Original Article

Prevalence of and factors related to tuberculosis in seropositive human immunodeficiency virus patients at a reference center for treatment of human immunodeficiency virus in the southern region of the state of Rio Grande do Sul, Brazil*

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ABSTRACT

Objective: In view of the relevance of co-infection with tuberculosis and human immunodeficiency virus, this study was designed to determine tuberculosis prevalence and identify factors related to tuberculosis in patients residing in a region in which both infections are highly prevalent. **Methods:** All patients treated during 1999 at the HIV/AIDS Clinic of the Universidade Federal do Rio Grande (Rio Grande Federal University) University Hospital were evaluated retrospectively, from the time of human immunodeficiency virus diagnosis, in terms of the incidence of tuberculosis and its relationship to sociodemographic, behavioral and immunological factors. **Results:** The sample included 204 patients, and tuberculosis prevalence was found to be 27%. The multivariate analysis showed a significant correlation between the development of tuberculosis and being of African descent (odds ratio: 4.76; 95% confidence interval: 1.93-11.72) and an inverse correlation between the development of tuberculosis and the TCD4+ lymphocyte count at the time of human immunodeficiency virus diagnosis (odds ratio: 0.995; 95% confidence interval: 0.993-0.997). When analyzed separately, other variables were found to be potential risk factors: being of the male gender (odds ratio: 2.49; 95% confidence interval: 1.15-5.39); and using illicit drugs (odds ratio: 2.1; 95% confidence interval: 1.02-4.31). **Conclusion:** The factors responsible for the development of tuberculosis among patients who are human immunodeficiency virus seropositive include immunological, socioeconomic and demographic factors. The high rate of tuberculosis prevalence among the seropositive patients underscores the urgent need to implement strategies that combine rapid identification and prompt treatment of individuals with active or latent infection, as well as of those with whom they have been in contact.

Keywords: HIV Infections/complications; AIDS-related opportunistic infections/complications; Tuberculosis/etiology; Tuberculosis/epidemiology

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INTRODUCTION

The incidence of tuberculosis (TB) has been increasing worldwide and this fact is strongly related to the infection with the human immunodeficiency virus (HIV). Approximately 11 million people worldwide are now coinfected with Mycobacterium tuberculosis and HIV.[1-3] The global distribution of TB is directly related to the socioeconomic status of the population.[1-3] Brazil ranks thirteenth worldwide in the total number of cases, belonging to a group of 22 countries that are responsible for 80% of all TB cases.[2]

The city of Rio Grande (in the state of Rio Grande do Sul) is located within a zone (the Third Regional Health District) that is considered an area of high TB prevalence according to the Rio Grande do Sul State Tuberculosis Control Program.[4] The city of Rio Grande, which has a port and is home to a university, ranks number 37 in the list of cities with the greatest numbers of HIV-infected patients in Brazil.[5] The Dr. Miguel Riet Corrêa, Jr. University Hospital has been a referral center for HIV-seropositive patients since the beginning of the epidemic and treats patients from 27 cities in the southern area of the state of Rio Grande do Sul. All HIV-positive patients living in the city of Rio Grande and surrounding areas are treated in this hospital, rather than only the most severe cases, as is common in other such referral centers. Therefore, epidemiological data from this hospital reflect regional prevalence with a certain degree of precision. In a previous study involving HIV-positive patients and carried out in the same hospital, it was reported that TB was found in 29% of the cases and was the main opportunistic infection that defined acquired immunodeficiency syndrome (AIDS) among the patients studied.[6]

Worldwide, TB is the most predominant opportunistic infection in AIDS patients. In addition, TB has a predilection for members of the more disadvantaged social groups[1-3] and is able to accelerate the course of HIV infection.[7] Diagnosing TB is often difficult. It has also been demonstrated that the survival of patients with AIDS is reduced after the development of active TB, especially in patients with more limited immunosuppression (CD4+ T-lymphocyte counts greater than 200 cells/mm3).[8-9] In terms of treatment, there are significant interactions between tuberculostatic and antiretroviral drugs, and resistant strains cause greater therapeutic difficulties.

The development of active TB in HIV-positive patients depends on immunosuppression status, high-risk behavior, lifestyle and history of contact with individuals with active TB, as well as the use of specific prophylaxis or antiretroviral therapy.[10-15]

In industrialized countries, these factors have been studied in depth. Such studies have shown that injection drug users and alcohol users are the most vulnerable members of the population.[12,15-16] In those countries, where the prevalence of latent infection with M. tuberculosis is low, and there are good health conditions, members of the general population is less often exposed to M. tuberculosis, although injection drug users have lifestyles that bring them into contact with the bacillus more often. In areas of high TB-HIV coinfection prevalence and poor health conditions, such as in some African countries, drug use is not part of the cultural behavior.[17]

After the advent of antiretroviral therapy, a decrease in the incidence of TB has been detected in countries where antiretroviral drugs are available.[18-20]

Brazil is one of the few countries in which there is a policy of universal access to antiretroviral therapy and a great number of coinfected individuals. Therefore, strategies to decrease the morbidity and mortality associated with TB-HIV coinfection have been established. The main measures for the control of the epidemic are early diagnosis, appropriate treatment of individuals with active TB and the identification of contacts.

The objectives of the present study were to determine the prevalence of TB in HIV-positive individuals treated at this facility and to identify the factors present at the time of HIV infection diagnosis that are correlated with the development of TB.

METHODS

A retrospective study was carried out including all patients treated during the year 1999 at the Federal University of Rio Grande Foundation Dr. Miguel Riet Jr. University Hospital HIV/AIDS Clinic. Data collected from the time of HIV diagnosis until the outset of the study were evaluated, with special attention given to information regarding the incidence of TB and events or factors leading up to that diagnosis.

The ethics research committee of the hospital approved the study. Patients were informed that refusal to enroll in the study would not affect their

follow-up treatment. Patients who agreed to participate gave written informed consent.

To construct the study sample, we used the following inclusion criteria: being infected with HIV, being older that 13 years of age, being in follow-up treatment at the specialized outpatient clinic or day-hospital of the institution and having been diagnosed with TB after being diagnosed with the HIV infection. Pregnant women were excluded, as were patients diagnosed with TB prior to being diagnosed with HIV.

The patients selected were asked to complete a structured questionnaire, and their medical records were reviewed in order to evaluate their immunological status at the time of HIV diagnosis. The questionnaire covered sociodemographic and behavioral variables. One of the authors of this study was responsible for the administration of the questionnaires. The variables under study were age, gender, race, educational level and means of exposure to HIV, as well as the use of tobacco, alcohol and illicit drugs prior to the time of the interview. Race was categorized as White or Black. Educational level was recorded in years of schooling, categorized as up to four, from 5 to 8 and more than 8. Smokers were defined as those who smoked at least one cigarette a day. Former smokers were defined as those who had quit smoking for at least 6 months prior, and nonsmokers were defined as those who had never smoked or who had smoked less than 100 cigarettes during their lifetime, but who had not smoked for at least 6 months prior. Based on their responses regarding illicit drug use, patients were categorized as users, nonusers or experimenters (those who had used illicit drugs less than 5 times during their lifetime). Alcohol users were categorized as daily drinkers, periodic drinkers (two to three times a week) or occasional drinkers. For the purpose of statistical analysis, individuals who had experimented with illicit drugs or cigarettes were classified as nonusers, as were the occasional drinkers. Individuals who fell into more than one HIV exposure category were interviewed separately for each category. For the statistical analysis, data were regrouped in accordance with the Hierarchical Classification of Transmission Categories.[6]

Immunosuppression status was determined by counting CD4+/CD8+ T-lymphocyte (CD4+TL) subpopulations and using the classification system established by the Centers for Disease Control in 1993. We used flow cytometry (FACSCount® system; Becton Dickinson, San Jose, CA, USA) for the CD4+TL count, carried out in the Laboratory for AIDS Support of the Department of Pathology of the Federal University of Rio Grande Foundation, which is linked to the Ministry of Health network of Viral Load and CD4+TL Laboratories. At the time of HIV diagnosis at the facility, CD4+TL counts were analyzed.

The final outcome measure was the development of TB between the time of HIV diagnosis at the HIV/AIDS Clinic and the time of the interview in 1999. Tuberculosis was diagnosed based on clinical profile, together with positive sputum smear microscopy or positive culture for M. tuberculosisFor those patients who were diagnosed with TB after having been diagnosed with HIV, data regarding the date, location and type of TB treatment (regular or irregular) were collected.

Data were entered into a database using the Excel program and were later transferred into the Stata 8.0 program. A descriptive analysis was carried by calculating means and proportions. In order to study the correlations between the outcome measure and each of the factors of interest, a bivariate analysis was carried out, including the calculation of odds ratios (ORs) and their respective 95% confidence intervals (95% CIs). In order to study the independent effect of the various factors, a multivariate analysis was carried out, using unconditional logistic regression with subsequent calculation of ORs and their respective 95% CIs. We used a p value of 0.2 (negative confounding) as a permanence criterion. The quality of the adjusted models was assessed using Hosmer-Lemeshow test. In all cases, for statistical decision, we adopted $p < 0.05$ for a two-tailed test. A linear tendency test was also conducted for ordinal categorical variables.

RESULTS

The sample comprised 204 patients, and 60% (122) were male. The mean age of sample was 34.04 years, with a standard deviation (SD) of 10.1 (range, 16-68 years). As shown in Table 1, the majority of patients were White (84% - 171 patients) with few years of schooling, only 34 (17%) having had more than 8 years of schooling. The principal means of contamination was sexual (74.6% - 150 patients), followed by injection drug use (25% - 51 patients).

TABLE 1

Sociodemographic and behavioral variables of HIV/AIDS patients studied in the city of Rio Grande (state of Rio Grande do Sul) in 1999 (n = 204)

Characteristic	Total patients n (%)		Patients with TB n (%)	
Gender				
Female	82	40.2	15	18.3
Male	122	59.8	40	32.5
Race				
White	171	83.8	38	22.2
Black	33	16.2	17	51.5
Educational level				
< 4 years	60	29.4	19	31.7
5–8 years	110	53.9	30	27.3
> 8 years	34	16.7	6	17.6
Mode of HIV transmission*				
Sexual	150	73.5	37	24.7
Blood	51	25.0	17	33.3
AIDS	111	54.4	55	49.5
Smoking	150	73.5	42	28.0
Alcohol	117	57.3	32	27.3
Illicit drugs	98	48.0	32	32.6
Injection drugs	53	25.9	15	28.3

*Three patients declined to state how they became infected with HIV; HIV: human immunodeficiency virus; AIDS: acquired immunodeficiency syndrome; TB: tuberculosis

At the time of the study, approximately half of the group (54.4% - 111 patients) met the criteria for AIDS, and the mean CD4+TL count was 187.27 (SD = 20.63).

Among the patients interviewed, 98 (48%) had a history of illicit drug use and 53 (26%) were injection drug users. Tobacco was used by 150 patients (73.5%), and 117 (57.8%) were alcohol users.

Of the 204 patients included in the study, 55 (27%) were diagnosed with TB after HIV infection. The mean age of this group of patients was 35.5 years (SD = 10.3). As shown in Table 1, the prevalence of TB was higher in males and in those with few years of schooling.

In the bivariate analysis of the characteristics correlated with TB (Table 2), showed that TB more often affected males (OR: 2.17; 95% CI: 1.10-4.28; p = 0.024), Blacks (OR: 3.72; 95% CI: 1.72-8.05; p = 0.001) and those with greater immunosuppression (initial CD4+TL: OR: 0.996; 95% CI: 0.994-0.998; p < 0.0001). Educational level was inversely correlated with the outcome measure, although this difference did not reach the cut-off point stipulated for significance.

TABLE 2

Crude and adjusted odds ratios for factors correlated with tuberculosis in HIV-1-positive individuals in the city of Rio Grande (state of Rio Grande do Sul) in 1999 (n = 204)

Risk factor	Crude OR (95% CI)	p	Adjusted OR (95% CI)	p
Age (years)	1.02 (0.99–1.05)	0.21	1.01 (0.97–1.05)	0.63
Gender				
Female	1		1	
Male	2.17 (1.10–4.28)	0.024	2.19 (0.99–4.84)	0.052*
Race				
Caucasian	1			
Black	3.27 (1.72–8.05)	0.001	4.76 (1.93–11.72)	< 0.0001*
Educational level				
d" 4 years		1		
4–8 years	0.81 (0.40–1.61)	0.69	(0.31–1.52)	
> 8 years	0.46 (0.16–1.30)	0.16#	0.39 (0.12–1.29)	0.1*#
HIV contamination				
Sexual	1		1	
Blood	0.65 (0.33–1.31)	0.23	0.88 (0.36–2.15)	0.77
Illicit drug use	1.75 (0.93–3.27)	0.08	1.78 (0.85–3.75)	0.1*
Injection drug use	1.58 (0.80–3.12)	0.18	0.64 (0.14–2.91)	0.56
Alcohol use	1.20 (0.62–2.33)	0.59	1.25 (0.57–2.73)	0.58
Smoking	1.23 (0.60–2.51)	0.58	1.11 (0.45–2.76)	0.81
Initial CD4+TL (/mm^3)	0.996 (0.994–0.998)	< 0.0001	0.995 (0.993–0.997)	< 0.0001*

*Final model: OR adjusted for gender, race, educational level, illicit drug use and initial CD4+TL count
#p test for linear tendency

Similarly, drug use should confer greater risk for TB, but the p value was not significant, although it was quite proximal to the level of significance (p = 0.08). The variables tobacco use, illicit drug use and alcohol use were not found to correlate with the development of TB.

Among the patients diagnosed with TB, extrapulmonary TB was more common than pulmonary TB, 39 (70.9%) presenting extrapulmonary TB and 16 (29.1%) presenting pulmonary TB (p = 0.003). Patients diagnosed with extrapulmonary TB had lower CD4+TL counts than did those diagnosed with pulmonary TB. The mean CD4+TL count was 203 (SD = 30.7) in patients with pulmonary TB and 180.7 (SD = 26.4) in those with extrapulmonary TB, although this difference was not statistically significant (p = 0.6).

In the multivariate analysis, as shown in Table 2, the final adjusted model showed that TB development correlated significantly with CD4+TL count and race. Patients with higher CD4+TL counts at the moment of diagnosis were less likely to be diagnosed with TB (OR: 0.995; 95% CI: 0.993-0.997). In addition, Black patients were more likely to be diagnosed with TB (OR: 4.93; 95% CI: 2.02-12.02). Three other variables (educational level, male gender and illicit drug use) presented p values less than or equal to 0.2 and therefore remained in the adjusted model. The effect of educational level increased after adjustments, but the p value was 0.1. The crude analysis of the male gender variable showed a significant correlation and an OR greater than 2. After adjustment to other variables, the effect of male gender remained the same, but the p value approached the level of significance (p = 0.053). The observed values for the variable illicit drug use remained virtually the same prior to and after adjustment.

A more detailed analysis showed that there was colinearity between illicit drug use and male gender so that withdrawing one of these variables from the model rendered the other significant. Consequently, when illicit drug use was withdrawn from the model, the OR for male gender increased to 2.49 (95% CI: 1.15-5.39), with a p value of 0.02. Similarly, when male gender was withdrawn from the model, the OR for illegal drug use rose to 2.1 (95% CI: 1.02-4.31), and the p value became 0.44.

Although injection cocaine use increased the risk for TB, its correlation with TB development was not statistically significant, and it therefore did not remain in the final model. The use of legal drugs, such as alcohol and tobacco, was not found to correlate with TB development.

DISCUSSION

The results of this study showed that gender, as well as CD4+TL count at the time of HIV diagnosis, correlates significantly with the development of TB. In addition, male gender and illicit drug can also be risk factors when studied separately.

Among the possible limitations of the present study, we could cite the temporal correlation between HIV infection and diagnosis with TB as the most significant. This aspect was minimized due to the exclusion of patients diagnosed with TB prior to HIV diagnosis. Of the 55 patients diagnosed with TB, 36 were diagnosed with TB and HIV simultaneously. Another limitation was that patients were not submitted to tuberculin tests, the results of which constitute a very important prognostic factor. The relationship between the results of this test and the development of the disease has been well established. Since tuberculin testing was unavailable in the country at the time the present study was carried out, this information was not included in the study.

Another relevant methodological aspect of every study in which attempts are made to identify users of licit or illicit drugs is the underestimation of their prevalence since subjects might withhold this type of information: actual values might therefore be even higher than those found. However, the reliability of data obtained from HIV-positive patients treated in our center seems to be better than that of those obtained from the population in general and, therefore, this aspect might be irrelevant.

We should emphasize that, although referral centers habitually receive the most severe, complex cases, with more diagnostic difficulties, this was not true in the hospital where the study was conducted. In addition to being a referral center for severe cases, this hospital participates in the evaluation and treatment of all seropositive cases in the city and neighboring towns. Therefore, the prevalence found in the study likely represents the prevalence in the region as a whole.

The demographic and socioeconomic characteristics found in the study group are similar

to those composing the national profile of HIV-positive patients in Brazil.[4]

In the present study, 73.5% of the participants reported having used tobacco. In contrast, in a study involving the general population of the state of Rio Grande do Sul, the prevalence of smokers found was 27.4%.[21] This difference between HIV-infected patients and the general population has been reported in other studies in which the prevalence of HIV+ smokers ranged from 31% to 88%.[22-24] This high prevalence might be related to the great number of people with a history of illicit drug use, which has been strongly correlated with smoking.

In the present study, 26% of the HIV-positive patients developed TB. These values are in agreement with findings reported in other studies. Since the development of TB is related to the socioeconomic conditions of the population, its prevalence or incidence varies depending on the group under study. The analysis of AIDS cases reported in Brazil from 1980 to March of 2000 revealed that, in 24% of cases, TB was diagnosed at the time the AIDS was reported.[25]

Similar prevalence rates have been reported in other studies conducted in areas of high TB and HIV prevalence,[9,13,26] in contrast with those found in studies carried out in industrialized countries, where the prevalence of the coinfection is rather lower.[1,3] Since TB is the only opportunistic infection that accompanies AIDS and is transmissible to other individuals, it is extremely important that we know the associated factors that may predispose patients to this infection in order to establish the diagnosis and initiate treatment as soon as possible.

In the present study pulmonary TB was definitively diagnosed in one-third of the patients, whereas extrapulmonary TB was responsible for 70% of the cases. Among the extrapulmonary forms, lymph node TB was the most frequent, which is in accordance with data in the literature on populations with such immunosuppression levels.[7,22]

The results of the present study showed that, after the adjustment with other variables, TB was more frequent in Black patients and in patients with lower CD4+TL counts. Regarding CD4+TL levels, although immunosuppression level is the most important isolated factor for the onset and form of presentation of TB,[7,26] the risk of TB infection in endemic areas for TB immediately after contamination with HIV, when the immune system of subjects is still preserved, may be higher than that previously expected. Some authors reported that the incidence of TB doubles in the first year after HIV infection and quadruples in the two following years.[28]

Regarding the higher risk for Blacks, studies have shown that the prevalence of TB in Blacks is higher than in Whites.[29] Although the relationship between this increased risk and the socioeconomic conditions in Africa may be more important than race, studies carried out in the USA involving socially disadvantaged populations have also shown a higher prevalence of TB among individuals of this race (African-Americans).[14,28]

Since the variables gender, illicit drug use and educational level met the pre-established criterion ($p < 0.2$), they were also included in the final model. The analysis showed that the p value for gender as a risk factor for the development of TB in HIV-positive patients was rather close to the level of significance ($p = 0.052$). Due to colinearity, the withdrawal of the illicit drug use variable caused the OR for the male gender variable to increase to 2.49 (95% CI: 1.15-5.39; $p = 0.02$) when compared to the variable female gender. The prevalence of TB is higher among adult males than among adult females.[10,13,15,17,25-27,31] However, it is not clear whether there is a real disparity in the prevalence of TB between genders or if confounding factors such as differences regarding access to treatment or stigmatization are involved.[30]

Although injection drug users are more vulnerable to TB,[10-12,15-16] we found no correlation with this variable in the present study. The lack of significant correlation in the adjusted model might be explained by the lack of power of the study sample since injection drug use has been associated with males[5] and, in the present study, there were only two female patients who presented these two conditions (TB and illicit drug use) in combination.

When drug use in general was studied, TB development was found to again be correlated with gender and illicit drug use in HIV-positive patients. As previously stated, the final model included both variables because their respective p values were within the pre-established value for remaining in the model ($p < 0.2$). With the withdrawal of the gender variable from the analysis, the illicit drug use variable presented an OR of 2.1 (95% CI: 1.03-4.27) and a p of 0.04, showing colinearity with gender.

The correlation between educational level and TB has been well documented in the literature.[14,17,25-26] Although the OR found in the present study revealed an inverse relationship between the frequency of TB and educational level, this correlation was not significant. Again, the reason for this lack of a correlation seems to be the lack of power of the study sample since, of the 204 individuals studied, only 6 of those developing TB had more than 8 years of schooling.

The results of the present study show that, except for the lower CD4+TL counts, the factors involved in the development of TB in HIV-positive patients mirror the risk factors found in the general Brazilian population (low educational level, being of the Black race, using illicit drugs, etc.) Consequently, HIV-related immunosuppression was found to correlate with those sociodemographic and behavioral characteristics that increase the risk of the disease. Therefore, in countries such as Brazil, where such sociodemographic factors have already resulted in high prevalence of the disease, there was an increase in the number of TB cases after the onset of the HIV epidemic, which explains the epidemiological differences found between Brazil and more developed countries.

Consequently, the difficulties in controlling the TB epidemic that existed prior to the HIV epidemic are today increased and potentiated by HIV coinfection. Successful experiences in the policy of HIV infection control and treatment must be applied in the TB control program. Controlling the HIV/TB coinfection epidemic will require a major global effort. Strategies combining the rapid identification of cases and contacts, as well as of individuals with latent forms of the infection, with early treatment should be implemented immediately.

REFERENCES

1. Who.int [homepage on the Internet]. New York: World Health Organization, [cited 2004 Sept 7] Available from: http://www.who.int/gtb/Country_info/index.htm
2. Ruffino-Netto A. Tuberculose: a calamidade negligenciada. Rev Soc Bras Med Trop. 2002;35(1):51-8.
3. Corbett EL, Watt CJ, Walker N, Maher D, Williams BG, Raviglione MC, et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. Arch Intern Med. 2003;163(9):1009-21.
4. Rio Grande do Sul. Secretaria da Saúde. Número de casos das doenças de notificação compulsória por CRS, RS, 2000-2001. [citado 2004 Ago 15]. Disponível em: http://www.saude.rs.gov.br
5. Bol Epidemiol AIDST [periódico na Internet]. 2004 [citado 2004 Nov 23];18(1: 01a a 26a Semanas Epidemiológicas, jan-jun. 2004):[cerca de 48p.]. Disponível em: http://www.aids.gov.br/final/dados/BOLETIM2.pdf
6. Barral-Martinez AM. Perfil epidemiológico dos pacientes com AIDS atendidos no Hospital Universitário da Fundação Universidade Federal do Rio Grande e caracterização dos subtipos de HIV-1 prevalentes [tese]. Belo Horizonte: Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais; 1999.
7. Michon C, Mortier E. La tuberculose. In: Girard PM, Katlama C, Pialoux G, editors. HIV édition 2001. Paris: Doin; 2001. p. 207-14.
8. Whalen CC, Nsubuga P, Okwera A, Johnson JL, Hom DL, Michael NL, et al. Impact of pulmonary tuberculosis on survival of HIV-infected adults: a prospective epidemiologic study in Uganda. AIDS. 2000;14(9):1219-28.
9. Badri M, Ehrlich R, Wood R, Pulerwitz T, Maartens G. Association between tuberculosis and HIV disease progression in a high tuberculosis prevalence area. Int J Tuberc Lung Dis. 2001;5(3):225-32.
10. Castilla J, Gutiérrez A, Guerra L, Pérez De La Paz J, Noguer I, Ruiz C, et al. Pulmonary and extra-pulmonary tuberculosis at AIDS diagnosis in Spain: epidemiological differences and implications for control. AIDS. 1997;11(13):1583-8.
11. Selwyn PA, Pumerantz AS, Durante A, Alcabes PG, Gourevitch MN, Boiselle PM, et al. Clinical predictors of Pneumocystis carinii pneumonia, bacterial pneumonia and tuberculosis in HIV-infected patients. AIDS. 1998;12(8):885-93.
12. Keizer ST, Langendam MM, Van Deutekom H, Coutinho RA, Van Ameijden E J. How does tuberculosis relate to HIV positive and HIV negative drug users? J Epidemiol Community Health. 2000;54(1):64-68.
13. Boffo MMS, Mattos IG, Ribeiro MO, Netto ICO. Tuberculose associada à AIDS: características demográficas, clínicas e laboratoriais em pacientes atendidos em um serviço de referência do sul do Brasil. J Pneumol. 2004;30(2):140-6.
14. Moss AR, Hahn JA, Tulsky JP, Daley CL, Small PM, Hopewell PC. Tuberculosis in the homeless. A prospective study. Am J Respir Crit Care Med. 2000;162(2 Pt 1):460-4.
15. Godoy P, Domínguez A, Alcaide J, Camps N, Jansà JM, Minguell S, et al Working Group of the Multicentre Tuberculosis Research Project. Characteristics of tuberculosis patients with positive sputum smear in Catalonia, Spain. Eur J Public Health. 2004;14(1):71-5.
16. O'Donnell AE. HIV in illicit drug users. Clin Chest Med. 1996;17(4):797-807.
17. Bates I, Fenton C, Gruber J, Lalloo D, Medina Lara A, Squire SB, et al. Vulnerability to malaria, tuberculosis, and HIV/AIDS infection and disease. Part 1. Determinants operating at individual and household level. Lancet Infect Dis. 2004;4(5):267-77.
18. Wolff AJ, O'Donnell AE. Pulmonary manifestations of HIV infection in the era of highly active antiretroviral therapy. Chest. 2001;120(6):1888-93.
19. Jones JL, Hanson DL, Dworkin MS, Alderton DL, Fleming PL, Kaplan JE, et al. Surveillance for AIDS-defining opportunistic illnesses, 1992-1997. MMWR CDC Surveill Summ. 1999;48(2):1-22.
20. Santoro-Lopes G, Pinho AM, Harrison LH, Schechter M. Reduced risk of tuberculosis among Brazilian patients with advanced human immunodeficiency virus infection treated with highly active antiretroviral therapy. Clin Infect Dis.

2002;34(4):543-6.
21. Oliveira Netto IC. Epidemiologia do tabagismo no Rio Grande do Sul [tese]. Porto Alegre: Faculdade de Medicina, Universidade Federal do Rio Grande do Sul; 1998.
22. Wallace JM, Rao AV, Glassroth J, Hansen NI, Rosen MJ, Arakaki C, et al. Respiratory illness in persons with human immunodeficiency virus infection. The Pulmonary Complications of HIV Infection Study Group. Am Rev Respir Dis. 1993;148(6 Pt 1):1523-9.
23. Conley LJ, Bush TJ, Buchbinder SP, Penley KA, Judson FN, Holmberg SD. The association between cigarette smoking and selected HIV-related medical conditions. AIDS. 1996;10(10):1121-6.
24. Wewers MD, Diaz PT, Wewers ME, Lowe M, Nagaraja HN, Clanton TL. Cigarette smoking in HIV infection induces a supressive inflammatory environment in the lung. Am J Respir Crit Care Med. 1998;158(5 Pt 1):1543-9.
25. Laguardia J, Mérchan-Hamann E. Factores de riesgo para la enfermedad tuberculosa en los casos de SIDA notificados en Brasil, 1980 a 2000. Rev Esp Salud Publica. 2003;77(5):553-65.
26. Song ATW, Schout D, Novaes HMD, Goldbaum M. Aspectos clínicos e epidemiológicos da comorbidade AIDS/tuberculose. Rev Hosp Clin Fac Med São Paulo. 2003;58(4):207-14.
27. Brito RC, Gounder C, Lima DB, Siqueira H, Cavalcanti HR, Pereira MM, et al. Resistência aos medicamentos anti-tuberculose de cepas de Mycobacterium tuberculosis isoladas de pacientes atendidos em hospital geral de referência para tratamento de AIDS no Rio de Janeiro. J Bras Pneumol. 2004;30(4):335-42.
28. Sonnenberg P, Glynn JR, Fielding K, Murray J, Godfrey-Fausset P, Shearer S. How soon after infection with HIV does the risk of tuberculosis start to increase? A retrospective cohort study in South African gold miners. J Infect Dis. 2005;191(2):150-8.
29. Centers for Disease Control and Prevention (CDC). Racial disparities in tuberculosis-selected southeastern states, 1991-2002. MMWR Morb Mortal Wkly Rep. 2004;53(25): 556-9.
30. Holmes CB, Hausler H, Numm P. A review of sex differences in the epidemiology of tuberculosis. Int J Tuberc Lung Dis. 1998;2(2):96-104.
31. Garcia GF, Corrêa PCRP, Melo MGT, Souza MB. Prevalência da infecção pelo HIV em pacientes internados por tuberculose. J Pneumol. 2000;26(4):189-93.