Original Article

Human immunodeficiency virus seroprevalence in patients with tuberculosis in the city of Londrina, in the state of Paraná, Brazil*

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ABSTRACT

Objective: To estimate the prevalence of human immunodeficiency virus seropositivity among patients with active tuberculosis residing in the city of Londrina, in the state of Paraná, Brazil and treated at the Pulmonology Clinic of the 17th Regional Health Facility of the State of Paraná, and to compare those coinfected with human immunodeficiency virus to those with active tuberculosis only in terms of the clinical form of tuberculosis, sputum smear microscopy, chest X-ray and tuberculosis treatment regimen. **Methods:** A transversal study involving 188 active tuberculosis patients was conducted. Tuberculosis and human immunodeficiency virus infection were diagnosed based on criteria established by the Brazilian Ministry of Health. In addition to the data obtained through individual tuberculosis investigation files, clinical and epidemiological information were collected by means of questionnaires, which were completed by all participating patients. **Results:** The prevalence of human immunodeficiency virus seropositivity among patients with tuberculosis was 14.9%. The rate of positive sputum microscopy results was higher in the tuberculosis-only group (p = 0.0275), and the ratio for patients treatment with alternative scheme was significantly higher in the co-infected group (p = 0.042). In 32.1% of the coinfected patients, the serological diagnosis of human immunodeficiency virus infection was made simultaneously to or following that of the tuberculosis. **Conclusion:** The results underscore the importance of routinely testing for human immunodeficiency virus antibodies in patients diagnosed with tuberculosis.

Keywords: Tuberculosis/complications; Tuberculosis/diagnosis; Soropositivity; HIV/immunology; HIV infections/complications; HIV infections/epidemiology; HIV infections/ drug therapy; Rifampin/therapeutic use; Disease progression

INTRODUCTION

Infection with the human immunodeficiency virus (HIV) is considered one of the principal risk factors for the progression from latent tuberculosis (TB) to active TB infection. The accumulated risk for developing active TB ranges from 5% to 10% during the lifetime of patients not infected with HIV, whereas the risk for HIV-infected patients accumulates at a rate of 10% per year.[1] Current estimates indicate that there are approximately five million individuals coinfected with HIV and TB in underdeveloped countries, especially in sub-Saharan Africa (3.8 million patients) and Asia (1.15 million patients).[1]

In Brazil, studies carried out in various states have shown that the prevalence of HIV/TB coinfection ranges from 6.2% to 44.3%.[2-3] The lowest prevalence was found in the city of Campinas (in the state of São Paulo), and the highest prevalence was in the city of Porto Alegre (in the state of Rio Grande do Sul). In the metropolitan area of the city of São Paulo, 5827 reported TB cases were investigated. Of these, only 1034 had been submitted to serologic tests for HIV, and, of these, 560 tested positive. In this case, the lowest prevalence was 9.6% (560/5827), whereas the highest prevalence was 54.2% (560/1034).[4] In a study carried out in the city of Londrina (in the state of Paraná), 186 TB patients were investigated. Only 65 of these were submitted to HIV antibody testing, revealing an HIV-infection rate of 17.2%.[5]

The World Health Organization has emphasized the importance of TB patients receiving counseling and being voluntarily submitted to HIV testing.[6] In the city of Londrina, this recommendation has not been routinely followed, as evidence by the fact that TB patients were submitted to HIV testing at rates of only 36.41% in 1997 and 42.29% in 1998.[7]

Routine HIV testing of TB patients is one means of evaluating the efficacy of epidemiological surveillance of HIV/TB coinfection.[8] As a result, the actual prevalence of such coinfection in the city of Londrina is unknown. The objective of the present study was to estimate HIV seroprevalence among patients with TB, as well as to compare those coinfected with HIV to those with active TB in terms of the clinical form of TB, sputum smear microscopy, chest X-ray and TB treatment regimen.

METHODS

A transversal study with descriptive and analytical components was conducted involving the population of patients with active TB treated at the Pulmonology Clinic of the Integrated Center for Infectious Diseases of Londrina.

A serially-selected convenience sample was recruited from January 1999 to June 2000. The sample size was based on a estimated TB patient population of 491[9] out of a total city of Londrina population of 426,607 inhabitants, with a mean HIV/TB coinfection prevalence of 15%,[5,10] a standard error of the estimate of 4% and a confidence level (CI) of 95%.

Participation in the study was voluntary. After giving written informed consent, 188 patients were interviewed by a skilled researcher. Data were obtained through individual TB investigation files and through the administration of a questionnaire created by the author and designed to collect data related to sociodemographic characteristics. The clinical and epidemiological variables in study were: HIV serologic testing results, age, gender, occupational status, clinical form of TB, sputum smear microscopy results, chest X-ray results and TB treatment regimen.

For the socioeconomic classification, we adopted the criteria recommended by the Associação Brasileira de Pesquisa de Mercado (Brazilian Marketing Research Association), considering the presence or absence of the following: television, radio, automobile, maid, bathroom, VCR, washing machine, refrigerator and vacuum cleaner. We also collected data regarding the educational level of the head of the household. Scoring these data led to the classification of the subjects into one of five economic levels (A, B, C, D or E).

Tuberculosis was diagnosed in accordance with the criteria recommended in the Guia de Vigilância Epidemiológica do Ministério da Saúde do Brasil (Brazilian Ministry of Health Epidemiological Surveillance Guide).[11] Patients with positive sputum smears were classified as having the pulmonary form of TB when there were: two positive microscopy results or one positive microscopy result and one positive culture result or one positive microscopy result and chest X-ray suggestive of pulmonary TB or at least two negative microscopy results and one positive TB culture result. Patients with negative sputum smears were classified as having pulmonary

TB when there were: two negative microscopy results but clinical findings and chest X-ray were compatible with TB or with other complementary tests that lead to a diagnosis of pulmonary TB. Patients were classified as having extrapulmonary TB when there was clinical evidence, together with laboratory or histopathological findings compatible with active extrapulmonary TB, which the physician had chosen to treat using a specific treatment regimen, or when there was at least one positive culture obtained from extrapulmonary samples and testing positive for mycobacteria.

Serologic testing was carried out in the immunology sector of the Laboratory of Clinical Investigation of the Hospital Universitário Regional do Norte do Paraná (Northern Paraná Regional University Hospital) and followed the technical guidelines of Edict 488/98 issued by the Secretaria de Vigilância Sanitária (Secretary for Sanitation Surveillance) of the Ministry of Health.[12]

Samples (blood) for HIV serologic testing were collected from all patients who had agreed to participate in the study, with the exception of for those who had been previously diagnosed with HIV/acquired immunodeficiency syndrome (AIDS). Patients in the latter group were submitted to the interview only.

The study was submitted to the Ethics Committee of the Universidade Estadual de Londrina (State University at Londrina), which approved the study design regarding the ethical assumptions for human research.

We used the chi-square test or Fisher's exact test for the comparison of the proportions of clinical and laboratory variables between the two groups of patients. We estimated the prevalence ratio and the 95% CI for the variables investigated in the study. The adopted significance level was 5% (0.05). We calculated p values for all statistical tests.

RESULTS

From January 1999 to June 2000, 258 patients with TB were treated. Of these, 32 were excluded from the study, 12 because they were children and 20 because they resided in other cities (Figure 1).

Of 226 patients selected for the study, 188 (83.2%) agreed to participate in the study and 38 (16.8%) refused or did not report for the interview (Figure 1).

In the serologic testing for HIV, 85.1% of the remaining 188 patients tested negative, and 14.9%
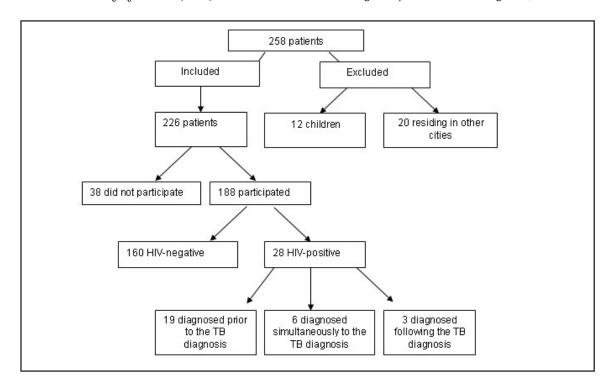

Figure 1 – Distribution of the 258 tuberculosis patients treated in Londrina, Paraná from January 1999 to June 2000

tested positive (95% Cl: 10.3% - 21%). All of the 28 coinfected patients met the criteria for a diagnosis of AIDS.[13]

Reviewing the medical files in the Pulmonology Clinic, we were able to obtain data concerning serologic results for HIV infection from the individual TB investigation files of the 38 patients who did not participate in the study. The distribution of the serologic results of these patients did not differ from those who participated in the study (p = 0.5526).

Table 1 shows the sociodemographic characteristics of patients coinfected with HIV and TB. The mean age was 37.2 years, with a standard deviation of 8.2.

Table 2 compares clinical and laboratory variables between the group of coinfected patients and that of patients diagnosed with TB alone. There was no statistically significant difference between the two groups concerning the form of TB (pulmonary or extrapulmonary) (p = 0.2031). In addition, there was no difference concerning the ratio of patients whose chest X-rays revealed alterations that indicated TB (p = 0.0613). The number of patients with positive results for sputum smear microscopy was significantly higher in the TB-only group (p = 0.0275). The ratio for patients treated with an alternative regimen was higher in the coinfected group (p = 0.0042).

DISCUSSION

The prevalence of HIV infection in patients with active TB (14.9%) found in this study is in concordance with that of a study carried out in 1994, in which it was predicted that, by the year 2000, approximately 13.8% of all patients with TB would also be coinfected with HIV.[10]

In accordance with the guidelines established by the Centers for Disease Control and Prevention, all patients with TB should be alerted to the fact that HIV infection alters the response to TB treatment. Therefore, serologic testing for the detection of HIV antibodies is a measure that

TABLE 1

Sociodemographic characteristics of 28 patients, coinfected with tuberculosis and the human immunodeficiency virus, treated in Londrina, Paraná from January 1999 to June 2000

Sociodemographic characteristics	HIV/TB	
	n	%
Population	28	14,9
Gender		
Male	23	82,1
Female	5	17,9
Ocupational Status		
Unemployed	11	39,2
Employed/self-employed/retired	17	60,8
Socioeconomic Classification		
A, B or C	10	35,7
D or E	18	64,3

TABLE 2

Clinical and laboratory variables of 188 patients, with TB only or coinfected with TB and HIV, treated in Londrina, Paraná from January 1999 to June 2000

Variable	HIV pos. (%)	HIV neg. (%) (IC 95%)	PR	p value
Clinical form of TB:				
Extrapulmonary	9 (32,1)	31 (19,4)	1,97	0,2031 *
Pulmonary	19 (67,9)	129 (80,6)	(0,74 - 5,16)	
Sputum smear microscopy				
Negative	9 (49,9)	26 (18,9)	2,98	0,0275 **
Positive	13 (59,1)	112 (81,1)	(1,04 - 8,50)	
Chest X-ray				
Normal or another alteration	7 (25,0)	17 (10,8)	2,75	0,0613 **
Suspicion of TB	21 (75,0)	140 (89,2)	(0,91 - 8,14)	
TB treatment regiment				
Alternative regimen	5 (17,9)	4 (2,5)	8,48	0,0042 **
Regimen 1	23 (82,1)	156 (97,5)	(1,80 - 41,3)	

*Chi-square test; **Fisher's exact test
HIV: human immunodeficiency virus; pos: positive; neg: negative; PR: prevalence ratio; Cl: confidence interval; TB: tuberculosis

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should be routinely adopted for patients with TB.[14] In Brazil, there is no consensus regarding the ordering of this serologic test since there are differences of opinion among researchers.[8,15-16] In 1993, the Brazilian Ministry of Health recommended HIV testing only in some special situations.[17]

There is also disagreement in the literature concerning the ideal criterion for HIV serologic testing of patients infected with TB. According to some of these studies, HIV antibody detection should only be ordered when there are clinical or epidemiological indicators that would justify such testing, thereby avoiding indiscriminate testing.[16] In contrast, it has been suggested that serologic testing should be required only in areas where the prevalence of HIV/TB coinfection is higher than 10%.[15] In addition, there are those who defend the idea that this testing should be part of the routine.[8]

The I Consenso Brasileiro de Tuberculose (First Brazilian Consensus on Tuberculosis), released in 1997, recommended that all patients with TB should be submitted to HIV serologic testing. This recommendation was based on a study carried out in Rio de Janeiro that demonstrated that only 70% of the patients coinfected with TB and HIV were identified without HIV testing, even after careful anamnesis and physical examination.[18] However, the Brazilian Ministry of Health Manual de Tuberculose (Tuberculosis Guidebook) makes no reference to HIV testing of patients with TB, although it does include the recommendation that HIV infection be considered an important factor in these patients.[19]

In the present study, 9 (32.1%) of the 28 coinfected patients were submitted to HIV serologic testing simultaneous to or following the TB diagnosis. This result underscores the importance of routine HIV testing of all patients with TB.

In the criteria adopted by the Centers for Diseases Control and Prevention in 1987 for use in defining AIDS in adolescents and adults, only the extrapulmonary form of TB was included in the list of diseases that would characterize AIDS. In 1993, these criteria were revised, and the pulmonary form of TB came to be considered a disease that would define the presence of AIDS. This inclusion occurred because of the strong epidemiological correlation between HIV infection and developing TB. In addition, according to the

Centers for Diseases Control and Prevention, the immunological condition of HIV-infected patients with pulmonary TB is similar to that of HIV-infected patients with extrapulmonary TB. The CD4 counts were lower than 200 cells/mm3 in 69% of the patients in the former group and in 77% of the patients in the latter group.[20]

Since 1992, the Caracas/Rio de Janeiro criteria have been used to define AIDS cases in adolescents and adults in Brazil.[21] In these criteria, patients with TB are only considered coinfected with AIDS: if there is extrapulmonary TB (especially in the central nervous system), including pulmonary forms, with typical or atypical chest X-rays, together with another extrapulmonary location; if there is extrapulmonary TB in more than one location (especially in the lymph nodes); or if there is pulmonary TB with atypical chest X-ray pattern (miliary TB or interstitial infiltrate, with no evidence of cavitation).

The above-described forms are equivalent to a score of 10 on the Caracas/Rio de Janeiro criteria scale, allowing the case to be reported as a case of AIDS. However, pulmonary TB with cavitation or other nonspecific forms of TB are equivalent to a score of only 5 points, insufficient to characterize the case as a case of AIDS. This difficulty increased when the Ministry of Health adopted an additional set of guidelines for the definition of AIDS, the modified Centers for Diseases Control and Prevention criteria, which do not include pulmonary TB as an AIDS-defining disease.[13]

Unfortunately, there are no clinical or epidemiological data that guarantee full efficacy in the detection of patients infected with HIV. If only those patients with TB that present risk behaviors for HIV infection are submitted to HIV serologic testing, a substantial number of patients coinfected with TB/AIDS will go undetected.[22] The sensitivity of the system of surveillance for the HIV/TB combination should be analyzed in terms of whether HIV testing has been performed or not. The lower the numbers of TB patients tested for HIV, the greater will be the uncertainty about the true magnitude of its prevalence.[8]

In areas where there is high prevalence of TB infection, TB is one of the diseases associated with AIDS. In 1993, of the 6716 AIDS cases reported in the state of Rio de Janeiro, 31.2% were individuals with TB, which was the second most often reported concomitant infection in individuals with AIDS,

surpassed only by candidiasis, which affected 58.4% of the patients.[23]

The TB problem in Brazil reflects the stage of social development in the country, in which the determinants of poverty, organizational weaknesses of the health care system and poor management have limited the use of technology and have therefore inhibited any sustained decrease in the number of diseases related to the social context. Regarding TB, two new causes have aggravated this situation: the AIDS epidemic and multidrug-resistance.[24]

In our sample, 9 (32.1%) of the 28 coinfected patients were diagnosed with extrapulmonary TB. Comparing this with data from the group of patients not infected with HIV, there was no association between coinfection and the clinical form of TB (pulmonary or extrapulmonary). We must highlight that the analytical power of this association was low due to the small number of coinfected patients.

The prevalence of the extrapulmonary form of TB in patients coinfected with AIDS ranges from 40% to 70% depending on the immunosuppression level at the moment patients are contaminated with TB.[25]

In the present study, we compared the group of coinfected patients with that of patients with TB only regarding positive sputum microscopy results. There was a statistically significant difference (p = 0.0275): the proportion of TB-only patients with positive sputum microscopy results was higher than that of coinfected patients.

In coinfected patients who are still in the early stage of HIV infection, with mild or moderate immunosuppression, the sensitivity of sputum smear microscopy is similar to that seen in patients not infected with HIV. However, in coinfected patients at an advanced stage of HIV infection, with severe immunosuppression, the sensitivity of the test decreases due to the low intensity of the pulmonary inflammatory process.[6]

Chest X-ray is the routine method for the diagnosis and follow-up examination of pulmonary TB patients. However, there is no particular image that is considered indicative of TB, although there are certain images that are suggestive of the disease.[6]

In the present study, chest X-ray examinations revealed suspicion of TB in 75% of the coinfected patients and normal findings or other alterations not suggestive of TB in 25%. In the group of patients diagnosed with TB only, these ratios were 89.2%

and 10.8%, respectively. The difference between the two groups was not statistically significant (p = 0.0943). It must be remembered that radiological data were only collected from the epidemiological files and could therefore be biased due to inaccurate entries or inappropriate interpretation of the results.

Rifampin, one of the most effective agents for TB treatment, cannot be used in combination with most antiretroviral protease inhibitors. This combination results in significant decrease in the serum levels of these anti-retroviral agents. Since rifampin cannot be used, physicians are forced to prescribe alternative TB treatment regimens, which are less effective and reduce treatment adherence.[19]

In the present study, the use of an alternative TB treatment regimen was significantly more frequent in the coinfected group than in the TB-only group (p = 0.0042). This occurred because this study was carried out during a period when it was recommended that, due to their clinical profile, HIV patients presenting clinical and laboratory evidence of severe immunosuppression and being treated for TB should be submitted to a regimen including more potent (protease inhibitor) antiretroviral agents as soon as possible. Therefore, the TB treatment regimen used for these patients was a combination of isoniazid, pyrazinamide, ethambutol and streptomycin.[26]

The main conclusion of this study was that HIV antibody testing should be performed in all patients with any form of TB, regardless of the presence of clinical or epidemiological evidence of AIDS.

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