

Outcomes of tuberculosis treatment among inpatients and outpatients in the city of São Paulo, Brazil*

Desfechos de tratamento de tuberculose em pacientes hospitalizados e não hospitalizados no município de São Paulo*

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Abstract

Objective: To compare inpatient and outpatient treatment of tuberculosis, in terms of outcomes, in the city of São Paulo, Brazil, as well to determine which variables are most frequently associated with hospitalization. **Methods:** A prospective, longitudinal study carried out between January and December of 2007, at two large hospitals and at outpatient clinics, in two regions of the city of São Paulo. For inpatients, data were collected with a structured questionnaire. Additional data were obtained from the São Paulo State Department of Health Tuberculosis Database. **Results:** Of the 474 patients included in the study, 166 were inpatients, and 308 were outpatients. The multivariate analysis showed that hospitalization for tuberculosis was associated with hospital/emergency room diagnosis of tuberculosis (OR = 55.42), with HIV co-infection (OR = 18.57), with retreatment (OR = 18.51), and with having previously sought treatment at another health care facility (OR = 12.32). For the inpatient and outpatient groups, the overall cure rates were 41.6% and 78.3%, respectively, compared with 30.4% and 58.5% for those who were co-infected with HIV, whereas the overall mortality rates were 29.5% and 2.6%, respectively, compared with 45.7% and 9.8% for those who were co-infected with HIV. **Conclusions:** Among inpatients, tuberculosis appears to be more severe and more difficult to diagnose, resulting in lower cure rates and higher mortality rates, than among outpatients. In addition, tuberculosis patients co-infected with HIV have less favorable outcomes.

Keywords: Tuberculosis; Hospitalization; Primary health care; Treatment outcome.

Resumo

Objetivo: Comparar os desfechos de tratamento de tuberculose em pacientes hospitalizados e aqueles tratados exclusivamente na atenção primária na cidade de São Paulo (SP), bem como determinar as variáveis mais associadas à internação. **Métodos:** Pesquisa prospectiva e longitudinal, realizada entre janeiro e dezembro de 2007 em dois hospitais de grande porte e em serviços de saúde em duas regiões na cidade de São Paulo. Os dados foram coletados através de um questionário estruturado, no caso dos pacientes internados, e no Banco de Dados de Tuberculose da Secretaria Estadual de Saúde de São Paulo. **Resultados:** Dos 474 pacientes incluídos no estudo, 166 estavam hospitalizados, e 308 eram pacientes ambulatoriais. A análise multivariada mostrou associações entre internação por tuberculose e diagnóstico de tuberculose em hospital/pronto-socorro (OR = 55,42), coinfeção por HIV (OR = 18,57), retratamento (OR = 18,51) e procura por outro serviço anteriormente (OR = 12,32). Para os pacientes hospitalizados e ambulatoriais, as taxas gerais de cura foram de 41,6% e 78,3%, respectivamente, ao passo que, para aqueles coinfectados por HIV, essas foram de 30,4% e 58,5%, enquanto as taxas gerais de mortalidade foram de 29,5% e 2,6%, respectivamente, ao passo que, para aqueles coinfectados por HIV, essas foram de 45,7% e 9,8%. **Conclusões:** Este estudo evidenciou maior gravidade, maior dificuldade de diagnóstico, menor taxa de cura e maior taxa de mortalidade nos pacientes internados que naqueles ambulatoriais. Além disso, os desfechos foram piores no subgrupo de pacientes coinfectados com HIV.

Descritores: Tuberculose; Hospitalização; Atenção primária à saúde; Resultado de tratamento.

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Introduction

Until 1980, nearly all tuberculosis cases were referred for hospitalization, although the Brazilian National Ministry of Health recommended home treatment over in-hospital treatment.⁽¹⁾ Although in-hospital treatment has become increasingly less common, it is still required for those who have a poor socioeconomic status, as well as for severe cases.⁽²⁾ This need is underscored by the concomitant presence of conditions such as alcoholism, malnutrition, and illicit drug use, as well as by the presence of comorbidities.⁽¹⁾

In developed countries, the leading causes of hospitalization are treatment failure and adverse drug effects, whereas the leading causes of hospitalization in developing countries are poor general health status and wasting, indicating not only the flaws in active surveillance but also the delay in diagnosis.⁽³⁾

It is estimated that 30% of the cases of tuberculosis in Brazil are detected only after they have become more severe and the patients have been hospitalized, either because access to the health care system is difficult or because the diagnosis is delayed. That rate is even higher in certain locations, being 33% in Rio de Janeiro and 42% in São Paulo.⁽⁴⁾

The city of São Paulo is among the priority cities for tuberculosis control, approximately 6,000 new cases being reported annually and approximately 13% of tuberculosis patients being co-infected with HIV, such cases being considered more severe and showing lower cure rates.⁽⁵⁾ In the city, most tuberculosis-related deaths (94%) occur in hospitals.⁽⁶⁾ Each of those deaths is the result of innumerable failures by health care and social systems, given that tuberculosis-related deaths are preventable.

In the state of São Paulo in 2004, 4,859 individuals were hospitalized for pulmonary tuberculosis; those hospitalizations resulted in costs for society and family members, as well as in a lower cure rate among such patients, given that hospitalized patients typically present with disease that is more severe and are therefore more likely to die.^(7,8) Tuberculosis/HIV co-infection increases tuberculosis-related morbidity and mortality.⁽⁹⁾

The objective of the present study was to compare patients treated at two large hospitals in the city of São Paulo with those treated exclusively at primary health care (PHC) clinics,

in terms of the outcomes of tuberculosis treatment. We also attempt to determine the risk factors that are most frequently associated with hospitalization and unfavorable outcome.

Methods

This was a descriptive, analytical, longitudinal study, conducted between January and December of 2007, comparing previously hospitalized tuberculosis patients with those treated exclusively at PHC clinics in two regions of the city of São Paulo, in terms of the outcomes of tuberculosis treatment.

We interviewed and analyzed all patients hospitalized with a confirmed diagnosis of tuberculosis at two large São Paulo city hospitals, both of which admit more than 50 such cases annually: the *Hospital São Paulo* (a university hospital affiliated with the Federal University of São Paulo Paulista School of Medicine), located in southeastern São Paulo, and the Mandaqui Hospital (a general and teaching hospital), located in northern São Paulo.

Subsequently, information regarding treatment outcomes (cure, transfer, treatment abandonment, death, and treatment failure) was collected from the hospital charts of the patients and from the São Paulo State Department of Health Tuberculosis Database. Patients whose diagnosis was changed and those whose hospitalization was unrelated to tuberculosis were excluded.

The group of patients being treated for tuberculosis exclusively at PHC clinics was composed of tuberculosis cases in southeastern and northern São Paulo, as registered in the São Paulo State Department of Health Tuberculosis Database. We analyzed a total of 513 tuberculosis reporting forms. Of those, 327 reported cases in southeastern São Paulo and 246 reported cases in northern São Paulo. We included all of the patients in whom the diagnosis of tuberculosis had been confirmed and whose treatment outcomes were registered in the Database during the study period. We thus excluded 157 and 95 cases of tuberculosis in southeastern and northern São Paulo, respectively, because they were cases in the prison system, cases in which the diagnosis was changed, or cases in which patients had been hospitalized for tuberculosis (as registered in the tuberculosis reporting form).

For inpatients, data were collected with a structured questionnaire comprising closed questions, as well as by analysis of their hospital charts. All of the patients or their legal guardians gave written informed consent. None of the patients declined to participate in the study.

We considered the following variables: age; gender; having sought treatment at another health care facility prior to the diagnosis of tuberculosis; facility at which the case was diagnosed; time elapsed between symptom onset and diagnosis; type of case; clinical presentation; results of sputum smear microscopy for AFB; tuberculosis/HIV co-infection or other comorbidities; and treatment outcome (classified in accordance with the Brazilian National Tuberculosis Control Program criteria).⁽¹⁰⁾ For inpatients, we collected information regarding the reason for hospitalization and the length of hospital stay.

The data collected were expressed as means, medians, standard deviations, and frequencies, together with ORs and the respective 95% CIs. The level of significance was set at $p < 0.05$.

The study was conducted in accordance with Brazilian National Health Council Resolution 196/96 and was approved by the Research Ethics Committees of the Federal University of São Paulo and the São Paulo Municipal Department of Health.

Results

During the study period, we included 474 patients with tuberculosis. Of those, 166 were hospitalized for tuberculosis and 308 were under outpatient treatment exclusively at PHC clinics.

In the group of inpatients, the mean age was 40.99 ± 13.67 years, 116 (69.9%) were male, and 97 (58.4%) had comorbidities, the most common being HIV infection (in 28.0%), diabetes (in 8.4%), and mental illness (in 3.0%). In the group of outpatients, the mean age was 39.13 ± 16.17 years, 204 (66.2%) were male, and 40 (13.0%) were co-infected with HIV. Among the inpatients, the reasons for hospitalization included elucidation of the diagnosis (in 48.2%), respiratory failure (in 18.7%), and hemoptysis (in 10.2%). For 101 inpatients (60.8%), the length of hospital stay was > 15 days, the mean length of hospital stay being 25.07 ± 19.56 days, and 113 (68.1%) of the inpatients were discharged to outpatient treatment. In 72.3% of the inpatients

and 38.3% of the outpatients, the diagnosis of tuberculosis was made in the emergency room or hospital.

The pulmonary form predominated in both groups, affecting 69.3% and 74.0% of the inpatients and outpatients, respectively. Sputum smear microscopy was positive for AFB in 81% and 63%, respectively. Information regarding HIV infection was unavailable for 27.1% and 23.7%, respectively. The mean time elapsed between the onset of symptoms and the diagnosis of tuberculosis was 14.2 ± 14.4 weeks (median, 8 weeks) for the inpatients and 12.6 ± 26.9 weeks (median, 8 weeks) for the outpatients.

Table 1 shows statistically significant associations between hospitalization for tuberculosis and the following variables: 30-39 year age bracket (OR = 2.17; 95% CI: 1.20-3.92; $p = 0.009$); 50-59 year age bracket (OR = 2.17; 95% CI: 1.15-4.08; $p = 0.010$); combination of pulmonary and extrapulmonary forms of tuberculosis (OR = 5.31; 95% CI: 2.02-13.9; $p < 0.001$); tuberculosis retreatment (OR = 2.66; 95% CI: 1.69-4.20; $p < 0.001$); seeking treatment at another health care facility prior to the diagnosis of tuberculosis (OR = 2.05; 95% CI: 1.37-3.08; $p < 0.001$); symptom duration of more than 12 weeks (OR = 2.23; 95% CI: 1.37-3.64; $p < 0.001$); and hospital/emergency room diagnosis of tuberculosis (OR = 4.68; 95% CI: 3.03-7.22; $p < 0.001$). Table 2 shows the results of the multivariate analysis, which revealed an association between hospitalization for tuberculosis and the following variables: hospital/emergency room diagnosis of tuberculosis (OR = 55.42); tuberculosis/HIV co-infection (OR = 18.57); retreatment (OR = 18.51); and having previously sought treatment for tuberculosis at another health care facility (OR = 12.32).

Table 3 shows the outcomes of tuberculosis treatment in the patients who were initially hospitalized. For those patients, the cure rate was low (41.57%) and the mortality rate was high (29.52%). For the subgroup of inpatients with tuberculosis/HIV co-infection, the cure rate was even lower (30.44%) and the mortality rate was even higher (45.65%). Table 4 shows the outcomes of tuberculosis treatment in the patients who were exclusively under outpatient treatment. For those patients, the cure rate was 78.25% and the mortality rate was 2.6%. For

Table 1 – Univariate analysis of the variables related to the hospitalization, clinical aspects, and epidemiological aspects of tuberculosis inpatients and tuberculosis outpatients treated exclusively at primary health care clinics in two regions of the city of São Paulo, 2007.

Variables	Inpatients	Outpatients	Total	OR	95% CI	p
	(n = 166)	(n = 308)	(n = 474)			
	n	n	n (%)			
Age bracket, years						
0-19	13	23	36 (36.11)	1.79	0.79-4.04	0.160
20-29	25	79	104 (24.00)	1.00		
30-39	44	64	108 (40.00)	2.17	1.20-3.92	0.009
40-49	33	58	91 (36.00)	1.79	0.96-3.44	0.062
50-59	33	48	81 (40.70)	2.17	1.15-4.08	0.010
> 60	18	36	54 (33.34)	1.58	0.76-3.25	0.213
Gender						
Male	116	204	320 (36.25)	1.18	0.78-1.77	0.419
Female	50	104	154 (32.47)	1.00		
Another facility ^a						
Yes	119	170	289 (41.18)	2.05	1.37-3.08	< 0.001
No	47	138	185 (25.40)	1.00		
Facility where the diagnosis was made						
Outpatient clinic	38	175	213 (17.84)	1.00		
ER/hospital	120	118	238 (50.42)	4.68	3.03-7.22	< 0.001
Other	8	15	23 (34.78)			
Time to diagnosis ^b						
< 12 weeks	87	91	178 (48.88)	1.00		
≥ 12 weeks	79	37	116 (68.00)	2.23	1.37-3.64	0.001
Type of case						
New	114	263	377 (30.24)	1.00		
Retreatment	52	45	97 (53.60)	2.66	1.69-4.20	< 0.001
Clinical form						
Pulmonary	115	229	344 (33.43)	1.00		
Extrapulmonary	35	73	108 (32.40)	0.95	0.60-1.51	0.844
Both	16	6	22 (72.70)	5.31	2.02-13.9	< 0.001
HIV status ^c						
Positive	46	41	52.88	2.90	1.76-4.77	0.001
Negative	75	194	27.88	1.00		

ER: emergency room. ^aPatients who previously sought tuberculosis treatment at another facility. ^bNo information available for 180 outpatients. ^cNo information available or not reported for 45 inpatients and 73 outpatients.

the subgroup of outpatients with tuberculosis/HIV co-infection, the cure rate was even lower (58.54%) and the mortality rate was even higher (9.76%).

Discussion

In the present study, we analyzed the treatment outcomes of 166 patients hospitalized for tuberculosis in 2007. Of those 166 inpatients, 68 had been admitted to the *Hospital São Paulo* and 98 had been admitted to the Mandaqui Hospital Complex, collectively

accounting for approximately 8% of the total number of patients hospitalized for tuberculosis that year in the city of São Paulo. Hospitalization rates for tuberculosis are usually higher in the northern regional health district (Santana) than in the southeastern regional health district (Vila Mariana).⁽⁸⁾

Of the 474 patients under study, 238 (50.2%) had been diagnosed with tuberculosis in the emergency room or hospital. In the city of São Paulo, it seems that hospitals are more accessible than are outpatient clinics and health care clinics, which operate at full capacity, are

Table 2 – Multivariate analysis of the variables that are most commonly associated with hospitalization for tuberculosis in two hospitals in the city of São Paulo, 2007.

Variables	OR	p
Facility where the diagnosis was made (ER/hospital vs. OC)	55.42	< 0.001
Previously sought tuberculosis treatment at another facility (yes/no)	12.32	< 0.001
Time to diagnosis (\geq 12 weeks vs. < 12 weeks)	2.89	0.891
Gender (male vs. female)	0.64	0.419
Type of case (retreatment vs. new)	18.51	< 0.001
Clinical form (pulmonary vs. other)	0.92	0.761
HIV status (positive vs. negative)	18.57	< 0.001

ER: emergency room; and OC: outpatient clinic.

understaffed, and offer a limited number of ancillary tests, hospitals therefore providing tuberculosis treatment more rapidly, with better results.

One group of authors⁽¹¹⁾ reported that 58% of the cases of tuberculosis in the city of São Paulo were diagnosed in an emergency room or hospital. This was also observed in the city of Londrina, Brazil, where 67.4% of the cases were diagnosed at hospitals.⁽¹²⁾ Those data suggest that hospitals are more accessible than are PHC clinics or that there was a real need for hospitalization (cases that were more severe and were accompanied by other diseases).⁽¹¹⁾

Excluding the reports in which there was no information regarding the outcome of tuberculosis treatment, we found that the cure rate for new cases in Brazil was 73% in 2006, being 57% for new cases of tuberculosis with HIV co-infection and 64.9% for cases of recurrence.⁽¹³⁾

In the present study, the cure rates for inpatients and outpatients were 41.6% and 78.3%, respectively. In 2001, the reported cure rates for inpatients and outpatients in the city of São Paulo were 32% and 72%, respectively.⁽⁸⁾

One group of authors reported that patients who are hospitalized for tuberculosis and are subsequently discharged do not always continue

the treatment on which they were started at the hospital.⁽¹⁴⁾ It is extremely important that epidemiological surveillance agencies take the necessary precautions and organize the flow of discharged patients, verifying that such patients seek outpatient treatment at a PHC clinic.

In the present study, the number of patients being retreated because of recurrence or treatment abandonment was higher among inpatients than among outpatients (31.0% vs. 14.6%). This partially explains why the cure rate was lower for the former. In addition, cases of retreatment can be more severe and refractory, as well as presenting with comorbidities and having higher treatment abandonment rates.⁽¹⁵⁾

In the state of São Paulo in 2007, the mean length of hospital stay for patients who were hospitalized for tuberculosis was 25 days, compared with 7.1 days for all hospitalized patients. That length of hospital stay might indicate the complexity and severity of the hospitalized cases of tuberculosis.^(7,16)

Infection with HIV was the comorbidity that was most commonly reported for the inpatients under study (27.7%). The HIV co-infection rate for all tuberculosis patients hospitalized in the city of São Paulo was 32.7% in 2001.⁽⁸⁾ Those data reflect the role of AIDS as one of the principal comorbidities in tuberculosis patients,

Table 3 – Treatment outcome in patients hospitalized for tuberculosis at either of two hospitals located in different regions of the city of São Paulo, 2007.

Outcome	HIV-negative, no information, or not reported	Co-infected with HIV/AIDS	Total
Cure	55 (45.83)	14 (30.44)	69 (41.57)
Transfer/no information	17 (14.17)	6 (13.04)	23 (13.85)
Abandonment	19 (15.83)	5 (10.86)	24 (14.46)
Death	28 (23.33)	21 (45.65)	49 (29.52)
Failure	1 (0.83)	0 (0.00)	1 (0.60)
Total	120 (100.00)	46 (100.00)	166 (100.00)

Table 4 – Treatment outcome in patients under outpatient treatment for tuberculosis in two different regions of the city of São Paulo, 2007.

Outcome	HIV-negative, no information, or not reported	Co-infected with HIV/AIDS	Total
Cure	215 (80.52)	24 (58.54)	239 (78.25)
Transfer/no information	8 (3.00)	1 (2.44)	9 (2.60)
Abandonment	40 (14.98)	12 (29.26)	52 (16.55)
Death	4 (1.50)	4 (9.76)	8 (2.60)
Failure	0 (0.00)	0 (0.00)	0 (0.00)
Total	267 (100.00)	41 (100.00)	308 (100.00)

HIV affecting younger individuals and causing clinical forms that are more severe, higher frequency of hospitalization, higher frequency of extrapulmonary or disseminated tuberculosis, a higher number of retreatment cases, lower cure rates, and higher mortality rates. In the present study, the cure rates for tuberculosis inpatients and outpatients co-infected with HIV were 30.4% and 58.4%, respectively, the corresponding mortality rates being 45.7% and 9.8%.

One group of authors collected information regarding tuberculosis treatment in 22 Brazilian capitals and showed that the outcome of tuberculosis treatment in patients with HIV/AIDS was favorable in only 33.3% of those with pulmonary tuberculosis and positive sputum smear microscopy results; when all forms of tuberculosis were considered, the outcome was favorable in 40.0% of the patients.⁽¹⁷⁾ A study conducted at a state referral center for HIV/AIDS in Recife, Brazil—a center that meets 50% of the HIV/AIDS treatment demand in the state of Pernambuco, Brazil—showed that the cure rate for tuberculosis patients co-infected with HIV was 58.7%.⁽¹⁸⁾ Another study, conducted in the city of Campinas, Brazil, found that the cure rate for such patients was 57.6%.⁽¹⁹⁾

Among the inpatients who died during their hospital stay in the present study, the underlying cause of death was listed as a disease/condition other than tuberculosis in 32.6%, as tuberculosis in 46.9%, and as tuberculosis/HIV co-infection in 20.4%. Of those in whom the cause of death was tuberculosis/HIV co-infection, 16% had not been started on specific treatment and 4.8% were diagnosed with tuberculosis only during the autopsy. Among all tuberculosis inpatients who died in the city of São Paulo in 2003, the underlying cause of death was listed as a disease/condition other than tuberculosis in 17.3%, as

tuberculosis in 35.3%, and as tuberculosis/HIV co-infection in 47.4%.⁽⁸⁾

Cure rates and treatment adherence rates are usually lower for tuberculosis patients who are co-infected with HIV than for those who are not. This is due to multiple drug use, adverse drug effects, lack of family support, and lack of training in tuberculosis/HIV co-infection management. The close relationship between tuberculosis and AIDS requires the coordinated efforts of tuberculosis control programs and HIV/AIDS control programs. The low cure rates for cases of tuberculosis/HIV co-infection and for those of readmission after treatment noncompliance underscore the need for public policies that address those populations in a different manner.⁽²⁰⁾

The limitations of the present study include data reporting and storage difficulties—complete data could not be collected in real time—as well as the impossibility of generalizing the data presented here to the entire city of São Paulo, given that only two regions of the city were analyzed. Taking into account the indicators of tuberculosis treatment outcome, we emphasize the importance of the following: active surveillance, diagnosis, and early treatment of cases of tuberculosis; investments in the training and continuing education of health care workers; initiation of supervised treatment whenever possible; and implementation of measures aimed at facilitating the diagnosis of cases that are more complex, including the creation of effective systems of referral and counter-referral (with the participation of experts) for rapid diagnosis.

In patients with HIV infection, active surveillance for tuberculosis, initiation of treatment for latent tuberculosis, and appropriate antiretroviral treatment reduce the incidence of tuberculosis, as well as reducing

morbidity and mortality. The surveillance of patients with tuberculosis/HIV co-infection should be redoubled because of the probability of treatment failure.

We conclude that the cure rates for patients who were previously hospitalized for tuberculosis are alarming, particularly in the subgroup of patients with tuberculosis/HIV co-infection. Various measures should be adopted in order to avoid cases of delayed diagnosis and disease dissemination, which lead to forms that are more severe. In addition, the integration between the surveillance systems of PHC clinics and those of hospitals must improve; patients hospitalized for tuberculosis must be monitored after discharge; and supervised treatment must be implemented in the PHC clinics that are closest to where those patients live.

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