Original Article

Treatment outcome and laboratory confirmation of tuberculosis diagnosis in patients with HIV/AIDS in Recife, Brazil*

Desfecho do tratamento e confirmação laboratorial do diagnóstico de tuberculose em pacientes com HIV/AIDS no Recife, Pernambuco, Brasil

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Abstract

Objective: To compare the frequency of unfavorable outcome (death or noncompliance and treatment failure) between tuberculosis (TB)/HIV co-infected patients treated for TB after laboratory confirmation of the diagnosis and TB/HIV co-infected patients who were so treated without diagnostic confirmation. **Methods:** A retrospective cohort of TB/HIV co-infected patients who started TB treatment between July of 2002 and June of 2004 at an HIV/AIDS referral center in Recife, Brazil. Laboratory confirmation of TB was analyzed based on three sets of variables: sociodemographic variables; HIV/AIDS-related variables; and TB-related variables. In order to evaluate the statistical significance of the results, we calculated odds ratios, with 95% confidence intervals, and p values (from chi-square tests and likelihood ratio tests). **Results:** A total of 262 patients were studied. No association was found between laboratory confirmation of the diagnosis of TB at treatment outset and unfavorable outcome, even after adjustment for confounders. In the final multiple logistic regression model, the following variables remained: the presence of other opportunistic diseases; CD4 lymphocyte count below 50 cells/mm^3; viral load between 10,000 and 100,000 copies/mL; dyspnea; the disseminated form of TB; and change in the TB treatment regimen due to adverse reactions or intolerance. **Conclusions:** Our results suggest that TB treatment in TB/HIV co-infected patients without etiologic confirmation of TB, at the discretion of experienced physicians in referral centers, did not increase the risk of unfavorable outcomes. In addition, it allowed the identification of groups that should be closely monitored due to a greater risk of unfavorable outcomes.

Keywords: Tuberculosis; Diagnosis; Therapeutics; Treatment outcome; HIV infections.

Resumo

Objetivo: Comparar a freqüência de desfecho desfavorável (óbito, abandono e falência de tratamento) entre pacientes com co-infecção tuberculose (TB)/HIV submetidos a tratamento para TB com confirmação etiológica do diagnóstico e pacientes co-infectados com TB/HIV e tratados sem confirmação diagnóstica. **Métodos:** Coorte retrospectivo de pacientes co-infectados com TB/HIV que iniciaram tratamento para TB entre julho de 2002 e junho de 2004, em um serviço de referência para HIV/AIDS no Recife (PE) Brasil. A exposição principal, confirmação laboratorial da TB, foi ajustada pelas variáveis de três blocos: variáveis sócio-demográficas; variáveis relacionadas ao HIV/AIDS; e variáveis relacionadas à TB. Para avaliar a significância estatística dos resultados, utilizaram-se o intervalo de confiança de 95% das *odds ratios* e o valor de p (teste de qui-quadrado e razão de verossimilhança). **Resultados:** Foram estudados 262 pacientes. Não se observou associação entre confirmação laboratorial do diagnóstico de TB e desfecho desfavorável, mesmo após o ajuste pelos fatores de confusão. Permaneceram no modelo final da regressão logística múltipla: coexistência de outras doenças oportunistas; contagem de linfócitos CD4 abaixo de 50 células/mm^3; carga viral entre 10.000 e 100.000 cópias/mL; dispnéia; forma disseminada de TB; e mudança do tratamento da TB por reação adversa ou intolerância. **Conclusões:** Os resultados sugerem que o tratamento para TB sem confirmação etiológica, em pacientes co-infectados, baseado na decisão de profissionais experientes em serviços de referência, não aumentou o risco de desfecho desfavorável do tratamento para TB. Além disso, identificaram-se grupos com maior risco de desfecho desfavorável, os quais devem ser cuidadosamente monitorados.

Descritores: Tuberculose; Diagnóstico; Terapêutica; Resultado de tratamento; Infecções por HIV.

Introduction

The interaction between *Mycobacterium tuberculosis* and HIV results in more rapid progression of tuberculosis (TB) and HIV-induced immunosuppression, which can render the diagnosis of TB more difficult in these patients, due to the possibility that immunodeficiency will modify the clinical and radiological profile, as well as to the low sensitivity of

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sputum smear microscopy.[1,2] These alterations can result in the delayed diagnosis of TB, which, in turn, is associated with an increased risk of death and of contamination of close contacts.[2-4]

In suspected cases of pulmonary or extrapulmonary TB in which the health status of the patient is severe and the isolation of the *M. tuberculosis* strain is difficult, the diagnostic studies can significantly delay treatment. Therefore, it is recommended that, in such cases, treatment be initiated even before the bacteriological results are known. Once started, treatment should not be interrupted, unless a rigorous clinical and laboratory review indicates a change in the diagnosis.[5]

To date, there have been virtually no comparative studies investigating TB treatment outcomes in patients co-infected with HIV who initiated treatment with diagnostic confirmation and those who initiated treatment without diagnostic confirmation.[6] The few such studies that have been conducted have provided discrepant results.

One study,[7] involving patients with extrapulmonary TB and co-infected with HIV, revealed that, in patients without diagnostic confirmation of TB, the mortality rate was four times greater than in those with confirmed diagnosis. In another study,[8] an association between negative sputum smear microscopy and greater risk of death was observed in TB/HIV co-infected patients. In contrast, one group of authors[9] found that positive sputum smear microscopy was associated with a greater risk of death in TB/HIV co-infected patients, as were drug resist-

Table 1 - Associations between unfavorable outcome of the treatment for tuberculosis and HIV/AIDS-related variables.[a]

HIV/AIDS-related variables	Outcome				Gross OR	95% CI	p	Adjusted OR	95% CI	p
	Unfavorable		Favorable							
	n	%	n	%						
Duration of anti-retroviral treatment										
≤1 year	29	70.7	58	82.9	1.00	-	-	1.00		
>1 year	12	29.3	12	17.1	2.00	0.73-5.50	0.1342	3.26	1.12-9.45	0.0298
Total	41	100.0	70	100.0	-	-	-	0.74	0.38-1.45	0.3757
Other concomitant opportunistic diseases										
No	20	18.5	60	39.0	1.00	-	-	1.00	-	-
Yes	88	81.5	94	61.0	2.81	1.51-5.26	0.0004	4.12	1.83-9.31	0.0006
Total	108	100.0	154	100.0	-	-	-	-	-	-
CD4 count (cells/mm^3)										
No data	46	42.6	28	18.2	5.95	2.39-14.84	<0.001	4.44	1.02-19.33	0.0474
≤50	27	25.0	33	21.4	2.97	1.17-7.54	0.022	1.77	0.52-6.02	0.3576
51-200	27	25.0	64	41.6	1.53	0.63-3.78	0.356	0.91	0.28-2.96	0.8765
>200	8	12.9	29	23.0	1.00	-	-	1.00		
Total	108	100.0	154	100.0	-	-	<0.001			
Plasma viral load (copies/mL)										
No data	44	40.7	37	24.0	4.61	1.89-11.24	0.001	1.37	0.33-5.23	0.6652
>100,000	36	33.3	69	44.8	2.02	0.84-4.85	0.115	1.77	0.63-4.95	0.2752
10,001-100,000	20	8.5	17	11.0	4.56	1.66-12.53	0.003	4.52	1.38-14.83	0.0127
≤10,000	8	7.4	31	20.1	1.00	-	-	1.00		
Total	108	100.0	154	100.0	-		0.001			
Laboratory test criterion for treatment initiation										
With etiologic confirmation	35	32.4	58	37.7	1.00		1.00	-		
Without etiologic confirmation	73	67.6	96	62.3	1.26	0.73-2.19	0.3816	1.41	0.73-2.70	0.3025
Total	108	100.0	154	100.0	-	-	0.3816			

[a]Due to a lack of data for some variables, the number of individuals varied depending on the variable studied.

Table 2 - Associations between unfavorable outcome of the treatment for tuberculosis and variables related to clinical manifestations of tuberculosis.[a,b]

Variables related to clinical manifestations of tuberculosis	Outcome				Gross OR	95% CI	p
	Unfavorable		Favorable				
	n	%	n	%			
Cough							
No	15	13.9	30	19.5	1.00	-	-
Yes	93	86.1	124	80.5	1.50	0.73-3.12	0.2375
Total	108	100.0	154	100.0	-	-	-
Fever							
No	4	3.7	24	15.7	1.00	-	-
Yes	104	96.3	129	84.3	4.84	1.53 -17.02	0.0021
Total	108	100.0	153	100.0	-	-	-
Lymph node enlargement							
No	89	82.4	112	72.7	1.00	-	-
Yes	19	17.6	42	27.3	0.57	0.30-1.09	0.0680
Total	108	100.0	154	100.0	-	-	-
Dyspnea							
No	32	29.6	95	61.7	1.00	-	-
Yes	76	70.4	59	38.3	3.82	2.19-6.70	<0.0001
Total	108	100.0	154	100.0	-	-	-
Chest pain							
No	80	74.1	116	75.3	1.00	-	-
Yes	28	25.9	38	24.7	1.07	0.58-1.95	0.8185
Total	108	100.0	154	100.0	-	-	-
Weight loss							
No	25	23.1	42	27.3	1.00	-	-
Yes	83	76.9	112	72.7	1.25	0.68-2.29	0.4513
Total	108	100.0	154	100.0	-	-	-
Asthenia							
No	34	31.5	67	43.5	1.00	-	-
Yes	74	68.5	87	56.5	1.68	0.97-2.90	0.0490
Total	108	100.0	154	100.0	-	-	-
Hepatosplenomegaly							
No	89	81.4	137	89.0	1.00	-	-
Yes	19	17.6	17	11.0	1.72	0.80-3.69	0.1293
Total	108	100.0	154	100.0	-	-	-
Pleural effusion							
No	89	82.4	136	88.3	1.00	-	-
Yes	19	17.6	18	11.7	1.61	0.76-3.43	0.1768
Total	108	100.0	154	100.0	-	-	-
Duration of cough (in months)							
≤1	57	77.0	61	62.2	2.03	0.98-4.25	0.0386
>1	17	23.0	37	37.8	1.00	-	-
Total	74	100.0	98	100.0	-	-	-
Duration of fever (in months)							
≤1	58	74.4	63	58.3	2.07	1.05-4.12	0.0237
>1	20	25.6	45	41.7	1.00	-	-
Total	78	100.0	108	100.0	-	-	-
Laboratory test criterion for treatment initiation							
With etiologic confirmation	35	32.4	58	37.7	1.00	-	-
Without etiologic confirmation	73	67.6	96	62.3	1.26	0.73-2.19	0.3816
Total	108	100.0	154	100.0			0.3816

[a]Due to a lack of data for some variables, the number of individuals varied depending on the variable studied.[b]After the multivariate analysis of this block, only the variable dyspnea remained (OR = 3.82; 95% CI: 2.19-6.70; p < 0.0001). When the variables etiologic confirmation of the diagnosis and dyspnea were introduced into the model, no association was observed between etiologic confirmation of the diagnosis of tuberculosis and unfavorable outcome: dyspnea (OR = 3.79; 95% CI: 2.24-6.42; p < 0.0001); etiologic confirmation of the diagnosis (OR = 1.18; 95% CI: 0.68-2.03; p = 0.2527).

ance, weight loss, recurrent TB and atypical X-ray findings.

Other authors,[10] based on data regarding TB treatment in 22 Brazilian capitals, demonstrated that TB treatment outcomes in patients with HIV/AIDS were favorable in only 33.3% of those with pulmonary TB and positive sputum smear microscopy results, compared with 40% for all patients with TB. Although the treatment noncompliance rate was similar in the two groups (approximately 32%), death and treatment failure rates were higher in patients with pulmonary TB and positive sputum smear microscopy results than in those with any form of TB.

The objective of the present study was to compare the frequency of unfavorable outcome (death, noncompliance or treatment failure) in patients with HIV/AIDS treated for TB without etiologic diagnostic confirmation with that observed in those treated with etiologic diagnostic confirmation, with the aim of contributing to the definition of specific monitoring and treatment procedures of these patients.

Methods

A retrospective cohort study was carried out at the Correa Picanço Hospital, a state referral center for HIV/AIDS in Recife, Brazil, meeting 50% of the HIV/AIDS treatment demand in the state.

Individuals with HIV/AIDS who initiated treatment for TB between July of 2002 and June of 2004 were included in the study.

Bearing in mind the established objectives, we devised a form specifically for use in this study. which was filled out based on information from medical charts by The principal researcher and two medical students, recipients of grants from the National Council for Scientific and Technological Development, were charged with transferring data from medical charts to the specially prepared form.

The principal factor under study was the treatment of TB without initial or subsequent diagnostic confirmation of the etiology through direct testing or culture for *M. tuberculosis* in clinical specimens. Patient data were divided into those related to patients in whom such testing was performed and those related to patients in whom it was not. Evidence of TB in cytological or histopathological examinations was also considered.

Unfavorable outcomes were defined as death, noncompliance and treatment failure. Discharge due to cure, with or without etiologic confirmation of the diagnosis of TB, was considered a favorable outcome.

Table 3 - Associations between unfavorable outcome of the treatment for tuberculosis and presentation form/tuberculosis diagnostic criterion.[a]

Presentation form and definition criterion of the diagnosis of tuberculosis	Outcome				OR	95% CI	p
	Unfavorable		Favorable				
	n	%	n	%			
Presentation form of tuberculosis[b]							
Pulmonary	58	53.7	74	48.1	1.00	-	-
Extrapulmonary	21	19.4	43	27.9	0.62	0.32-1.22	0.1364
Disseminated	15	13.9	6	3.9	3.19	1.07-9.90	0.0192
Pulmonary or extrapulmonary	14	13.0	31	20.1	0.58	0.26-1.25	0.1303
Total	108	100.0	154	100.0	-	-	0.007
Criterion of the diagnosis of tuberculosis							
Positive sputum smear microscopy or culture	33	30.5	48	31.1	1.00	-	-
Clinical or radiological	73	67.6	96	62.4	1.11	0.62-1.96	0.7132
Histological or cytological	2	1.9	10	6.5	0.29	0.04-1.56	0.0958
Total	108	100.0	154	100.0	-	-	0.195

[a]Due to a lack of data for some variables, the number of individuals varied depending on the variable studied. [b]When the variables etiologic confirmation of the diagnosis and presentation form of tuberculosis were introduced into the model, no association was observed between etiologic confirmation of the diagnosis of tuberculosis and unfavorable outcome: presentation form (extrapulmonary, OR = 0.61; 95% CI: 0.32-1.14; p = 0.1193—disseminated, OR = 3.14; 95% CI: 1.15-8.61; p = 0.0262—pulmonary or extrapulmonary, OR = 0.59; 95% CI: 0.29-1.214; p = 0.1521); etiologic confirmation of the diagnosis (OR = 1.24; 95% CI: 0.73-2.12; p = 0.4289).

Variables were grouped into three blocks for analysis:

- sociodemographic variables (gender, age bracket, level of education and city of residence)
- HIV/AIDS-related variables (time since being identified as HIV seropositive, use of antiretroviral therapy, duration of antiretroviral therapy, other concomitant opportunistic diseases, CD4 T-lymphocyte counts and quantification of plasma HIV viral load)
- TB-related variables, which, in turn, were divided into three groups: signs and symptoms; form of presentation/diagnostic criterion; and treatment-related variables.

Incidence was determined by calculating the odds of having an unfavorable outcome in relation to having a favorable outcome. The outcome odds ratio among patients with TB confirmation was expressed as a/b, whereas that for those without such confirmation was expressed as c/d, and the odds ratio between the two odds ratios was expressed as a/b:c/d. Initially, univariate analysis was employed to determine the association between each variable and TB treatment outcome. The magnitude of the association was expressed through the odds ratio. In order to evaluate statistical significance, the confidence interval of odds ratios and the p value obtained (chi-square test) were used. Values of $p < 0.05$ were considered statistically significant.

Based on the determination of the variables that presented an association with the outcome ($p < 0.20$) in the univariate analysis, multivariate analysis was performed using the multiple logistic regression model in each block of variables. The model was initially saturated and the step-by-step removal of each variable of the model was tested, observing the p value obtained in the maximum likelihood test. In the analyses including two or more independent variables, variables presenting more than three categories were submitted to category grouping in order to ensure greater statistical stability of results. In the multiple logistic regression model, the antilogarithm of the coefficient for each variable corresponds to the odds ratio that estimates the magnitude of the association between the factor and the outcome, controlling the effect of all other variables in the model.

Table 4 - Associations between unfavorable outcome of the treatment for tuberculosis and variables related to the treatment of tuberculosis.[a]

Variables related to the treatment of tuberculosis	Outcome				Gross OR	95% CI	p	Adjusted OR	95% CI	p
	Unfavorable		Favorable							
	n	%	n	%						
History of treatment	108	100.0	154	100.0						
No	91	84.3	129	83.8	1.00					
Yes	17	15.7	25	16.2	0.96	0.47-1.98	0.9147			
Follow-up treatment regimen at treatment initiation	108	100.0	154	100.0						
Outpatient treatment	17	15.7	68	44.2	1.00	-	-	1.00	-	-
Hospitalization	91	84.3	86	55.8	4.23	2.22-8.15	<0.0001	4.19	2.24-7.83	>0.0001
Change in treatment regimen due to adverse reactions or intolerance	108	100.0	154	100.0						
No	75	69.4	138	89.6	1.00	-	-	1.00	-	-
Yes	33	30.6	16	10.4	3.79	1.87-7.75	<0.0001	3.71	1.84-7.44	0.0002
Laboratory criterion for treatment initiation	108	100.0	154	100.0						
With etiologic confirmation	35	32.4	58	37.7	1.00	-	-	1.00	-	-
Without etiologic confirmation	73	67.6	96	62.3	1.26	0.73-2.19	0.3816	1.14	0.66-1.99	0.6341
Total	108	100.0	154	100.0						

[a]Due to a lack of data for some variables, the number of individuals varied depending on the variable studied.

The variables selected in each block were introduced into the final model, and the variables were selected according to the procedure described above. The variable "etiologic confirmation of the diagnosis of TB" was introduced into each block of the multivariate model and into the final multivariate model.

Data were registered, stored and analyzed using the Epi Info statistical program, version 6.04, and the Statistical Package for Social Sciences, version 8.0 (SPSS Inc., Chicago, IL, USA).

This study was approved by the Ethics in Research Committee of the Correia Picanço Hospital.

Results

Between July of 2002 and June of 2004, 288 patients who initiated treatment for TB were identified. Of these patients, 26 were excluded from the analysis: 23 due to a lack of data regarding treatment outcome; and 3 due to having been transferred to other facilities.

Of the 262 patients studied, 180 (68.7%) were male. The mean age was 36 years. The outcome of the treatment for TB was unfavorable in 108 patients (41.2%) and favorable in 154 (58.8%). There were 7 patients (2.7%) with laboratory confirmation who were cured, 147 (56.1%) without etiologic confirmation who were cured, 30 (11.5%) who abandoned treatment, 2 (0.8%) who experienced treatment failure due to the development of resistance and 76 (29%) who died. Etiologic confirmation of the diagnosis was obtained in only 93 patients (35.5%). No association was observed between the etiologic confirmation of the diagnosis of TB and unfavorable outcome (p = 0.3816). Since this result could be distorted by other variables, the variable

Table 5 - Final general model of the associations between related variables and outcome of the treatment for tuberculosis.

Variable	Gross OR	95% CI	p	Adjusted OR	95% CI	p
Other opportunistic diseases						
No	1.00	-	-	1.00	-	-
Yes	2.67	1.16-6.17	0.0212	2.17	1.06-4.17	0.0344
CD4 count (cells/mm^3)						
No data	3.93	0.81-19.14	0.0903	4.28	1.14-16.08	0.0311
Up to 50	1.22	0.34-4.33	0.7595	1.47	0.50-4.33	0.4795
From 51 to 200	0.68	0.20-2.29	0.5295	0.80	0.28-2.28	0.6772
>200	1.00	-	-	1.00	-	-
Plasma viral load (copies/mL)						
No data	0.70	0.15-3.25	0.6489	1.05	0.27-4.07	0.9435
>100,000	1.36	0.45-4.11	0.5822	1.43	0.52-3.96	0.4886
10,001-100,000	3.88	1.09-13.79	0.0361	3.77	1.14-12.43	0.0293
≤10,000	1.00	-	-	1.00	-	-
Dyspnea						
No	1.00	-	-	1.00	-	-
Yes	2.34	1.15-4.78	0.0197	2.52	1.32-4.78	0.0048
Presentation form of tuberculosis						
Pulmonary	1.00	-	-	1.00	-	-
Extrapulmonary	1.28	0.56-2.92	0.5603	1.19	0.56-2.55	0.6488
Disseminated	3.93	1.15-13.42	0.0284	3.82	1.18-12.34	0.0253
Pulmonary or extrapulmonary	0.44	0.16-1.22	0.1139	0.72	0.31-1.66	0.4404
Change in treatment regimen due to adverse reactions or intolerance						
No	1.00	-	-	1.00	-	-
Yes	3.52	1.57-7.90	0.0023	3.51	1.63-7.56	0.0013
Laboratory criterion for treatment initiation						
With etiologic confirmation	1.00	-	-	1.00	-	-
Without etiologic confirmation	1.26	0.73-2.19	0.3816	1.08	0.58-1.99	0.8156

etiologic confirmation of the diagnosis of TB was introduced into the final model of each group of variables (sociodemographic variables; HIV/AIDS-related variables; and TB-related variables), thus eliminating the influence of the variables of each group on the estimation of this association. In the multivariate models, no association was observed between etiologic confirmation of the diagnosis of TB and unfavorable outcome.

We found etiologic confirmation of the diagnosis of TB to be associated with the HIV/AIDS-related variables, as well as with the TB-related variables. The comparison between the groups of patients with and without etiologic confirmation showed a p value of 0.066, which is near the cut-off point for the variable "presentation form of TB". For the remaining variables (CD4 count, plasma viral load and TB treatment outcome) the difference was not statistically significant (data not shown).

A statistically significant association was observed between unfavorable outcome and the following HIV/AIDS-related variables: duration of anti-retroviral use; other concomitant opportunistic diseases; CD4 count; and plasma viral load (Table 1).

A statistically significant association was observed between unfavorable outcome and the following variables related to signs and symptoms of TB: fever; dyspnea; asthenia; duration of cough; and fever (Table 2). However, in the final model of the multivariate analysis, only dyspnea presented an association ($p < 0.0001$), which was independent of the outcome.

A statistically significant association was observed between unfavorable outcome and the presentation form of TB (Table 3), as well as between unfavorable outcome and patient follow-up regimen at treatment initiation for TB ($p < 0.0001$) and when there was change in the treatment regimen due to adverse reactions or intolerance ($p < 0.0001$). This association remained statistically significant after the mutual adjustment of these two variables (Table 4).

Final multivariate analysis model

For each of the groups, all variables presenting associations that were independent of the outcome were introduced into the final multivariate model. The following variables remained in the final model: other concomitant opportunistic diseases; CD4 count; plasma viral load; dyspnea; the disseminated form of TB; and change in the TB treatment regimen due to adverse reactions or intolerance, thus constituting the group and variables with the closest association with the outcome (Table 5).

Discussion

In this study, only 35.5% of the patients initiated treatment for TB after etiologic diagnostic confirmation. No association was observed between the outcome of the treatment for TB and the etiologic confirmation of the diagnosis of this disease, even after adjustment for confounders.

The retrospective cohort study design might imply some methodological limitations. There were 26 patients who were lost to follow-up (there were no data regarding treatment outcome on the charts of 23 patients, and 3 patients were transferred). Since the magnitude of the loss was relatively small (9%), we do not believe that it had a significantly effect on the results. Since the data were not registered specifically for this study, it was not possible to obtain information on all individuals for all variables, thus generating an effect similar to that of lack of response. However, one of the characteristics that set this study apart from most previous studies is the fact that we analyzed HIV/AIDS- and TB-related variables, thus using the effect of each to control that of the each of the others.

The high percentage of individuals without etiologic diagnostic confirmation is probably related to the high number of patients with the extrapulmonary and disseminated form of the disease. Other studies have also shown traditional diagnostic methods to have low yields. One group of authors,[11] working in the United States, found positive sputum smear microscopy results in only 29% of patients with HIV/AIDS, compared with 61% of HIV-negative patients, whereas others,[12] working in Malaysia, found positive sputum smear microscopy results in 51% of TB/HIV co-infected individuals with respiratory symptoms.

The lack of an association between outcome of the treatment for TB and etiologic confirmation of the diagnosis in HIV co-infected patients has been reported in the literature.[7,8,13] Some authors suggest that waiting for the results of cultures or histopathological tests is often detrimental to the patient and that early treatment of TB can lower morbidity and

mortality rates, thus becoming a useful procedure in establishing a diagnosis of TB.[14-16]

Regarding all outcomes observed, the percentage of cure in the present study was 58.7%, similar to that found in another study conducted in the city of Campinas, Brazil,[13] according to which the cure rate was 57.6% among TB/HIV co-infected patients. A lower percentage (43.4%) was found in another study[17] involving TB/HIV co-infected patients in Spain.

The percentage of noncompliance observed (11.5%) is within the range of rates reported nationwide in Brazil (4.5-20.3%).[18] The frequency of noncompliance with treatment in patients with HIV/AIDS has presented significant variation. Whereas a study conducted in Malawi[7] reported a noncompliance rate of approximately 6% for all forms of TB, another, conducted in Thailand,[19] found that 33% of TB/HIV co-infected patients abandoned treatment.[19]

In the present study, only two patients (0.8%) experienced treatment failure. A low rate of treatment failure (0.4%) was also found in the Malawi study,[7] as well as in the Campinas study.[13]

In our study, the mortality rate was high (29%), which is intermediate between the 38.9% reported in the Malaysia study[12] and the 21.5% reported in the study conducted in Spain.[17] Since the Correia Picanço Hospital is a referral center, the condition of the patients treated at this hospital is critical, and the diagnosis, or suspected diagnosis, of TB/HIV co-infection is usually made when the infection is in an advanced stage. This is confirmed by the findings of a study conducted in the northeast of Brazil,[20] in which half of the HIV/AIDS patients already presented signs or symptoms of immunosuppression when they arrived at specialized clinics, suggesting that the diagnosis and the treatment of HIV infection are both delayed.

In the final multivariate model, unfavorable outcome of the treatment for TB was associated with CD4 count, plasma viral load, other concomitant opportunistic diseases, dyspnea, the disseminated form of TB and changes in the treatment regimen due to adverse reactions or intolerance.

All of the associations described above reflect, in practice, the intimate relationship between *M. tuberculosis* and HIV in terms of the mechanisms of immunological response that occur. The following variables were strongly associated with unfavorable outcome: low CD4 count (severe immunosuppression); high plasma viral load (high risk of progression to AIDS); other concomitant opportunistic diseases (overlapping of symptoms and treatments); dyspnea (extensive pulmonary involvement); the disseminated form of TB (the most severe form of the disease); a change in the treatment regimen due to adverse reactions or intolerance (adopting less potent regimens or interrupting treatment for prolonged periods); initiation of in-hospital treatment for TB (disease severity and potential comorbidities); non-use of antiretroviral therapy.

Studies suggest that the level of immunosuppression is the principal determinant of survival in TB/HIV co-infected patients.[21,22] Low CD4 counts have been associated with a greater risk of opportunistic infections and atypical presentations of TB, as well as with predominance of the extrapulmonary and disseminated forms of the disease, all of which are factors that can make diagnosis more difficult and delay treatment.[23] (≤200 /mm^3)In the present study, the chance of an unfavorable outcome was greater for patients with extremely low CD4 counts (≤200 cells/mm^3), especially for those presenting <50 cells/mm^3, than for those with higher counts (>200 cells/mm^3). The greater chance of unfavorable outcome in those patients with no data on CD4 counts probably reflects delayed diagnosis of HIV infection, since there was not sufficient time to obtain results before initiating TB treatment.

Patients with plasma viral loads of 10,001-100,000 copies/mL had a greater chance of presenting an unfavorable outcome and a greater risk of death than did those with plasma viral loads ≤10,000 or >100,000 copies/mL. The unexpected finding that the chance of an unfavorable outcome was lower for patients with plasma viral loads >100,000 copies/mL might have been due to the fact that those were the same patients who most often used antiretroviral therapy.

The chance of an unfavorable outcome of the treatment for TB was nearly four times greater for patients with the disseminated form of TB. This is considered one of the most severe forms of the disease and presupposes severe immunosuppression.[24]

We observed an association between a change in the treatment regimen due to adverse reactions or intolerance and unfavorable outcome of the treatment for TB. In a study conducted in Porto,

Portugal,[25] 25.7% of the TB/HIV co-infected patients evaluated were found to present complications of the treatment for TB due to adverse reactions, and this was more common in patients later presenting an unfavorable outcome. The concomitant use of antiretroviral therapy and TB treatment regimens is controversial, principally regarding the potential complex interaction among drugs, overlapping adverse reactions and noncompliance with treatment, as well as increased frequency and intensity of paradoxical reactions.[26,27]

The Brazilian National Ministry of Health recommends that, when possible, antiretroviral treatment be initiated only after the conclusion of the treatment for TB.[28] If the antiretroviral therapy is mandatory, antiretroviral regimens compatible with rifampicin should be used. In the present study, the non-use of antiretroviral therapy was associated with an increased risk of death. In a study conducted in London,[29] TB/HIV patients co-infected with TB and HIV during the pre-highly active antiretroviral therapy (HAART) era were compared with those co-infected during the post-HAART era. The authors observed that the use of HAART significantly reduced the risk of death (43 *vs.* 22%) and the appearance of new AIDS-defining events (69 *vs.* 43%). However, a study conducted in Rio de Janeiro[30] showed that the mortality rate in TB/HIV co-infected patients who used HAART was 8%, compared with 55% in those who did not.

The results of the present study show that, in the population studied, treatment for TB without etiologic diagnostic confirmation did not imply a greater chance of an unfavorable outcome, suggesting that in the cases in which it is not possible to confirm the diagnosis of TB using the laboratory test methods available in the clinic, empirical treatment for TB could be a useful procedure.

The study design also allowed us to identify the groups of individuals with a greater chance of presenting an unfavorable outcome of the treatment for TB: those presenting other concomitant opportunistic diseases/infections; those presenting dyspnea; those with the disseminated form of TB; those in whom the TB treatment regimen is modified due to adverse reactions or intolerance; those presenting a CD4 counts < 50 cells/mm^3; and those presenting a plasma viral load between 10,001 and 100,000 copies/mL. These groups should be closely monitored and should receive proper support in order to reduce the frequency of unfavorable outcomes.

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