

Smoking, HIV and non-fatal tuberculosis in an urban African population

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SUMMARY

Most previous studies on smoking and tuberculosis (TB) have not considered the role of human immunodeficiency virus (HIV) infection, and very few have been conducted in sub-Saharan Africa. We conducted a case-control study on smoking and TB in Addis Ababa, Ethiopia. Men aged 18–65 years with TB ($n = 72$) were compared to men with no history of TB ($n = 81$). Forty-three per cent of

cases smoked vs. 25% of controls (OR 2.3, adjusted for age, education and self-reported HIV status). Given that HIV appears to increase TB transmission in Africa, our finding that smoking also increases the risk of TB in Africa is of special concern.

KEY WORDS: smoking; tuberculosis; HIV; risk factors; Ethiopia; Addis Ababa

LIKE TWO EARLIER meta-analyses of epidemiological studies,^{1,2} Slama et al. demonstrate that both active and passive tobacco smoking are important contributors to fatal and non-fatal tuberculosis (TB).³ While 11 of the 28 studies assessed by Slama et al. considered human immunodeficiency virus (HIV) status as a risk factor, only three of the 11 and five of all 28 were conducted in Africa. These meta-analyses are also limited, as few studies have considered the role of HIV infection, which may alter the relationship between smoking and the development of TB. Moreover, few studies investigating tobacco use as a risk factor for respiratory diseases have been undertaken in Africa. Our study therefore aimed to assess the main risk factors for the development of TB in an urban African population.

METHODS

In 2006 we conducted a case-control study on the relationship between smoking and TB in Addis Ababa, Ethiopia, a city with high HIV prevalence.

Men aged 18–65 years undergoing treatment for pulmonary TB for at least 2 weeks (cases, $n = 72$) were compared to men with no history of TB, drawn from relatives of cases and matched for age within 5 years (controls, $n = 81$). (Data from women were collected but were excluded from the analysis, as smoking prevalence was nearly zero.) After obtaining written consent, we interviewed each person to obtain self-reported HIV status, use of tobacco and *khat* (a

mild narcotic commonly chewed in Ethiopia), exposure to second-hand smoke and indoor air pollution, alcohol use and other variables. We also obtained a carbon monoxide measurement.⁴

The study was approved by the St Peter's Tuberculosis Hospital Ethics Committee.

Data were double-entered. All statistical analyses were carried out using Stata 8.2 (StataCorp, College Station, TX, USA).

RESULTS

About 43% of men with TB smoked vs. 25% of controls (Table). This corresponds to an odds ratio (OR) of 2.3 (95% confidence interval [CI] 1.1–4.8), after adjusting for age, education and self-reported HIV status. About 28% of men with TB reported being HIV-positive vs. 7% of controls (OR 4.7, 95%CI 1.7–13.1, after adjustment for age, education and smoking). Compared to non-smokers, smokers of ≥ 10 years (OR 5.0, 95%CI 1.7–14.7) were at greater risk than smokers of < 10 years (OR 1.2, 95%CI 0.5–3.1), after adjustment for age, education and HIV status (test for trend of OR across strata = 0.01). Smoking-HIV interaction was non-significant in our model ($P = 0.43$). Relative to non-smokers, patients who smoked ≥ 10 cigarettes per day (OR 4.4, 95%CI 1.3–15.5) were at somewhat greater risk than those who smoked < 10 cigarettes per day (OR 1.8, 95%CI 0.7–4.0, after adjustments; test for trend of OR across strata = 0.03). Among controls, the sensitivity, specificity and

Table Risk factors for tuberculosis in Ethiopia

Risk factor	TB cases <i>n</i> (%)	Controls <i>n</i> (%)	OR (95%CI)	Attributable cases, %
Smoking				
Never	41 (57)	61 (75)	1*	
Ever	31 (43)	20 (25)	2.3 (1.1–4.8) [†]	25
Self-reported HIV status				
Negative/ unknown	52 (72)	75 (93)	1*	
Positive	20 (28)	6 (7)	4.7 (1.7–13.1) ^{‡§}	22

* Reference category.

[†] Adjusted for age, education and HIV; ORs were produced from logistic regression and the score test was used to test for trends in odds for dose-response, while the two-tailed z-test was used to test for differences in ORs; adjusting for *khat* and alcohol use has no additional effect ($P_{\log\text{-likelihood}} = 0.11$).

[‡] Adjusted for age, education and smoking.

[§] Smoking-HIV interaction non-significant ($P = 0.43$).

HIV = human immunodeficiency virus; TB = tuberculosis; OR = odds ratio; CI = confidence interval.

predictive value of the carbon monoxide meter against self-reported smoking status were respectively 100%, 35% and 30%.

DISCUSSION

Our study found that smoking status and HIV status were the two key risk factors for TB infection. These risks are too extreme to be due to chance, and are consistent with those observed in earlier meta-analyses of smoking and TB, as well as HIV and TB.^{1–3,5} Moreover, we show a dose-response relationship with duration and amount of smoking. A quarter of the controls smoked, which is higher than the proportion reported among adult males in Ethiopia (about one sixth).⁶

While our study was small and further tests for smoking and HIV interaction may be indicated, these results pose two suggestions. On one hand, we might commonly be underestimating the true risks of smoking and TB in Ethiopia. No major reductions in the relative risks of TB associated with smoking were seen on adjustment for levels of education, HIV status or *khat* or alcohol use, suggesting that residual confounding by socio-economic status or these other exposures is unlikely to explain much of the excess TB risk associated with smoking. On the other hand, only 7% of our controls reported being HIV-positive. Previous estimates of the overall prevalence of HIV among adult males and females aged 15–49 years are about 15% in Addis Ababa and about 4% nationally in Ethiopia.⁷ This suggests that we might have overestimated the risk of HIV for TB, particularly if positive HIV status was underreported in controls. This is possible given the fact that healthy controls have less reason to know their HIV status than TB-positive patients.

Although smoking has not historically been a major health concern in Africa, TB is of major concern, being

responsible for an estimated 0.3 million deaths a year in the region.⁸ If, as believed,^{2,3,9,10} smoking turns stable subclinical infection by the tubercle bacillus, which is widespread in Africa and elsewhere, into active disease, smoking would also be expected to contribute to the spread of TB infection by making latent disease more active and infectious. Given that HIV appears to increase TB transmission in Africa,⁵ our finding that smoking also increases the risk of TB in Africa is of special concern. Large-scale epidemiological studies in African and other countries are required to understand the relationship between smoking and HIV and TB acquisition, transmission and mortality.

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References

- 1 Lin H-H, Ezzati M, Murray M. Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis. *PLOS Med* 2007; 4: 173–189.
- 2 Bates M N, Khalakdina A, Pai M, et al. Risk of tuberculosis from exposure to tobacco smoke: a systematic review and meta-analysis. *Arch Intern Med* 2007; 167: 335–342.
- 3 Slama K, Chiang C-Y, Enarson D A, et al. Tobacco and tuberculosis: a qualitative systematic review and meta-analysis. *Int J Tuberc Lung Dis* 2007; 11: 1049–1061.
- 4 Mordan E, Weeks A, Geffrard M, et al. Expired carbon monoxide validation of self-reported smoking among emergency department patients. *Acad Emerg Med* 2005; 12 (Suppl 1): 45.
- 5 Corbett E L, Bandason T, Cheung Y B, et al. Epidemiology of tuberculosis in a high HIV prevalence population provided with enhanced diagnosis of symptomatic disease. *PLOS Med* 2007; 4: e22.
- 6 Mackay J, Eriksen M. The tobacco atlas. Geneva, Switzerland: World Health Organization, 2002. http://www.who.int/tobacco/resources/publications/tobacco_atlas/en/ Accessed September 2007.
- 7 Hladik W, Shabbir I, Jelaludin A, et al. HIV/AIDS in Ethiopia: where is the epidemic heading? *Sex Transm Infect* 2006; 82 (Suppl 1): i32–i35.
- 8 Lopez A D, Mathers C D, Ezzati M, Jamison D T, Murray C J L. Global burden of disease and risk factors. New York, NY, and Washington DC, USA: Oxford University Press and The World Bank, 2006.
- 9 Gajalakshmi V, Peto R, Kanaka T S, Jha P. Smoking and mortality from tuberculosis and other diseases in India: retrospective study of 43 000 adult male deaths and 35 000 controls. *Lancet* 2003; 362: 507–515.
- 10 Jha P, Jacob B, Gajalakshmi V, et al. A nationally representative case-control study of smoking and death in India. *N Engl J Med* 2008; 358: 1137–1147.

R É S U M É

La plupart des études antérieures sur les rapports entre le tabagisme et la tuberculose (TB) n'ont pas pris en compte le rôle de l'infection par le virus de l'immuno-déficience humaine (VIH), et très peu d'entre elles ont été menées en Afrique sub-saharienne. Nous avons entrepris une étude cas-contrôle sur le tabagisme et la TB à Addis-Abeba, Ethiopie. Des hommes âgés de 18 à 65 ans atteints de TB ($n = 72$) ont été comparés à des hommes

sans antécédents de TB ($n = 81$). Après ajustement pour l'âge, l'éducation et le statut VIH auto-rapporté, il y avait 43% de fumeurs parmi les cas vs. 25% parmi les contrôles (OR 2,3). Vu que le VIH semble accentuer la transmission de la TB en Afrique, notre observation sur l'augmentation due au tabagisme du risque de TB en Afrique par le tabagisme est particulièrement inquiétante.

R E S U M E N

En la mayoría de los estudios previos sobre tabaquismo y tuberculosis (TB) no se ha considerado el papel de la infección por el virus de la inmunodeficiencia humana (VIH) y pocos se han llevado a cabo en África subsahariana. Se realizó un estudio de casos y testigos sobre tabaquismo y TB en Addis Abeba, Etiopía. Se compararon hombres de 18 a 65 años de edad con TB ($n = 72$) con hombres sin antecedentes de esta enfermedad ($n =$

81). Cuarenta y tres por ciento de los casos presentaba antecedente de tabaquismo, comparado con 25% de los testigos (OR 2,3), corrigiendo los datos con respecto a la edad, la educación y el estado autorreferido de la serología el VIH. Considerando que la infección por el VIH pareciera aumentar la transmisión de la TB en África, este hallazgo de un aumento del riesgo de TB en África asociado con el tabaquismo es de particular importancia.