

The Association of Tuberculosis and HIV Infection in Burundi

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ABSTRACT

AIDS and tuberculosis (TB) are both endemic in Bujumbura, Burundi. An 11% failure rate to standard antituberculosis treatment ($n = 173$) was observed at the Tuberculosis Treatment Center of Bujumbura (CATB) in 1985–1986. All resistant cases ($n = 19$) were HIV seropositive. Among 328 consecutive cases with tuberculosis at the CATB during a 3 month period in 1986, 54.5% were HIV seropositive, which is five times higher than the prevalence in the general population in Bujumbura.

More female patients than male cases were HIV antibody positive (62 versus 49%, respectively; $p < 0.02$). Persistent weight loss, cough, and an anergic tuberculin test were more common in the HIV-seropositive group. Among 48 household members of HIV-seropositive patients with tuberculosis, 6 (12.5%) new cases of tuberculosis were identified, compared with none among 28 household members of HIV-seronegative patients with tuberculosis (odds ratio, 3.8; 95% confidence interval, 0.43–33.2).

HIV infection is a new risk factor for tuberculosis in Africa, and HIV-infected cases of tuberculosis may be more infectious than HIV-negative patients. The AIDS epidemic may drastically complicate the diagnosis, management, and control of tuberculosis in populations in which both infections are endemic.

INTRODUCTION

A CORRELATION BETWEEN TUBERCULOSIS (TB) and human immunodeficiency virus (HIV) in Africa has been reported for the first time in Kinshasa, where a high HIV seroprevalence rate of 33% was found among patients with tuberculosis.¹ This alarming observation suggested that in HIV endemic areas tuber-

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culosis is strongly associated with HIV infection and that the incidence of tuberculosis may greatly increase in populations in which both HIV infection and tuberculosis are endemic. Questions have been raised concerning the management and the control of tuberculosis in Africa. At the end of 1985 an 11% failure rate to standard antituberculous treatment among 178 patients was observed at the Centre Anti-Tuberculeux of Bujumbura (CATB) in Burundi. All the failures ($n = 19$) were found to be HIV seropositive.² Subsequently a study was performed to define the rate of HIV infection among patients with pulmonary tuberculosis and to estimate the rate of tuberculosis disease among household members of HIV-infected patients with tuberculosis.

METHODS

Overall 328 consecutive patients (207 males and 121 females) with pulmonary tuberculosis seen at the CATB were enrolled in a cross-sectional study from September to October 1986. All cases were patients with pulmonary tuberculosis confirmed by microscopic examination or by culture, before starting standard treatment for tuberculosis (2 months on streptomycin, 1 g daily, 6 days a week; isoniazide, 300 mg daily; ethambutol, 800 mg daily; and 10 months on streptomycin, 1 g 2 days a week, and isoniazide, 600 mg 2 days a week). All patients underwent a physical examination and a tuberculin test.

For a survey on additional tuberculosis cases among household members, 24 households of adult HIV-1-seropositive patients with tuberculosis and 14 of adult HIV-1-seronegative cases of tuberculosis were selected. Selection of patients was made to obtain a homogeneous group in age, sex, marital status, place of living in Bujumbura, and assiduity to the TB treatment. Most of the selected HIV-positive adult cases were living in the poor and overcrowded parts of Bujumbura (Bwiza and Buyenzi), where we find only a limited number HIV-seronegative TB cases who met the selection criteria. All cases were patients under ambulatory standard antituberculous treatment for at least 10 months. In every family, only two persons were selected (one adult and one child preferentially) because of the limited resources and time available to investigate the whole family. If no adult was present at the first visit, the two oldest children were selected. Home visits were performed between 5 and 7 p.m. of every workday to have the greatest chance to meet most of the family members. The selected persons underwent, as for the patients with tuberculosis, a questionnaire, a clinical examination, a tuberculin test, a chest x-ray, a microscopic sputum examination (if cough was present) with culture, and serologic tests for HIV antibody. The questionnaire included demographic features, clinical signs and symptoms, and possible risk behaviors for HIV infection. The study had to be stopped prematurely for reasons beyond the control of the investigators. Serologic tests for HIV-1 antibody included an enzyme-linked immunosorbent assay (ELISA; Organon Teknika, Oss) performed at the national laboratory of Bujumbura, confirmed by an immunofluorescence test (IMT, Antwerp, Belgium) and by Western blot analysis (DuPont de Nemours, Geneva).³ Both confirmation tests were performed at the Institute of Tropical Medicine in Antwerp, Belgium. Sera were considered positive for HIV-1 antibody if they reacted with at least one band representative of HIV-1 core proteins and one band representative of the envelope glycoproteins.

Statistical tests used included Z and F statistics, chi-square, and Fisher's exact test.

RESULTS

The overall prevalence rate of HIV antibody among the 328 patients with tuberculosis was 54% (95% confidence interval, 49–59%). Figure 1 shows the different age distributions of HIV-infected and noninfected cases of tuberculosis. Variance equality between both groups was nonsignificant (F distribution, 3.6; $n_1 = 177$ and $n_2 = 147$; $p < 0.05$). Between the ages of 20 and 40, 62% of the cases were HIV antibody positive, compared with 2.5% below 20 years and 35.5% above 40 years. For the noninfected group the percentages were 45, 9.5, and 45.5%, respectively.

The prevalence rate was significantly different between the sexes, with 62% of the women HIV seropositive compared with 49% of the men ($X = 5.26$; $p < 0.02$). Among the HIV-infected sexually active age group (aged 15–44 years), women with tuberculosis were younger than men with both infections

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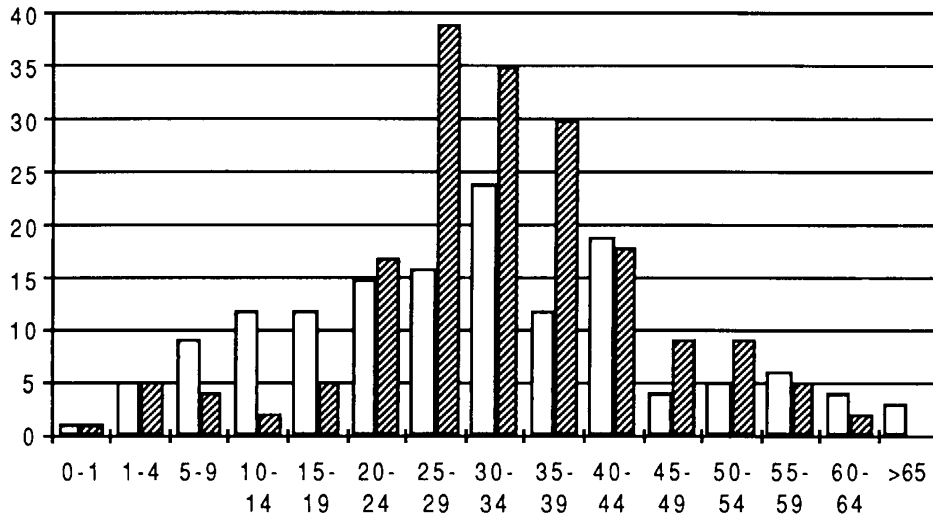


FIG. 1. Age distribution of the 328 patients with tuberculosis: solid bars, HIV negative; hatched bars, HIV positive.

[mean age of the women ($n = 67$) 30.2, compared with 33.4 for men ($n = 75$), t statistics = 2.95, $p < 0.005$].

More HIV-positive women were single or in a concubinage relationship (37 of 67) compared with the men (23 of 75), who were mostly married ($X = 8.72$; $p < 0.01$). Unmarried female HIV-seropositive patients with tuberculosis were preferentially living in those parts of Bujumbura (Buyenzi and Bwiza) where prostitution activity is more prevalent (24 of 30; 80%), whereas only 14 of 26 (54%) unmarried male HIV-seropositive TB cases were living in these areas ($X = 4.36$; $p < 0.05$).

Among 48 household members (mean age 14 years; female-male ratio, 0.71) of HIV-seropositive patients with tuberculosis, 6 (12.5%) new cases of tuberculosis were found, compared with none among 28 household members (mean age 12 years; female-male ratio 1.33) of HIV-seronegative patients with tuberculosis (odds ratio 3.8; 95% CI, 0.43–33.28; $p = 0.11$ by the Fisher's exact test, two-sided). The six secondary cases of tuberculosis occurred in five families, all with a female HIV-seropositive index case. These were four boys and two girls, with a mean age of 7 years. Among the 76 household members six new HIV-seropositive cases were found in five families (two men and four women, all older than 18 years). Two were observed in the household of one HIV-seronegative TB case and the four others were found among the household contacts of the HIV antibody-positive patients with tuberculosis, but none was diagnosed with tuberculosis.

Clinical differences between the HIV-seropositive and the HIV-seronegative patients with tuberculosis are given in Table 1. Persistent weight loss and cough and an anergic tuberculin test result were more common in the HIV-positive group. It was difficult to classify the HIV-seropositive group in acquired immunodeficiency syndrome (AIDS) and AIDS-related complex (ARC) patients, but at least 10 patients at the moment of selection of the study fulfilled the criteria of the World Health Organization (WHO) clinical case definition of AIDS.⁴

DISCUSSION

This study confirms the association between tuberculosis and HIV infection as reported earlier from the United States and Zaire.^{1,5-7} The observed HIV seroprevalence rate of 54% among tuberculosis cases is more than five times higher than the prevalence rate in the general population of Bujumbura.⁸ The demographic features of the HIV-seropositive patients with tuberculosis were similar to those observed among

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TABLE 1. CLINICAL FEATURES OF HIV-SEROPOSITIVE AND HIV-SERONEGATIVE PATIENTS WITH TUBERCULOSIS IN BUJUMBURA

<i>Feature</i>	<i>HIV antibody positive (n = 24)</i>	<i>HIV antibody negative (n = 14)</i>	<i>p^b</i>
Resistance to treatment ^a	5	—	0.16
Anergic tuberculin test	10/20	1	0.02
Weight loss	22	4	0.003
Cough	18	6	0.01
Polyadenopathy	6	—	0.10
Dermatitis	5	—	0.16
Scarification practice	13	3	0.10
Recent STD infection	14	4	0.14
Herpes zoster infection	6	—	0.10
Thrush	2	—	0.7

^aDefined as positive sputum by microscopic and culture analysis after 10 months of standard antituberculous treatment.

^bFisher's exact test.

AIDS cases in Bujumbura and elsewhere in Africa.^{8,9} Thus women with tuberculosis and HIV infection were younger than the HIV-positive men and were more often single. The greatly increased risk for the development of tuberculosis among persons with HIV infection may lead to increasing numbers of cases of tuberculosis, particularly in populations in which both infections are common, as among sexually active young adults in some parts of Africa.

This has been documented recently in the United States, where the increasing incidence of tuberculosis is thought to be due to the current AIDS epidemic.¹⁰ Similarly, an increase of 24% in the number of reported cases of tuberculosis was observed in Bujumbura between 1983 and 1986, when 1046 and 1301 new cases were diagnosed, respectively.¹¹ During this period, no methodological modifications in the detection of cases of tuberculosis occurred and no major demographic changes were noted in Bujumbura.

Although the number of household contacts studied is small because of the inadvertent end to the survey, our results are consistent with the hypothesis that HIV-infected patients with tuberculosis may be more infectious than patients without HIV infection. If confirmed, this increased secondary transmission rate may also contribute to an increased incidence of tuberculosis among the HIV-seronegative population, particularly among young children. This is consistent with observations in Bujumbura, where the greatest increase in the number of cases of tuberculosis between 1983 and 1986 was found in children below 10 years of age as the number of newly diagnosed cases rose from 19 to 92.¹¹

Studies in the United States and Zaire suggest that the clinical presentation of tuberculosis is different in HIV-infected individuals.^{5,6,12} In particular, various types of extrapulmonary tuberculosis are more frequent, and skin anergy to tuberculin is common in patients with both tuberculosis and HIV infection. The latter was also found in the present survey, which documented cutaneous anergy in half the patients with confirmed pulmonary tuberculosis. In addition, our observations also suggest that HIV infection may be associated with failure of standard antituberculosis therapy, although the present study was not designed to address this question.

Tuberculosis remains a major health problem throughout Africa. The emergence of the AIDS epidemic may enormously complicate the diagnosis, management, and control of tuberculosis in several parts of the continent. Priority areas for further studies include an assessment of the efficacy of standard treatment regimens for tuberculosis in HIV-infected patients, the evaluation of routine chemoprophylaxis to prevent relapse following therapy, and the estimate of the infectiousness of HIV-positive cases of tuberculosis.

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