The increasing burden of tuberculosis in rural South Africa — impact of the HIV epidemic

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Objective. To determine the impact of the HIV epidemic on tuberculosis caseload in rural South Africa.

Setting. Hlabisa health district, KwaZulu-Natal.

Methods. Demographic and clinical data were extracted from the tuberculosis database for the period, May 1991 - June 1995. The attributable fraction of HIV-infected tuberculosis cases was estimated from the prevalence of HIV infection in tuberculosis cases and the prevalence of HIV infection in women attending antenatal clinics.

Results. Between 1991 and 1995, the annual tuberculosis caseload increased from 301 to 839 cases. Tuberculosis accounted for 4.7% of all admissions in 1989 and 8.3% in 1995 ($P < 0.0001$). The incidence of tuberculosis increased from 154/100 000 in 1991, to 413/100 000 in 1995. The proportion with smear-positive pulmonary disease fell from 65% to 56% ($P = 0.04$), and pleural tuberculosis accounted for 7.5% of disease in 1991 and 18% in 1995 ($P = 0.002$). The minimum HIV prevalence in patients with tuberculosis increased from 8.7% in 1991 to 28.3% in 1995, and the proportion of tuberculosis cases attributable to HIV infection was estimated to be at least 44% in 1995.

Conclusion. The burden of HIV-related tuberculosis is increasing rapidly in rural South Africa and is exerting a negative impact. Innovative approaches to control will be needed to cope with it effectively.

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Infection with the human immunodeficiency virus (HIV) is the greatest risk factor for subsequent development of active tuberculosis,[1] and HIV is considered responsible in large part for the recent upsurge in incidence of tuberculosis in sub-Saharan Africa.[1-3] Tuberculosis is the commonest HIV-related disease in the developing world.[1,2]

Little is known about the burden and impact of HIV-related tuberculosis in South Africa. Notification data do not yet reflect any increase in tuberculosis incidence, but the reporting system is fragmented and unreliable.[4] It is therefore

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necessary to rely on sentinel surveillance to gain insight into the impact of HIV on tuberculosis in the country in order for appropriate planning and resource allocation to occur. This is especially pertinent as a new tuberculosis control programme is currently being planned and implemented.

This paper reports on the increasing caseload of tuberculosis in a rural South African health district, correlates it with the rapidly rising prevalence of HIV in the community and estimates the proportion of tuberculosis caseload attributable to HIV infection.

Methods

Setting

The study took place in the rural Hlabisa health district of KwaZulu-Natal. The district is home to about 205 000 people who rely on migrant labour remittances, pension payments and subsistence farming for a living. The area is generally rural and is relatively resource-poor. The tuberculosis control programme has been described in detail.[5,6]

Case definitions

All patients with suspected tuberculosis in the district are referred to Hlabisa Hospital where they are admitted for diagnosis based on smear microscopy (culture is not routinely available) and chest radiography. Standard case-definitions are employed.[7]

HIV infection was diagnosed when two different enzyme-linked immunosorbent assays were reported as positive. HIV status was determined when infection was clinically suspected, except in 1993 when a cohort study was undertaken. HIV status (stratified by gender) is therefore reported as: (*i*) the proportion of tuberculosis patients tested; (*ii*) the proportion of those tested found to be HIV infected; and (*iii*) the minimum rate of HIV infection (number shown to be infected divided by the total number of patients). The prevalence of HIV in adults with tuberculosis was also estimated in 1993[8] and 1995[9] in two cross-sectional studies.

Data collection and analysis

Comprehensive demographic, clinical and case-management data were collected prospectively from May 1991 to June 1995 on all tuberculosis patients and entered into an Epi-Info database. Accurate data on the number of admissions were available in full for the years, 1989 - 1995.

The attributable fraction (AF) represents the proportion of HIV-positive tuberculosis patients in whom tuberculosis was attributable to HIV infection (the excess incidence of tuberculosis in HIV-infected persons). It is calculated as AF = 1 – (1/RR),[10] where RR is the relative risk of HIV infection in people with tuberculosis compared with those without tuberculosis. Women attending antenatal clinics were chosen as the group in whom the risk of HIV infection without tuberculosis was measured. Although this probably overestimates the risk in the general population from which people who develop tuberculosis originate, this group was chosen because accurate data are available and because a conservative estimate of the AF will be obtained.

Analysis was by means of Epi-Info version 6.02, and categorical data were compared by the chi-square test and continuous data by the non-parametric Kruskal-Wallis test. Given the relatively low specificity of the diagnosis of tuberculosis in children, the analysis focuses on tuberculosis in adults (age > 14 years).

Results

Number of cases and rates

The total number of cases of tuberculosis increased significantly between 1989 and 1995, from 301 to 839 (Fig. 1). Though stable between 1989 and 1991, the number doubled in 1992 and increased steadily thereafter. Tuberculosis accounted for 8.3% of hospital admissions in 1995 compared with 4.7% in 1989 ($P < 0.0001$). Similarly, tuberculosis accounted for 2.8% of outpatient consultations in 1995 compared with 1.1% in 1989 ($P < 0.0001$). Using population estimates for the district derived from the 1991 census, the estimated incidence of tuberculosis increased from 154/100 000 in 1991 to 413/100 000 in 1995. These changes took place while the prevalence of HIV infection in women attending antenatal clinics in KwaZulu-Natal increased from 1.61% in 1990 to 18.23% in 1995 (Fig. 1).[11]

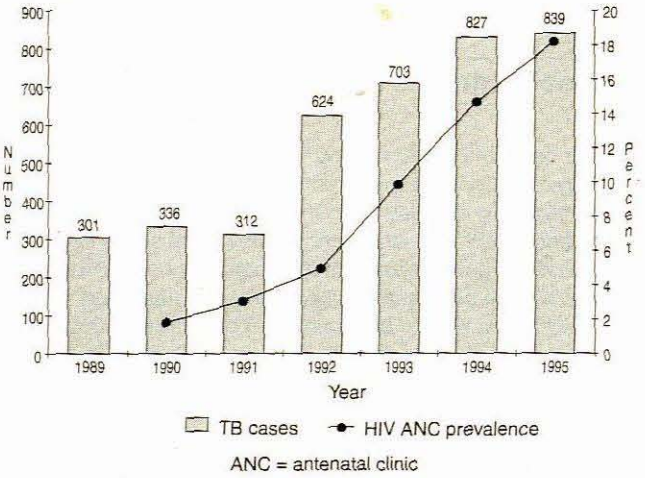

Fig. 1. Tuberculosis caseload and HIV prevalence.

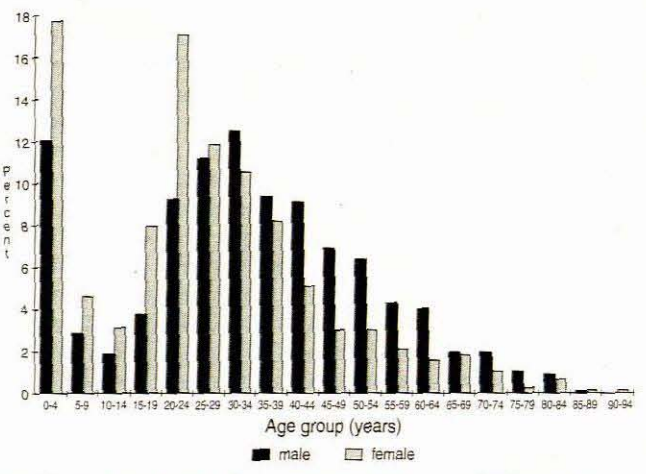

Fig. 2. Age/sex distribution — tuberculosis cases 1991 - 1995.

Age and sex distribution

In all, 2 397 adults were admitted between May 1991 and June 1995 and data were available for 98.5% of them. Forty per cent were women, and this proportion increased from 28% in 1991 to 37% in 1995 ($P = 0.04$). The age distribution was broadly similar in both sexes (Fig. 2), but the mean (SD) age of women was 33.4 (14.1) years compared with 39.5 (14.8) years in men ($P < 0.0001$). A higher proportion of the disease in women occurred in younger age groups than in men (23% v. 11% in the 20 - 24-year age group, $P < 0.0001$).

The mean age of women with tuberculosis fell from 39.1 (15.6) years in 1991 to 31.7 (12.4) years in 1995 ($P = 0.002$). There was no significant fall in the mean age of men with tuberculosis over the same period.

Spectrum of disease

As shown in Table I, most disease (74%) was pulmonary. The proportion of pulmonary cases fell from 80% in 1991 to 73% in 1995 ($P = 0.1$), and the proportion of smear-positive pulmonary cases from 65% to 56% ($P = 0.04$) over the same period. The number of extrapulmonary cases increased over time. Pleural tuberculosis accounted for 7.5% of all cases in 1991 and 18% in 1995 ($P = 0.002$); disseminated tuberculosis increased from 2% to 5% ($P = 0.11$), and while no cases of pericardial tuberculosis were diagnosed in 1991, 7 were seen in the first half of 1995.

Table I. Spectrum of tuberculosis in adults (age > 14 years)

Type	No.	%
Pulmonary	1 777	74
Smear positive	1 333	56
Smear negative	444	18
Extrapulmonary*	620	26
Pleural	296	12
Disseminated	142	6
Lymphatic	48	2
Pericardial	27	1
Meningitic	17	1
Total*	2 397	100

* Not all sub-categories of extrapulmonary tuberculosis are shown.

HIV and tuberculosis

The proportion of patients tested for HIV infection ranged from 28% in 1992 to 55% in 1995 and 80% in 1993. The minimum HIV seroprevalence in adults with tuberculosis increased from 8.7% in 1991 to 28.3% in 1995 (Table II). Women were consistently tested for HIV infection more frequently than men, and both the proportion of those tested who were shown to be infected and the estimated minimum prevalence were consistently higher in women than in men.

The prevalence of HIV infection in adults with tuberculosis was 58% in 1995,[9] and the risk of HIV infection in adults without HIV infection was estimated at 14% from a local survey of women attending antenatal clinics (unpublished data). The RR of HIV infection is therefore 58/14 = 4.14. The AF is calculated as 1 – (1/4.14) = 0.76, i.e. the proportion of HIV-infected patients with tuberculosis due to HIV infection is estimated at 76%. Therefore, in 1995, the number of adult cases of tuberculosis due to HIV infection — the population AF — is equal to the number of adult cases that year (663) multiplied by the fraction known to be HIV infected (0.58) x AF (0.76) = 292. This is equal to 44% of the adult cases of tuberculosis diagnosed in 1995.

Table II. HIV test results in adults with tuberculosis, 1991 - 1995

	Year				
	1991	1992	1993	1994	1995
Proportion tested	30%	28%	80%	46%	55%
Male	24%	25%	77%	44%	49%
Female	44%	32%	84%	51%	68%
Proportion HIV positive of those tested	29%	42%	43%	46%	55%
Male	25%	36%	37%	39%	40%
Female	43%	50%	51%	57%	68%
Minimum HIV prevalence	8.7%	11.8%	34.5%	21.1%	28.3%
Male	5%	9%	29%	17%	20%
Female	19%	16%	43%	29%	46%

Discussion

This study reports, for the first time that we are aware, the impact of the HIV epidemic on tuberculosis in rural South Africa. Tuberculosis caseload increased almost three-fold in recent years in the Hlabisa district, and the proportion of cases due to HIV infection is estimated at 44%. The current prevalence of HIV in adults with tuberculosis in this area is around 60%.[9]

That much of the increased caseload is due to HIV is supported by several observations. The caseload increased in tandem with the carefully documented rising prevalence of HIV among women attending antenatal clinics (Fig. 1). The minimum prevalence of HIV in adults with tuberculosis increased over the same time period (Table II). The spectrum of tuberculosis has also changed recently, with those forms of the disease associated with HIV infection (extrapulmonary and smear-negative pulmonary disease) becoming more common. There has also been a shift in the age distribution of women with tuberculosis (but not men), probably reflecting the significantly different age distributions of HIV-infected men and women in Africa. In the Hlabisa cohort,[7] the mean age of HIV-infected women with tuberculosis was 29 years compared with 37 years in their HIV-negative counterparts.

There are at least three other possible reasons for the recent dramatic increase in caseload. In 1991 a new tuberculosis control programme was introduced in Hlabisa:[5,6] diagnosis and reporting of cases probably improved, and patients diagnosed in neighbouring hospitals but resident in Hlabisa were transferred to Hlabisa for continued care. The community-based directly observed therapy programme employs a very short period of hospital stay and this seems to be popular — it is possible that the new programme attracted patients with existing disease in 1992. Finally, the hospital became busier as medical staffing increased from two doctors in 1991 to 11 in 1995; however, the proportion

of both inpatient and outpatient workload attributable to tuberculosis also increased over that time period.

It is estimated that of the 663 adult cases seen in 1995, 234 (35%) would have occurred anyway (if the caseload had remained stable after 1991); 292 (44%) are attributable to HIV; and 137 (21%) may be due to the other factors listed above.

The estimate that 44% of adult cases of tuberculosis are due to HIV infection is probably conservative. This estimate depends on calculation of the AF, the accuracy of which largely depends on the risk of HIV infection in the population from which patients with tuberculosis originate. As this is not known, the risk in a surrogate group must be used, and the choice usually lies between blood donors and women attending antenatal clinics. Women attending antenatal clinics probably have a higher prevalence of HIV infection than adults in the broader community,[12] and blood donors a lower rate (because of voluntary exclusions). Compared with an AF of 76% reported here, in a Tanzanian study[13] an AF of 86% was calculated by using the rate of HIV infection in blood donors as a control group. Using a population prevalence of 4% (South African blood donors) for the data reported here, the proportion of tuberculosis cases attributable to HIV was estimated at 54%. It is therefore reasonable to suggest that the proportion of cases of tuberculosis due to HIV infection in Hlabisa is at least 44% and probably greater.

Monitoring trends in extrapulmonary disease may be a useful way of monitoring trends in HIV-related tuberculosis, without doing HIV testing. Extrapulmonary disease is strongly associated with HIV infection.[8] In high tuberculosis prevalence settings most cases of large pleural effusion are tuberculous.[7] As most cases of HIV-related tuberculosis are pulmonary and difficult to distinguish from cases in HIV uninfected patients, pleural cases may prove to be a useful sensitive and specific indicator of the proportion of cases due to HIV infection. Monitoring the prevalence of HIV in patients tested for clinical indications provides useful information on trends, particularly when linked to data obtained from cross-sectional surveys (Table II).

Within a few years the tuberculosis caseload has increased markedly in this area, and much of it seems to be directly attributable to HIV infection. HIV has had a rapid adverse impact on the tuberculosis service. While the spectrum of disease has changed and HIV-associated clinical problems are more common, most adult disease remains pulmonary and most of this is smear positive. Much of the increased burden appears to be borne by women; women were more likely to be tested for HIV in this study (suggesting more clinically suspected HIV infection), and minimum prevalence was consistently higher in women. In a cross-sectional study undertaken in 1993, 46% of women were HIV-positive compared with 29% of men.[8] Furthermore, the on-treatment tuberculosis mortality rate doubled from 5% to 10% between 1991 and 1994,[6] and defaulting has also increased.[6,8]

In order to cope with the increased burden of disease and to maintain high completion rates (85% between 1991 and 1994[6]), the Hlabisa community-based directly observed therapy programme has been expanded. Colleagues in similar settings may wish to consider a similar approach, as hospital care is either impractical (not enough beds are available) or too expensive. The burden of HIV infection on tuberculosis in rural South Africa is already considerable and while the impact is adverse, strategies do exist that allow a relatively resource-poor health system to cope.

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