TUBERCULOSIS

Association between smoking and tuberculosis infection: a population survey in a high tuberculosis incidence area

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Thorax 2005;**60**:555–557. doi: 10.1136/thx.2004.030924

Received 5 July 2004
Accepted 6 April 2005

Background: Associations between smoking and tuberculosis disease including death from tuberculosis have been reported, but there are few reports on the influence of smoking on the risk of developing *Mycobacterium tuberculosis* infection. The aim of this study was to determine the association between smoking and *M tuberculosis* infection.

Methods: In a cross sectional population survey, data on smoking and tuberculin skin test (TST) results of 2401 adults aged ⩾15 years were compared.

Results: A total of 1832 (76%) subjects had a positive TST (⩾10 mm induration). Of 1309 current smokers or ex-smokers, 1070 (82%) had a positive TST. This was significantly higher than for never smokers (unadjusted OR 1.99, 95% confidence interval (CI) 1.62 to 2.45). A positive relationship with pack-years was observed, with those smoking more than 15 pack-years having the highest risk (adjusted OR 1.90, 95% CI 1.28 to 2.81).

Conclusion: Smoking may increase the risk of *M tuberculosis* infection.

In a recent large epidemiological study, 50% of deaths from tuberculosis among Indian men was attributed to smoking.[1] While an association between smoking and tuberculosis disease has been shown in various studies,[2–7] it is less clear to what extent smoking increases the risk of *Mycobacterium tuberculosis* infection, the risk of progression from infection to disease, or the risk of death among tuberculosis patients.

We report here a population survey conducted in two urban communities in Cape Town, South Africa that provides evidence that smoking may increase the risk of tuberculosis infection. The study area in which we have performed epidemiological research for more than 10 years has a population of 36 334 and 97.9% are of mixed ethnicity (categorised as ''coloured''; Statistics South Africa: Census 2001). The tuberculosis notification rate in the area is 238 new smear-positive cases per 100 000 population per year (1993–8),[8] and the prevalence of HIV infection is estimated to be lower than the overall rate for the Western Cape province at the time of the survey (12.4% (8.8–15.9%) in 2002).[9]

METHODS

A random sample of 15% of the residential addresses was selected. Of the 833 selected addresses, the head of the household of 218 (26%) declined to participate. These addresses were replaced by neighbouring addresses according to fixed rules. Written informed consent was obtained from every adult (⩾15 years) and the study was approved by the research ethics committees of Stellenbosch University and the University of Cape Town.

Data collection methods included a tuberculin skin test (TST) and a precoded questionnaire with questions on smoking. For the TST we used an intradermal injection of 2 TU (0.1 ml) PPD RT 23 into the ventral aspect of the left forearm. The induration was measured 48–72 hours later.

Smoking was defined as having ever smoked for at least 1 year. The average number of cigarettes smoked per day was recorded for all ex-smokers and current smokers. The number of pack-years smoked was calculated as the average number of cigarettes smoked per day multiplied by the duration of smoking divided by 20. Infection with *M tuberculosis* was defined as a TST of 10 mm or more, referred to as a positive TST. The 10 mm cut off point is conventionally used and appeared justified in this population since intermediate reactions to TST, usually attributed to environmental mycobacteria, were uncommon (fig 1).

The following potential confounders were considered: age, sex, education level, body mass index (BMI), and individual monthly income. The possible interactions between pack-years and the variables age and sex were investigated. Odds ratios (OR) and their 95% confidence intervals (95% CI) were determined to identify risk factors, and random effects logistic regression was used to control for confounding as well as for possible clustering at the address level.

RESULTS

Of 3512 adults who completed the questionnaire, a TST result was recorded in 2443 (70%). Data on smoking habits were incomplete in 42 individuals so analyses were performed on 2401. Compared with subjects excluded from the analyses, those included were less often male (unadjusted OR 0.57, 95% CI 0.49 to 0.65), were less often current or ex-smokers (unadjusted OR 0.82, 95% CI 0.70 to 0.94), and fewer had an income above 2000 Rand (300 US$) (unadjusted OR 0.62, 95% CI 0.51 to 0.76).

Of the 2401 adults analysed, 1832 (76%) had a positive TST and 1309 (55%) were current or ex-smokers; 82% (n = 1070) of the 1309 current or ex-smokers had a positive TST compared with 70% (n = 762) of the 1092 never smokers (unadjusted OR 1.99, 95% CI 1.62 to 2.45). Men were more likely to have a positive TST than women (unadjusted OR 1.34, 95% CI 1.08 to 1.65; table 1). A positive TST was more common in the 25–44 year age group than in other age groups. The proportion of individuals with a positive TST increased with income, but not with education level or BMI (data not shown).

In the multiple logistic regression analyses, income and sex did not confound the association between smoking and infection. However, as sex was associated with smoking and with having a positive TST, it was retained in the model. The

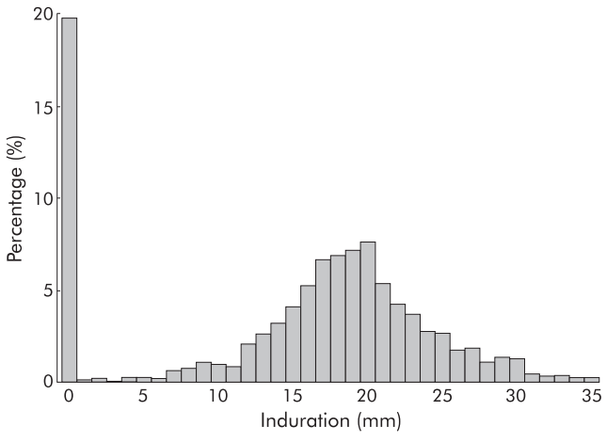

Figure 1 Distribution of induration of tuberculin skin test in 2401 adults.

association between infection and pack-years smoked was not significantly different for the different age and sex strata. After adjusting for age and sex, there was a significant association between smoking and a positive TST (adjusted OR 1.77, 95% CI 1.41 to 2.21). The probability of a positive TST seemed to increase slightly with the number of pack-years smoked, although the differences between the different pack-year categories were not significant (table 1).

DISCUSSION

This study shows that current or ex-smokers had a higher prevalence of *M tuberculosis* infection than never smokers and that there was a slightly higher risk of infection for those who smoked more than 15 pack-years than for those who smoked less, although this was not significant. This suggests that the increased risk of disease and death from tuberculosis among smokers may be due, at least in part, to an increased risk of smokers becoming infected with *M tuberculosis*.

An unexpected finding was the positive association between a positive TST and income. It should be noted, however, that the mean incomes in the study area are low, and that the categorisation threshold used in the analyses identifies only the poorest in the community. Nevertheless, the reason for their lower TST rates requires further study, including the possibility of lower risk of exposure through fewer social contacts.

Our study confirms previous studies that showed an association between smoking and tuberculosis infection in at risk groups.[3 10–14] For example, in an immigrant population Plant *et al*[10] reported a higher risk of infection among smokers which increased with duration of smoking. In contrast to previous studies investigating specific high risk groups,[10–14] the current study is the first to investigate the association between smoking and tuberculosis infection in a cross sectional population survey in a high incidence community.

The reason for the increased risk of infection in smokers is unclear, but may be explained by the effects of smoking on pulmonary host defences. Smoking has been shown to reduce natural killer cytotoxic activity, to suppress T cell function in both lung and blood, to impair mucociliary clearance of particles, and to increase numbers of alveolar macrophages in the lower respiratory tract. Cells of the macrophage-phagocytic group influence immediate or innate immunity through their handling and elimination of mycobacteria, and products of cigarette smoke may therefore favour persistence and/or replication of ingested mycobacteria by impairing the macrophage or dendritic cell function.[15 16]

To take possible sources of bias into account we have considered the following. Men and persons in the highest income category are under-represented, but this is unlikely to be of significance as neither sex nor income was a confounder for the association between smoking and positive TST. Smokers and ex-smokers were also slightly under-represented but still comprised 55% of the sample, and we can see no reason to assume that the smokers who had undergone a TST might be different from those who had not. A weakness of the study is that we did not test the HIV status

Table 1 Risk factors for *M tuberculosis* infection

				Odds ratio	
	TST ⩾10 mm	Total	% TST ⩾10 mm	Unadjusted (95% CI)	Adjusted* (95% CI) n = 2328
Smoking (pack-years)					
Never smoked	769	1102	70	1	1
<5	443	550	81	1.86 (1.42 to 2.43)	1.77 (1.33 to 2.35)
5–15	343	407	84	2.39 (1.74 to 3.29)	1.77 (1.25 to 2.50)
⩾15	236	288	82	2.00 (1.40 to 2.84)	1.90 (1.28 to 2.81)
Unknown	41	54	76		
Sex					
Female	1100	1477	74	1	1
Male	731	923	79	1.34 (1.08 to 1.65)	1.24 (0.99 to 1.56)
Unknown	1	1	100		
Age (years)					
15–24	432	651	66	1	1
25–34	444	498	89	4.47 (3.14 to 6.37)	4.30 (3.00 to 6.17)
35–44	412	484	85	3.16 (2.28 to 4.37)	2.82 (2.00 to 3.99)
45–54	263	330	80	2.11 (1.50 to 2.97)	1.96 (1.35 to 2.85)
⩾55	264	408	65	0.88 (0.66 to 1.18)	0.88 (0.64 to 1.22)
Unknown	17	30	57		
Income (Rands)†					
<500	804	1088	74	1	
500–1999	685	893	77	1.18 (0.94 to 1.48)	
⩾2000	315	381	83	1.93 (1.38 to 2.68)	
Unknown	28	39	72		
Total	1832	2401			

*Adjusted for pack-years, age, sex, and taking into account possible clustering at address level.
†R6.50 = US$1.00.

of participants and were therefore not able to correct for HIV status. Confounding factors that were taken into consideration were individual monthly income, BMI, and education level. However, we cannot entirely discount the possibility that socioeconomic and behavioural differences other than smoking may have affected the relationship between smoking and tuberculous infection.

We conclude that smoking may increase the risk of *M tuberculosis* infection. We propose that further studies be conducted to investigate this association and to establish whether smoking reduction strategies contribute to tuberculosis control.

ACKNOWLEDGEMENTS

The authors thank Dr Ivan Toms, Director of Health, City of Cape Town for permission to work in the community, Neil White and Elvis Irusen for their contribution to the design of the study, Kathy Lawrence for the data management, the sisters and the fieldworkers for their help in gathering data, and the people of Ravensmead and Uitsig for their participation.

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This study was funded by Stellenbosch University through funding from the South African Department of Trade and Industry (THRIP fund) and the Glaxo Smith Kline Action TB Programme, and the University of Cape Town Lung Institute. MWB and SV were supported by Areas Global TB Vaccine Foundation. None of the funding sources had any role in the study design; the collection, analyses, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

NB, EB, SvL, DE, and MB were involved in the study design and writing of the manuscript. SdB performed the statistical analysis and wrote the paper. Advice on statistics was given by CL, SV and MB. All authors participated in interpretation of the results. NB supervised the data collection and MB the statistical analyses.

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