Original Article

Epidemiological aspects of human immunodeficiency virus/tuberculosis co-infection in Ribeirão Preto, Brazil from 1998 to 2003*

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ABSTRACT

Objective: This study aimed to characterize the epidemiological profile of tuberculosis cases reported in the city of Ribeirão Preto between 1998 and 2003, according to patient HIV status, gender, age bracket and treatment outcome. **Methods:** This was a descriptive epidemiological study that employed the Brazilian National Tuberculosis Notification Database as an instrument of data collection. The study sample consisted of all cases of human immunodeficiency virus/tuberculosis co-infection occurring in residents of Ribeirão Preto and reported between 1998 and 2003. **Results:** During this period, 1273 new cases of tuberculosis were reported, 377 of which were in HIV-positive individuals, for a co-infection rate of 30%. Of the cases of co-infection, 76% were in men, and the majority occurred in individuals in the 20-59 age bracket. In terms of treatment outcome, cure was achieved in 52%, treatment abandonment was reported in 11%, and death occurred in 32%. The predominant clinical form of tuberculosis was the pulmonary form, which accounted for 58% of the cases. **Conclusion:** A high prevalence of co-infection was observed in the community studied. The treatment outcomes seen among the cases in our study sample underscore the need to adopt special strategies to monitor this clientele. Comparing the cases of tuberculosis in isolation with the cases of co-infection, no gender-related or age-related differences were observed.

Keywords: Tuberculosis; HIV infections; Comorbidity

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INTRODUCTION

Tuberculosis (TB) is an infectious disease that is still a significant cause of morbidity and mortality. Advances in the understanding of TB, as well as in the technology available for the control of this disease have not been sufficient to have a significant impact on TB-related morbidity and mortality, especially in developing countries. In Brazil, despite the fact that patients have access to efficacious chemotherapy and up-to-date diagnostic and preventive methods, TB continues to be a significant public health problem.[1]

In a number of countries, the rate of decline in TB incidence has tended to slow in recent years, and, in some countries, the annual number of new cases has even increased.[2] In the mid 1980s, developed countries, in which the annual incidence of TB had been on the decline, began to see an increase. It is estimated that 10 million people are infected with Mycobacterium tuberculosis in the USA.[2]

According to a World Health Organization report, Brazil ranks fifteenth among the twenty-two countries that are responsible for 80% of the total number of cases of TB worldwide. It has been estimated that approximately two billion individuals are currently infected with TB worldwide, which corresponds to approximately 30% of the global population. Annually, eight million of these two billion individuals will develop the active form of TB, and two million will die from it.[3]

It has been estimated that TB has killed one hundred million people over the past 100 years, being considered the second leading cause of death worldwide, being surpassed only by the human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS).[4]

In Brazil, the estimate is 120,000 new cases and 6000 deaths per year. A cure is achieved in only 72% of patients, treatment abandonment is seen in 11.7%, and death occurs in 7%.[3]

Some socioeconomic factors have been implicated in this scenario. Poverty has increased, making it more difficult for certain individuals to access health care services. In addition, the growth of ghettos and the migration of individuals in search of a better quality of life have complicated the health care equation. Furthermore, the efficiency of public health care facilities has fallen in recent decades.[5]

In 1981, with the advent of AIDS, a growing number of reported cases of TB in individuals co-infected with HIV were seen, in developed and developing countries.

It was estimated that, in the year 2000, 11% of all adults with TB also presented co-infection with HIV or had AIDS.[4]

In 2003, 9762 cases of HIV and AIDS were reported in Brazil, 41.13% occurring in the state of São Paulo.[6] Infection with HIV had a visible impact on the epidemiology, natural history and clinical evolution of TB.[4]

Preliminary data indicated that mortality rates in patients co-infected with HIV and TB were higher than in those diagnosed with HIV infection alone. Being infected with HIV is today a significant risk factor for the development of TB, and, if it is not the most relevant, it is the most characteristic in terms of morbidity, not only because of the pathological interaction, but also due to a combination of factors that favor the evolution of the disease in both conditions. The combination of TB and HIV infection affects mortality in two ways: TB presents significant lethality for those infected with HIV; and HIV acts as an indirect cause of the increase in the incidence of TB and consequent increase in TB-related mortality among HIV-negative individuals by increasing the reservoir of M. tuberculosis.[7]

It was recently shown that, in one patient infected with HIV, exposure to chronic exogenous infection resulted in increased viral expression and greater infectiousness.[8] In areas where there is a high prevalence of TB/HIV co-infection, noncompliance with TB treatment regimens by patients co-infected with HIV and TB can result in increased resistance against anti-TB medications, as well as in the risk of transmission of M. tuberculosis and HIV to those who come into contact with such patients.

Consequently, the National Coordination of the Tuberculosis Control Program suggests that HIV serological testing be made available for patients diagnosed with TB, and the National Tuberculosis Control Plan (2004-2007) recommends that all patients diagnosed with TB be submitted to serological investigation for HIV.

From 1993 to 2003, the number of requests for serological testing for HIV of patients diagnosed with TB in the city of Ribeirão Preto rose from 34% to 86%. Over the past few years, health care teams have begun to incorporate this practice into

their routine practice. Offering serological testing for HIV might help determine the rates of the TB/HIV co-infection. It has been conjectured that the combination of TB and HIV has had a disastrous effect on the global TB scenario, rendering TB control programs ineffective.[9] In this context, it is necessary to develop epidemiological profiles of individuals co-infected with HIV and TB in order to facilitate the planning of control measures against such co-infection.

The objective of the present study was to describe the epidemiological profile of the patients co-infected with TB and HIV residing in the city of Ribeirão Preto, according to age bracket, gender, clinical form and treatment outcome.

METHOD

This was a retrospective epidemiological study, the results of which might suggest explanations for the frequency variations. Therefore, further studies on this topic, especially analytical studies, could be based on the present study, which attests to the strong investigational component inherent to the field of epidemiology.[10]

The city of Ribeirão Preto is located in the state of São Paulo, 319 km from the capital, with a population of approximately 551,000 inhabitants, according to the Information Technology Department of the Unified Health Care System. This city has a wide network of public, private and philanthropic health care clinics and hospitals, which include primary, secondary and tertiary health care facilities.

Regarding the activities of the TB control program, the city is organized around the hierarchical and regionalized principles proposed by the Unified Health System. Consequently, the basic health care clinics are responsible for identifying individuals who present respiratory symptoms, as well as for diagnostic examinations (sputum smear microscopy). After the diagnosis has been confirmed, the patient is referred to the referral health care clinic in the district in which the patient resides.

Due to the high incidence of the TB/HIV co-infection in the city of Ribeirão Preto, the staff of such health care clinics include professionals who work in both specialties (Tuberculosis and Infectious Diseases), which has improved patient treatment and follow-up evaluation. Such clinics also allow a better articulation and interface with the local interlocutor of the sexually transmitted diseases/AIDS program.

There is also the Special Unit for the Treatment of Infectious and Contagious Diseases, managed by the of the University of São Paulo School of Medicine Hospital das Clínicas in Ribeirão Preto. This unit treats outpatients with TB/HIV co-infection and is responsible for hospitalizing patients who present more severe symptoms and require specialized care.

The cases are reported when patients are diagnosed with TB, at which time HIV serological testing is offered. The tests are performed in a municipal laboratory using the ELISA method (two samples). Samples testing positive are sent to the Referral Laboratory of the Adolfo Lutz Institute for confirmatory tests.

The population evaluated in the present study consisted of all cases of TB/HIV co-infection occurring in residents of Ribeirão Preto and reported between 1998 and 2003.

Data were collected from the Epi-TB database, centralized in the Epidemiological Surveillance Division of the Municipal Secretary of Health of Ribeirão Preto. This database uses a software program compatible with Epi Info and was created by the State of São Paulo Tuberculosis Control Division, being officially used in all cities in the state.

In accordance with standard practice, the TB reporting forms are filled out by the professionals working in the health care clinics, entered into the database and then sent to the central office.

RESULTS

From 1998 to 2003, 1273 new cases of TB were reported in Ribeirão Preto, 377 of which were in HIV-positive individuals. The mean co-infection rate was 30% during this period.

Of the cases of co-infection, 76% were in men (Table 1).

The majority of cases occurred in individuals in the 20-59 age bracket. Table 2 shows that 91% of the reported cases were in individuals in this age bracket.

Of the cases of co-infection, the predominant clinical form of TB was the pulmonary form, which

TABLE 1

Cases of tuberculosis according to time period, gender and HIV serological status. Ribeirão Preto, SP, 1998-2003

Cases	Reporting Period 1998 - 2000 n	%	2001 - 2003 n	%	Total n	%
Females						
HIV-positive	54	25.0	36	22.0	90	24.0
HIV-negative	162	75.0	127	78.0	289	76.0
Subtotal	216	100.0	163	100.0	379	100.0
Males						
HIV-positive	175	36.0	112	27.0	287	32.0
HIV-negative	308	64.0	299	73.0	607	68.0
Subtotal	483	100.0	411	100.0	894	100.0
Total per period	699	55.0	574	45.0	1273	100.0

accounted for 74.5% of all cases. Among the HIV-negative patients, the incidence of the pulmonary clinical form of TB was 86%. The extrapulmonary clinical form of TB was more common in HIV-positive patients than in HIV-negative patients (25.5% vs. 14%).[11-13]

In terms of treatment outcome, we used only the following outcome measures: cure, abandonment, death or relocation. Of the TB/HIV co-infected patients, 52.5% were cured, 11% abandoned treatment, 33% died, and 3.5% were relocated.

TABLE 2

Pacientes com tuberculose e sorologia positiva para o HIV, segundo período da notificação e faixa etária. Ribeirão Preto, SP, 1998-2003.

Age Bracket	Reporting Period 1998 - 2000 n	%	2001 - 2003 n	%	Total n	%
0 - 4	2	0.8	1	0.6	3	0.8
10 - 14	1	0.4	1	0.6	2	0.5
15 - 19	1	0.4	3	2.0	4	1.0
20 - 29	50	21.8	31	20.9	81	21.4
30 - 39	135	58.9	66	44.5	201	53.3
40 - 49	31	13.5	34	22.9	65	17.2
50 - 59	7	3.0	9	6.0	16	4.2
60 ou +	2	0.8	3	2.0	5	1.3
Subtotal	229	100.0	148	100.0	377	100.0

Table 3 shows that there was a high mortality rate in the HIV-positive population that was being treated for TB. Of the 377 HIV-positive cases, death occurred in 123 (33%) during the TB treatment. In a more comprehensive analysis, we detected that, of these 123 patients, 30% died during the first month of treatment in the tertiary-care referral center. This rate increased to 50% in the second month, to 60% in the third month and to 80% in the sixth month.

Since many of these patients died at the beginning of treatment, only 33% were submitted to supervised treatment.

Among those who died, there was a predominance of males (Table 4). Individuals in the 20-49 age bracket accounted for 92% of the deaths (Table 5).

TABLE 3

Patients with tuberculosis and HIV-positive serological test results, by time period and treatment outcome. Ribeirão Preto, SP, 1998-2003

Cases Outcome	Reporting Period 1998 - 2000 n	%	2001 - 2003 n	%	Total n	%
Cure	120	52.0	78	53.0	198	52.5
Abandonment	27	12.0	15	10.0	42	11.0
Death	69	30.0	54	36.4	123	33.0
Relocation	13	6.0	1	0.6	14	3.5
Subtotal	229	100.0	148	100.0	377	100.0

TABLE 4

Patients with tuberculosis and HIV-positive serological testing results who died, according to the notification period of tuberculosis and gender. Ribeirão Preto, SP, 1998-2003

Cases	Reporting Period 1998 - 2000 n	%	2001 - 2003 n	%	Total n	%
Female	19	27.6	14	26	33	27.0
Male	50	72.0	40	74	90	73.0
Subtotal	69	100.0	54	100.0	123	100.0

TABLE 5

Patients with tuberculosis and HIV-positive serological test results who died, by time period and gender. Ribeirão Preto, SP, 1998-2003

	Reporting Period					
	1998 - 2000		2001 - 2003		Total	
Age Bracket	n	%	n	%	n	%
15 - 19	1	1.4	0	0	1	0.8
20 - 29	22	32.0	9	16.7	31	25.0
30 - 39	34	49.3	27	50.0	61	50.0
40 - 49	8	11.6	13	24.0	21	17.0
50 - 59	3	4.3	3	5.5	6	5.0
60 ou +	1	1.4	2	3.8	3	2.5
Subtotal	69	100.0	54	100.0	123	100.0

DISCUSSION

In Brazil, 8.1% of the reported cases of TB are accompanied by HIV infection. In the state of São Paulo, this rate is 15%. These values might represent an underestimation, since they depend on the availability and performance of HIV serological testing. In the city of Ribeirão Preto, the availability of such testing has been increased in recent years in order to facilitate the early detection of this co-morbidity.

Some authors[11] have reported that TB/HIV co-infection is more common in males, a condition not observed among individuals infected with TB alone. In the present study, a similar situation was observed: males were more often affected by such co-infection than were females.

The age distribution of the cases of TB/HIV co-infection in Ribeirão Preto followed a pattern similar to that reported for Africa, which has one of the highest rates of this co-morbidity.[12]

In Ribeirão Preto, we found that the extrapulmonary clinical form of TB was more common than the pulmonary clinical form in HIV-positive patients, a situation not observed among HIV-negative patients. This finding is in agreement with those of other epidemiological studies conducted in Brazil.[11-13]

In terms of TB treatment, we found that treatment outcomes during the study period were better among HIV-negative patients than among HIV-positive patients. Among the HIV-negative patients, cure was achieved in 83.5%, treatment abandonment was reported in 5.2%, death occurred in 9%, and relocation was reported in 2.2%.

The higher mortality rate due to TB in males in this city was similar to that reported in the literature and can be attributed to the fact that females seek treatment sooner than do males.[8]

In the municipality studied, the prevalence of TB/HIV co-infection was found to be high, which shows the need for further studies describing the magnitude of the role played by the HIV/AIDS epidemic in the dynamics of TB transmission. This panorama is essential for the good administration and evaluation of the control programs.

It has been reported that, in the regions that are more affected by HIV, various patients died before concluding the treatment for TB. The mortality rate for patients co-infected with TB/HIV in Ribeirão Preto was 33%.

This scenario demands reflections upon the quality of health care. We can presuppose that some factors interfere with the process of case follow-up. Are HIV/AIDS patients being diagnosed with TB too late? Are there too many therapeutic tests being requested? How has the prescription of chemoprophylaxis been being used with HIV/AIDS patients?

These questions should be further investigated, consequently demanding further studies. It is recommended that a TB surveillance plan be established in order to stimulate the collection and improve the quality of the information that is being compiled through the verification of the number of deaths, using methods to identify diagnostic errors. Studies on mortality are relevant not only from the perspective that mortality is a marker of the quality and availability of treatment, but also because evaluating the deaths of patients who died undiagnosed might reveal failings in the health care facilities, such as underdiagnosis and underreporting.

Still within this context, we emphasize that the individuals most often affected by TB/HIV co-infection are young adults, which has serious social implications, since this group should be in the labor market supporting their families.

Consequently, we suggest that special strategies be developed for the follow-up treatment of such patients, and that such strategies focus on the early detection of TB/HIV co-morbidity.

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