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Profile of tuberculosis patients progressing to death, city of São Paulo, Brazil, 2002

ABSTRACT

OBJECTIVE: To profile adult patients dying of tuberculosis in the city of São Paulo with respect to biological, environmental and institutional factors.

METHODS: Descriptive study covering all tuberculosis deaths (N=416) among individuals aged over 15 years in 2002. Data were obtained from hospital records, the local Mortality Information System, Coroner's Service, and tuberculosis Surveillance System. The estimates of relative risk and 95% confidence intervals (95% CI) were based on the reference group, i.e., females aged 15 to 29 years, originally from the State of São Paulo (Brazil). A comparative analysis was conducted using Pearson's chi-square test and Fisher's exact test for categorical variables and Kruskal-Wallis test for continuous variables.

RESULTS: Of all tuberculosis deaths identified, 78% had pulmonary form. Tuberculosis diagnosis was made after death in 30% and in primary health care units in 14%. Of them, 44% had not started treatment; 49% were not notified; and 76% were men. The median age was 51 years; 52% had up to four years of schooling; 4% were probably living in the streets. Mortality rate increased with age; it was 5.0/100,000 for the entire city, ranging between zero to 35 according to the district. Previous treatment was reported for 82 out of 232 patients, and of them, 41 defaulted treatment. Diabetes (16%), chronic obstructive pulmonary disease (19%), HIV infection (11%), smoking (71%), and alcohol abuse (64%) were also reported.

CONCLUSIONS: Adult males over 50, migrants and living in lower Human Development Index districts were more likely to die of tuberculosis. Low schooling and comorbidities are relevant characteristics. Low involvement of primary care units in tuberculosis diagnosis and high underreporting of cases were also seen.

DESCRIPTORS: Tuberculosis, mortality. Comorbidity. Health Profile. Epidemiology, Descriptive. Brazil.

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INTRODUCTION

Brazil ranks among the countries with the highest rates of tuberculosis (TB) morbidity and mortality with around 85,000 new TB cases and 6,000 deaths every year.[6] From 1980 to 1995, the proportion of deaths associated to TB compared to total deaths due to infectious diseases (International Classification of Diseases – 10th Revision [ICD-10]; Chapter I) increased from 10.1% to 15.5%.[13] This data point to the high endemicity of TB in Brazil and evidence this disease trend which contrast with the marked decline that seen for most other infectious diseases in the last 20 years.[4,a]

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[a] Ministério da Saúde. Situação da prevenção e controle das doenças transmissíveis no Brasil. Brasília; 2003. Saúde Brasil 2004: uma análise da situação de saúde. p. 301-37.

For the city of São Paulo, TB morbidity and mortality rates are close to mean rates reported nationwide; however, they are higher than that seen in the interior of the State of São Paulo[a] (Galesi 1998). In 2000, the city of São Paulo had an incidence rate of 65 per 100,000 inhabitants, 60% of them new bacillary TB cases and a mortality rate of 5.7 per 100,000. Incidence rates varied widely by districts ranging from 18.7 to 261.1 per 100,000, while mortality rates were nil in some districts and as high as 20.9 per 100,000 in the poorest districts.[b]

Data available on TB control activities in the city of São Paulo are consistent with the seriousness of this endemic, i.e., in 2000, there were about 70% of cure, 20% of treatment default and 13% of case-fatality rate.[b]

The objective of the present study was to profile adult patients dying of TB in the city of São Paulo with respect to biological, environmental and institutional factors.

METHODS

The city of São Paulo has approximately 10 million inhabitants and is characterized by a wide-ranging Human Development Index (HDI), from 0.245 in poorer districts to 0.811 in well-off ones.[c]

This is a descriptive study including all patients, both males and females, aged 15 years or more, living in the city of São Paulo who progressed to death due to any clinical form of TB as a main cause of death (codes A15 to A19, ICD 10) between January and December 2002.

The following variables were studied: gender; age; race/ethnicity; origin; marital status; schooling; district of residence; place of death; clinical form; type of service where the diagnosis was made; criteria for diagnosis; time between symptom onset and diagnosis; treatment duration of TB episode progressing to death; length of hospital stay before death; type of treatment; past history of TB; outcome of prior treatment (cure, default), comorbidities and other conditions (diabetes, cancer, chronic obstructive pulmonary disease, TB/HIV co-infection, alcohol abuse, smoking) and case reporting to TB Surveillance System.

Data was obtained from the following information sources: Mortality Information System of the City of São Paulo (PROAIM) for identification of TB deaths and collection of data from death certificates; hospital records where TB deaths occurred; Coroners Service of the State of São Paulo for anatomopathology (macroscopic) examination results; TB Surveillance System, Center for Disease Control of the City of São Paulo (CCD) for ascertainment of cases reported and data collection; Brazilian Institute of Geography and Statistics (IBGE) for population data used in estimates of mortality rates. Data obtained from TB Surveillance System were updated as for September 2003.

A pre-coded form was used for data collection from all the different sources. Data were double entered and a database was created using EpiInfo software program, version 6.4.

Mortality rates by gender, age group, district of residence and origin were calculated using the number of deaths identified in the study in the numerator and population aged 15 years or more estimated as for July 1st, 2002 in the denominator. Estimates of relative risks and 95% confidence intervals (95% CI) were based on female gender, age group between 15 to 29 years and originally from the State of São Paulo as reference.

TabWin program was applied for mapping mortality rates by city district. In the comparative analysis, Pearson's chi-square test and Fisher's exact test were used for categorical variables and Kruskal-Wallis test for continuous variables. All estimates were performed using EpiInfo version 6.4 and SPSS software programs version 14.

The study was approved by the Research Ethics Committee of Universidade de São Paulo School of Medicine.

RESULTS

A total of 416 deaths due to TB as primary cause were identified in 2002. The most common clinical forms were pulmonary (77.9%) and disseminated (17.5%). Of them, 44.1% were untreated cases, 51.1% received regimen 1 (isoniazid, rifampicin and pyrazinamide) and 4.8% regimen 1R (isoniazid, rifampicin, pyrazinamide, and ethambutol); 20.2% and 38.5% were treated for at least one week or up to one month, respectively, before dying.

Among those treated patients, 82/232 (35.3%) had past history of TB, of which 50% had defaulted prior treatment and 34/82 (41.5%) had TB in the last two years. For 30.4% TB diagnosis was made only after death.

Of all deaths identified, 86.0%, 11.1% and 2.9% took place in hospitals, at home and in a public road, respectively. Of those who died in a hospital, 20.1% and 43.1% died within the first 24 and 72 hours after admission, respectively. Criteria for diagnostic confirmation were: bacteriological examination in 31.8%, anatomopathology (macroscopic) examination in 38.9%, clinical-radiology evaluation in 27.2% and histopathology examination in 2.1%.

[a] Galesi VMN. Mortalidade por tuberculose no município de São Paulo, análise de uma década, 1986 a 1995 [dissertação de mestrado]. São Paulo: Faculdade de Saúde Pública da USP; 1998.
[b] Secretaria Municipal de Saúde. Centro de Controle de Doenças. *Informe TB*. 2002;2:1-4.
[c] City of São Paulo. Department of Development, Labor and Solidarity. Human Development Index, HDI: City of São Paulo, 2002.

Of 416 deaths, 19.5% received home visits to search for TB cases among household contacts. Of those cases not reported (n=206; 49.5%), 187 were untreated. Address information was missing for 15 patients (3.6%), and personal identification was also missing for six of them and none of these cases had been reported, suggesting they were homeless.

Median age was 51 years (16 to 98 years), 53 years in women (17 to 98 years) and 50 in men (16 to 93 years) (p> 0.05); and 75.5% of deaths were in males. According to death certificate information, 54.7% were White, 27.2% were mixed; 16.1% were Black, and 2.0% were Asian.

Of 202 deaths with schooling information, 51.9% had less than four years of schooling, 32.7% had four to seven, and 15.4% had more than seven. Schooling in those originally from the State of São Paulo was 37.2%, 43.0% and 19.8%, respectively; and in those born in other Brazilian states was 63.6%, 26.1% and 10.2% (p<0.005), respectively.

The proportion of married individuals (38.2%; 140/377) was lower than that of single, widowed, divorced and those with no steady partners (61.8%; 233/377) (p<0.001).

Overall TB mortality rate was 5.1 per 100,000 inhabitants per year, 8.3 in men and 2.3 in women, and increasing with age (Figure 1). Mortality rates in those originally from the State of São Paulo, in the south and central-west regions and in a combination of the north, northeast, and southeast regions, excluding the State of São Paulo, were 2.5, 3.7 and 6.1 per 100,000 inhabitants per year, respectively. Taking the former as reference, relative risks were 1.48 (95% CI: 0.79;2.66) and 2.48 (95% CI: 1.98;3.01), respectively.

There were no deaths reported in 8/96 (8.3%) districts of the city, whereas in 11/96 (11.5%) mortality rates were equal to or higher than twice the mean rates in São Paulo, reaching as high as 34.3 per 100,000 inhabitants per year. Figure 2 illustrates the distribution of mortality rates and HDI per district. The percent distribution of deaths shows that 2.6%, 52.2%, 34.6% and 4.1% lived in districts with HDI below 0.40, 0.40 to 0.50, 0.51 to 0.69 and above 0.69, respectively.

TB patients also had diabetes (16%), chronic obstructive pulmonary disease (19%), HIV infection (11%), smoking (71%) and alcohol abuse (64%). Of all cases, 84.6% had respiratory symptoms and 89.3% had weight loss.

When those who were untreated or treated for up to one week were classified as not effectively treated, no significant differences were found between treated and untreated patients by gender, age, marital status, schooling and ethnicity (p>0.05) (Table 1).

After a similar comparison was carried out for diabetes, cancer, chronic obstructive pulmonary disease, HIV co-infection, pulmonary symptoms at the time of diagnosis, weight loss, smoking and alcohol abuse, it was evidenced that untreated patients were more likely to have HIV infection (p<0.005) and history of alcohol abuse (p<0.01) (Table 2).

DISCUSSION

A decline in TB mortality has been seen in the city of São Paulo since 1996, which could be in part attributed to the introduction of new antiretroviral therapies. These

Table 1. Distribution of deaths due to all tuberculosis clinical forms, in untreated and treated patients, among individuals aged 15 or more, according to sociodemographic characteristics. São Paulo, Brazil, 2002. N=416

| Sociodemographic characteristics | Total | TB patients* | | | | p-value |
| | | Untreated** | | Treated | | |
	n	n	%	n	%	
Gender						>0.05
Female	102	66	64.7	36	35.3	
Male	314	201	64.2	113	36.0	
Total	416	267	64.3	148	35.7	
Age						>0.05
15–19	5	5	100.0	0	0.0	
20–49	190	121	63.7	69	36.3	
50–59	84	55	65.5	29	34.5	
60 or +	133	83	62.4	50	37.6	
Total	412	264	64.1	148	35.9	
Marital status						>0.05
Single	166	109	65.7	57	34.3	
Married	140	81	57.9	59	42.1	
Widowed	47	30	63.8	17	36.2	
Divorced	19	12	63.2	7	36.8	
Other	4	3	75.0	1	25.0	
Total	376	235	62.5	141	37.5	
Schooling						>0.05
<4 years	105	47	44.8	58	55.2	
4–7 years	66	40	60.6	26	39.4	
>7 years	31	15	48.4	16	51.6	
Total	202	102	50.5	100	49.5	
Ethnic group						>0.05
Black	65	45	69.2	20	30.8	
White	217	138	63.6	79	36.4	
Mixed	108	72	66.7	36	33.3	
Asian	8	3	37.5	5	62.5	
Total	398	258	64.8	140	35.2	

* TB patients progressing to death
** Untreated patients or those who did receive treatment for less than seven days

Table 2. Distribution of deaths due to all tuberculosis clinical forms, in untreated and treated patients, among individuals aged 15 or more, according to comorbidities, clinical conditions and presentations. São Paulo, Brazil, 2002. N=416

Clinical and comorbidity characteristics	Total	TB patients*				p-value
		Untreated**		Treated		
	n	n	%	n	%	
Diabetes						>0,05
No	237	116	48.9	121	51.1	
Yes	44	23	52.3	21	47.7	
Total	281	139	49.5	142	50.5	
Cancer						>0.05
No	285	147	51.6	138	48.4	
Yes	6	4	66.7	2	33.3	
Total	291	151	51.9	140	48.1	
Chronic obstructive pulmonary disease						>0.05
No	169	75	44.4	94	55.6	
Yes	39	23	59.0	16	41.0	
Total	208	98	47.1	110	52.9	
HIV infection						<0.005
No	128	45	35.2	83	64.8	
Yes	15	11	73.3	4	26.7	
Total	143	56	39.2	87	60.8	
Smoking						>0.05
No	24	10	41.7	14	58.3	
Yes	64	39	60.9	25	39.1	
Total	88	49	55.7	39	44.3	
Alcohol abuse						<0.01
No	81	32	39.5	49	60.5	
Yes	142	82	57.7	60	42.3	
Total	223	114	51.1	109	48.9	
Cough at the time of diagnosis						>0.05
No	42	24	57.1	18	42.9	
Yes	231	114	49.4	117	50.6	
Total	273	138	50.5	135	49.5	
Weight loss						>0.05
No	30	18	60.0	12	40.0	
Yes	251	151	60.2	100	39.8	
Total	281	169	60.1	112	39.9	

* TB patients progressing to death
** Untreated patients or those who did receive treatment for less than seven days

treatments have reverted the growing trends started from mid-80s due to the impact of TB-HIV co-infection.[1,2] Despite this mitigation, TB has remained a major cause of death in the city, affecting mostly those living in lower HDI districts, evidencing a strong impact of socioeconomic factors, as seen in other Brazilian capitals.[14]

Yet, the data found in the present study reveal only part of the problem. If TB deaths as an associated cause were also included, the observed magnitude would be dramatically greater.[17] In addition, the results are likely to be underestimated since the number of deaths among those people presumably homeless was relatively low based on social indicators of the city of São Paulo.[a] On the other hand, no reporting of deaths among patients originally from other Latin American countries contrasts with the current growing migration flows from areas with high TB prevalence.[16]

A close examination of the characteristics of patients progressing to death revealed that mortality rates by gender and age groups found in the present study were corroborated in the literature.[14,17,20] Higher TB risk seen among the elderly was probably due their lower immunity, more difficult diagnosis of TB as well as to the fact that older cohorts were more exposed to infection in the past.[22]

Higher TB death rates found among migrants from other Brazilian regions may be because they are usually older,[2,5] belong to the poorest segments of society and come from areas with high TB prevalence.[3]

High TB prevalence among patients with diabetes, chronic obstructive pulmonary disease, smokers and those with past history of alcohol abuse suggest that biological, socioeconomic, and behavioral factors played a role in increasing their vulnerability and favored TB progressing to more severe forms and death.[3,5,12,22]

The prevalence of TB-HIV co-infection found in the study is lower than that reported in studies conducted in 1990s,[2,20] but similar to Oliveira et al[15] recent findings of reduced mortality in TB-HIV co-infected people probably due to the introduction of new highly active antiretroviral therapy.

The high proportion of cases diagnosed after death or untreated, treated for less than a month and progressing to death right after hospital admission make clear the failure of health services to identify and timely treat a substantial number of TB patients in the city of São Paulo. These characteristics make these cases potentially preventable and they should be a priority in targeted public health interventions.

Allied to that, the predominance of bacillary forms and the small proportion of cases identified in primary care services and of those receiving home visit to improve treatment compliance scale up the risk of disease transmission among those exposed, reducing or neutralizing the impact of TB control activities.[8,11] Similarly to that seen in other Brazilian regions,[20] about half of TB deaths were underreported cases and thus gone unidentified by TB Control Program before their deaths.

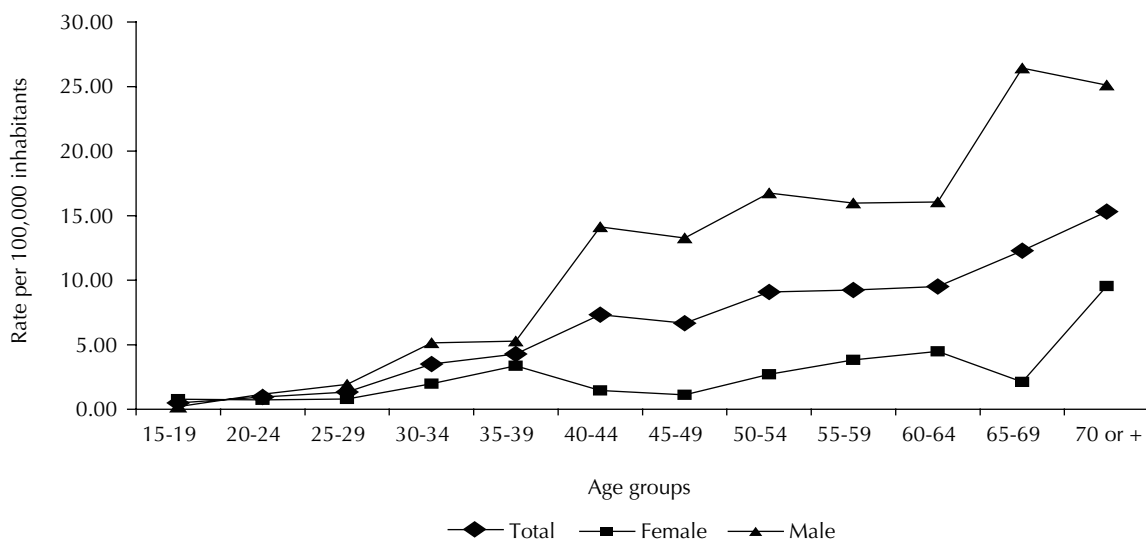[a] Department of Development, Labor and Solidarity. Human Development Index – HDI. São Paulo; 2002.

Figure 1. Tuberculosis mortality rate due to all clinical forms in individuals aged 15 or more living in the city of São Paulo, according to age group and gender. São Paulo, Brazil, 2002.

Low schooling of patients progressing to death may have contributed to their inability to perceive the disease. But a recent study in a Brazilian capital city did not show any association between difficult access to health services and delay in TB diagnosis and treatment.[18] This finding is consistent with free and universal access to TB diagnosis and treatment in Brazil and broad coverage provided in primary care services in the city of São Paulo.
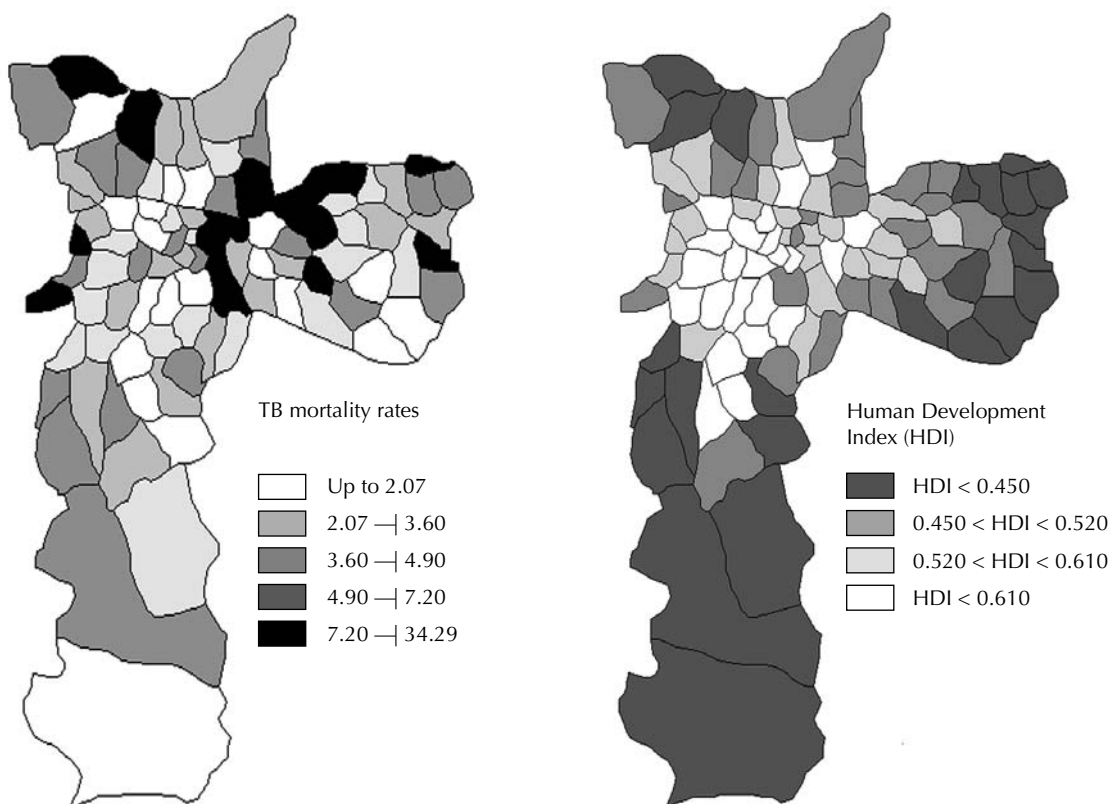

Figure 2. Tuberculosis mortality rates due to all clinical forms as main cause of death among individuals aged 15 or more, by district and Human Development Index. São Paulo, Brazil, 2002.

Since a large proportion of patients here studied showed TB typical signs and symptoms, it suggests that health providers failed to suspect TB in high-risk groups or in those with clinical presentations indicative of infection.

The high proportion of patients with past history of TB in the two years prior to their death and treatment default, and the fact that some of them have been treated with 1R regimen (isoniazid, rifampicin, pyrazinamide, and ethambutol) allow to assuming that, at least, part of these deaths may be associated to multidrug-resistant *Mycobacterium tuberculosis*.[5,21] In addition, it suggests inadequate follow-up of patients and their close contacts during treatment and for at least two years after treatment.

The high prevalence of patients infected with *Mycobacterium tuberculosis* hinders a significant decline in TB rates in the short run in Brazil. However, the study findings indicate that widely implementing the Directly Observed Therapy Short-Course (DOTS) strategy and prioritizing migrant population, districts with the lowest HDI as well as targeting those at higher risk of progressing to severe disease will favor a rapidly reduction of TB mortality as achieved by other countries where TB was also a serious public health concern.[6,7,19]

Free and universal access to TB diagnosis and treatment, broad coverage of primary care services and low prevalence of multidrug-resistant *Mycobacterium tuberculosis*[4,21] will create favorable grounds for rapidly reducing TB mortality in Brazil.

Hence, it would be advisable to change the DOTS strategy in São Paulo since it has aimed at providing universal coverage to TB patients but lacks a special focus on high-risk groups for TB death. On the other hand, there is a need for further studies to better understanding TB death predictors in the Brazilian scenario. From an operational perspective, given Brazil's large population size, huge poverty-stricken areas and high incidence rates of TB, it is crucial to provide adequate infrastructure for diagnosis which could facilitate systematic search of TB cases among patients with respiratory symptoms seeking care at primary health units.

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