

Prevalence of HIV Infection in Patients Hospitalized for Tuberculosis in Bahia, Brazil

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HIV infection is an important risk factor for the development of tuberculosis (TB), and also affects its morbidity and mortality. This study estimated the prevalence of HIV infection in patients hospitalized for TB in Bahia (in northeastern Brazil) and to evaluate its impact on in-hospital mortality. A total of 375 patients with TB, admitted consecutively to a TB reference hospital in Salvador (Bahia, Brazil), were evaluated between July 2001 and July 2003. Anti-HIV serology was performed in all patients irrespective of clinical and/or epidemiological data suggestive of HIV infection. Death during hospitalization was the principal event-dependent variable. Mean age of patients was 41.4 ± 16.2 years and the male/female ratio was 3.4:1.0. The prevalence of HIV infection was 8.8% (95%CI: 6.2-12.0%). Patients in the HIV-positive group were younger than those in the HIV-negative group (37.1 versus 41.9 years; $p=0.05$). In-hospital mortality was 10.9% for the whole group (95%CI: 9.4-15.9%), but was significantly greater in the HIV-positive group compared to the HIV-negative group (27.3% versus 9.4%; RR=2.9; 95%CI: 1.5-5.6; $p=0.002$). The prevalence of HIV infection in patients hospitalized for TB in Bahia (northeastern Brazil) is relatively high (8.8%) and mortality is significantly higher (2.9-fold) in the HIV-positive group. These findings justify carrying out HIV testing, as recommended by the Brazilian Ministry of Health, in all TB patients, particularly those requiring hospitalization.

Key-Words: Tuberculosis, HIV infection, prevalence, Brazil, Bahia.

HIV infection is a known risk factor for the development of tuberculosis (TB), and also affects its morbidity and mortality. According to a study carried out by the World Health Organization, the global prevalence of HIV infection in patients with TB is estimated at 8% [1]. However, some regions of the world have significantly higher rates of TB-HIV co-infection, such as Africa, where prevalence ranges between 31 and 66% [2-5]. In South America, the few studies that have been published report a wide variability in prevalence rates, ranging from 1.6% in Chile [6] and Paraguay [7] to 21% in Argentina [8].

In Brazil, prevalence has varied from region to region, with higher rates in the south and southeast of the country [9-14]. A previously published study carried out in Bahia in 378 TB patients who had been hospitalized during the period from 1993 to 1995 reported an estimated HIV prevalence rate of 7.1% and a significant impact of TB-HIV co-infection on the prognosis of these patients, with a higher rate of mortality in

the HIV-positive group [15]. Another more recent local study involving only treatment-naïve outpatients followed up in health centers in the city of Salvador (Bahia), reported a prevalence of TB-HIV co-infection of 3.6% [16]. In a multicenter trial carried out in patients with multidrug-resistant TB in Brazil, Dalcolmo et al. reported a 1.9% prevalence of HIV infection, lower than that conventionally observed in other countries [17].

The objective of this study was to estimate the prevalence of HIV infection in patients hospitalized with tuberculosis in Bahia and to evaluate the impact of co-infection on in-hospital mortality.

Materials and Methods

Between July 2001 and July 2003, 400 patients with an initial diagnosis of TB were evaluated prospectively, following hospitalization at the "Octavio Mangabeira Hospital", a tertiary care public hospital that is a reference for TB and accounts for approximately 85% of all the beds available for the hospitalization of TB patients in the state of Bahia (northeastern Brazil).

All patients had serum samples tested for the presence of HIV-1/-2 at the same laboratory (a reference public health laboratory in Bahia). The methods used were ELISA followed by Western Blot or indirect immunofluorescence for confirmation of HIV-positivity. Diagnosis of TB was based on the criteria established in the II Brazilian Guidelines for Tuberculosis: 1) presence of positive direct smear examination (Ziehl-Neelsen method) and/or positive culture for *M. tuberculosis* (in Löwenstein-Jensen medium); and 2) presence of clinical, epidemiological and radiological findings compatible with TB, associated with a favorable response to treatment with anti-TB drugs [18].

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Twenty-five of the 400 enrolled patients were excluded from the study due to a later change in diagnosis (patients with non-tuberculous pneumopathies), and therefore, the remaining 375 patients comprised the final study population. With respect to tuberculin testing, individuals were considered reactors when the area of induration due to PPD inoculation was: 1) ≥ 5 mM for patients in the HIV-positive group; and 2) ≥ 10 mM for patients in the HIV-negative group.

Statistical analysis was carried out using the SPSS software program, version 9.0. The chi-square or Fisher's exact tests were used to compare proportions, and measurement of the association was used to express relative risk (RR) of death. Logistic regression was used to evaluate the probable confounding factor of age in the principal association. The 95% confidence interval (95%CI) was used to describe the precision of the point estimates of the proportions, using the statistical software program PEPI.

Results

The characteristics of the study population are shown in Table 1. Of the 375 patients, 290 (77.3%) were male. The mean age of patients was 41.2 years (ranged from 15-82 years). The mean age of the HIV-positive patients was significantly lower than that of the patients in the HIV-negative group (37.1 *versus* 41.9 years, $p=0.05$). One hundred and thirty-three patients (35.5%) were retreatment cases and, of these, 57.1% (76/133) reported having abandoned previous treatments. There was no significant difference between the HIV-positive and HIV-negative groups with respect to whether they had abandoned previous treatment.

With respect to the tuberculin test, there was no statistically significant difference between the 2 groups in the

proportions of PPD reactors. Of the 375 patients in the study, it was possible to establish the duration of the illness prior to hospitalization in 364 (31/33 in the HIV-positive group and 333/342 in the HIV-negative group). The distribution of the duration of illness in the HIV-positive and HIV-negative groups, respectively, was: a) =1 month: 12.9% (4/31) *versus* 21.3% (71/333) ($p=0.381$); b) 1-3 months: 51.6% (16/31) *versus* 30.9% (103/333) ($p=0.032$); c) 3-12 months: 29.0% (9/31) *versus* 30.0% (100/333) ($p=0.929$); and d) =12 months: 6.5% (2/31) *versus* 17.7% (59/333) ($p=0.175$). Except when the duration of disease prior to hospitalization was 1-3 months ($p=0.032$), there were no statistically significant differences between the HIV-positive and HIV-negative groups. In addition, there was no statistically significant difference in the mean time interval between admission and death when comparing the 2 groups of patients (20.9 days in the HIV-positive group *versus* 33.6 days in the HIV-negative group; $p=0.401$).

Of the 375 participants in the study, 33 were HIV-positive (prevalence: 8.8%; 95%CI: 6.2-12.0%). Of the whole study group, 41/375 patients died during the period of hospitalization (in-hospital mortality rate of 10.9%; 95%CI: 7.3-15.6%). In the HIV-positive group, 9/33 (27.3%) patients died during hospitalization, while in the group of HIV-negative patients, death occurred in 32/342 (9.4%). A strongly positive association between HIV infection and death was observed in patients hospitalized with TB, the risk of death being 2.9-fold in the population of HIV-positive patients compared to the HIV-negative group (RR=2.9; 95%CI: 1.5-5.6; $p=0.002$). Logistic regression was carried out to adjust for age as a probable confounding factor, and results still confirmed the strongly positive association between TB-HIV co-infection and death in this sample. These data are shown in Table 2.

Table 1. General characteristics of patients in the study population and according to HIV serological status (n=375)

	HIV-negative (n=342)	HIV-positive (n=33)	Total (n=375)	P
Age (years)				
Mean \pm SD	41.9 \pm 15.9	37.1 \pm 7.8	41.2 \pm 15.6	0.05*
Range	15 - 82	15 - 49	15 - 82	
Male, n (%)	266 (77.8)	24 (72.7)	290 (77.3)	NS
PPD reactive, n (%)	178 (52.1)	14 (42.4)	193 (51.5)	NS
Retreatment, n (%)	120 (35.1)	13 (39.4)	133 (35.5)	NS
History of abandoning treatment, n/N (%)	69/120 (57.5)	7/13 (53.8)	76/133 (57.1)	NS

*Statistically significant. NS=not statistically significant.

Table 2. Relative risk (RR) of death in patients hospitalized with TB according to HIV status (n=375)

HIV Status	Death during hospitalization				RR (95%CI)	p
	Yes (n=41)		No (n=334)			
	n/N	%	n/N	%		
Positive (n=33)	9/33	27.3	24/33	82.7	2.9 (1.5 - 5.6)	0.002
Negative (n=342)	32/342	9.4	334/342	91.2	1 (reference group)	
Total	41/375	10.9	334/375	89.1	—	—

Data on the number of CD + cells was not available for analysis as a predictor of mortality, since this was not part of the methodology of the present study. None of the 33 HIV-positive patients in this study had previously used antiretroviral therapy, since they had not been previously aware of their HIV seropositivity. No case of immune reconstitution was observed in the 33 HIV-positive patients in this sample.

Discussion

The present study showed a prevalence of 8.8% of HIV infection among patients hospitalized with a diagnosis of tuberculosis. The HIV-positive group was younger and had higher in-hospital mortality. The 2 groups had similar proportions of PPD reactivity and similar intervals between the onset of symptoms of tuberculosis and hospitalization.

In Brazil, a country of continental magnitude with wide socioeconomic inequalities and extremely diverse cultures, the prevalence of TB-HIV co-infection varies greatly from one geographic region to another. In a review paper published in 1995 evaluating data from 1987 to 1992, TB-HIV co-infection ranged from 0.5% to 12% in outpatients and 1.9-20.7% among inpatients [9]. Recent studies carried out in the southeast of the country found estimated prevalence rates of 21.8-42% in hospitalized patients, which are significantly higher rates ($p < 0.001$) than those observed in our study [10,12-14]. Two plausible explanations may justify the differences in the estimates of TB-HIV co-infection in the southeast of Brazil compared to the data reported in this present study: 1) geographical and cultural differences (for example, the use of intravenous drugs) that may interfere in the prevalence of HIV infection in the populations of the regions in question (southeast and northeast of the country); 2) a possible selection bias, since the above-mentioned studies were carried out in reference hospitals for AIDS. Two studies carried out in patients hospitalized in TB reference hospitals, one in the state of Minas Gerais [19] and the other in the state of Goiás [20] reported estimated prevalence rates of co-infection of 10.1% and 9.2%, respectively. These findings are similar to those observed in the present study and were also based on populations of patients hospitalized with TB in tertiary care reference hospitals for this disease.

The point-prevalence observed in the present study (8.8%) was slightly but not significantly higher ($p = 0.401$) than that reported in a previous study carried out in Salvador (Bahia, northeastern Brazil) in 378 patients hospitalized with TB during the period 1993-1995 (7.1% prevalence) [15]. Another study carried out at the same time as the present study in outpatients in Salvador (Bahia, Brazil) reported an estimated prevalence of HIV infection of 3.6% in treatment-naïve patients or patients initiating TB treatment [16]. There is a statistically significant difference between this prevalence rate and the rate found in the present study (3.6% *versus* 8.8%; $p = 0.006$). The different estimated prevalence rates found during the same timeframe may be explained by the difference between the populations

studied (outpatients *versus* inpatients, respectively). It is plausible to expect subgroups of patients with a greater prevalence of TB-HIV co-infection to be in a more serious clinical condition that would more often require hospitalization.

The strong association between HIV-TB co-infection and death from TB observed in the present study irrespective of age ($RR = 2.9$) is in agreement with data reported from various other studies [15,21,22]. This finding is very pertinent since it provides confirmation that systematic routine identification of HIV-seropositive patients should indeed be incorporated into the routine healthcare provided within the basic healthcare network, a fact that is even more relevant when dealing with inpatients. Early identification of this group at greater risk of death, with particular focus on specific care, may lead to a reduction in mortality.

Based on the findings of this study, we conclude that the prevalence of HIV infection in hospitalized patients with tuberculosis in Bahia (northeastern Brazil) is relatively high (8.8%), and that mortality is significantly greater (2.9-fold) in the HIV-positive group. These data justify carrying out HIV testing in all patients with TB, particularly in those requiring hospitalization, as recommended by the Brazilian Ministry of Health.

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References

1. Dye C., Scheele S., Dolin P., et al. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project. *JAMA* **1999**;282:677-86.
2. Corbett E.L., Watt C.J., Walker N., et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. *Arch Intern Med* **2003**;163:1009-21.
3. Connolly C., Davies G.R., Wilkinson D. Impact of the human immunodeficiency virus epidemic on mortality among adults with tuberculosis in rural South Africa, 1991-1995. *Int J Tuberc Lung Dis* **1998**;2:919-25.
4. Kelly P.M., Cumming R.G., Kaldor J.M. HIV and tuberculosis in rural sub-Saharan Africa: a cohort study with two year follow-up. *Trans R Soc Trop Med Hyg* **1999**;93:287-93.
5. Van Gorkom J., Kibuga D., Adallah S., et al. HIV sero-prevalence among tuberculosis patients in Kenya. *East Afr Med J* **1999**;76:452-6.
6. Grupo de estudio de tuberculosis y sida. Prevalencia de soropositividad en pacientes tuberculosos activos de la región metropolitana: 2 estudio. *Rev Chil Enferm Respir* **1993**;9:142-8.
7. Mingo E., Estigarriba L.C., Marin M.E. Prevalencia de infección por el virus VIH en pacientes tuberculosos. *Bol Inst Patol Reg* **1993**;15:22-3.
8. Israel A.M., Sued O., Tesi N., et al. Tuberculosis: formas clínicas y prevalencia. *Rev Asoc Méd Argent* **1999**;112:37-41.

9. Kritski A., Dalcolmo M., del Bianco R., et al. [Association of tuberculosis and HIV infection in Brazil]. *Bol Oficina Sanit Panam* **1995**;118:542-54.
10. Belo M.T.C.T., Trajman A., Belo Neto E., et al. Aspectos clínicos da tuberculose associada à infecção pelo HIV. *J Pneumol* **1996**;22:299-302.
11. Fandinho F., Kritski A., Hofer C., et al. Drug resistance patterns among hospitalized tuberculous patients in Rio de Janeiro, Brazil, 1993-1994. *Mem Inst Oswaldo Cruz* **1999**;94:543-7.
12. Brito R.S., Gouder C., Lima D.B., et al. [Drug-resistant *Mycobacterium tuberculosis* strains isolated at an AIDS reference center general hospital in Rio de Janeiro.]. *J Bras Pneumol* **2004**;30:335-342.
13. Ribeiro S.A., Matsui T.N. Admission for tuberculosis to a university hospital. *J Pneumol* **2003**;29:9-14.
14. Selig L., Belo M., Cunha A.J.L.A., et al. [Deaths attributed to tuberculosis in the state of Rio de Janeiro]. *J Bras Pneumol* **2004**;30:417-24.
15. Pedral-Sampaio D.B., Martins Netto E., Pedrosa C., et al. Co-Infection of Tuberculosis and HIV/HTLV Retroviruses: Frequency and Prognosis Among Patients Admitted in a Brazilian Hospital. *Braz J Infect Dis* **1997**;1:31-5.
16. Marinho J.M. Infecção pelo retrovirus HTLV1 como fator de risco para tuberculose. Departamento de Medicina. Salvador: Escola Bahiana de Medicina e Saúde Pública, **2003**.
17. Dalcolmo M.P., Fortes A., Fiuza de Melo A.F., et al. Estudo de efetividade de esquemas alternativos para o tratamento da tuberculose multirresistente no Brasil. *J Pneumol* **1999**;25:70-7.
18. Dalcolmo M.P., Fiuza de Melo A.F., Pereira Pinto W. II Consenso Brasileiro de Tuberculose: Diretrizes Brasileiras para Tuberculose 2004. *J Bras Pneumol* **2004**;30(supl 1):S2-S56.
19. Garcia GF, Corrêa P.C.R.P., Melo M.G.T., Souza M.B. Prevalência da infecção pelo HIV em pacientes internados por tuberculose. *J Pneumol* **2000**;26:189-93.
20. Rabahi M.F., Rodrigues A.B., Queiroz de Mello F., et al. Noncompliance with tuberculosis treatment by patients at a tuberculosis and AIDS reference hospital in midwestern Brazil. *Braz J Infect Dis* **2002**;6:63-73.
21. Fabiani M., Accorsi S., Aleni R., et al. Estimating HIV prevalence and the impact of HIV/AIDS on a Ugandan hospital by combining serosurvey data and hospital discharge records. *J Acquir Immune Defic Syndr* **2003**;34:62-6.
22. Okamura M.N. [Epidemiological profile of tuberculosis patients assisted at an university general hospital.]. Departamento de epidemiologia. São Paulo: Universidade de São Paulo, **2003**:120.