Original Article

Factors associated with death from tuberculosis in the eastern part of the city of São Paulo, 2001*

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Abstract

Objective: To identify factors associated with death from TB, evaluating TB cases reported for 2001 in the city of São Paulo (specifically in the neighborhoods of Cidade Tiradentes, Guaianazes, Itaquera and São Mateus) and comparing those evolving to death with those evolving to cure. **Methods:** We investigated all deaths in which TB was given as the principal cause (n = 48), analyzing medical charts and conducting home visits to interview the caregiver(s). In parallel, we investigated 96 TB cases in which the patient had been discharged after a cure had been achieved. Patients with HIV were excluded from both groups. **Results:** There were no differences between the two groups in terms of the clinical form of tuberculosis, laboratory test confirmation of the diagnosis and type of treatment. Death from TB was found to be associated, in a statistically significant manner, with being male, being over 50 years of age, having had less than 3 years of schooling, suffering from alcoholism and being unemployed. The logistic regression showed that the variables presenting the strongest associations with death from TB were suffering from alcoholism and being over 50, whereas being a new treatment and being employed were found to be protective. The combination of suffering from alcoholism, being unemployed and being over 50 increased the chance of evolving to death by 25 times (95% CI: 6.43-97.20). **Conclusion:** Ongoing education of health professionals, prompt epidemiological interventions and efficient patient referral systems could improve the indices related to this disease.

Keywords: Tuberculosis/mortality; Epidemiologic studies; Death certificates.

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Submitted: 11 May 2006. Accepted, after review, 15 September 2006.

Introduction

Tuberculosis (TB) is one of the principal causes of morbidity and mortality in Brazil.[1-3] It is estimated that, worldwide, 30% of the population is infected with *Mycobacterium tuberculosis*.[4,5] It is known that 75% of the cases occur in the economically active population of adults between 20 and 49 years of age.[4] In addition, TB corresponds to 25% of the total number of avoidable deaths in adults in developing countries.

Early diagnosis and treatment of TB are necessary in order to reduce morbidity and mortality, as well as to decrease transmission of the disease.[2,6] To that end, priority lines of epidemiological research in Brazil, recommended by TB guidelines, are the registration of deaths and studies regarding trends in the TB-related data collected (new cases and deaths),[7] by region, as well as by city and state, differentiating the subgroup of HIV-positive patients.

Death from TB should be a rare event. The factors associated with TB mortality are as follows: late diagnosis, noncompliance with treatment, multidrug-resistant TB, socioeconomic factors, comorbidities, age, gender, and site of the disease.[8]

The objective of this study was to identify the socioeconomic and epidemiological factors most closely associated with the evolution to death from TB, comparing them with cured cases of TB, in the neighborhoods of Cidade Tiradentes, Guaianazes, Itaquera, and São Mateus, in the eastern part of the city of São Paulo, in 2001.

Methods

This was a descriptive study, using secondary data from morbidity/mortality databases, review of clinical charts, and home visits.

The city of São Paulo is politically and administratively divided into 31 submunicipalities (regions). The region studied comprised four neighborhoods: Itaquera, Guaianazes, Cidade Tiradentes, and São Mateus, which, together, compose Region 5. Region 5 is characterized as highly populated, with approximately 1.2 million inhabitants, and is considered a dormitory community. Part of this region has been rapidly occupied in an unplanned manner, without proper urban infrastructure and with poor-quality housing. Another important phenomenon is the construction of large housing units in isolated areas with few social resources, such as schools, day care centers, health care facilities, and hospitals. Approximately 10% of the deaths from TB in the city occur in this region.

Using information contained in the São Paulo Municipal Mortality Database,[9] in which all deaths of city residents are registered, we studied only deaths occurring in Region 5 and in which tuberculosis was listed as the principal cause of death. However, we excluded cases in which the individual had presented co-infection with HIV, and we limited our search to the year 2001. A total of 52 such deaths were initially identified. Home visits and reviews of clinical charts were performed for all cases of death from TB. An investigation form designed specifically to register demographic, epidemiological, and clinical data was used in the review of the clinical charts. In the home visit, the caregiver filled out a standardized questionnaire regarding sociodemographic data and answered questions on access to health care services, as well as on comorbidities, symptoms, and type of treatment prior to death. There was no address information for the victims of four of the deaths, which were therefore excluded from the analysis. In addition, in the review of the clinical charts, the diagnoses of two of these deaths were found to be unrelated to TB. Therefore, 48 cases of death from TB were studied. There were 3 cases in which the individual died at home, and, in those cases, TB was confirmed by the City of São Paulo Mortality Registry. Data from the Tuberculosis Control Program database of the Tuberculosis Epidemiology database were cross-checked with the records obtained in home visits and from hospital charts. When possible, the staff of the treatment unit was asked to clarify situations in which the data were incomplete or nonexistent.

Cure was achieved in 860 of the TB cases reported in the region. Of those 860, only 258 (30%) were in HIV-negative patients. Of those 258, official discharge after cure and completion of the epidemiological chart occurred in only 109 (42%). There were 13 patients who were excluded from the analysis because their places of residence, when georeferenced, were too far from those of the cases of death. Therefore, the cases of death were compared with those of 96 patients discharged after cure, the latter group chosen for residing in a geographical region proximal to that of the cases of death in order to ensure similar social and living conditions.

For the statistical analysis, the data obtained were analyzed using the STATA® program. The chi-square test or (when less than 20% presented expected frequencies < 5) Fisher's exact test was used in order to determine the association between the cases of death and the cured cases (response variable) in relation to independent variables. For the multivariate analysis, logistic regression was used in order to select the variables which, together, were most closely associated with death, adjusted for the type of patient/treatment. All variables presenting $p < 0.20$ in the univariate analysis were included in the initial regression model. Subsequently, one by one, all the variables that presented $p > 0.05$ were withdrawn from this initial model, starting with the higher p values. To better understand this set of variables, we opted to present the final results in a stratified table, so that the cells resulting from the possible combinations of the different categories of the three variables that composed the final logistic regression model were listed from first to last in ascending order according to the probability of death. Proportion ratios and their respective confidence intervals regarding the contrast of the probability observed in the cell in question with the first cell - or reference cell, which shows the lower probability of death, are presented to the side of each cell. In summary, in each cell, the respective proportion ratio reflects the chance of dying from TB in the presence of the conditions mentioned, in contrast to the conditions presented in the first cell. The level of significance was set at $p < 0.05$.

The study protocol was approved by the Ethics in Medical Research Committee of the Federal University of São Paulo.

Results

In 2001, the following incidence coefficients for all forms of TB were registered: in the state of São Paulo, 47.7/100,000 inhabitants; in the city of São Paulo, 63.4/100,000 inhabitants; and, in Region 5, 57.6/100,000 inhabitants.[10] In this same period, there were 494 deaths from TB in the city of São Paulo, excluding the cases of HIV co-infection; of these, 52 deaths occurred in Region 5, corresponding to 10.5% of all TB-related deaths.[9] The age of the cases of death ranged from 26 to 82 years (mean, 49.1 years; median 47.5 years), and the age of the cured cases ranged from 1 to 73 years (mean, 36.4 years; median, 36 years). Most of the deaths (94%) occurred in hospitals, with only 3 (6%) occurring in the home. Of the facilities in which the deaths occurred, 33 were public hospitals, 12 were philanthropic hospitals, and 4 were private hospitals.

In 24 (50%) of the 48 deaths studied, data regarding the death were not entered into the Tuberculosis Control Program database/Tuberculosis Epidemiology database until after the death certificate had been issued. Based on the information available in the Tuberculosis Epidemiology database, 9/24 (37.5%) of the cases were reported during hospitalization (prior to death), and 15/24 (62.5%) of the cases had been previously reported by the basic health care clinics.

Regarding the length of hospital stay of the patients prior to death, except for the 3 deaths occurring in the home, death occurred within the first 48 h in 21% of the cases, within 3-7 days in 36%, and after the first week of hospitalization in 43%.

Home visits revealed that the contacts of the cases of death were not properly instructed regarding the disease and its transmission.

Table 1 shows the distribution of cases of death from TB and cured cases according to sociodemographic variables and characteristics of TB. Regarding the variables age bracket, gender, years of schooling, associated diseases, and occupation, there was a statistically significant difference between the two groups. The pulmonary form of TB was predominant in both groups. There was no statistically significant difference between groups regarding the diagnostic confirmation (testing for acid-fast bacilli in sputum, culture for mycobacteria, or biopsy) in 77% of the deaths and in 73% of the cured cases, according to the type of patient (treatment-naïve or undergoing retreatment).

In the initial logistic regression model, the variables that correlated positively with death from TB (adjusted for treatment-naïve patients) were being over 50 years of age and being an alcoholic, whereas being employed and being treatment-naïve were shown to be factors of protection against death (Table 2).

Considering that the epidemiological charts did not always include data on all of the variables studied, and that, in some cases, it was not possible to obtain those data, even from the clinical charts maintained at the basic health care clinics, we tried

Table 1 - Distribution of deaths and cured cases of tuberculosis by age bracket, gender, schooling, accompanying diseases, occupation, characteristics of tuberculosis, and diagnosis of tuberculosis (São Paulo, Region 5, 2001).

		Deaths (n = 48)		Cured cases of TB (n = 96)		Total cases (n = 144)		p
		n	%	n	%	n	%	
Age bracket (years)	0 to 50	25	52.1	83	86.5	108	75.0	< 0.001
	> 51	23	47.9	13	13.5	36	25.0	
Gender	Male	37	77.1	57	59.4	94	65.3	0.035
	Female	11	22.9	39	40.6	50	34.7	
Years of schooling	0 to 3	24	50.0	22	22.9	46	34.1	< 0.001
	> 4	24	50.0	65	77.1	89	65.9	
Associated diseases	Alcoholism	34	70.8	10	10.4	44	31.0	< 0.001
	Other	6	12.5	12	12.5	18	12.7	
	None	8	16.7	72	75.0	80	56.3	
Occupation	Employed	22	45.8	59	64.8	81	58.3	0.013
	Unemployed/Other	26	54.2	32	35.2	58	41.7	
Clinical form	Pulmonary	41	85.4	78	81.3	119	82.6	0.534
	Extrapulmonary	7	14.6	18	18.8	25	17.4	
Laboratory test confirmation of diagnosis	Yes	37	77.1	70	72.9	107	74.3	0.589
	No	11	22.9	26	27.1	37	25.7	
Type of patient	Treatment-naïve	41	85.4	88	91.7	129	89.6	0.247
	Retreatment	7	14.6	8	8.3	15	10.4	

TB: tuberculosis.

to establish *odds ratios* and prevalence ratios based on the data available for 137 patients (48 deaths and 89 cured cases of TB). In the final model, the three variables that were found to be most closely correlated with death were alcoholism, occupation, and age (Tables 3 and 4).

The combination of being an alcoholic, being unemployed, and being over 50 was found to increase the chance of evolving to death by 25 times (Table 4).

Discussion

Considering the variables studied, it was determined that being over 50 years of age, being an alcoholic, and being unemployed were the variables most closely associated with death from TB. Being treatment-naïve proved to be a factor of protection against death.

In cities with chaotic urbanization and large pockets of poverty, deficiencies of the health care

Table 2 - Original model of (saturated) logistic regression with all variables studied.

Variable*	*Odds ratio*	95% CI	p > z
Age bracket (≥50 years/<50 years)	8.91	2.49-31.94	0.001
Gender (M/F)	1.75	0.47-6.59	0.405
Years of schooling (≤3/>3)	2.27	0.75-6.92	0.149
Accompanying diseases (alcoholism/other)	25.04	7.06-88.84	<0.001
Occupation (employed/other)	0.23	0.67-0.76	0.017
Clinical presentation (pulmonary/extrapulmonary)	1.49	0.38-5.82	0.567
Laboratory test confirmation of diagnosis (yes/no)	0.55	0.16-1.90	0.343

*adjusted for type of patient/treatment.

Table 3 - O*dds ratios* for prognostic factors of death from TB.

Variable*	*Odds ratio*	95% CI	p > z
Alcoholism	30.79	9.46-100.20	<0.001
Employed	0.32	0.11-0.94	0.038
Over 50 years of age	8.60	2.52-29.31	0.001

*adjusted for type of patient/treatment; 95% CI: 95% confidence interval.

system are probably responsible for the high rates of TB-related morbidity and mortality.

The poor quality of the databases and clinical charts made it difficult to analyze the data in the present study. Among the obstacles encountered, we can mention the difficulty in locating the clinical charts within the hospital files, limited legibility of entries or errors in reporting test results, and the lack of test results. Similarly, complications, when registered at all, were recorded in a disorganized manner, which prevented adequate data recovery.

Inconsistencies, duplications, incomplete records, and lack of updating in the epidemiological charts, as well as the methods used in the collection of some data, such as level of education and reason for hospitalization, negatively affected our analysis.

Since only reported cases of TB are supposedly eligible to receive medication at basic health care clinics, most unreported cases of death might never have been treated. In the hospitals, the epidemiological surveillance teams, or their equivalents, are responsible for ensuring the reporting and referral of patients to the basic health care clinics at the time of discharge. The hospitals are also in charge of instructing contacts.

A study of deaths from TB in the state of Rio de Janeiro revealed that 41.7% of the deaths occurred in cases that had not previously been reported.[8] According to another study conducted in the city of São Paulo, only 35.8% of the deaths from TB occurring between 1986 and 1995 were reported.[11]

Regarding the severity of the disease, 21% of the patients had been hospitalized for less than 48 h prior to their death, and 36% had been hospitalized for 3 to 7 days, which demonstrates the severity of the disease at the time of diagnosis. Due to a lack of data, patients receiving a late diagnosis could not evaluated in comparison with those who had achieved cure before discharge.

Since most deaths occur in hospitals (94% in the present study), a continuous process of investment in education and epidemiological surveillance of TB in the hospitals is necessary.

Late detection of the disease, noncompliance with treatment, and epidemiological interventions that fail to detect all the cases of TB are factors that perpetuate the transmission of the disease and were not evaluated in this study.

Pulmonary TB, which is the most common clinical manifestation, perpetuates the transmission of the

Table 4 - Proportion ratio and confidence intervals of the alcoholism, occupation and age variables of the cases of death and cured cases of tuberculosis (São Paulo, Region 5, 2001).

Variables			Deaths (n = 48)	Cured cases (n = 89)	Proportion	Proportion ratio	95% CI
Not alcoholic	Employed	Age <50	2	48	0.04	1.0	
		Age >50	4	5	0.45	11.1	2.4-51.9
	Unemployed	Age <50	4	19	0.17	4.4	0.9-22.1
		Age >50	4	8	0.33	8.3	1.7-40.3
Alcoholic	Employed	Age <50	11	7	0.61	15.3	3.7-62.4
		Age >50	6	1	0.86	21.4	5.3-86.1
	Unemployed	Age <50	8	1	0.89	22.2	5.6-88.1
		Age >50	9	0	1.00	25.0	6.4-97.2

95% CI: 95% confidence interval.

disease and has a high mortality rate. Through tests such as acid-fast bacilli smear microscopy, culture, and biopsy, the diagnosis was confirmed in 72.9% of the cured cases, a percentage similar to that found for the state of São Paulo.[10] Regarding age, studies conducted in different geographic regions in the country indicate increased death risk by TB among the elderly, due to the aging of the population and the influence of the TB control programs, which manage to decrease mortality in the younger age brackets. In addition, patients over 50 years of age are more frequently affected by other diseases, use medication for chronic diseases and are more likely to forget to take antituberculosis medication or use it irregularly, unless under supervised treatment for TB.

Higher prevalence among males, confirmed in most states in Brazil and in other countries, can be explained by genetic and nongenetic factors.[12] Among the nongenetic factors, it is important to highlight a lack of self-care, not displaying treatment-seeking behavior, treatment noncompliance, and greater exposure to communicable diseases.

In addition, individuals with less schooling, which is frequently associated with various other unfavorable social conditions, are less aware of their health and show less self-care, causing a delay in seeking health care, which results in late diagnosis and treatment. When under treatment, they frequently tend to be noncompliant or to use medications incorrectly. Since TB is a social disease, a greater incidence of cases and deaths is expected in the poorly-qualified, low-schooling strata, which present a higher number of unemployed or never-employed individuals.[13,14]

Various comorbidities were more common in the group at greater risk of death from TB. However, due to the small number of deaths and incomplete epidemiological charts in the present study, we were only able to demonstrate that being an alcoholic was the leading comorbidity associated with an unfavorable outcome. Alcoholism as a risk factor has previously been associated with an unfavorable outcome.[15] Therefore, any strategy for the prevention of death and for TB control should include alcoholism-related interventions.

It is known that TB is marked by a strong social nature and that the high mortality rate prevails in individuals in the higher age brackets. Multiprofessional efforts in the approaches taken to treating the sick individual, as well as addressing comorbidities and social problems, will bring better results in decreasing TB mortality, which should be a rare and exceptional event.

The identification of predisposing factors for death should increase alertness in TB treatment teams with prompt institution of measures to assist patients at risk, such as supervised treatment, social work assistance, occupational therapy, psychological support, and treatment for alcoholism, as well as incentives for out-of-work patients and elderly individuals.

Therefore, ongoing training of health teams in hospitals, together with prompt epidemiological surveillance and efficient patient referral systems, will greatly improve the indicators of the disease.

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