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Smoking and Pulmonary Tuberculosis

Tuberculosis (TB) is one of the world's leading infectious causes of death. It has been reported that currently, one-third of the world's population is infected with the TB bacillus and approximately 2 million individuals die each year of TB, with more than 90% of infections and deaths occurring in low- and middle-income countries. About 80% of all new TB cases are seen in 23 countries; more than half are concentrated in 5 countries (Bangladesh, China, India, Indonesia and Nigeria).¹¹²

Even in India, pulmonary TB is a highly prevalent disease and a major cause of death. Thus, ascertaining the role of smoking in the development and progression of TB is of paramount importance. Very early studies from the West did point out some association between smoking and TB, but by the time large cohort studies were launched, TB had declined considerably in those countries.

Global evidence

Some studies related to smoking and TB had been conducted in developed countries, where pulmonary TB as a cause of death had already become uncommon. In developing countries, the major increase in smoking is relatively recent for the full hazards to have materialized.^{115–117} Hence,

Box 4.4 Pathogenesis of tuberculosis among smokers

TB occurs predominantly among socially and economically disadvantaged people and in immunocompromised patients. Smoking decreases immune defences and increases susceptibility to pulmonary TB.¹¹³ Cigarette smoking has been found to affect pulmonary function; it can damage the respiratory mucosa, thereby impairing host resistance to infection.¹¹⁴

the potential importance of the association between persistent smoking and TB has been underestimated. For example, the disease was not even indexed in two major reports on smoking and health by the US Surgeon-General.^{118,119} Some major reports on smoking and health mentioned the association between smoking and TB only to dismiss it.^{120–122} In India, as in many other countries, TB still remains a major cause of premature death, both in early adult life and in middle age, particularly among men who smoke.

Indian evidence

This section reviews the available case-control and cohort studies of the association between smoking and death from TB in India, case-control studies of smoking in patients recently diagnosed by TB clinics as having active TB, and population surveys that correlate the self-reported prevalence of ever smoking and of ever having TB.

Tamil Nadu studies

Mortality from TB: Urban and rural case-control studies

A case-control study (1995–2002) of tobacco use was conducted among deceased adult men who were 25 years of age and above at the time of death in an urban and a rural area in the south Indian state of Tamil Nadu.¹²³ Urban cases were from Chennai during 1995–1997 and the rural cases were from the district of Viluppuram during 1997–1998. The controls were living men aged 25 years or above, either married to a woman who had died during the same period as the cases (1995–1997) or a male family member living in the same home as the deceased woman. The study in the urban area included 27,000 cases (2200 of whom had died of TB) and 20,000 controls. The rural study included 16,000 cases (1800 of whom had died of TB) and 15,000 controls. The probable underlying cause of death was assigned by verbal autopsy (VA). The VA procedure used for adult deaths had a sensitivity of 94% to identify cancer in the age group of 25–69 years.^{124–126}

In the urban area, among those 25–69 years of age, 78.9% of those who were diagnosed to have died of TB had been smokers, but only 39.2% of the controls were smokers (Table 4.6). The risk among smokers of dying from TB was more than four times that among non-smokers, in both urban and rural areas. Seventy-nine per cent of the 1840 deaths from TB in the urban area involved smokers, and it can be estimated that 61% (1127/1840) of all male TB deaths in this age range would have been avoided on the assumption that the smokers would have had non-smoker TB death rates. Of the 1529 deaths from TB in the rural area, 73% of those who had died of TB had smoked, and 56% (853/1529) of the deaths from TB would have been avoided.¹²³

Age-specific comparisons between the men whose deaths were attributed to pulmonary TB and the controls show that in urban Chennai the smoker versus non-smoker risk ratios decreased slightly with age, from 5.1 in early adult life (25–34 years) to 3.4 in old age (75+), but in each age group the excess TB mortality among smokers was substantial and highly significant. Likewise, in rural Viluppuram the excess mortality from TB was substantial and highly significant in all age groups.¹²³

Urban Tamil Nadu (cross-sectional survey) in Chennai: Self-reported prevalence of ever having smoked and ever having had TB

In a cross-sectional survey, among all men and

Table 4.6 Death from pulmonary tuberculosis, by smoking and age: Men in urban and in rural areas of Tamil Nadu, south India¹²³

A: Urban (Chennai): 2231 tuberculosis deaths (cases) and 20,162 controls

Age group (years)	TB deaths (cases)		Unmatched controls		Risk ratio, ever/never-smoked* (95%CI)	Smoking-associated		
	No. smoked	%	No. smoked	%		No.	%	
25–34	205	73.7	1787	31.7	5.1	(3.6–7.1)	121	59
35–44	415	80.2	3847	40.7	4.6	(3.6–6.0)	261	63
45–54	517	82.4	5079	41.5	5.2	(4.1–6.6)	344	67
55–64	494	78.9	4171	39.8	4.4	(3.5–5.5)	301	61
65–69	209	72.2	1604	36.3	3.4	(2.4–4.8)	107	51
70–74	177	74.0	1570	37.8	4.1	(2.9–5.9)	99	56
75+	214	64.0	2104	30.8	3.4	(2.5–4.6)	96	45
Subtotal:								
25–69	1840	78.9	16,488	39.2	4.5	(4.0–5.0)	1127	61
All medical causes	16,076	60.0	16,488	39.2	2.1	(2.0–2.2)	5021	31

B: Rural (Viluppuram): 1841 tuberculosis deaths (cases) and 15,128 controls

Age group (years)	TB deaths (cases)		Unmatched controls		Risk ratio, ever/never-smoked* (95%CI)	Smoking-associated		
	No. smoked	%	No. smoked	%		No.	%	
25–34	119	64.7	2738	43.1	2.4	(1.6–3.5)	44	37
35–44	291	79.7	4068	51.8	4.1	(3.1–5.6)	176	61
45–44	471	75.8	3510	47.8	4.0	(3.2–5.1)	268	57
55–64	461	74.4	2183	39.4	5.5	(4.3–6.9)	280	61
65–69	167	59.9	864	34.3	3.2	(2.3–4.6)	77	41
70–74	139	51.1	794	36.1	2.2	(1.5–3.3)	39	28
75+	173	49.1	971	29.4	2.5	(1.8–3.5)	51	29
Subtotal:								
25–69	1529	73.3	13,363	44.0	4.2	(4.7–4.8)	853	56
All medical causes	10,121	52.0	13,363	44.0	1.6	(1.5–1.7)	2057	20

*Standardized for age, educational level and tobacco chewing

CI: confidence interval

Table 4.7 Prevalence of ever having had pulmonary tuberculosis by smoking and age: Survey of 250,000 men in urban Chennai, Tamil Nadu, South India¹²³

Age group (years)	Ever-smoker		Never-smoker		TB prevalence ratio, ever/never-smoked* (95% CI)	
	Ever TB/total	%	Ever TB/total	%		
35–44	233/42,813	0.5	134/71,273	0.2	2.4	(1.9–3.0)
45–54	254/27,293	0.9	123/42,196	0.3	2.7	(2.1–3.3)
55–64	214/15,159	1.4	73/24,162	0.3	3.9	(3.0–5.1)
65–69	68/4171	1.6	25/8034	0.3	4.6	(2.8–7.3)
Subtotal:						
35–69	769/89,436	0.86	355/145,665	0.2	2.9	(2.6–3.3)
70+	63/4448	1.4	53/11,468	0.5	2.8	(1.9–4.0)

*Standardized for age, educational level and tobacco chewing.

women aged 35 years or above in Chennai during 1998–2001, which included 251,000 men and 225,000 women, 67% of the men with a history of TB and 37% of other men (age ≥ 35 years) in the general population were found to be smokers. In the age range of 35–69 years, the standardized self-reported TB prevalence ratio was 2.9. This self-reported prevalence of TB (both in middle and old age) was 3 times higher among ever-smokers compared to never-smokers. This provides strong evidence that smoking substantially increases the probability of ever having clinical TB. Among ever-smokers aged 35–69 years, the TB prevalence ratio was positively related to daily smoking, both of cigarettes and, particularly, of *beedis* (Table 4.7).^{123,126}

Case–control study in rural Tamil Nadu: Prevalence of ever-smoking among patients with smear/culture-positive TB

A population survey was carried out to identify TB cases among 60,000 subjects 10 years of age and above in 30 villages in the Tiruvallur district

Table 4.8 Prevalence of confirmed pulmonary tuberculosis (TB) by smoking in men (cases vs controls) 20–50 years of age in rural Tamil Nadu¹²⁷

Smoking status	Cases (n=85)	Controls	Age-adjusted TB prevalence ratio, ever/never-smoked (95% CI)
Never-smokers	21	206	1.0
Ever-smokers	64	253	2.2 (1.3–3.9)

of the state of Tamil Nadu, south India, during 1993–1996.¹²⁷ The results of the study are provided in Table 4.8. Seventy-five per cent of cases and 55% of controls were smokers. The age-adjusted relative risk of developing TB was over 2-fold among ever-smokers compared to never-smokers.¹²⁷

Preliminary results of two ongoing studies in Kerala

Population survey in an urban area: Self-reported prevalence of ever having smoked and ever having had TB

An urban population survey of 106,637 males aged 25 years and above in the city of Thiruvananthapuram, Kerala showed that the percentage of ever-smokers among those with a self-reported history of TB was 74%, as against 49% in other adults. A history of TB was reported by 1.5% of ever-smokers and 0.5% of never-smokers (Table 4.9), yielding a risk ratio (RR) of 3.0.¹²⁸

Case–control study in a rural area: Incidence of TB

A case–control study is being conducted in four districts of Kerala. Over 4 months, 808 confirmed male TB cases under treatment by the local TB

Table 4.9 Prevalence of self-reported pulmonary tuberculosis in men aged 25 years and above in Kerala, south India¹²⁸

Smoking status	Tuberculosis		Risk of tuberculosis RR (95% CI)
	Yes	No	
Never-smokers	267	51,495	1.0
Ever-smokers	748	55,142	3.0 (2.6–3.5)

control programme and 878 population controls were recruited. About 86% of cases and 68% of controls were smokers, yielding a risk ratio of 2.9 for developing TB among smokers (95% CI: 2.3–3.7) (Table 4.10).¹²⁸

Table 4.10 Incidence of confirmed pulmonary tuberculosis among men in Kerala, south India¹²⁸

Smoking status	Cases	Controls	Risk ratio (95% CI)
Never-smokers	115	280	1.0
Ever-smokers	693	598	2.9 (2.3–3.7)

Mumbai, Maharashtra study

Prospective study of 100,000 adults (age 35+ years) in an urban area: Mortality from TB

A baseline survey of 99,598 individuals aged 35 years and above in Mumbai (population: 3.4 million) was conducted between 1991 and 1994. The study showed that the relative risk for all-cause mortality for ever-smokers compared to never-smokers was 1.6 in men and 1.3 in women. Comparing ever-smokers to never-smokers, the age-adjusted relative risk of death due to TB was 2.6, but this decreased to 2.1 on standardizing for education (Table 4.11). A higher relative risk was seen for *beedi* smokers compared to cigarette smokers.¹²⁹

Chandigarh study

Case-control study in urban Chandigarh: Incidence of active TB

In a case-control study in Chandigarh, the cases were 200 patients (males and females) with active pulmonary TB, as confirmed by either positive sputum smears or strong clinical and radiographic evidence with documented response to anti-tubercular drugs. They were matched, by age and sex, with 200 healthy individuals

Table 4.11 Death from pulmonary tuberculosis by smoking: Prospective study of men aged 35 years and above, in Mumbai, Maharashtra¹²⁹

Smoking status	TB deaths (cases)	Adjusted relative risk	
		By age	By education
Never-users	30	1.0	1.0
Ever-smokers	86	2.6	2.1

(healthy controls) and with 200 patients (patient controls) who attended the chest clinic, excluding those with chronic obstructive pulmonary disease and lung cancer.¹³⁰ Thirty-five per cent of cases, 11% of controls with other respiratory disorders and 12.5% of healthy controls were smokers. Comparing the cases with the healthy controls, the ever-smoker versus never-smoker odds ratio standardized for age, sex, socioeconomic status and history of exposure to TB was 4.4.¹³⁰

National Family Health Survey

The National Family Health Survey (NFHS-2) was conducted among a representative sample of 492,197 persons in 92,486 households in India. The survey results indicated that the overall prevalence of TB in India was 0.6% in rural areas and 0.4% in urban areas. The prevalence was 0.62% among males and 0.46% among females, and increased with age. It was estimated that about 2 million people in India develop TB each year.^{131,132}

Summary of the evidence

The studies done in India show a 2- to 4-fold TB prevalence/incidence ratio among males based on the age range analysed in the study, and the smoking-associated proportion was 41%–56%. In 2000, the prevalence of all reported cases of TB among males aged 15 years and above in 1998–1999 was 552 per 100,000 population.¹³³ The burden of TB in India among those aged 15–59 years was 4.0 million (Table 4.12). The death of about half of all TB cases among males would have been avoided if the smokers had had non-smoker TB death rates. The death of about half of all TB cases in 2000—about one million—would have been avoided if the smokers had had non-smoker TB death rates.

Table 4.12 Burden of tuberculosis (TB) in India in 2000^{131,133}

Age range (years)	Interview-reported history of TB (%)	Population in 2000 (millions)	Estimated number with a history of TB (millions)
<15	0.15	338	0.5
15–59	0.68	594	4.0
60+	1.37	77	1.1

Despite some limitations in a few of the studies discussed here, a strong, consistent association does emerge in them. TB is known to be strongly associated with socioeconomic status and other factors such as alcohol use. Thus, confounding from some unknown risk factors remains a possibility but, given the magnitude of the risk, it is highly unlikely to nullify the observed association with smoking.

The studies done in Tamil Nadu estimated that in India, at the death rates of the year 2000, there would be about 700,000 deaths a year due to tobacco smoking, of which about 200,000 would involve pulmonary TB. Half of these tobacco-attributed TB deaths are of men still in their thirties, forties and early fifties.¹²³ The percentage of smokers among those who died of TB in the Tamil Nadu and Mumbai studies was much higher than the percentage of smokers in the general population. After standardization for age, educational level and tobacco chewing, the results in both the urban and rural areas in Tamil Nadu indicate a mortality ratio (ever-smoker versus never-smoker) of about 4. The results of the Mumbai

study indicate an age-standardized mortality ratio of about 3. The magnitude of these RRs are too high to be explained by only confounding.

In general population surveys and case-control studies, the proportion of adults who reported a current or previous history of TB (self-reported TB) and the proportion with confirmed TB (by laboratory tests) are substantially higher among ever-smokers than among never-smokers. This indicates that smoking acts more to increase the incidence of clinical disease than to increase the probability that clinical disease will lead to death from TB. This is because an increased case fatality rate among smokers would selectively remove smokers from the population of patients with TB, and would therefore tend to reduce rather than increase the proportion of smokers in live patients who are detected to have the disease in a survey or a case-control study. Further evidence of causality is that the heavier the exposure (either to cigarettes or *beedis*), the greater the prevalence of TB among smokers. Thus, smoking seems to be an important cause of death from TB.

4.5 SMOKING AND PULMONARY TUBERCULOSIS

KEY MESSAGES

- Tuberculosis is a major cause of premature death in India, both in early adult life and in middle age (25–69 years), particularly among men who smoke.
- The prevalence of TB is about three times higher among ever-smokers than among never-smokers.
- The heavier the smoking, either cigarettes or *beedis*, the greater the prevalence of TB among smokers.
- Mortality from TB is three to four times higher in ever-smokers than in never-smokers.
- Smoking contributes to half the male deaths from TB in India and a quarter of all male deaths in middle age (25–69 years).
- In India, there are an estimated 200,000 deaths per year due to smoking in those with pulmonary TB, out of 700,000 tobacco smoking-related deaths (base year 2000). Half of these tobacco-attributed TB deaths are of men still in their thirties, forties and early fifties.