



Factors associated with tuberculosis and multidrug-resistant tuberculosis in patients treated at a tertiary referral hospital in the state of Minas Gerais, Brazil

Valéria Martins Soares¹ , Isabela Neves de Almeida² ,
Lida Jouca de Assis Figueredo² , João Paulo Amaral Haddad³ ,
Camila Stefanie Fonseca de Oliveira³ , Wânia da Silva Carvalho⁴ ,
Silvana Spindola de Miranda² 

1. Hospital Júlia Kubitschek, Fundação Hospitalar do Estado de Minas Gerais, Belo Horizonte (MG) Brasil.
2. Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte (MG) Brasil.
3. Escola de Veterinária, Universidade Federal de Minas Gerais, Belo Horizonte, Belo Horizonte (MG) Brasil.
4. Faculdade de Farmácia, Universidade Federal de Minas Gerais, Belo Horizonte (MG) Brasil.

Submitted: 5 December 2018.

Accepted: 22 April 2019.

Study carried out in the Júlia Kubitschek Hospital, Fundação Hospitalar do Estado de Minas Gerais, Belo Horizonte (MG) Brasil.

ABSTRACT

Objective: To evaluate the risk factors for the development of tuberculosis and multidrug-resistant tuberculosis (MDR-TB) in patients treated at a tertiary referral hospital. **Methods:** This was a cross-sectional study based on data obtained from patients treated at the Júlia Kubitschek Hospital, located in the city of Belo Horizonte, Brazil, between October of 2012 and October of 2014. We evaluated sociodemographic, behavioral, clinical, and radiological variables. The outcome considered to identify associations between tuberculosis and the explanatory variables was the treatment prescribed. To evaluate the associations between MDR-TB and the same explanatory variables, the change in MDR-TB treatment was considered. **Results:** The factors associated with tuberculosis were alcoholism, comorbidities, pulmonary cavitations, and a radiological pattern suggestive of tuberculosis. Cavitation and previous treatment for tuberculosis were associated with MDR-TB. **Conclusions:** Despite the significant progress made in the fight against tuberculosis, there is a need for coordinated actions that include social protection measures and patient support.

Keywords: Tuberculosis; Risk factors; Tuberculosis, multidrug-resistant.

INTRODUCTION

Tuberculosis continues to be a serious public health problem worldwide and, according to the World Health Organization (WHO), is the leading cause of death from diseases caused by a single infectious agent, ahead of HIV.⁽¹⁾ In 2017, 10 million new cases of tuberculosis were reported worldwide.⁽²⁾

In 2017, 79,222 new cases of tuberculosis were reported in Brazil⁽²⁾ and 13,347 cases of retreatment were reported, corresponding to 16.1% of all cases reported in the same period.⁽¹⁾ The state of Minas Gerais recorded incidence and mortality rates of 15.8/100,000 population and 1.3/100,000 population, respectively, and 3,343 new cases of tuberculosis were reported.⁽¹⁾

In 2017, 2,000 cases of drug-resistant tuberculosis were diagnosed. Those results were obtained by using the rapid molecular test for tuberculosis or drug susceptibility testing, with 1.5% of the total corresponding to new cases and 8.0% corresponding to cases of retreatment (relapse or readmission after treatment noncompliance).⁽²⁾ In 2016, 752 cases of patients who were started on treatment for drug-resistant tuberculosis were reported in the Special Tuberculosis Treatment Database. Of those 752 patients, 177 (23.5%) had single-drug resistant tuberculosis, 330

(43.9%) had rifampin-resistant tuberculosis (detected by using the rapid molecular test), 49 (6.5%) had polyresistant tuberculosis, 193 (25.7%) had multidrug-resistant tuberculosis (MDR-TB), and no results were available for 3 (0.3%).⁽³⁾

Mycobacterium tuberculosis infection is associated with factors such as incarceration, smoking, alcoholism, a history of drug use, low body mass index (which is a risk factor and a sign of infection), diabetes mellitus (DM), hepatitis C, HIV/AIDS, and depression.⁽⁴⁾ Although efforts to control the epidemic have reduced its mortality and incidence, there are several predisposing factors to be controlled to reduce the disease burden.⁽⁵⁾

The combination of tuberculosis and other comorbidities (multimorbidity), as well as some social habits, should be considered and evaluated in populations exposed to tuberculosis, because it may be a complicating factor in clinical treatment.⁽⁶⁾ In recent years, it has been observed that active tuberculosis develops more frequently in patients with poor glycemic control and that, radiologically, patients with tuberculosis and DM have more extensive lesions and, more frequently, present multilobar disease and the presence of cavitation.^(5,7)

Regarding social habits, observational studies have shown that exposure to smoking is associated with tuberculosis

Correspondence to:

Silvana Spindola de Miranda. Avenida Alfredo Balena, 190, Santa Efigênia, CEP 30130-100, Belo Horizonte, MG, Brasil.

Tel.: 55 31 3409-9905. E-mail: silvanaspindola@gmail.com

Financial support: This study received financial support from the *Fundação de Amparo à Pesquisa do Estado de Minas Gerais* (FAPEMIG, Foundation for the Support of Research in the State of Minas Gerais; Project nos. APQ-03266-13 and APQ-00094-12) and the Brazilian *Conselho Nacional de Desenvolvimento Científico e Tecnológico* (CNPq, National Council for Scientific and Technological Development; Project nos. 446796/2014 e 310174/2014-7).

infection, active tuberculosis, and tuberculosis-related mortality.^(5,8,9) In addition, although alcohol consumption is considered socially acceptable in most countries, it influences not only the incidence of tuberculosis but also its clinical evolution and outcomes.^(5,10)

The WHO recognizes that the measures taken to combat tuberculosis should be applied at the primary, secondary, and tertiary levels of health care, including prisons. Clinical and operational research has recently indicated that such approaches are most effective when responding to local sociocultural characteristics, health service organization, and the types of community activities.⁽¹¹⁾ Within this context, the study and monitoring of factors related to tuberculosis exposure may be important tools to disrupt the maintenance of the tuberculosis transmission chain and to increase the impact of disease control program interventions.^(2,5) Therefore, the aim of the present study was to evaluate the factors associated with tuberculosis and MDR-TB in patients treated at a tertiary referral hospital.

METHODS

Study design

This is a cross-sectional study based on data obtained from patients treated between October of 2012 and October of 2014 at the Júlia Kubitschek Hospital (JKH), a public general hospital that is a tertiary referral center for the treatment of tuberculosis and drug-resistant tuberculosis, located in the city of Belo Horizonte, which conducts educational and medical activities in the state of Minas Gerais, Brazil. Every month, the JKH Microbiology Laboratory receives approximately 200 samples from suspected tuberculosis patients, and, on average, 12 present a confirmed diagnosis of tuberculosis.

The study was approved by the Research Ethics Committee of the Federal University of Minas Gerais (UFMG, *Universidade Federal de Minas Gerais*) in 2013 (CAAE: 02232412.7.1001.5149) and by the Research Ethics Committee of the Minas Gerais State Hospital Foundation in 2012 (Ruling no. 018B / 2012).

Study population

We included patients ≥ 18 years of age with suspected tuberculosis (pulmonary or extrapulmonary) who were treated at the outpatient clinics, emergency rooms, and hospital wards of the JKH and who had their clinical samples sent to the JKH Microbiology Laboratory. All of the patients included gave written informed consent. Patients diagnosed with nontuberculous mycobacterial infection were excluded.

Measurements and procedures

The participants were interviewed with a standardized questionnaire, and missing data were located by consulting medical records. The questionnaires were applied by researchers from the Mycobacterial Research Group of the UFMG School of Medicine, all of who had been trained in its use. The questionnaire

contained sociodemographic, behavioral, clinical, and radiological data. To assess alcoholism, we applied the **C**ut down, **A**nnoyed, **G**uilty, and **E**ye-opener (CAGE) questionnaire, which has been validated for use in Brazil.⁽¹²⁾ The CAGE questionnaire, which comprises four questions, was utilized with a cutoff point of two affirmative answers suggesting positivity for alcohol abuse or dependence.⁽⁴⁾

The presence of pulmonary cavitation and the chest X-ray pattern were evaluated according to the following classification⁽¹³⁾: suggestive, defined as the presence of infiltrate in the upper lobes(s) or apical segment of the lower lobe; typical, defined as mediastinal enlargement or an enlarged hilar lymph node, together with a miliary pattern or pleural effusion; and atypical, defined as any other pattern.

The patients were interviewed at the time of suspicion of tuberculosis and at the end of treatment to assess the outcomes (cure, death, and treatment noncompliance or maintenance of treatment).

Outcome measures of the study: dependent variable

The outcome considered to identify associations between tuberculosis and the explanatory variables was the treatment prescribed. The cases of tuberculosis were diagnosed according to the Brazilian National Tuberculosis Control Program through clinical, epidemiological, mycobacteriological, radiological, histopathological, and complementary examinations.⁽¹³⁾ To evaluate the association between drug-resistant tuberculosis and the same explanatory variables, the authors considered any change in the treatment prescribed for MDR-TB.

Outcome measures of the study: exposure factors

The variables used were grouped according to sociodemographic characteristics (age, gender, skin color, income, and education); behavioral characteristics (alcoholism, smoking, marital status, and homelessness); clinical characteristics (fever, cough, hemoptysis, dyspnea, expectoration, previous treatment for tuberculosis, and presence of comorbidities); and radiological characteristics.

To categorize the level of education, we established a dichotomous variable ($<$ or ≥ 9 years of schooling). To categorize income, the third quartile was considered the cutoff point.

The comorbidities considered were alcoholism (assessed using the CAGE questionnaire),⁽⁴⁾ DM, COPD, pulmonary silicosis, liver diseases, malignant neoplasms, diffuse lung disease, chronic kidney disease, HIV/AIDS, drug use, corticosteroid use, malnutrition, anemia, depression, asthma, and high blood pressure.

Statistical analysis

Databases were created with the 2003 version of Microsoft Excel. The first database included all patients

with suspected tuberculosis regardless of a positive or negative diagnosis for tuberculosis. A descriptive analysis was performed using frequency distribution of the categorical variables. For the continuous variables, the measures of central tendency and dispersion (mean and standard deviation) were evaluated. In the second database, only patients with a confirmed diagnosis of tuberculosis (sensitive or resistant) were selected. That second database was created to test the association between the explanatory variables and MDR-TB.

The magnitude of the association was expressed in ORs and 95% CIs. For all the analyses conducted, the level of significance was set at $p < 0.05$.

Variables with a $p \leq 0.20$ in the uncorrected chi-square test in the univariate analysis were manually selected to start the multivariate model via a stepwise regression selection procedure. Multivariate analysis was used in order to assess the association between exposure factors and the dependent variable. After the multivariate analysis, only the variables with a $p \leq 0.05$ were retained in the final model, and the collinearity of the variables inserted in this model was verified by calculating the generalized variance inflation factor. The variables were considered collinear when the coefficient was greater than 5.⁽¹⁴⁾ The analyses were performed using the programs Epi Info, version 7, and RStudio, version 1.2.5019 (RStudio, Inc., Boston, MA, USA).

Sample size

The sample size was determined by considering a 10% margin of error, 95% CI, and a frequency of 50% to determine the population of patients who underwent mycobacteriology tests during the 2-year study. The minimum sample size was calculated to be 184 patients.

RESULTS

During the study period, we included 251 patients with suspected tuberculosis, of whom 176 (70.12%) were male. The mean age was 55.4 ± 15.7 years. The mean monthly income, in Brazilian reais (R\$) was $R\$1,244.00 \pm 1,151.06$. The sociodemographic, behavioral, clinical, and radiological variables are presented in Table 1.

Of the 251 patients, 95 (38.6%) were diagnosed with tuberculosis. Of those patients, 71 (74.7%) were cured; 11 (11.6%) abandoned treatment; 3 (3.2%) died from tuberculosis; 4 (4.1%) died from other causes; 2 (2.1%) were receiving ongoing treatment; and 4 (4.2%) were lost to follow-up.

In the sample as a whole, the most common comorbidities were alcoholism, in 59 patients (23.5%); COPD, in 35 (13.9%); and type 2 DM, in 25 (10.0). Of the 11 patients (4.4%) with HIV/AIDS, only 1 presented coinfection with tuberculosis.

The presence of comorbidities, COPD, dyspnea, fever, alcoholism, pulmonary cavitation, and a radiographic pattern suggestive of tuberculosis were significantly associated with tuberculosis (Table 2).

The final multivariate model included four variables as independent factors associated with tuberculosis (Table 3): alcoholism, comorbidities, pulmonary cavitation, and a radiological pattern suggestive of tuberculosis. However, COPD and symptoms such as dyspnea and fever were not considered risk factors for tuberculosis after the multivariate analysis. The values of the collinearity coefficient were as follows: alcoholism = 1.210070; comorbidities = 1.206232; pulmonary cavitation = 1.147316; and a radiological pattern suggestive of tuberculosis = 1.135740. Therefore, there was no collinearity between the variables presented as factors associated with tuberculosis.

Of the 95 patients who were started on a tuberculosis treatment regimen of rifampin, isoniazid, pyrazinamide, and ethambutol, 12 (12.6%) switched to a standard regimen (due to secondary resistance as a result of treatment noncompliance in 11 patients; and due to primary resistance in 1). Of those 12 patients, 11 (91.6%) were classified as having MDR-TB via drug susceptibility testing, and the treatment was changed to a standardized resistance regimen in 1 (8.4%) because that patient reported having had contact with a family member with MDR-TB (primary resistance), as well as presenting clinical worsening, although the drug susceptibility testing did not show resistance to rifampin. Regarding the outcome of those 12 patients, 8 (66.7%) were cured, 2 (16.7%) were still undergoing treatment at the end of the study, and 2 (16.7%) abandoned treatment.

Table 4 presents the factors associated with MDR-TB. There was a significant association with previous treatment for tuberculosis and pulmonary cavitation. Multivariate analysis was not performed due to the limited number of patients with MDR-TB.

DISCUSSION

In the present study, behavioral determinants (especially alcoholism), suggestive radiological changes, and other potential risk factors were important for the development of tuberculosis. Pulmonary cavitation and previous treatment for tuberculosis were also shown to be associated with MDR-TB. Increasingly, it is necessary to prioritize investments in public policies that address behavioral and clinical factors, thereby promoting intersectoral coordination in the health care system, as well as supervised treatment and the encouragement of societal participation in tuberculosis control.

Most participants were male, and the mean age was 55.4 years, which was higher than that reported in other studies conducted in Minas Gerais.^(15,16) This is probably due to the profile of the population treated at the JKH. Age, gender, skin color, income, and level of education were not found to be associated with tuberculosis and MDR-TB in the present study.

Alcoholism, when evaluated separately, was associated with tuberculosis. Despite being a risk factor for tuberculosis (OR = 3.70; 95% CI: 1.33-10.98), alcoholism

Table 1. Descriptive analysis of the sociodemographic, behavioral, clinical, and radiological characteristics of the patients in the study (N = 251).

Characteristic	n	%
Age, years		
18-40	41	16.3
≥ 41	210	83.7
Gender		
Male	176	70.1
Female	75	29.9
Skin color		
White	45	22.3
Non-White	157	77.7
Income		
≥ R\$ 1,875.00	48	21.6
< R\$ 1,875.00	174	78.4
Years of schooling		
< 9	76	31.0
≥ 9	169	67.0
Alcoholism		
Yes	59	24.1
No	185	75.8
Smoking status		
Current or former smoker	161	74.2
Never smoker	56	25.8
Marital status		
Single/separated/widowed	112	50.9
Married/living as married	116	49.1
Homeless		
No	238	94.8
Yes	13	5.2
Treatment prescribed for tuberculosis		
Yes	95	38.6
No	151	61.4
Change of treatment due to resistance		
Yes	12	12.6
No	83	87.4
Previous treatment for tuberculosis		
Yes	88	39.1
No	137	60.9
Presence of comorbidities		
Yes	183	74.1
No	64	25.9
Type 2 diabetes mellitus		
Yes	25	10.0
No	223	90.0
HIV/AIDS		
Yes	11	4.4
No	240	95.6
Pulmonary cavitation		
Yes	43	28.3
No	109	71.7
Chest X-ray pattern		
Suggestive/typical	89	54.9
Atypical	73	45.1
Fever		
Yes	95	40.2
No	141	59.7
Cough		
Yes	220	88.7
No	28	11.3
Hemoptysis		
Yes	69	29.6
No	164	70.4
Dyspnea		
Yes	160	65.6
No	84	34.4
Expectoration		
Yes	187	76.3
No	58	23.7

R\$: Brazilian reals.

Table 2. Comparison between patients with a confirmed diagnosis of tuberculosis and those with suspected tuberculosis but without a confirmed diagnosis, by risk factors.

Risk factor	Tuberculosis ^{a,b}		OR (95% CI)	p
	Confirmed (n = 95)	Suspected (n = 156)		
Age, years				
18-40	14 (14.8)	24 (15.9)	0.91 (0.44-1.87)	0.806
≥ 41	81 (85.2)	127 (84.1)		
Gender				
Male	24 (25.3)	50 (33.1)	0.68 (0.38-1.21)	0.191
Female	71 (74.7)	101 (66.9)		
Skin color				
White	16 (22.2)	27 (21.3)	1.05 (0.52-2.13)	0.874
Non-White	56 (77.8)	100 (78.7)		
Income				
≥ R\$ 1,875.00	64 (78.1)	106 (78.5)	0.97 (0.50-1.89)	0.935
< R\$ 1,875.00	18 (21.9)	29 (21.5)		
Years of schooling				
< 9	64 (69.6)	103 (69.1)	1.02 (0.58-1.79)	0.942
≥ 9	28 (30.4)	46 (30.9)		
Alcoholism				
Yes	60 (64.5)	121 (82.3)	2.55 (1.40-4.66)	0.001
No	33 (35.5)	26 (17.7)		
Smoking status				
Smoker or former smoker	32 (35.6)	45 (35.1)	0.93 (0.50-1.73)	0.833
Never smoker	58 (64.4)	81 (64.3)		
Marital status				
Single/separated/widowed	45 (51.7)	70 (51.1)	1.02(0.59-1.75)	0.926
Married/living as married	42 (48.3)	67 (48.9)		
Homeless				
No	87 (91.6)	146 (96.7)	0.37 (0.11-1.17)	0.081
Yes	8 (8.4)	5 (3.3)		
Dyspnea				
No	41 (45.1)	43 (28.7)	2.04 (1.18-3.51)	0.009
Yes	50 (54.9)	107 (71.3)		
Fever				
Yes	44 (50.0)	94 (64.8)	0.54 (0.31-0.93)	0.025
No	44 (50.0)	51 (35.2)		
Cough				
Yes	13 (14.0)	15 (9.9)	1.47 (0.66-3.25)	0.335
No	80 (86.0)	136 (90.1)		
Hemoptysis				
Yes	59 (72.0)	102 (68.9)	1.15 (0.63-2.09)	0.630
No	23 (28.0)	46 (31.1)		
Previous treatment for tuberculosis				
Yes	58 (61.7)	78 (60.9)	1.03 (0.59-1.78)	0.908
No	36 (38.3)	50 (39.1)		
Presence of comorbidities				
Yes	32 (33.7)	31 (21.0)	0.52 (0.29-0.93)	0.027
No	63 (66.3)	117 (79.0)		
Type 2 diabetes mellitus				
Yes	87 (91.6)	131 (88.5)	0.70 (0.29-1.71)	0.442
No	8 (8.4)	17 (11.5)		
HIV/AIDS				
No	94 (99.0)	141 (93.4)	0.15(0.01-1.19)	0.054
Yes	1 (1.0)	10 (6.6)		
COPD				
No	90 (94.7)	118 (79.7)	0.22 (0.08-0.60)	0.001
Yes	5 (5.3)	30 (20.3)		
Cavitation pulmonary				
Yes	30 (49.2)	76 (86.4)	6.54 (2.97-14.40)	< 0.001
No	31 (50.8)	12 (13.6)		
Chest X-ray pattern				
Suggestive/typical	9 (13.4)	62 (67.4)	13.31 (5.82-30.43)	< 0.001
Atypical	58 (86.6)	30 (32.6)		

R\$: Brazilian reals. ^aValues expressed in n (%). ^bMissing data in some cases.

Table 3. Multivariate analysis of factors associated with tuberculosis.

Factor	OR	p	95% CI
Alcoholism	3.70	0.012	1.33-10.98
Presence of comorbidities	0.24	0.004	0.09-0.64
Pulmonary cavitation	2.88	0.032	1.09-7.62
Chest X-ray pattern	7.43	< 0.001	2.82-19.58

Table 4. Factors associated with multidrug-resistant tuberculosis using univariate analysis.

Factors	Groups ^{a,b}		ORs	p
	DS-TB (n = 84)	MDR-TB (n = 11)		
Skin color				
White	15 (24.2)	1 (10.0)	2.87 (0.33-24.56)	0.439
Non-White	47 (75.8)	9 (90.0)		
Income				
≥ R\$ 1,875.00	54 (76.1)	10 (90.9)	0.31 (0.03-2.66)	0.441
< R\$ 1,875.00	17 (23.9)	1 (9.1)		
Years of schooling				
< 9	57 (71.2)	7 (58.3)	1.77 (0.50-6.15)	0.501
≥ 9	23 (28.7)	5 (41.7)		
Alcoholism				
Yes	51 (63.0)	9 (75.0)	0.56 (0.14-2.25)	0.528
No	30 (37.0)	3 (25.0)		
Smoking status				
Smoker or former smoker	58 (73.4)	8 (72.7)	1.03 (0.25-4.27)	1.000
Never smoker	21 (26.6)	3 (27.2)		
Homeless				
No	75(90.4)	12(13.8)	Undefined	0.590
Yes	8(9.6)	0 (0.0)		
Previous treatment for tuberculosis				
Yes	55 (67.1)	3 (25.0)	6.11 (1.52-24.42)	0.008
No	27 (32.9)	9 (75.0)		
Presence of comorbidities				
Yes	28 (33.7)	4 (33.3)	1.01 (0.28-3.67)	1.000
No	55 (66.3)	8 (66.7)		
Type 2 diabetes mellitus				
Yes	76 (91.6)	11 (91.7)	0.98 (0.11-8.80)	1.000
No	7 (8.4)	1 (8.3)		
HIV/AIDS				
Yes	82 (98.9)	12 (100)	Undefined	1.000
No	1 (1.2)	0		
Pulmonary cavitation				
Yes	29 (55.8)	1 (11.1)	10.08 (1.17-86.57)	0.026
No	23 (44.2)	8 (88.9)		
Chest X-ray pattern				
Suggestive/typical	9 (15.8)	0 (0.0)	Undefined	0.335
Atypical	48 (84.2)	10 (100.0)		

DS-TB: drug-susceptible TB; and MDR-TB: multidrug-resistant tuberculosis. ^aValues expressed in n (%). ^bIncomplete data in some cases.

was not associated with MDR-TB, unlike what has been reported in other studies.^(17,18) The in vivo and in vitro association between alcohol consumption and tuberculosis has long been known. Alcohol use significantly alters the immune response, thereby increasing susceptibility to tuberculosis.⁽⁵⁾ In addition, alcohol abuse influences not only the incidence of tuberculosis but also its clinical course and outcomes, with higher rates of treatment noncompliance and relapse due to precarious living

conditions and the increased risk of hepatotoxicity.⁽⁵⁾ This association underscores the need to try to achieve the goals proposed by the WHO described in Pillar 1 (prevention and integrated patient-centered care) of the National Plan, likewise supported by the Brazilian National Ministry of Health, to eliminate tuberculosis as a health problem.^(1,3)

Although we found no association between smoking and tuberculosis, some authors, through observational

analyses, have shown an unfavorable association between smoking and the global tuberculosis epidemic, as well as having pointed out the psychosocial aspects of smoking that are related to lower treatment compliance rates.⁽⁵⁾

Despite the low socioeconomic conditions in Belo Horizonte, homelessness was not associated with tuberculosis, although such an association has been reported by other authors.⁽⁶⁾ That can probably be explained by the small number of homeless individuals among the patients selected in the present study.

The classic symptomatology of pulmonary tuberculosis is characterized by cough, sputum (sometimes bloody), chest pain, weakness, weight loss, fever, and night sweats.⁽¹⁹⁾ Of those symptoms, only fever and dyspnea were associated with tuberculosis. For the other three symptoms (sputum, cough, and hemoptysis) there was no association with tuberculosis, probably because they are also associated with other diseases found in patients treated at the JKH, which, in addition to being a tertiary referral hospital for tuberculosis, is a comprehensive regional general hospital. Therefore, those data constitute not only a warning but also an indication of the diagnostic confusion and difficulties that occur when differentiating tuberculosis from other important diseases.

The presence of comorbidities (alcoholism, DM, pulmonary silicosis, chronic kidney disease, HIV/AIDS, etc.) is associated with tuberculosis. In fact, some studies^(5,20) show that tuberculosis is approximately three times more prevalent in patients with DM. However, comorbidities, except for alcoholism when analyzed separately, were not found to be risk factors for tuberculosis in our sample. That may be related to the high prevalence of comorbidities among our patients, which acts as a protective factor. The JKH treats patients with highly complex diseases, which shows the need for patient follow-up with a multidisciplinary team, because comorbidities may increase costs, alter the course of the disease, and modify its outcome.⁽¹⁾

In 2016, the WHO estimated that 10% of the 10.4 million patients with tuberculosis are also infected with HIV.⁽²⁾ In the present study, only 1 patient presented tuberculosis-HIV coinfection, possibly because coinfecting patients are typically referred to the Minas Gerais State Referral Hospital for Infectious Diseases, located in the same city.

Atypical or typical chest X-ray findings presented a strong association in the final model (OR = 7.43; 95% CI: 2.82-19.58), as did the presence of pulmonary cavities (OR = 2.88; 95% CI: 1.09-7.62). That demonstrates that chest X-ray, which is still the most widely used imaging examination, is an important tool for diagnostic investigation and enables the differentiation of images suggestive of tuberculosis,^(15,19) thereby underscoring the relevance of radiological data.

In recent years, the Brazilian National Ministry of Health has used the targets proposed by the WHO in tuberculosis control: diagnose at least 70% of the

expected cases; properly treat 100% of the diagnosed cases; cure at least 85% of those cases; and maintain treatment noncompliance at levels considered acceptable (below 5%). Among the patients who were started on tuberculosis treatment in the present study, the cure rate was 74.7%, below the level recommended by the WHO and close to the 67.2% and 76.2% reported for the state of Minas Gerais in 2013⁽¹⁵⁾ and 2014,⁽¹⁶⁾ respectively. In addition, the treatment noncompliance rate was 11.6%, close to the 9.0% and 11.5% reported for Brazil as a whole in 2013 and 2014, respectively, and more than double the target recommended by the WHO.⁽¹⁾

In recent years, there has been a reduction in tuberculosis mortality in Brazil.⁽³⁾ Although not the object of the present study, the outcomes were analyzed due to the importance of those data. There were 3 deaths due to tuberculosis in our study, which demonstrates the need for continued efforts to improve the quality of care given to people with the disease. The rates of cure and treatment noncompliance among the patients with MDR-TB were comparable to those reported by the Brazilian National Ministry of Health in 2017 (66.5% and 16.7%, respectively).⁽³⁾

In the univariate analysis, an association between pulmonary cavitation and the occurrence of MDR-TB was observed, because primary and acquired resistance are phenomena that are dependent on bacillary load and active multiplication, which are higher in the presence of cavitory disease.^(17,18) In addition, MDR-TB was associated with previous treatment for tuberculosis, as has previously been reported.^(18,21) That finding is of concern, because there were 13,347 cases of retreatment in the country, corresponding to 16.1% of all cases reported, during the study period.⁽¹⁾ Those data underscore the importance of giving special attention to patients who have previously been treated for disease, because they are at a higher risk of being infected with a drug-resistant strain of *M. tuberculosis*.

One of the main limitations of our study was that the small number of MDR-TB cases included limited the statistical power, precluding a multivariate analysis of resistance exposure factors. Another limitation was the fact that the study was conducted at only one center.

In conclusion, alcoholism, a chest X-ray with a pattern suggestive of tuberculosis, the presence of comorbidities, and the presence of pulmonary cavitations were factors associated with tuberculosis. MDR-TB was associated with previous treatment for tuberculosis and cavitation. Despite the significant progress made in the fight against tuberculosis, there is a need for coordinated actions that include social protection measures and patient support.

ACKNOWLEDGMENTS

We thank Prof. Cristiane Menezes de Padua, of the Social Pharmacy Department of the UFMG School of Pharmacology, for her assistance. We are also grateful to the Graduate Program in Health Sciences, Tropical

Medicine, and Infectology of the UFMG School of Medicine, the Brazilian Office for the Advancement of Higher Education, the Brazilian National Council for Scientific and Technological Development, the Foundation for the

Support of Research in the State of Minas Gerais, the UFMG Dean's Office for Research, the Brazilian Tuberculosis Research Network, and the Júlia Kubitschek Hospital of the Hospital Foundation of the state of Minas Gerais.

REFERENCES

1. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Implantação do plano nacional pelo fim da tuberculose como problema de saúde pública no Brasil: primeiros passos rumo ao alcance das metas. Boletim Epidemiológico. 2018;49(11). [Adobe Acrobat document, 18p.].
2. World Health Organization [homepage on the Internet]. Geneva: World Health Organization [cited 2018 Dec 1]. Global tuberculosis report 2018. [Adobe Acrobat document, 265p.]. Available from: http://www.who.int/tb/publications/global_report/gtbr2017_main_text.pdf
3. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Indicadores prioritários para o monitoramento do Plano Nacional pelo fim da tuberculose como problema de saúde pública no Brasil. Boletim Epidemiológico. 2017;48(8). [Adobe Acrobat document, 11p.].
4. Hermosilla S, You P, Aifah A, Abildayev T, Akilzhanova A, Kozhamkulov U, et al. Identifying risk factors associated with smear positivity of pulmonary tuberculosis in Kazakhstan. PLoS One. 2017;12(3):e0172942. <https://doi.org/10.1371/journal.pone.0172942>
5. Silva DR, Muñoz-Torrico M, Duarte R, Galvão T, Bonini EH, Arbex FF, et al. Risk factors for tuberculosis: diabetes, smoking, alcohol use, and the use of other drugs. J Bras Pneumol. 2018;44(2):145-152. <https://doi.org/10.1590/s1806-37562017000000443>
6. Valenzuela-Jiménez H, Manrique-Hernández EF, Idrovo AJ. Association of tuberculosis with multimorbidity and social networks. J Bras Pneumol. 2017;4(1):51-53. <https://doi.org/10.1590/s1806-37562016000000075>
7. Muñoz-Torrico M, Caminero Luna J, Migliori GB, D'Ambrosio L, Carrillo-Alduenda JL, Villareal-Velarde H, et al. Comparison of bacteriological conversion and treatment outcomes among MDR-TB patients with and without diabetes in Mexico: Preliminary data. Rev Port Pneumol (2006). 2017;23(1):27-30. <https://doi.org/10.1016/j.rppnen.2016.11.009>
8. Bates MN, Khalakdina A, Pai M, Chang L, Lessa F, Smith KR. The risk of tuberculosis from exposure to tobacco smoke: a systematic review and meta-analysis. Arch Intern Med. 2007;167(4):335-42. <https://doi.org/10.1001/archinte.167.4.335>
9. Lin HH, Ezzati M, Murray M. Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis. PLoS Med. 2007;4(1):e20. <https://doi.org/10.1371/journal.pmed.0040020>
10. Molina PE, Happel KI, Zhang P, Kolls JK, Nelson S. Focus on: Alcohol and the immune system. Alcohol Res Health. 2010;33(1-2):97-108.
11. Kritski A, Andrade KB, Galliez RM, Maciel ELM, Cordeiro-Santos M, Miranda SS, et al. Tuberculosis: renewed challenge in Brazil. Rev Soc Bras Med Trop. 2018;51(1):2-6. <https://doi.org/10.1590/0037-8682-0349-2017>
12. Masur J, Monteiro MG. Validation of the "CAGE" alcoholism screening test in a Brazilian psychiatric inpatient hospital setting. Braz J Med Biol Res. 1983;16(3):215-8.
13. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Programa Nacional de Controle da tuberculose. Manual de Recomendações para o controle da tuberculose no Brasil. 2nd ed. Brasília: Ministério da Saúde; 2019.
14. O'Brien RM. A Caution Regarding Rules of Thumb for Variance Inflation Factors. Qual Quant. 2007;41:673-690. <https://doi.org/10.1007/s11135-006-9018-6>
15. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Detectar, tratar e curar: desafios e estratégias Brasileiras frente à tuberculose. Boletim Epidemiológico. 2015;46(9). [Adobe Acrobat document, 18p.].
16. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Perspectivas brasileiras para o fim da tuberculose como problema de saúde pública. Boletim Epidemiológico. 2016;47(13). [Adobe Acrobat document, 15p.].
17. Skrahina A, Hurevich H, Zalatskaya A, Sahalchyk E, Astrauko A, Hoffner S, et al. Multidrug-resistant tuberculosis in Belarus: the size of the problem and associated risk factors. Bull World Heal Org. 2013;91(1):36-45. <https://doi.org/10.2471/BLT.12.104588>
18. Barroso EC, Mota RM, Santos RO, Barroso JB, Rodrigues JL. Risk factors for acquired multidrug-resistant tuberculosis. J Pneumol. 2009;29(2):89-97. <https://doi.org/10.1590/S0102-35862003000200008>
19. Brasil. Ministério da Saúde. Boletim Brasileiro de Avaliação de Tecnologias em Saúde: Xpert MTB/RIF no diagnóstico da tuberculose pulmonar. 2011;16(4). [Adobe Acrobat document, 18p.].
20. Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med. 2008;5(7):e152. <https://doi.org/10.1371/journal.pmed.0050152>
21. Feliciano CS, Nascimento MM, Anselmo LM, Pocente RH, Bellissimo-Rodrigues F, Bollela VR. Role of a Genotype MTBDRplus line probe assay in early detection of multidrug-resistant tuberculosis at a Brazilian Reference Center. Braz J Med Biol Res. 2015;48(8):759-764. <https://doi.org/10.1590/1414-431x20154458>