Original Article

Factors associated with death from tuberculosis and treatment default in a General Hospital in the city of Rio de Janeiro, 2007 to 2014

Fatores associados ao óbito e ao abandono do tratamento da tuberculose em um hospital geral do município do Rio de Janeiro, 2007 a 2014

Factores asociados con la muerte y el abandono del tratamiento de la tuberculosis en un hospital general del municipio de Río de Janeiro, 2007 a 2014

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RESUMO

Justificativa e Objetivos: a tuberculose permanece como relevante problema de saúde pública e a cura dos casos diagnosticados é uma estratégia para redução da elevada morbimortalidade. O objetivo deste estudo é identificar fatores associados ao óbito por tuberculose e ao abandono do tratamento em pacientes diagnosticados no Hospital Federal dos Servidores do Estado (HFSE) de 2007 a 2014. **Métodos:** estudo observacional, analítico, de todos os 670 casos confirmados notificados neste período na base local do Sistema de Informação de Agravos de Notificação (SINAN), com encerramento registrado como cura (383), óbito por tuberculose (159) ou abandono do tratamento (128). Este sistema é alimentado a partir de ficha de investigação epidemiológica padronizada, contendo variáveis sociodemográficas e clínicas. A análise estatística envolveu variáveis disponíveis no SINAN e considerou desfecho desfavorável

aquele composto por óbito ou abandono. Variáveis com razões de chances elevadas na análise bivariada e/ou importância clínica foram consideradas para inclusão em modelo multivariado de regressão logística. Como medida de associação para análise dos fatores associados a desfecho desfavorável *versus* cura, foram estimadas as razões de chance e seus intervalos de 95% de confiança. **Resultados:** foram identificados como fatores estatisticamente associados a chance aumentada do desfecho desfavorável idade ≥60 anos, raça/cor não branca, tratamento prévio para tuberculose ou situação de tratamento prévio desconhecida, resultado de anti-HIV positivo, forma pulmonar e sobretudo forma extrapulmonares grave. **Conclusão:** esses resultados reforçam a necessidade de investir em políticas que garantam o acesso e a adequada assistência aos pacientes, especialmente àqueles com condições que predispõem a não adesão ao tratamento e formas graves.

DESCRITORES: Tuberculose. Vigilância Epidemiológica. Resultado de Tratamento. Modelos Logísticos.

ABSTRACT

Background and Objectives: tuberculosis remains a relevant public health problem and the cure of diagnosed cases is a strategy to reduce high morbidity and mortality. The objective of our study is to identify factors associated with death due to tuberculosis and treatment default in patients diagnosed in the HFSE from 2007 to 2014. **Method:** we performed an observational, analytical study of all 670 confirmed cases reported in this period at the local SINAN reporting base, of which outcome was recorded as cure (383), death from tuberculosis (159) or treatment default (128). This system received information from a standardized epidemiological investigation sheet containing socio-demographic and clinical variables. Statistical analysis involved variables available in SINAN and considered as unfavorable outcome that consisting of death or treatment default. Variables with high odds ratios in the bivariate analysis and/or clinical relevance were considered for inclusion in a logistic regression model. As a measure of association for the analysis of factors associated with unfavorable outcome *versus* cure, odds ratios and their 95% confidence intervals were estimated. **Results:** the final model identified the following as statistically associated with an unfavorable outcome: age ≥60 years, non-white ethnicity/skin color, history of previous treatment for tuberculosis, or unknown history of previous treatment, positive anti-HIV test, pulmonary form of disease and presence of severe extrapulmonary forms. **Conclusion:** the results confirm the need to invest in policies that guarantee access and fair care to patients, especially those with conditions that predispose to treatment default and severe forms of the disease.

KEYWORDS: Tuberculosis. Epidemiological surveillance. Treatment outcome. Logistic Models.

RESUMEN

Justificación y objetivos: la tuberculosis permanece como relevante problema de salud pública y la cura de los casos diagnosticados es una estrategia para reducir la elevada morbimortalidad. El objetivo de este estudio es identificar factores asociados al fallecimiento por tuberculosis y al abandono del tratamiento en pacientes diagnosticados en el HFSE de 2007 a 2014. **Métodos:** em el presente estudio se analizaron todos los 670 casos confirmados notificados en este período en la base local del SINAN, con cierre registrado como cura (383), muerte por tuberculosis (159) o abandono del tratamiento (128). Este sistema es alimentado a partir de una ficha de investigación epidemiológica estandarizada, conteniendo variables sociodemográficas y clínicas. El análisis estadístico involucró variables disponibles en el SINAN y consideró desenlace desfavorable aquel compuesto por muerte o abandono. Las variables con razones de

posibilidades elevadas en el análisis bivariado y/o la importancia clínica se consideraron para su inclusión en el modelo de regresión logística. Como medida de asociación para el análisis de los factores asociados a desenlace desfavorable frente a la curación, se estimaron las razones de probabilidad y sus intervalos de confianza del 95%. **Resultados:** fueron identificados como factores estadísticamente asociados a un desenlace desfavorable edad ≥60 años, raza / color no blanco, tratamiento previo para tuberculosis o situación de tratamiento previo desconocido, resultado de anti-VIH positivo, forma pulmonar y sobre todo forma extrapulmonar grave. **Conclusiones:** los resultados refuerzan la necesidad de invertir en políticas que garanticen el acceso y la adecuada asistencia a los pacientes, especialmente a aquellos con condiciones que predisponen a la no adhesión al tratamiento ya formas graves.
DESCRITORES: Tuberculosis. Vigilancia Epidemiológica. Resultado del tratamento. Modelos Logísticos.

INTRODUCTION

Tuberculosis is an endemic infectious disease in several countries. According to data from the World Health Organization (WHO), it is estimated that 10.4 million individuals had the disease in 2016, and Brazil was the 20th country in the world with the highest disease burden. In that year, tuberculosis was the 9th leading cause of death worldwide, with more than 1.6 million deaths.[1]

In Brazil, 67,599 new cases were diagnosed in 2015: 5.8% abandoned treatment and 2.8% died. Considering that 27,091 cases still remain without closure information, this scenario may be even more disturbing.

The Southeast region accounted for 46.8% of the cases, of which 10,236 were diagnosed only in the state of Rio de Janeiro (RJ). The incidence rate in the state of Rio de Janeiro was 61.7 cases / 100,000 inhabitants (the 2nd highest in the country) and in the city of Rio de Janeiro, 77.6 cases / 100,000, the 6th highest in the state.[2]

The cure of patients diagnosed with tuberculosis is one of the main strategies to reduce this situation of high morbidity and mortality. The WHO recommends that the goal of cure be ≥85% and that of treatment default be <5.0%.[1,4]

For these goals to be achieved, interventions must be carried out aiming not only at fighting specific risks in the public health field, but also at reducing poverty and promoting social security, education and community autonomy.[1,3,4]

Several studies have associated the occurrence of tuberculosis with unfavorable socioeconomic conditions.[3,5-7] Treatment default has been associated with factors related to medication, to the patient and those related to health care services.[5,8-11] The consequences of non-adherence to treatment are varied: reduction in the cure rate; death from tuberculosis; development of more severe clinical forms and multidrug resistance.

Coinfection with the human immunodeficiency virus (HIV) is another relevant factor associated with an unfavorable outcome.[5,7,10,12]

Considering the relevance of tuberculosis as a public health problem and the inclusion of Hospital Federal dos Servidores do Estado (HFSE) in the Brazilian Unified Health System (SUS), this study aimed to analyze the factors associated with an unfavorable outcome of tuberculosis treatment (treatment default or death from tuberculosis) in patients notified at the unit and diagnosed from 2007 to 2014.

METHODS

This was an observational, analytical study developed at the HFSE, which analyzed tuberculosis notifications registered at the local Disease Notification Information System (SINAN-NET), from 2007 to 2014. HFSE is a general teaching hospital, a referral one for infectious-parasitic diseases and for epidemiological surveillance in the hospital setting in the state of Rio de Janeiro, Brazil. The hospital is located at the Port area of the city of Rio de Janeiro, in the Saúde neighborhood, near Morro da Providência, areas known for the high incidence rates of the disease.[3]

After performing the database duplicity, consistency and completeness analyses, a total of 1,642 confirmed cases of tuberculosis were identified in the HFSE that were notified in the period, of which 593 cases had no closure information (36.1%). As strategies for information retrieval, the following were reviewed: copies of the 593 files of epidemiological investigation filed locally; 201 medical records; and an active search for closure information was carried out in several sectors of the hospital. A total of 361 closure reports were recovered, with records and database being updated. The closure situation in the updated bank was as follows: cure - 383 cases (23.3%); treatment default -128 (7.8%); death from tuberculosis: 159 (9.7%); death from other causes: 85 (5.2%); transfer to another health unit - 488 (29.7%); change in diagnosis - 93 (5.7%); multidrug resistance: 74 (5.7%); ignored - 232 (14.1%). There was no record of treatment failure.

For the purposes of this study, the non-probabilistic sample involved the selection of all 670 cases of tuberculosis, diagnosed and notified from 2007 to 2014, confirmed by laboratory test or clinically, and containing closure information recorded as cure, treatment default or death from tuberculosis.

The outcomes of interest considered in the study were: death from tuberculosis or treatment default, considered as composite unfavorable outcome; and cure. The cases classified as multidrug resistance were referred from other units with a pre-established resistance diagnosis; thus, they were excluded from this study. Also excluded were cases

recorded as deaths from other causes, because they were not directly associated with the disease; and unit transfers.

The initial descriptive analysis was performed with the Epi Info 2000 software. The analyzed variables were all categorical, except age: gender, ethnicity/skin color, place of residence, schooling, age, type of treatment, clinical form, comorbidities, laboratory tests (smear results, culture for *Mycobacterium tuberculosis*, histopathological analysis, anti-HIV test, chest x-ray), treatment (tuberculostatic drug treatment) and closure (cure, death from tuberculosis, treatment default). The categories were those standardized by SINAN[4] and are detailed in Table 1 of the results. After the initial descriptive analysis, some categories were regrouped, such as ethnicity/skin color, as white vs. non-white. For the study of the association between the independent variables and the unfavorable tuberculosis treatment outcome, a multivariate analysis was performed using logistic regression. This analysis included the variables that showed an association with the unfavorable outcome in the previous bivariate analysis, compared with the cure outcome, with $p < 0.10$ (Chi-square test), and those considered of clinical importance. The logistic regression model was developed using the SPSS program, v. 18; a *p* value <0.05 was considered statistically significant. The Odds Ratios (OR) and their respective 95% confidence intervals (95% CI) were estimated.

The study was considered approved by the Ethics and Research Committee of the HFSE, called "Epidemiological surveillance and clinical-epidemiological profile of the compulsory notification cases treated at Hospital Federal dos Servidores do Estado since the implementation of the Epidemiology Service (CEP-HFSE 000.534 of 07/14/2014).

RESULTS

A total of 670 cases were included, of which 383 had a cure outcome, 128 treatment default, and 159 died from tuberculosis. Table 1 shows the sample's general profile: 52.7% were males; 112 (16.7%) were 19 years of age or younger, of which 48 were children younger than 13 years (of which 24 were 1 year old or younger) and 64 were adolescents; 12.7% were 60 years or older.

The percentage of ignored schooling level was high (27.2%); excluding the categories of ignored and does not apply data (preschoolers or infants), the level of schooling of 49.9% of the cases was at most unfinished elementary school. Regarding ethnicity/skin color, 56% were black or brown; in 7.6% of the cases, it was ignored. Regarding the place of residence, 70.6% lived in the municipality of Rio de Janeiro and 26.0% in the municipalities of Baixada Fluminense.

As for the type of treatment, 74.2% were new cases. Regarding the clinical form, 50.8% had some extrapulmonary form (isolated or associated with the pulmonary form). As SINAN allows filling out two fields to specify the type of extrapulmonary form, the authors identified 385 extrapulmonary forms described among the cases, with the most frequent ones being ganglionary (29.1%), pleural (20.5%), meningoencephalic (11.9%), miliary (10.6%) and disseminated TB (5.5%). The patient with more than two extrapulmonary forms had its clinical form considered as the disseminated type.

A chest x-ray was not performed in 13.1% of cases or there was no information about it; in most cases, the information regarding the radiological pattern was described as suspected of tuberculosis.

Anti-HIV serology was not performed in 29.0% of the cases and was positive in 48.1%. In addition to alcoholism (8.1%), illicit drug use (3.0%), diabetes (5.1%) and mental illness (1.5%), other comorbidities were reported for 215 cases (32.1%), especially: rheumatic diseases - 39 (5.8%); arterial hypertension - 27 (4.0%); renal diseases - 23 (3.4%); pneumopathies - 14 (2.1%); cardiovascular disease - 12 (1.8%); hematological diseases - 12 (1.8%); neoplasms - 10 (1.5%), liver diseases - 8 (1.2%).

Laboratory confirmation was obtained in 66.3% of the cases; 231 cases (34.5%) had at least one positive smear test (any material); 386 (57.6%) had a positive culture for *Mycobacterium tuberculosis*; 89 (13.3%) had a histopathological test with suggestive/positive result for tuberculosis (35 with positive AFB and 54 with suggestive result for tuberculosis). Sputum smear microscopy was not performed in 289 (43.1%) cases. Considering only the 330 cases with the isolated pulmonary form, sputum smear microscopy was not performed in 104 (31.5%) cases; 133 (40.3%) had a positive result at the sputum smear microscopy. Overall, of the 439 cases in which the smear microscopy of sputum or other material was initially negative, confirmation by culture was possible in 42.1% of cases. Histopathological examination was performed in 151 cases (22.5%).

Table 1 - Profile of tuberculosis cases of with a known closure situation (cure, treatment default and death from tuberculosis), HFSE, RJ, Brazil, 2007 to 2014.

Variables	N (670)	%
Gender		
Female	317	47.3
Male	353	52.7
Age range		
≤ 19 years	112	16.7
20 to 29 years	109	16.3
30 to 39 years	154	23.0
40 to 49 years	111	16.6

50 to 59 years	99	14.8
≥ 60 years	85	12.7
Level of schooling		
Illiterate	8	1.2
Unfinished Elementary School	220	32.8
Finished Elementary School	108	16.1
Finished High School	87	13.0
Finished College/University	34	5.1
Does not apply	31	4.6
Unknown/No information	182	27.2
Ethnicity/skin color		
White	240	35.8
Black	177	26.4
Asian	4	0.6
Brown	198	29.6
Unknown	51	7.6
Type of treatment		
New case	497	74.2
Relapse	46	6.9
Previous default	50	7.5
Unknown	39	5.8
Transfer	38	5.7
Clinical form		
Pulmonary	330	49.3
Extrapulmonary	156	23.3
Pulmonary associated to extrapulmonary	184	27.5
Chest X-ray		
Suspected	488	72.8
Normal	81	12.1
Suggestive of another pathology	13	1.9
Not performed/No information	88	13.1
Alcoholism	54	8.1
Illicit drug use	20	3.0
Diabetes mellitus	34	5.1
Mental disease	10	1.5
Anti-HIV serology		
Positive	322	48.1
Negative	149	22.2
Ongoing	5	0.7
Not performed	194	29.0
Laboratory confirmation of tuberculosis		
Yes	444	66.3
No	226	33.7
Closure situation		
Cure	383	57.2
Treatment default	128	19.1
Death from tuberculosis	159	23.7

Treatment was initiated with RHZE (R: rifampicin; H: isoniazid; Z: pyrazinamide; and E: ethambutol) in 294 cases (43.9%); RHZ in 276 (41.2%); and other regimens were used in 57 (8.5%) cases. There were 28 cases of primary treatment default (4.2%) and 15 deaths from tuberculosis prior to the start of treatment (2.2%). In 7 of the 570 cases

(1.2%) that started the RHZ / RHZE regimen, it was necessary to definitively change treatment due to intolerance.

The overall profile of the 670 selected cases was similar to the total of 1,642 cases reported and diagnosed in the period regarding gender, age range, type of treatment and clinical form. However, the percentage of cases with positive anti-HIV serology was higher in the selected cases (48.1%) than in the total notified cases (35%).

Table 2 shows the results of the bivariate analysis for variables that showed a significant association ($p < 0.05$) with type of outcome: ethnicity / skin color, previous treatment, use of illicit drugs, alcoholism, chest X-ray, anti-HIV and clinic form / severity of the disease. Although the variables age range and level of schooling did not show a statistically significant difference in the bivariate analysis, heterogeneity was observed in outcome distribution and we chose to include them in the multivariate model. To study the association with the outcome of interest, the variable ethnicity/skin color was categorized as White *versus* Non-white, including in the latter category the 51 cases with missing data.

This decision was taken after the empirical confirmation that the analysis in the original subdivisions did not significantly modify the observed effect of a higher percentage of cure in favor of the White category; furthermore, the resulting bias would be a conservative one (the existence of White ethnicity/skin color cases among the ignored ones would tend to decrease the observed final effect).

Table 2 – Bivariate analysis of tuberculosis cases according to the closure situation (cure, treatment default or death from tuberculosis), HFSE, RJ, Brazil, 2007 to 2014.

Variables	Cure (n=383)		Default or death from tuberculosis (n=287)		(p-value)
	f	%	f	%	
Age range					**0.246**
≤ 19 years	72	64.3	40	35.7	
20 – 59 years	263	55.6	210	44.4	
≥ 60 years	48	56.5	37	43.5	
Level of Schooling					**0.098**
Illiterate	5	62.5	3	37.5	
Elementary School (finished or nor)	178	54.3	150	45.7	
Finished High School	55	63.2	32	36.8	
Finished College or University	26	76.5	8	23.5	

Unknown/Does not apply	119	55.9	94	44.1	
Ethnicity/skin color					<0.001
White	161	67.1	79	32.9	
Non-white [1]	222	51.6	208	48.4	
Previous treatment					<0.001
No (new case)	319	64.2	178	35.8	
Yes (relapse or previous default)	37	38.5	59	61.5	
Unknown/transfer	27	35.1	50	64.9	
Alcoholism					0.035
No [1]	360	58.4	256	41.6	
Yes	23	42.6	31	57.4	
Illicit drug use					0.001
No	379	58.3	271	41.7	
Yes	4	20.0	16	80.0	
Chest X-ray					0.003
Normal	60	74.1	21	25.9	
Suspected	276	56.6	212	43.4	
Suggestive of another pathology	6	46.2	7	53.8	
Not performed/unknown	41	46.6	47	53.4	
Anti-HIV					<0.001
Negative	109	73.2	40	26.8	
Positive	139	43.2	183	56.8	
Not performed	135	67.8	64	32.3	
Clinical forma /severity					<0.001
Isolated pulmonary	190	57.6	140	42.4	
Isolated non-severe extrapulmonary	98	74.8	33	25.2	
Pulmonary associated to non-severe extrapulmonary	59	56.2	46	43.8	
Severe extrapulmonary associated or not to pulmonary	36	34.6	68	65.4	

[1] **Includes cases with unknown information / no information.**

The variables that showed statistical significance in the bivariate analysis and those with clinical relevance were selected for the logistic regression model. The following remained in the studied final models: age, ethnicity / skin color, previous treatment, illicit drug use, anti-HIV test and clinical form / severity. The following types were considered severe extrapulmonary clinical forms: disseminated, miliary and meningoencephalic.

In the multivariate analysis, the isolated pulmonary form was initially considered as the reference category for the variable "clinical form / severity" (table 3).

It was observed that the non-severe isolated extrapulmonary form showed a lower chance of unfavorable outcome in relation to the isolated pulmonary form and there was no significant difference between the pulmonary form alone or associated with non-severe extrapulmonary form. Thus, in the final model, we chose to consider the non-

severe isolated extrapulmonary form as the reference category for that variable, without any important changes in the fit of the model.

The final logistic regression model shown in table 4, with 69.6% of agreement, showed the following categories with a statistically significant association with an unfavorable treatment outcome for tuberculosis: age ≥ 60 years (OR = 2.0, 95% CI: 1.1-3.9; reference: age up to 19 years); ethnicity / non-white skin color (OR = 1.6; 95% CI: 1.1-2.4; reference: ethnicity / white skin color); history of previous treatment, including relapse and previous default (OR = 2.0, 95% CI: 1.2-3.3, reference: new case); positive anti-HIV test (OR = 2.9, 95% CI: 1.8-4.5, reference: negative anti-HIV test); (OR = 1.9, 95% CI: 1.2-3.2, reference: non-severe, isolated extrapulmonary form); and especially presence of the severe extrapulmonary form, associated or not with the pulmonary form (OR = 4.3, 95% CI: 2.3-7.9; reference: non-severe, isolated extrapulmonary form). The fit of the model was evaluated by the Hosmer-Lemeshow test, with a satisfactory result (13.03; p = 0.11). The selection of the reference category and the definition of the categories analyzed for each variable took into account intermediate analyses that did not find any significant associations for other subsets.

Table 3 – Multivariate analysis of the factors associated with the unfavorable outcome of tuberculosis treatment (treatment default or death from tuberculosis) in 670 patients diagnosed at HFSE, RJ, Brazil, from 2007 to 2014 - model 1.

Variable	Parameter	Standard Error	Pr>χ_2 P	OR (95%CI)
Intercept	-1.698	0.313	0.000	
Age range (reference: ≤ 19 years)				
20 to 59 years	0.231	0.244	0.344	1.3 (0.8-2.0)
≥ 60 years	0.713	0.328	0.029	2.0 (1.1-3.9)
Ethnicity/skin color (reference: White)				
Non-white	0.503	0.185	0.006	1.7 (1.2-2.4)
Previous treatment (reference: new case)				
Yes (relapse or previous default)	0.679	0.253	0.007	2.0 (1.2-3.2)
Unknown /transfer	1.271	0.279	0.000	3.6 (2.1-6.2)
Illicit drug use (reference: No)				
Yes	1.138	0.604	0.060	3.1(1.0 a 10.2)
HIV (reference: negative HIV)				
Positive	1.054	0.235	0.000	2.9 (1.8-4.6)
Not performed	0.132	0.260	0.611	1.1 (0.7-1.9)
Clinical form/severity (reference: isolated pulmonary)				
Non-severe isolated extrapulmonary	-0.704	0.246	0.004	0.5 (0.3-0.8)
Pulmonary associated to non-severe extrapulmonary	-0.080	0.250	0.749	0.9 (0.6-1.5)
Severe extrapulmonary, associated or not to pulmonary	0.752	0.257	0.003	2.1 (1.3-3.5)
Fit of the model	Concordance=69.6% ĉ (Hosmer-Lemeshow) = 12.824 (8 GL; p=0,118)			

Table 4 - Multivariate analysis of the factors associated with the unfavorable outcome of tuberculosis treatment (treatment default or death from tuberculosis) in 670 patients diagnosed at HFSE, RJ, Brazil, from 2007 to 2014 - final model.

Variable	Parameter	Standard Error	Pr>χ2 P	OR (95%CI)
Intercept	-2.403	0.367	0.000	-
Age range (reference: ≤ 19 years)				
20 to 59 years	0.232	0.244	0.342	1.3 (0.8-2.0)
≥ 60 years	0.717	0.327	0.028	2.0 (1.1-3.9)
Ethnicity/skin color (reference: White)				
Non-white	0.498	0.184	0.007	1.6 (1.1-2.4)
Previous treatment (reference: new case)				
Yes (relapse or previous default)	0.682	0.253	0.007	2.0 (1.2-3.3)
Unknown /transfer	1.275	0.279	0.000	3.6 (2.1-6.2)
Illicit drug use (reference: no)				
Yes	1.135	0.604	0.060	3.1 (1.0-10.2)
HIV (reference: negative HIV)				
Positive	1.053	0.235	0.000	2.9 (1.8-4.5)
Not performed	0.143	0.258	0.580	1.2 (0.7-1.9)
Clinical form/severity (reference: non-severe isolated extrapulmonary)				
Pulmonary associated or not to non-severe extrapulmonary	0.684	0.238	0.004	1.9 (1.2-3.2)
Severe extrapulmonary associated or not to pulmonary	1.458	0.310	0.000	4.3 (2.3-7.9)
Fit of the model	Concordance=69.6%			
	ĉ (Hosmer-Lemeshow) = 13.032 (8 GL; p=0.111)			

DISCUSSION

Treatment default constitutes a limitation for the control and cure of the disease, contributes to the maintenance of transmission, thus increasing the cost and time of treatment. A study published by the Ministry of Health identified a positive association between default rates (new pulmonary cases) and tuberculosis mortality coefficient in the period from 2001 to 2014: for every 1% increase in treatment default, an increase of 4% was observed in that mortality coefficient.[12] This study described for Brazil a default rate of 11% of new pulmonary cases in 2015; in the State of Rio de Janeiro it was 13%, the highest in the Southeast region. The goal recommended by the Ministry of Health is a default rate <5%.[4,12]

The percentage of treatment default (7.8%) and death from tuberculosis (9.7%) found in the cohort of 1,642 notified cases in the HFSE, which originated the sample of this study is high, partly attributable to the fact that HFSE is a referral hospital for cases with comorbidities, especially HIV coinfection, and severe clinical forms.

The prevalence of the male gender, non-white ethnicity/skin color, young adults and with low level of schooling is reported in the literature.[3,8,10,13,14] However, our percentage of female gender is higher than that reported by other authors, a fact that may

be related to the presence of a high-risk maternity ward, which is a reference for HIV-positive pregnant women.[10,13,15]

The predominance of individuals at the economically active age group and with low level of schooling corroborates the results of other studies. [3,8,10,13,14] The low level of schooling reflects a group of unfavorable socioeconomic determinants, which may increase vulnerability to tuberculosis and contribute to the increase in its incidence.[3]

A study carried out with data from the National Household Sample Survey (PNAD) of 2003 found that the black ethnicity/skin color had twice the chance of becoming infected with tuberculosis than whites.[16]

Regarding the place of residence, 70.6% were from the city of Rio de Janeiro, the largest municipality in the state and where the hospital is located, followed by 26.0% from Baixada Fluminense. This is justified, since the HFSE is a tertiary referral hospital, of easy access to populations living in other municipalities.

The predominance of new cases and pulmonary form is in agreement with other studies.[3,13] However, the proportion of 50.8% of cases with some type of extrapulmonary form is higher in the present study, reflecting the profile of HFSE care. In this hospital, a case diagnosed with the isolated pulmonary form and no comorbidities will be referred to the basic health unit and the local closure will be patient transfer.

As for the chest X-ray, 13.1% of the cases did not undergo the examination. Radiography is a diagnostic method of utmost importance in the investigation of tuberculosis, and it is recommended for all patients with clinical suspicion of pulmonary tuberculosis. A high percentage (16.4%) of not performed / unknown test is reported by other authors.[13]

Laboratory confirmation was obtained in 66.3% of the cases and 33.7% started empirical treatment. The percentage of 57.6% of confirmation through culture in the HFSE is higher than that reported by other authors (20.2%).[13] These authors also reported 50% of positive sputum smear microscopy and 24.2% of non-performed tests, but its percentage of isolated pulmonary form is 85.3%, quite higher than ours. Sputum smear microscopy can detect 60% to 80% of cases of pulmonary tuberculosis, which is important from the epidemiological point of view, since smear-positive cases are responsible for the maintenance of the transmission chain.[4,12] In 2012, sputum smear microscopy and culture were performed in 77.4% and 13.1% of the cases of pulmonary tuberculosis reported in the state of Rio de Janeiro.[17]

The percentage of tuberculosis-HIV coinfection in this study is high, since the unit is a reference for HIV patients; 48.1% were HIV-positive and 29.0% had not performed

anti-HIV serology. In 2015, the percentage of new tuberculosis cases that were submitted to HIV testing was 68.9% for Brazil and 65.8% for the state of Rio de Janeiro.[12] The results of the HIV testing among new cases of tuberculosis disclosed 9.7% of people with HIV-TB coinfection in Brazil. The Ministry of Health recommends that the test for the diagnosis of HIV be offered as soon as possible to every individual diagnosed with tuberculosis, regardless of bacteriological confirmation. [4,11,12]

Tuberculosis / HIV coinfection increases the risk of death in relation to HIV and tuberculosis infection alone; HIV-infected patients have a higher risk of latent tuberculosis reactivation, contributing to the continuity and dissemination of the disease, and the development of multidrug-resistant forms.[10] The occurrence of severe forms increases among patients with AIDS, especially the severely immunocompromised ones. The knowledge of the percentage of tuberculosis/HIV coinfection is crucial for the planning of appropriate TB control actions for these patients.[10,12,18]

As for alcohol consumption, 8.1% of the selected patients declared they consumed it. Alcohol consumption is a factor that can aggravate the disease and impair the therapeutic regimen, increasing the chance of treatment default.[5,7]

As for diabetes, reported in 5.4% of the cases, it has been described as a risk factor for death from tuberculosis, and is also related to the chance of relapse and of developing multidrug-resistant tuberculosis.[19]

Social and demographic factors exert great influence on treatment default.[15] The association between default and lower level of schooling has been described by several authors.[8,15,20] Significant associations have been described with higher chances of default due to alcoholism, low level of schooling, unemployment and rehospitalization post-treatment default.[5,7,12,15]

Individuals aged 60 years or older were more likely to have an unfavorable outcome for tuberculosis treatment. A study that analyzed the multiple causes of death of a cohort of patients with tuberculosis found a higher frequency of deaths among the elderly.[21] Other authors have also found an association between older age groups and death; however, regarding the default outcome, an association has been described with the age range of young adults, perhaps related to social factors, alcoholism and drugs.[8,9,20,22,23]

The ethnicity / skin color reported as non-white showed a 1.6-fold higher chance of having an unfavorable outcome when compared to whites. The Annual Report on Racial Inequalities in Brazil of 2009-2010 showed a decrease in the quality of life and life expectancy of the black population, and a higher chance of incidence of the disease

and death from tuberculosis among individuals with brown and black ethnicity/skin color, in addition to lower access to health services.[23] A study carried out with data from PNAD's supplementary health survey found that the black ethnicity/skin color is twice as likely to become infected with tuberculosis than whites.[16] Other studies have corroborated the higher chance of treatment default among the brown and black ethnicity/skin color.[5,8,13]

A history of previous treatment (relapse or previous default) was associated with a higher chance of unfavorable outcome in comparison to a new case. However, the category of unknown previous treatment or transfer was also associated with a greater chance of an unfavorable outcome, which may be related to the fact that HFSE is a referral hospital for severe forms of the disease and patients with comorbidities. Data from the Ministry of Health indicate treatment default in 26.1% of cases of pulmonary tuberculosis retreatment with laboratory confirmation, almost three times of that reported for new cases.[12]

Other authors have also reported an association between retreatment and an unfavorable outcome (death from tuberculosis, treatment default or failure).[9,15,22,24,25] Alcohol consumption and illicit drug use have been pointed out by several authors as factors related to treatment default.[5,15,20]

In the present study, alcohol consumption and illicit drug use were associated with an unfavorable outcome in the bivariate analysis; however, they did not reach statistical significance in the multivariate analysis, although the odds ratio associated with illicit drug use remained high.

Regarding the anti-HIV testing, individuals with a positive result were more likely to have an unfavorable outcome, corroborating other studies, both in relation to treatment default and death.[13,15,18,22,24,25] TB/HIV coinfection increases the likelihood of an unfavorable outcome, since these patients are immunocompromised, have more adverse drug reactions and have higher lethality rates, aggravated by the late diagnosis of these forms. HIV seropositivity is often discovered together with the tuberculosis diagnosis. Moreover, tuberculosis is the leading cause of death among individuals living with HIV, with a 20% death rate in the presence of coinfection.[20] In coinfected patients, the young adult age range is associated with a greater chance of treatment default, whereas the age range ≥60 years is associated with a greater chance of death; black ethnicity/skin color is associated with high rates of default and death, as well as alcohol consumption.[25,26]

A study carried out in Zimbabwe on tuberculosis mortality found a higher risk associated with HIV coinfection and a protective effect associated with the antiretroviral therapy start.[24] The coinfection increases the probability of treatment default, considering the association of both treatments. However, the present study also showed a greater chance of unfavorable outcome, in cases in which the anti-HIV test was not performed in comparison to those with a negative result, although not a significant one.

Another Brazilian study described a greater chance of treatment default and death in cases with an unknown anti-HIV result in comparison to a negative test result, in addition to the association with higher rates of treatment default and, mainly, higher rates of death with an HIV-positive result.[22] An African study found a greater chance of treatment default associated with an unknown HIV test result, in addition to a greater chance of treatment default found in the seropositive individuals in comparison to the seronegative ones.[9]

Regarding the clinical form of tuberculosis, a greater chance of unfavorable outcome was observed in the presence of some type of severe extrapulmonary form (with or without associated pulmonary form) compared to the non-severe isolated extrapulmonary form. Higher risk of death associated with the presence of both pulmonary and extrapulmonary forms was described in a study carried out in Nigeria.[25]

The directly supervised treatment strategy is not available in the HFSE, which in other studies has shown a protective effect against treatment default.[12,22]

Some limitations of this study included: failure to locate some medical records, record-keeping problems in the medical record systems, lack of information about the closure of cases, and discordant information. Strategies for retrieving information from the epidemiological surveillance database reduced the percentage of unknown closure from 36.1% to 14.1%; however, this percentage remains high. The quality of information, including underreporting and incompleteness of data, is an important limitation for the use of data from health information systems, which may compromise the evaluation and the decision-making process.[3,11,15]

The present study, despite its limitations, has contributed to the improvement in the quality of the HFSE tuberculosis database. In addition to the resolution of duplicities, active search strategies reduced the percentage of unknown closure and allowed the correction of inconsistent and missing data.

The final logistic regression model identified the following categories with a statistically significant association with an unfavorable outcome for tuberculosis treatment in the population of selected cases at HFSE: age ≥ 60 years, non-white

ethnicity/skin color, history of previous treatment, anti-HIV positive testing and presence of the severe extrapulmonary form of the disease, associated or not to the pulmonary form. These results corroborate data from the current literature and reinforce the need to invest in policies that guarantee access and adequate assistance to patients diagnosed with tuberculosis, especially those with conditions that predispose them to treatment non-adherence and the potentially fatal, severe forms of the disease.

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