	Non-Smokers
Control	69(48%)	46(32%)	28(20%)	347
Case	58(38%)	55(37%)	37(25%)	161
Odd's Ratio	2.6	2.94	3.25	

Table 1: Distribution of subjects with different grades of smoking

Table 1 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 2.6, 2.94 and 3.25 respectively.

	<10 years	11-20 years	>20 years	Non-Smokers
Control	60(42%)	47(33%)	36(25%)	347
Case	41(27%)	48(33%)	60(40%)	161
Odd's Ratio	1.68	2.51	4.1	

Table 2: Distribution of Subjects with duration of smoking showing cumulative effect of smoking on occurrence of PTB

Table 2 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 1.68, 2.51, and 4.10 respectively, were obtained for the three categories.

DISCUSSION: 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 exculpta*). The Tendu leaf is odourless and tasteless when smoked. Because of its smaller size, “beedi” may produce less smoke than a cigarette.

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This study showed that frequency of smoking in TB patients in the region is more prevalent than was expected. The present study showed that cigarette smoking is an important risk factor for tuberculosis than those previously documented in literature (OR, 3.2 vs. 2.3). A review of recent published reports, showed that cigarette smoking as a risk factors for TB indicated a variation of odds ratio in different areas, ranging between 2.1 to 3.13.12-20 There is potential explanation of stronger association between smoking and TB in our study, too.

This suggests that it is important for Indian health policy makers to further develop strategies at community level, for controlling cigarette use, in order to reduce the impact of TB in India.

Previous similar studies had shown male preponderance among smoker TB patients. In the region of our study, males are usually at higher risk for cigarette smoke exposure because of their high risk social behaviors. They also take part in parties or activities, putting them at higher risk of smoking and this was the reason, we have observed the records of male patients only.

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 absence so there is little chance of recall bias.

The finding that smoking is an important risk factor for TB in our region has obvious TB control implication. High prevalence of smoking in TB patients requires high attention, focused on fighting against increasing trend of cigarette smoking in our population especially young people.

Limitations of the Study: The study has several limitations. First, our finding is based on the retrospective observations; we cannot, therefore, exclude the possibility of confounding variables that may be associated with each of the exposures. Second, we compared TB patients with non TB patients and frequency of smoking in each group was analyzed. Our control group may not truly represent to the whole local population as far as habits and socioeconomic status is concerned.

CONCLUSION: Cigarette smoking may be an important risk factor for developing tuberculosis. The association does not show dose-dependency. However, further prospective study including large population of smokers and non-smokers is needed for determining the smoking as a risk factor for TB.

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