Original Article

Indicators related to delays in diagnosis and in implementation of measures to control airborne infection among patients with pulmonary tuberculosis in a tertiary-care hospital*

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Background: The risk for nosocomial transmission of tuberculosis exists in health care institutions.

Objective: To evaluate indicators of transmission risk among patients with pulmonary tuberculosis treated at a university hospital.

Method: A retrospective study covering the January 1997 to September of 1999 period and evaluating patients admitted to the Hospital de Clínicas of the Universidade Estadual de Campinas with pulmonary tuberculosis. Three intervals were determined: from admission to collection of sputum for acid-fast bacilli microscopy; from admission to implementation of airborne infection control measures; from sputum collection to the initiation of treatment.

Results: The final sample included 63 cases. Concomitant human immunodeficiency virus-positivity was found in 31.7%. Forty patients (63.5%) were admitted through the emergency room. In 42 (66.7%) patients, TB was suspected at admission. The interval between admission and sputum collection exceeded 12 hours in 27.5% of cases admitted through the emergency room and in 30.4% of those admitted directly to wards ($p = 0.803$). Delayed respiratory isolation occurred in 31 cases (49.2%). The delay in isolation was correlated to no diagnosis of tuberculosis at admission ($p < 0.000$) and lower bacillary load in the sputum ($p = 0.032$). Co-infection with human immunodeficiency virus ($p = 0.530$), hospitalization ward ($p = 0.284$) and underlying diseases ($p = 0.541$) were not correlated with delayed isolation. The interval between sputum collection and initiation of treatment was greater than 24 hours in 15.9% of the cases.

Conclusion: Delayed isolation was observed in many cases. Policies of continuing education are called for, especially in high-risk areas.

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INTRODUCTION

For several decades, it has been known that there is a high risk for nosocomial transmission of tuberculosis (TB) in health care institutions. However, appropriate control measures to prevent the dissemination of the disease in these institutions have yet to be implemented[1,2]. In the 1990s, several institutional outbreaks were reported in developing countries, accompanied by high attack rates, rapid progression from infection to active disease and significant nosocomial dissemination among patients and health care professionals[2].

In order to prevent TB dissemination in health care institutions, the Centers for Disease Control and Prevention in Atlanta, Georgia (USA) proposed guidelines for transmission control in 1994[3]. In 1999, the World Health Organization established similar guidelines to be used in countries with limited resources[4]. These guidelines prioritize administrative measures and establish the need for an evaluation of indicators that make it possible to estimate the risk for disease transmission in a given institution.

In Brazil, the National Tuberculosis Control Program has recommended that outpatient treatment be used as a tool for TB detection, appropriate treatment and control[5]. However, the number of cases that are diagnosed and treated in hospitals is significant, resulting from the disorganization of the health care system as well as from TB concomitance with the human immunodeficiency virus (HIV) and other diseases[6]. Some hospitals aggregate a significant number of TB patients and susceptible individuals, and practice inappropriate measures for the control of nosocomial transmission, thereby favoring the dissemination of Mycobacterium tuberculosis.

The objective of the present study was to evaluate indicators of TB transmission risk for patients with pulmonary TB treated at a university hospital in Brazil.

METHODS

The present study was carried out at the Hospital das Clínicas da Universidade Estadual de Campinas (HC-Unicamp, University of Campinas Clinical Hospital), a 408-bed university hospital that is a referral center for the region surrounding the city of Campinas (in the state of São Paulo) and admits approximately 100 to 150 new TB cases annually. Since 1996, measures for preventing patient-to-patient airborne transmission of TB have been recommended and adopted for patients with a suspected or confirmed diagnosis of pulmonary TB[7]. However, despite the adoption of measures for preventing airborne transmission at the HC-Unicamp, the hospital lacked engineering controls at the time of the study. Surveillance and notification of TB cases were carried out by the HC-Unicamp Center for Epidemiological Surveillance through an active search of cases first admitted to the emergency room and cases admitted directly to wards, in addition to the monitoring of the results of microbiological exams and the specific medicines distributed by the hospital pharmacy. Positivity for acid-fast bacilli (AFB) in respiratory samples is immediately reported to the HC-Unicamp Center for Epidemiological Surveillance by the Mycobacterium Sector of the Microbiology Laboratory.

We carried out a retrospective and descriptive study in which we evaluated the January 1997 to August 1999 period.

Inclusion criteria were being an inpatient (hospital stay equal to or longer than 24 hours) and having pulmonary TB (positivity for AFB in sputum or tracheal fluid microscopy). Patients whose culture revealed mycobacteria other than M. tuberculosis, or whose clinical and epidemiological data were incomplete, were excluded.

Patient charts, as well as case report forms, were reviewed using a standardized research tool in order to collect demographic data, data relating to TB, data relating to clinical suspicion, the interval between admission and collection of sputum for microscopy (for AFB), the interval between collection of sputum and the implementation of measures for preventing airborne transmission, length of hospital stay, area of stay, HIV co-infection and other comorbidities.

The criteria used for the reporting and investigation of cases were those established by the Brazilian Health Ministry[8]. Bacillary load was evaluated based on the result of the sputum microscopy for AFB (performed using the Ziehl-Neelsen method) and was considered high if +++ or ++++ and low if + or ++. Based on data from the case report forms, chest X-rays were classified as "suspect" (infiltrate in any location, cavitations, and pleural effusion or pneumothorax), "normal" or "presenting other alterations". Respiratory patients who presented cough for more than three weeks were categorized as symptomatic. The indicators evaluated were those defined by the Centers for Diseases Control and Prevention, 1994[3]. Three indicators were defined:

Interval 1 - interval between admission and collection of sputum for smear microscopy (for AFB), Interval 2 - interval between admission and implementation of airborne infection control measures, and Interval 3 - interval between collection of sputum for smear microscopy (for AFB) and the initiation of treatment. Delay in clinical suspicion was defined as no diagnostic hypothesis of TB at admission. Cases in which a patient was not immediately isolated (Interval 2 diferent 0) were categorized as cases of delayed respiratory isolation, and those in which Interval 3 was greater than 24 hours were categorized as cases of delay in the initiation of treatment.

Results were analyzed using Epi Info, version 6.04b[9]. Differences in the proportions for categorical variables were analyzed using the chi-square test with Yates' correction, when appropriate. Differences in the means for continuous variables were analyzed using the Kruskall-Wallis test. Values of $p < 0.05$ were considered statistically significant.

RESULTS

During the study period, the HC-Unicamp Center for Epidemiological Surveillance reported a total of 260 patients with pulmonary TB: 178 outpatients (68.5%) and 82 inpatients (31.5%). Among the inpatients, 19 (23.2%) were excluded. Of those, 14 (17.1%) were excluded because their data were incomplete, and 5 (6.1%) because they presented cultures positive for mycobacteria other than M. tuberculosis.

The final sample included 63 cases (76.8%), with a median age of 37 years. The clinical history showed that 61 patients had reported cough. Of those, 47 (74.6%) presented cough for more than three weeks. Fifty-three patients (85%) presented pulmonary form and the remaining 10 (15%) presented extrapulmonary involvement. Twenty patients (31.7%) were HIV-positive and 15 (20.6%) presented other comorbidities: 5 had diabetes mellitus, 2 had chronic liver disease, 2 had pancreatitis, 2 had paracoccidioidomycosis, 1 had cranioencephalic trauma, 1 had chronic renal insufficiency, 1 had systemic lupus erythematosus and 1 had multiple sclerosis.

In 41 patients (65.1%), TB was suspected at admission and 12 patients (19%) were initially diagnosed as having other lung diseases. In 10 patients (15.9%), the initial diagnostic hypothesis was neither TB nor any other lung disease, and the main reason for hospitalization was related to other comorbidities. Of the 47 patients who experienced respiratory symptoms, 34 (72.3%) were admitted with clinical suspicion of TB. Chest X-rays were classified as abnormal in all cases. Sputum microscopy was positive for AFB in the first sample collected in 72.3% of the cases. Although M. tuberculosis patterns of susceptibility to drugs were not systematically evaluated, multidrug resistance was detected in 2 cases.

Forty patients (63.5%) were first admitted to the emergency room, whereas 23 (36.5%) were admitted directly to wards. The median emergency room stay was 21 hours (minimum = 1, maximum = 336 hours), and 14.3% remained in the emergency room throughout the treatment. Most of the patients (69.8%) were admitted to infectious diseases wards (31.7%), pulmonology wards (27%) and internal medicine wards (11.1%). The median ward stay was 9 days (minimum = 1, maximum = 63 days), and there was no difference between patients who were HIV-positive and those who were not.

Table 1 shows the intervals evaluated. The longest Interval 1 (27 days) was observed in an HIV-positive patient who was admitted with a head injury. The median Interval 1 was comparable between patients who were HIV-positive (11.5 hours) or those who were not (12 hours) ($p = 0.09$).

Sputum microscopy for AFB was performed prior to hospitalization in 5 patients (12.55) first admitted to the emergency room and in 13 (56.5%) of the patients admitted directly to wards. Interval 1 was greater than 12 hours in 11 patients (27.5%) first admitted to the emergency room and in 7 patients (30.4%) admitted directly to wards ($p = 0.803$). Delay in diagnosis was longer than 12 hours in 28.6% of cases.

TABLE 1

Indicators related to infection control in the management of patients with pulmonary tuberculosis in a tertiary-care hospital in Brazil

	Indicators evaluated		
	Interval 1	Interval 2 (hours)	Interval 3
Minimum	1.0	0	0
25th percentile	4.5	0	2.5
Median	12.0	0	6.0
75th percentile	25.5	21.0	15.0
Maximum	648.0	816.0	168.0

Delay in the implementation of airborne infection control measures, evaluated through Interval 2, occurred in 31 cases (49.2%). There was no statistically significant difference in the occurrence of delay among the various years evaluated (p = 0.467). Thirteen patients (9 in the emergency room and 4 in the wards) were not isolated at any time. In these cases, the result of the sputum microscopy for AFB was not known until after patient discharge or death. No clinical suspicion of TB at admission, as well as lower bacillary load in the sputum, was found to correlate with delay in the implementation of airborne infection control measures (Table 2).

In 17 patients (27%), TB treatment was started prior to hospitalization. Interval 3 was greater than 24 hours in only 7 cases (15.9%). Of those 7, 5 were HIV-positive and the remaining 2 received no treatment.

DISCUSSION

The present study identified a need to revise practices related the management of patients with active pulmonary TB in order to prevent the dissemination of the disease. We observed that a great number of new cases of sputum-positive pulmonary TB (63.5%) were first admitted to the emergency room, and that the length of stay was long. Since these types of patient care facilities, which include infectious diseases wards, pulmonology wards and general adult wards, present high concentrations of inpatients with transmissible forms of the disease, they should be considered high-risk areas for TB transmission and areas of priority for the continuing education of professionals.

The identification of patients with respiratory symptoms in emergency units has been a strategy adopted to optimize the treatment of suspected cases of TB in certain hospitals in developing countries, as well as in hospitals that are referral centers for the treatment of infectious diseases in Brazil[10]. Since it is difficult to implement screening procedures in general hospital emergency rooms, it is necessary to consider other methods, such as the method of syndromic surveillance for pulmonary diseases, or other forms of continuing education. Sokolove et al.[11]observed that, although risk factors and TB-related symptoms are present among patients treated in the emergency room, they do not generally become known to the emergency room team, a fact which makes it difficult to implement triage criteria in these units.

In the present study, delayed diagnosis occurred in 28.6% of the cases. We advise caution in

TABLE 2

Risk factors correlated with delayed isolation of patients with pulmonary tuberculosis

	Delayed isolation			
	Yes	No	*p* value	OR (95% CI)
Initial diagnosis				
TB	13	29	< 0.001	13.38 (2.94-69.9)
No TB	18	3		
Hospitalization Ward *				
ID, Pulmonol, GWA1	7	27	0.294	2.38 (0.49-12.09)
Other	6	4		
First admitted to the emergency room				
Yes	20	20	0.869	1.09 (0.35-3.45)
No	11	12		
Sputum microscopy for AFB				
+ and ++	20	12	0.033	3.03 (0.97-9.7)
+++ and ++++	11	20		
HIV co-infection				
Yes	11	9	0.533	1.41 (0.43-4.67)
No	20	23		

*9 patients were excluded for having remained in the emergency room during hospitalization
TB: tuberculosis; ID: Infectious diseases, Pulmonol: Pulmonology; GWA: General Ward for Adults; AFB: acid-fast bacilli; OR: odds ratio; 95% CI: 95% confidence interval.

comparing this finding to those of other studies carried out in other countries due to the diverse epidemiological profiles, as well as differences in inclusion criteria and treatment strategies. In a multicentric hospital-based study carried out in North America, the inclusion criterion was positive culture, and delayed diagnosis occurred in 26.6% of the cases. Delayed TB diagnosis was independently correlated with absence of cavitary pulmonary disease, absence of meningeal disease and absence of hemoptysis, as well as with negativity for AFB in sputum microscopy. In a hospital-based study conducted in Turkey, inpatients who were AFB positive were evaluated[13]. The authors found that the median interval between admission and collection of sputum for AFB microscopy was 3 days, and that there was a high rate of delayed diagnosis (69.4%).

In contrast to developed countries, the occurrence of TB is frequent in developing countries and clinicians are familiar with the typical presentations of the disease. However, comorbidities, especially HIV co-infection, in patients treated at referral hospitals hinder the clinical diagnosis of TB due to the broad spectrum of clinical-radiological manifestations. In order to prevent long delays in diagnosing pulmonary TB in this group of patients, as well as in immunosupressed and lung disease patients, a significant degree of suspicion is required, even when the main reason for hospitalization was unrelated to pulmonary disease[14]. Models to predict TB based on clinical parameters have been evaluated in developed countries[15]. However, it is not possible to extrapolate such models for use in Brazil, and a national TB diagnosis model should be developed.

Although the clinical suspicion was confirmed in 71.4% of cases, airborne infection control measures were not implemented for all suspected cases, which caused a delay in isolation in 49%. Delays in implementing airborne infection control measures among TB inpatients have frequently been observed in the United States: 39% in a hospital in Boston[16], 30% and 56%, respectively, in two Californian hospitals[17], and 20.6% in a university hospital in Texas[18]. In a study carried out at the university hospital of the Rio de Janeiro Federal University, researchers reported that, prior to the implementation of the nosocomial TB control program, the mean interval between admission and respiratory isolation was 1.5 days (range, 0-18 days)[19].

The delay in isolation identified in the present study was correlated with the absence of clinical suspicion of TB at admission and with lower bacillary load in the sputum. Although no statistically significant correlation was found between HIV co-infection and delay in isolation, long intervals were found for some HIV-positive patients, as has been previously reported by other authors[14,20]. Studies carried out in developed countries have shown that the following factors were correlated with delayed diagnosis: advanced age, HIV co-infection, non-cavitary disease on chest X-ray, no cough or expectoration, and negativity for AFB in sputum microscopy[21-23].

It should be emphasized that, although the interval between admission and collection of sputum for AFB microscopy was satisfactory in most of the cases, the delay in implementing control measures was longer, demonstrating that, despite the fact that there was suspicion and sputum was collected, the implementation of control measures were not made based on clinical suspicion. The study design does not allow the analysis of why patients under clinical suspicion of having the disease were not isolated. Some hypotheses may be put forward and should be tested in future studies: inefficiency of health care facilities in making an early diagnosis of the disease (resulting in patients later seeking treatment at tertiary-care hospitals); high traffic and lack of organization in the emergency rooms of general hospitals; lack of perception of transmission risk on the part of health care professionals; and not having hospital beds specifically designated for TB patients.

According to the guidelines established by the Centers for Disease Control and Prevention, the result of the sputum microscopy for AFB should be available within 24 hours after collection of the sputum sample[3]. In the present study, the initiation of treatment occurred promptly after the sputum collection (Interval 3), within a median of 6 hours. This is due to the fact that the HC-Unicamp Microbiology Laboratory efficiently reported positivity for AFB in sputum microscopy to the Center for Epidemiological Surveillance. This result calls attention to the need for TB control programs in hospitals, either as an independent program in large-scale hospitals or as an integral

part of the hospital epidemiological activities (epidemiological surveillance and hospital infection control), as at HC-Unicamp. A study carried out at a university hospital in the city of Rio de Janeiro demonstrated the impact of the implementation of a nosocomial TB control program on the indicators related to disease transmission[24].

The present study had several limitations. Its retrospective design did not allow us to analyze other proposed parameters (adherence to control measures and predictability of clinical suspicion of TB). In addition, it was not possible to detail some variables, such as the radiographic findings. In addition, data on tuberculin conversion and the development of M. tuberculosis among health care professionals were not evaluated, nor were these indicators evaluated in the period prior to the implementation of transmission-based control measures.

In developing countries such as Brazil, the determination of indicators related to TB transmission (as a basis for the evaluation of disease control programs in the hospital and community) should be implemented and guaranteed by hospital administrations and should be regulated by local, state and national disease control programs.

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