Original Article

Tuberculosis in a Psychiatric Hospital in the state of Goiás, Brazil*

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ABSTRACT

Objective: To investigate the prevalence of infection, disease and eventual institutional outbreak of tuberculosis in a psychiatric hospital using the PPD test, as well as testing for mycobacteria in material collected from the bronchial tree and using molecular tracking technique based on insertion sequence *6110* (IS6110). **Methods:** Between February and August of 2002, PPD tests were given to 74 inpatients and 31 staff members at a psychiatric hospital in the city of Rio Verde, located in the state of Goiás, Brazil. In addition, bronchial tree material collected from the inpatients was submitted to testing for *Mycobacterium tuberculosis*. **Results:** Among the patients analyzed, mycobacteria were isolated from five (6.8%): four identified as M. tuberculosis and one as *M. chelonae*. The *M. tuberculosis* isolates were sensitive to isoniazid and rifampicin, and, when submitted to the restriction fragment length polymorphism/IS6110 technique, presented unique genetic profiles, totally distinct from one another, suggesting that all of the tuberculosis cases were due to endogenous reactivation. It was not possible to characterize this group of cases as an institutional outbreak. Performing the two-step tuberculin test in the patients, the infection rates were 23% and 31%, compared with 42% among staff members, who were submitted to the one-step test. **Conclusion:** The results indicate a high incidence of tuberculosis infection among inpatients and hospital staff, as well as a high occurrence of the disease among inpatients.

Keywords: Tuberculosis/epidemiology; Hospitals, psychiatric; *Mycobacterium tuberculosis*; Tuberculin test; *Mycobacterium chelonae*

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INTRODUCTION

Although we know the etiologic agents and forms of transmission of tuberculosis (TB), as well as having efficient treatments available for it, it is still the leading cause of adult death from infection worldwide.[1] In Brazil, there are an estimated 111,000 new cases of TB and 6000 TB-related deaths per year. In 2001, 81,432 cases were reported.[2]

The incidence of TB among patients and professionals that work in hospitals, mental health clinics, and prisons is higher than that seen in the general population and poses risks of institutional outbreaks. Studies show that the transmission rate in these environments is very high, and the prevalence of TB is sixteen-times higher in institutionalized patients than in the general population.[3] In addition, it has been shown that there is great risk of dissemination of multidrug-resistant forms of TB in hospitals.[4] Some authors[5] found a high rate of drug resistance (17.2%) among 58 samples of Mycobacterium tuberculosis isolated from convicts at a prison psychiatric hospital for men in the city of Rio de Janeiro, Brazil.

The identification of the species alone is not sufficient to investigate TB outbreaks in institutions. As of the end of the 1980s and beginning of 1990s, molecular techniques to differentiate M. tuberculosis strains have been implemented, detecting and characterizing repetitive elements in the genome of bacteria belonging to the M. tuberculosis complex.[6-7] Among the several repeated elements identified, the same insertion sequence applied in the diagnosis - insertion sequence 6110 (IS6110) - has been used as a marker to differentiate among M. tuberculosis strains. The irregular insertion of IS6110 in the genome of mycobacteria allows the discrimination of strains through the DNA fingerprinting technique and the restriction fragment length polymorphism (RFLP) analysis. Its use has been widely recommended, and it can be performed in a reproducible and standardized way.[8] The method most often used for molecular characterization of M. tuberculosis strains[9] has been the RFLP analysis. It results from the combination of the Southern blot and hybridization techniques, the latter using probes constructed on the basis of the IS6110 DNA sequence (RFLP-IS6110). One group of authors[10] used the RFLP methodology to conduct an epidemiological study of inpatients at a psychiatric hospital in Havana, Cuba. In that study, the RFLP methodology served as instrument of disease control.

It is of fundamental importance to estimate the prevalence of infection by M. tuberculosis among institutionalized patients, as well as among the professionals that are in constant contact with those patients. The most widely accepted method of doing so is to quantify the skin response to the tuberculin test, including the retest in order to evaluate the booster effect.

The aim of this study was to assess the prevalence of TB infection and active TB among the inpatients of a permanent psychiatric institution in order to evaluate the possibility of intra-institutional transmission of the identified cases and estimate the prevalence of infection in the staff.

METHODS

Between February and August of 2002, material (sputum or saliva samples) collected from the bronchial trees of 74 inpatients (39 women and 35 men), with or without respiratory symptoms, under treatment at a psychiatric hospital in the city of Rio Verde, in the state of Goiás, Brazil, was submitted to testing for mycobacteria. The hospital has an area of 384 m2 and employs 21 nurses. The outpatient sector is separated into male and female wards.

The study was approved by the hospital ethics committee and was monitored by a team of physicians specialized in general clinical medicine, radiology, and phthisiology. All patients were submitted to clinical, radiological, and laboratory tests. Samples were collected from the bronchial tree of each patient on three consecutive days. The patients and the 31 staff members (12 kitchen assistants, 11 nurses, 3 administrative employees, 3 physicians, 1 psychologist, and 1 pharmacist) were simultaneously submitted to the tuberculin test. Two smears were submitted to Ziehl-Neelsen staining for the mycobacteria testing. The remaining samples were used cultured using the Kudoh and Kudoh technique.[11] The colonies that presented characteristics of mycobacteria were submitted to subculture in new Ogawa tubes to be identified through the classical methodology recommended by the Health Department[12] and through mycolic acid analysis.[13] M. tuberculosis complex mycobacteria were defined as those presenting slow growth and testing positive for nitrate reductase, positive for

urease, and negative for arylsulfatase. The inverse criteria were used to define M. chelonae complex mycobacteria. The isolates were then submitted to the sensitivity test using the proportions method.[12]

M. tuberculosis strains were also submitted to the RFLP technique for molecular typing, using the methodology proposed by van Soolingen et al.[14] Initially, the DNA extraction was performed using lysozyme, proteinase K, and chloroform/isoamyl alcohol (24:1). Subsequently, approximately 3 g of DNA from each sample were digested with 5 U of Pvu II enzymes, and submitted to electrophoresis on a 1% agarose gel to separate the fragments. The fragment hybridization was performed using a digoxigenin-labeled probe. The genetic profile of each strain was analyzed using the GelCompar II program, version 2.0, for Windows (Applied Maths, Kortrijk, Belgium).

For the tuberculin test employed to evaluate the prevalence of the infection in patients and employees, the purified protein derivative (PPD) RT-23 was used in two steps. For each patient or employee, 0.1 ml of PPD-RT23, corresponding to 2 UT, were injected in the anterior aspect of the left forearm, and the result was read after 48 to 72 hours, when the size of the induration was measured.[15] Three weeks later, the patients presenting an induration of less than 10 mm were submitted to a second application in order to evaluate the booster effect. For operational reasons, the second test was not performed in health professionals.

RESULTS

Among the 74 inpatients analyzed, 64 were receiving treatment for a mental disorder, five were alcohol-dependent, and the others presented both problems concomitantly. No cases of illicit drug use were observed. According to the medical charts, none of the patients had a history that was suggestive of or would raise the suspicion of infection with the human immunodeficiency virus. Of the 39 women, 36 were between 21 and 50 years of age, and three were over 50. Of the 35 men, 30 were between 21 and 50 years of age, and five were over 50. The hospital stays of the patients analyzed varied from 3 to 19 months (mean, 9 months). The sputum smear microscopy was positive in only one patient and negative in the other 73 patients. However, through culture, mycobacteria were isolated from the samples of five patients (6.8%): four were M. tuberculosis strains and one was a M. chelonae strain. Although there were more female patients, all cases of TB occurred in male patients. However, M. chelonae, the only species of nontuberculous mycobacteria (NTM), was isolated from a woman. The M. tuberculosis strains were sensitive to isoniazid and rifampin, and the M. chelonae strains were resistant to both of the drugs tested. Images on conventional chest X-rays were not suggestive of TB (absence of cavities) among patients with positive sputum culture.

In the genomic DNA analysis using the RFLP-IS6110 technique, the four M. tuberculosis isolates presented 10 to 13 copies of IS6110. The genetic profiles obtained were evaluated using the GelCompar II program, version 2.0 (Applied Maths), and the results are shown in Figure 1.

The four M. tuberculosis complex isolates presented unique genetic profiles, that is, profiles

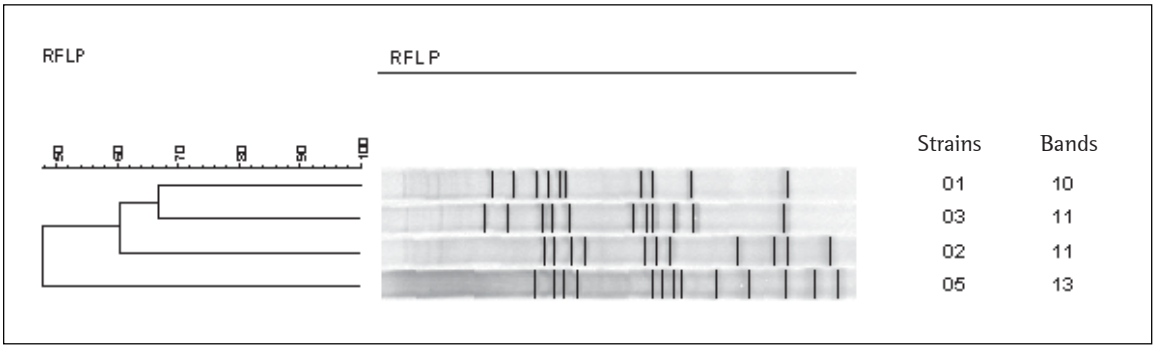

Figure 1 - Profile of the four M. tuberculosis isolates defined through the RFLP-IS6110 technique. The bands were aligned using the Mt 14323 strain as a reference
RFLP: restriction fragment length polymorphism

TABLE 1

Correlation between the genetic profiles of the strains obtained through restriction fragment length polymorphism and epidemiology of patients with tuberculosis identified by the M. tuberculosis culture

	Strains			
	1	2	3	4
Genetic profile	I	II	III	V
Gender	Male	Male	Male	Male
Age (years)	46	49	39	53
Accompanying disease	Alcoholism	Alcoholism	Alcoholism	Schizophrenia
Origin (city)	Rio Verde	Pedreira	Rio Verde	Maurilândia
Hospital stay (months)	3	6	19	9
Sharing the same room?	No	No	No	No

TABLE 2

Distribution of tuberculin test results among patients according to the different variables

Patients	Age		Mean hospital stay	Accompanying diseases		
(74)	21-50	>50		Alco	MD	Alco+MD
PPD + (19)	18	1	Média de 16 meses	4	12	3
PPD - (55)	48	7	Média de 09 meses	5	49	1
Booster (04)	4	-	Média de 16 meses	-	4	-

Alco: alcoholism; MD: mental disorder; PPD: purified protein derivative (tuberculin) test

that were completely different from one another. No genetic group, identified by samples that share the same band profile, was observed. These data are supported by the absence of an epidemiological correlation, which was also verified through the analysis of medical charts. The correlation results are shown in Table 1.Among the patients, the two-step tuberculin test and the retest showed initial positivity of 25.7% (19/74) and 31.1% (23/74), respectively. The booster effect was confirmed in four patients (Table 2). Among the professionals, the positivity was 42% (13/31), as can be seen in Table 3. The positivity rate on the tuberculin test was higher among the professionals who had been in the job for a longer mean period (30 months vs.18 months, respectively, for the groups presenting positive and negative tuberculin test results). Being a nurse, followed by being a kitchen assistant, were the variables that presented the highest risk. The positivity rate in these groups was 55.5% and 46%, respectively. The rate of infection was identical (33.3%) for physicians and administrative assistants. However, due to the small sample size, these results are shown exclusively as detected data, and not as a trend to be analyzed.

TABLE 3

Distribution of tuberculin test results among professionals according to the different variables

Variables	Profissionals (31)	
	PPD + (13)	PPD - (18)
Age (years)		
21 - 50	13	15
>50	-	3
Months on the job (mean)	30	18
Profession		
Nurse (17)	6	11
Kitchen assistant (17)	5	12
Administrative assistant (4)	1	3
Physician (04)	1	3
Pharmacist/Psychologist (2)	-	2

PPD: purified protein derivative (tuberculin) test

DISCUSSION

The patients had long been confined to the psychiatric hospital and typically left it only if some urgent medical procedure was required. Due to the fact that they sleep in groups of five per room, with poor ventilation, and that they share the

recreation and dining rooms, there is a high risk of TB transmission among inpatients and even among the professionals working in the hospital.

This study identified one case of mycobacteriosis caused by NTM. Although there have been no Brazilian studies, some authors[16] have found the incidence of infection with NTM to be 5% to 7% in some confined environments in Tel Hashomer, Israel. Isolation of M. chelonae is in agreement with the observation of a worldwide increase in the incidence of NTM infection since the advent of the acquired immunodeficiency syndrome epidemic.[17-18] In this study, M. chelonae was isolated from one patient, who, according to her hospital history, was receiving treatment for alcoholism and did not present acquired immunodeficiency syndrome. Infection with NTM is more likely to occur in patients presenting altered immunological status, either due to alcohol dependence or immunosuppression. The M. chelonae strain was resistant to the drugs analyzed - isoniazid and rifampicin, confirming the data in the literature showing that NTMs are refractory to the drugs used in TB treatment.

In relation to the epidemiological study of TB, it is important to highlight that active TB can occur either by the progression of a recent infection, by exogenous infection, by re-infection, or by the reactivation of a latent infection, known as endogenous reactivation. These events can be determined by the intrinsic characteristics of the host, of M. tuberculosis, or both.[19] According to some authors,[20] the TB cases associated with M. tuberculosis strains with identical genetic profiles are a result of the recent transmission of the bacilli. On the other hand, cases of the disease caused by strains with unique profiles are a result of the endogenous reactivation of a latent infection. In addition, there must be an epidemiological connection among patients infected with strains that have identical genetic profiles according to the RFLP technique.[21]

In the present study, the genetic profiles of the four strains were different from one another. No genetic groups were observed. Therefore, it was not possible to establish a previous or current correlation between the molecular study and the epidemiological data in patients identified as having TB. In this sense, considering the absence of an epidemiological connection, it is plausible that the M. tuberculosis isolates with unique genetic profiles, such as we have found, are a consequence of endogenous reactivation. This evidence is supported by the negative sputum results, with bacilli recovered only from cultures, combined with the radiological examination results, which were atypical for TB, with absence of cavities, suggesting impaired pulmonary function with paucibacillary lesions and a low possibility of transmission.

The immunosuppressive factors, such as nosocomial diseases and prolonged confinement, to which the patients are subjected might have caused the reactivation of latent infections. This could also explain the high incidence of TB among the patients in this hospital (4 of the 74 inpatients), compared with 47.2/100,000 inhabitants[2] in Brazil as a whole and 26/100.000 inhabitants[22] in the city of Rio Verde, where the study was carried out.

The inpatient infection rate of 31% reveals a high risk for infected patients to become sick, due to conditions inherent to the prolonged hospital stay. The difference of 6% in the infection prevalence detected by the booster effect reinforces the idea of immunosuppression in institutionalized patients, indicating the need for chemoprophylaxis in this population.

The infection rate of 42% among employees, higher than that of the inpatients, even without the tuberculin retest, demonstrates the occupational risks and the need for a biosafety policy. In one study carried out in 1998,[23] a similarity was observed between the infection rates of employees of a university hospital and a control group composed of salary-matched employees of a restaurant located in a bank (56% vs. 53%), both located in the city of São Paulo. This result can support our findings, that is, the fact that the rates of tuberculin test positivity are similar between the nursing staff and the kitchen staff of the hospital analyzed (Table 3). In another study,[24] the prevalence by M. tuberculosis infection was found to be 51% among the health professionals of a university hospital in the city of Rio de Janeiro. Even among medical students, some authors[25] have verified increasing positivity rates - 4%, 6.4%, and 13%, according to the progress of their participation in practical activities. This increase was also indicated by other authors[26] among the employees of a referral clinic for TB in the city of São Paulo.

In confined environments such as a psychiatric hospital, there is a predisposition for the dissemination of TB. Therefore, we can suggest that there is the need for a constant monitoring of patients through the culture of sputum samples, detecting cases of TB in the paucibacillary phase, so that its transmission can be avoided.

The fact that we cannot characterize the findings as an institutional outbreak can either be a result of specific conditions of the institution where the study was carried out or a result of the low possibility of transmission of the disease in the identified cases.

In Brazil, three recent molecular epidemiology studies mapped strains of bacilli using the RFLP technique and observed similar genetic groups corresponding to recent infections and diseases resulting form exogenous re-infection. The rates of infection were as follows: 23% and 37% (between 1991 and 1994) in the states of Rio de Janeiro and Rio Grande do Sul, respectively[27]; 33% (between 1995 and 1997) in the city of São Paulo[28]; and 29% (between 2000 and 2002) in the city of Araraquara.[29] Although these studies are initial and limited, they indicate that new cases in Brazil result predominantly from endogenous reactivation of latent infection, which account for approximately 70% of the cases. In a certain way, this supports the findings of the present study.

As a consequence of this study, patients with TB were treated, and those presenting positive tuberculin test results were submitted to chemoprophylaxis. The board of directors of the institution is also studying the possibility of submitting new admissions to the tuberculin test. In addition, tuberculin tests and chest X-rays were adopted as obligatory for all employees hired in the future.

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