Factors associated with unfavorable treatment outcomes of tuberculosis in older adults in Brazil: a multinomial analysis

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Abstract

Objective: To identify, within the three axes of vulnerabilities (individual, social, and programmatic), the factors associated with unfavorable treatment outcomes of tuberculosis (TB) among older adults in Brazil between 2015 and 2019. *Method:* This is a cross-sectional study utilizing secondary data from the Notifiable Diseases Information System (SINAN) regarding reported TB cases in Brazil, among individuals aged 60 years or older. The covariates associated with the outcome of interest ($p \leq 0.20$) were included in a multinomial logistic regression model using the cure category as the reference. *Results*: Older adults self-identified as black or mixed-race, experiencing homelessness, with mental health disorders, living with the human immunodeficiency virus (HIV), and engaging in the use of licit and illicit drugs had higher odds of loss to follow-up. Furthermore, older adults experiencing homelessness, with mental health disorders, engaging in the use of licit and illicit drugs, and who did not undergo bacilloscopy, presented higher odds of death due to TB. For the outcome of death due to other causes, individuals living with diabetes mellitus and HIV, engaging in the use of licit and illicit drugs, also had higher odds of experiencing this outcome. *Conclusion*: The results highlighted the influence of factors on TB treatment outcomes in older adults, encompassing the individual, social, and programmatic axes. Aspects such as advanced age, race, female sex, comorbidities, and homelessness were identified as relevant determinants, emphasizing the need for integrated approaches to improve outcomes and promote a favorable treatment outcome for TB in older adults.

Keywords: Tuberculosis. Older Adult. Measures of Association. Exposure. Risk or Outcome.

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There was no funding for the execution of this work.

The authors declare that there is no conflict in the conception of this work.

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Received: November 09, 2023
Approved: April 29, 2024

http://dx.doi.org/10.1590/1981-22562024027.230244.en

INTRODUCTION

Tuberculosis (TB), despite being an ancient infectious disease, treatable, and curable, remains a major global public health problem in the twenty-one century[1]. Worldwide, in 2022, it is estimated that 10.6 million people fell ill with TB, and approximately 1.3 million cases resulted in death[1,2]. Data from 2020 and 2021 showed a sharp decline in TB diagnosis and a significant increase in the number of deaths from the disease, an impact related to the Covid-19 pandemic coupled with difficulties in accessing healthcare services and similarities in transmission and clinical manifestation between the two diseases[1].

In Brazil, concerning the incidence rate, there was a decline in the number of reported cases between 2012 and 2015, followed by an increase between 2016 and 2019[2]. In 2022, there was a significant national increase in this rate, reaching 38.0 per 100,000 inhabitants after two years of decline related to the impact of the Covid-19 pandemic[2]. It is noteworthy that Brazil is among the 30 countries with the highest burden of TB, deemed a priority by the World Health Organization (WHO) for disease control[3].

Among the groups at higher risk for TB development are older adults, who exhibit a higher mortality rate when compared to younger individuals[4,5]. This phenomenon may be explained by the age-related decline in immunity, coexisting morbidities such as diabetes mellitus (DM), a greater likelihood of adverse drug reactions, and lower treatment adherence[4-6].

The identification of TB symptoms among older adults is also hindered due to their association with common age-related diseases that share similarities with the clinical presentation of TB, such as respiratory, cardiovascular, and systemic illnesses[4]. It is also noteworthy that other age-related characteristics, such as speech problems and memory deficits, may contribute to the delayed diagnosis of the disease[7].

The delay in TB diagnosis in older adults entails prolonged exposure to the disease, which may contribute to increased numbers of hospitalizations and cases that result in death in this age group, as well as to heightened transmission of *Mycobacterium tuberculosis*[8].

Regarding health vulnerabilities, they can be defined as a condition in which individuals, groups, or communities face an increased risk of experiencing health problems due to various circumstances, characteristics, or unfavorable factors[9,10]. These vulnerabilities can result from a range of elements, including socioeconomic, demographic, geographic, cultural, access to healthcare services, and other factors[10].

Thus, to assist in describing and understanding the epidemiological profile of TB in older adults, as well as in identifying factors influencing the occurrence of unfavorable outcomes in this age group, we will utilize in the present study the hierarchical model of TB determinants proposed by Maciel and Reis[9]. This model relates TB determinants and considers the multicausality of the disease across three axes of vulnerabilities: individual or behavioral, programmatic or institutional, and social or contextual. The arrangement of vulnerabilities across these three axes allows for different forms of analysis, as it encompasses determinants ranging from proximal to distal, considering both the individual and the collective[9].

The axes of vulnerability contribute to understanding health issues, especially when it comes to vulnerable populations such as older adults. Considering these axes in studies and healthcare practices provides an effective and comprehensive approach to promoting health and well-being in this population[9].

In this sense, the objective of this study was to identify, within the three axes of vulnerabilities, the factors associated with unfavorable outcomes of loss to follow-up, death due to tuberculosis, and death due to other causes among older adults in Brazil between 2015 and 2019.

METHOD

This is a cross-sectional study using secondary data from the Notifiable Diseases Information System (SINAN). The data are collected from healthcare services through the completion of specific notification and investigation forms for TB, which feed into the national system.

The study population included TB cases reported in SINAN between January 1, 2015, and December 31, 2019, among individuals aged 60 years or older with the outcome variable filled. The exclusion criteria comprised post-mortem notifications and outcomes involving transfer, diagnostic change, treatment regimen change, and drug-resistant TB. The response variable used for the study was "closure status", categorized as: cure (when the patient presents two negative bacilloscopy results); loss to follow-up (which includes abandonment and primary abandonment, meaning patients who interrupted medication use for more than 30 days, whether this interruption occurred before or after 30 days of treatment); TB-related death (death caused by tuberculosis); and death from other causes (death caused by any underlying cause, even if TB is an associated cause)[2].

The explanatory variables in the study were divided according to the vulnerability axes proposed by Maciel and Reis[9], encompassing individual, social, and programmatic variables. Within the axis of individual vulnerabilities, the following were considered: age (60-69 years; 70-79 years; ≥80 years), race (white; black; mixed-race; other [yellow, indigenous]), sex (male; female), and education level (no education; up to 4 years; 4 to 8 years; more than 8 years). Within the social vulnerability axis, the variables considered were: place of residence (urban; rural; peri-urban), government benefit (no; yes), population deprived of liberty (no; yes), homeless population (no; yes), healthcare worker (no; yes), alcoholism (no; yes), smoking (no; yes), other drugs (no; yes), diabetes (no; yes), human immunodeficiency virus (HIV) (no; yes). Finally, the programmatic axis comprised the following variables: Types of hospitalization (new case; relapse; re-entry after abandonment; unknown; transfer), clinical form of TB (pulmonary; extrapulmonary; pulmonary + extrapulmonary), Sputum bacilloscopy (negative; positive; not performed), chest radiography (normal; suspected; other pathology; not performed), sputum culture (negative; positive; in progress; not performed).

Additionally, a sensitivity analysis was conducted, wherein the response variable also included treatment failure as an outcome (defined by the persistence of positive sputum bacilloscopy at the end of treatment), aiming to identify factors related to this event. However, there were no statistically significant differences due to the small number of observations for this outcome, and therefore, it was not included as a variable in the study.

The participants' characteristics in the study were described using absolute and relative frequency measures. The Pearson chi-square test or likelihood ratio was used to compare proportions. The covariates associated with the outcome of interest, i.e., with a p-value of ≤0.20, were included in a multinomial logistic regression model, following the hierarchical model proposed by Maciel and Reis[9], to estimate the effect measure (odds ratio, OR). In this model, the cure variable was used as the reference for the response variable and compared with the other categories (cure vs loss to follow-up; cure vs TB-related death; cure vs death from other causes).

The first stage of the multinomial logistic regression model involved analyzing individual variables; in the second stage, contextual characteristics were included; in the third stage, variables related to comorbidities were added, and in the fourth stage, TB-related characteristics were included (Figure 1). The final multinomial logistic regression model included all predictors with p-values <0.05.

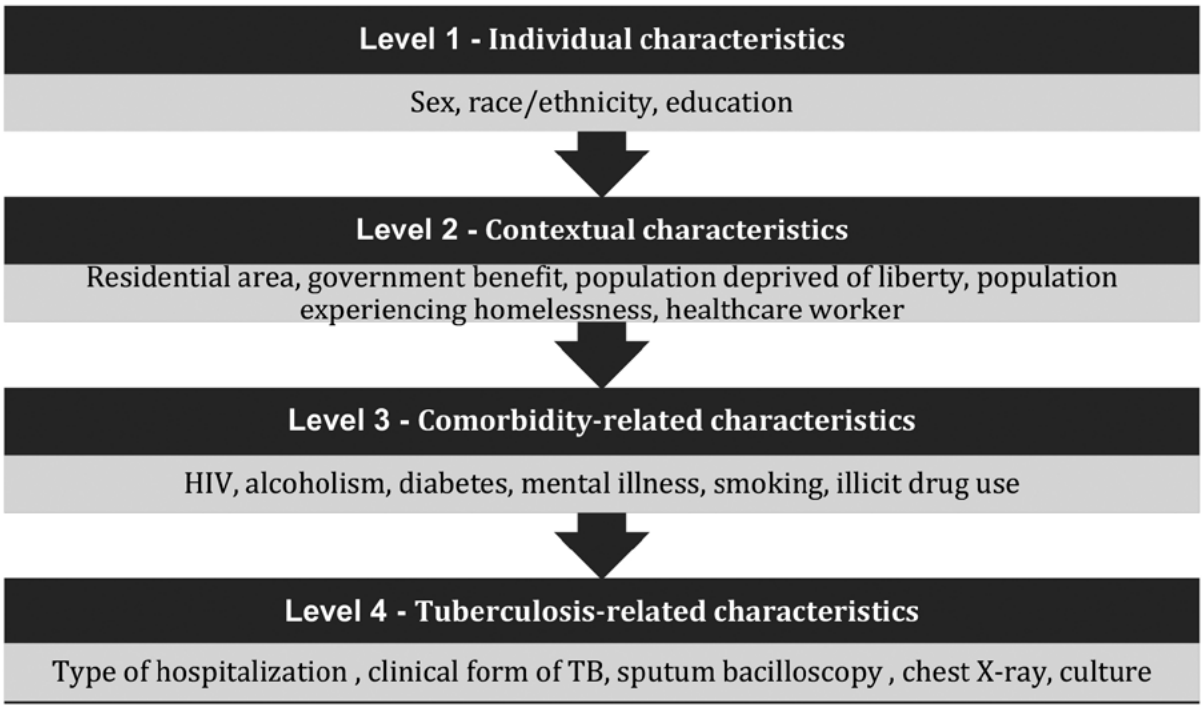

Figure 1. Flowchart of the variables included at each level of multinomial analysis. Brazil, 2015-2019.

Source: Authors.

The database was made available by the Ministry of Health through the Electronic System of Citizen Information Service (e-SIC), ensuring confidentiality and non-disclosure of individual identifiers. The project was developed following the ethical and legal principles outlined in Resolutions number 466/12 and number 510/2016 of the National Health Council. Additionally, it was submitted for review by the Ethics Committee of the Universidade Federal do Espírito Santo (UFES) and was approved under protocol number 2,088,338.

DATA AVAILABILITY

The entire dataset supporting the findings of this study is available upon request from the corresponding author.

RESULTS

Initially, the database contained 75,565 TB notifications recorded in SINAN between 2015 and 2019 in individuals aged 60 years or older. After applying the exclusion criteria, there were 70,833 notifications remaining. Of these, 44,562 (73.9%) resulted in cure after treatment, while 16,802 (26.1%) had unfavorable outcomes, including loss to follow-up (6.2%), TB-related death (9.4%), or death from other causes (10.3%).

It was identified that the majority of TB cases in older adults were male (66.5%), aged between 60-69 years (59.7%), of mixed-race (46.1%), with low education levels (61.8%), and residing in urban areas (86.9%). Clinically, the majority of cases were pulmonary TB (84.8%) and resulted in cure (73.9%). All studied variables were associated with the unfavorable treatment outcome ($p \leq 0.05$) (Table 1).

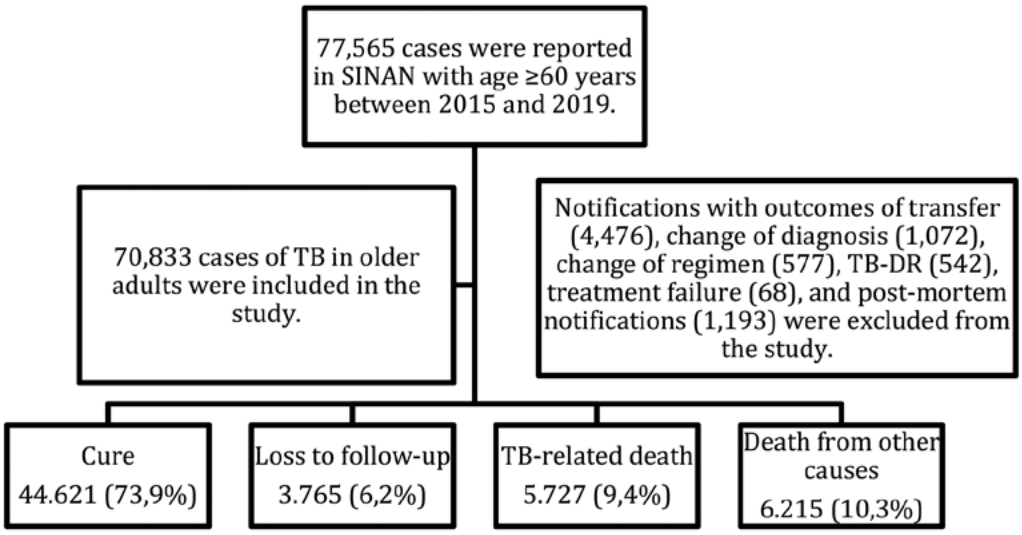

Figure 2. Flowchart of the tuberculosis case sample from the Notifiable Diseases Information System. Brazil, 2015-2019.

Source: Authors' elaboration based on SINAN data.

Table 1. Distribution of clinical characteristics of older individuals notified with tuberculosis in the Notifiable Diseases Information System according to treatment outcome. Brazil, 2015-2019.

Variables (N)[a]	Cure N (%[b]);	Loss to follow-up N (%)	Death from tuberculosis N (%)	Death from other causes N (%)	p-value
Age (years)					
60-69	27,616 (77.0)	2,403 (6.7)	2,800 (7.8)	3,027 (8.4)	<0.001
70-79	12,553 (72.5)	962 (5.5)	1,798 (10.3)	1,996 (11.5)	
≥ 80	4,392 (61.8)	394 (5.5)	1,127 (15.8)	1,118 (16.7)	
Sex (61.478)					
Male	29,150 (72.2)	2,569 (6.3)	4,258 (10.5)	4,357 (10.8)	<0.001
Female	15,464 (77.3)	1,193 (5.9)	1,468 (7.3)	1,857 (9.2)	
Race/ethnicity (56.907)					
White	17,206 (75.5)	1,163 (5.1)	1,998 (8.7)	2,399 (10.5)	<0.001
Black	4,625 (72.4)	515 (8.0)	598 (9.3)	643 (10.0)	
mixed-race	18,697 (73.6)	1,709 (6.7)	2,447 (9.6)	2,518 (9.9)	
Other	1,050 (76.7)	76 (5.5)	131 (9.5)	111 (8.1)	
Years of education (43.188)					
No education	5,203 (73.2)	465 (6.5)	710 (10.0)	725 (10.2)	<0.001
Up to 4	20,313 (76.8)	1,569 (5.9)	2,141 (8.1)	2,412 (9.1)	
5 to 8	5,003 (79.0)	377 (5.9)	427 (6.7)	522 (8.2)	
≥8	2,206 (83.1)	116 (4.3)	145 (5.4)	186 (7.0)	
Residential area (47.261)					
Urban	29,773 (73.4)	2,708 (6.6)	3,892 (9.6)	4,176 (10.3)	0.001
Rural	4,278 (74.8)	312 (5.4)	495 (8.6)	627 (10.9)	
Peri-urban	201 (73.6)	18 (6.5)	26 (9.5)	28 (10.2)	

to be continued

Continuation of Table 1

Variables (N)[a]	Cure N (%[b]);	Loss to follow-up N (%)	Death from tuberculosis N (%)	Death from other causes N (%)	p-value
Population deprived of liberty (51.492)					
No	37,196 (74.2)	3,032 (6.0)	4,703 (9.3)	5,177(10.3)	0.003
Yes	442 (76.7)	49 (8.5)	42 (7.2)	43 (7.4)	
Population experiencing homelessness (51.463)					
No	37,088 (74.6)	2,882 (5.8)	4,604 (9.2)	5,134 (10.3)	<0.001
Yes	415 (50.5)	198 (24.1)	136 (16.5)	72 (8.7)	
Healthcare worker (49.804)					
No	36,044 (74.2)	2,982 (6.1)	4,533 (9.3)	5,012 (10.3)	<0.001
Yes	367 (87.1)	16 (3.8)	21 (4.9)	17 (4.0)	
Government benefit (32.297)					
No	21,410 (75.5)	1,846 (6.5)	2,364 (8.3)	2,736 (9.6)	0.054
Yes	2,672 (74.0)	255 (6.2)	330 (9.1)	381 (10.5)	
HIV[c] status (61.241)					
Negative	35,330 (78.5)	2,327 (5.1)	3,347 (7.4)	3,994 (8.8)	<0.001
Positive	8,792 (60.3)	1,378 (9.4)	2,284 (15.6)	2,116 (14.5)	
Not performed	401 (70.2)	48 (8.4)	56 (9.8)	66 (11.5)	
Alcoholism (57.294)					
No	37,018 (76.3)	2,686 (5.5)	3,995 (8.2)	4,806 (9.9)	<0.001
Yes	5,159 (65.1)	771 (9.7)	1,116 (14.9)	872 (11.0)	
Smoking (51.858)					
No	30,754 (76.3)	2,296 (5.7)	3,320 (8.2)	3,932 (9.7)	<0.001
Yes	7,382 (69.1)	806 (7.5)	1,305 (12.2)	1,189 (11.1)	
Other drugs (51.683)					
No	37,553 (75.1)	2,934 (5.8)	4,459 (8.9)	5,025 (10.0)	<0.001
Yes	523 (57.7)	147 (16.2)	143 (15.8)	92 (10.1)	
Diabetes (57.299)					
No	33,775 (74.3)	2,882 (6.3)	4,195 (9.2)	4,597 (10.1)	<0.001
Yes	8,396 (76.3)	558 (5.0)	926 (8.4)	1,115 (10.1)	
Mental illness (56.868)					
No	41,054 (75.0)	3,309 (6.0)	4,883 (8.9)	5,496 (10.4)	<0.001
Yes	870 (66.2)	107 (8.1)	188 (14.3)	149 (11.3)	
Types of hospitalization (59.848)					
New case	38,992 (75.0)	2,823 (5.4)	4,751 (9.1)	5,378 (10.3)	<0.001
Relapse	3,389 (73.1)	352 (7.6)	471 (10.1)	422 (9.1)	
Re-entry after abandonment	1,135 (53.8)	477 (22.6)	290 (13.7)	206 (9.7)	
Unknown	117 (46.2)	20 (7.9)	59 (23.3)	57 (22.5)	
Transfer	988 (71.1)	93 (6.7)	156 (11.2)	152 (10.9)	
Clinical form of tuberculosis (61.479)					
Pulmonary	38,110 (74.2)	3,273 (6.3)	4,931 (9.6)	5,008 (9.7)	<0.001
Extrapulmonary	5,578 (74.5)	418 (5.5)	513 (7.1)	955 (12.7)	
Pulmonary + Extrapulmonary	933 (61.3)	74 (4.8)	263 (17.3)	250 (16.4)	

to be continued

Continuation of Table 1

Variables (N)[a]	Cure N (%[b]);	Loss to follow-up N (%)	Death from tuberculosis N (%)	Death from other causes N (%)	p-value
Sputum bacilloscopy (61.448)					
Negative	10,413 (73.0)	941 (6.5)	1,104 (7.7)	1,810 (12.8)	<0.001
Positive	22,360 (77.3)	1,597 (5.5)	2,763 (9.5)	2,179 (7.5)	
Not performed	10,552 (68.5)	1,114 (7.2)	1,702 (11.0)	2,033 (13.2)	
Chest X-ray (58.784)					
Normal	2,457 (79.4)	183 (5.9)	147 (4.7)	306 (9.8)	<0.001
Suspected	32,045 (73.3)	2,663 (6.0)	4,393 (10.0)	4,609 (10.5)	
Other pathology	726 (63.8)	67 (5.8)	143 (12.5)	202 (17.7)	
Not performed	7,427 (76.1)	714 (7.3)	801 (8.2)	817 (8.3)	
Culture (61.198)					
Negative	5,248 (80.9)	314 (4.8)	377 (5.8)	541 (8.3)	<0.001
Positive	7,918 (79.3)	593 (5.9)	785 (7.8)	687 (6.8)	
in progress	729 (69.6)	61 (5.8)	135 (12.9)	121 (11.5)	
Not performed	30,527 (71.7)	2,784 (6.5)	4.398 (10.3)	4,836 (11.3)	

a. Absolute value; b. Relative value; c. Human Immunoeficiency Virus

Source: Authors' elaboration based on SINAN data.

In the multivariate analysis (Table 2), it was observed that older individuals aged 80 years or older had a higher risk of TB-related and other-cause deaths compared to those aged 60-69 years. Additionally, self-declared black individuals had a higher risk of loss to follow-up, while mixed-race individuals showed a lower risk of death from other causes compared to white individuals. However, women had a lower risk of TB-related and other-cause deaths compared to men.

Regarding the level of education, having any level of education reduced the risk of TB-related and other-cause deaths compared to having no education. Older individuals experiencing homelessness had a higher risk of treatment abandonment and TB-related death. Also, individuals with diabetes mellitus had a lower risk of loss to follow-up, while those with mental illness had a higher risk of TB-related death.

The presence of HIV also stood out, as older individuals living with HIV had a higher chance of loss to follow-up, TB-related death, and death from other causes. Furthermore, tobacco and alcohol consumption were associated with a higher likelihood of unfavorable outcomes.

Cases of relapse showed a higher likelihood of loss to follow-up compared to new cases. Furthermore, instances of re-entry after abandonment exhibited an even greater likelihood of loss to follow-up and tuberculosis-related mortality. Regarding the clinical form of TB, pulmonary TB + extrapulmonary TB demonstrated a higher likelihood of TB-related mortality and mortality from other causes compared to the pulmonary form.

With respect to diagnostic methods, positive bacilloscopy was associated with a reduced risk of loss to follow-up and mortality from other causes, whereas failure to undergo the test increased the risk of TB-related mortality and decreased the risk of mortality from other causes. Additionally, chest radiography results suspicious for TB increased the risk of TB-related mortality. Lastly, failure to undergo culture testing was associated with a higher risk of unfavorable outcomes.

Table 2. Multivariable multinomial logistic regression analysis with a hierarchical model of sociodemographic and clinical covariates associated with tuberculosis treatment outcomes in older adults reported with tuberculosis in the Notifiable Diseases Information System. Brazil, 2015-2019.

Level	Variables	Cure-loss to follow-up OR[a] (95% CI[b])	Cure-tuberculosis-related mortality OR (95% IC)	Cure-mortality from other causes OR (95% CI)
	Age (years)			
	60-69	Reference	Reference	Reference
	70-79	0.98 (0.87-1.10)	1.47 (1.33-1.62)	1.48 (1.35-1.62)
	≥ 80	1.13 (0.96-1.33)	2.66 (2.36-3.00)	2.46 (2.20-2.76)
	Sex			
	Male	Reference	Reference	Reference
	Female	0.93 (0.84-1.04)	0.69 (0.63-0.76)	0.74 (0.67-0.80)
	Race/ethnicity			
1[c]	White	Reference	Reference	Reference
	Black	1.48 (1.27-1.74)	1.01 (0.88-1.17)	1.05 (0.92-1.19)
	Mixed-race	1.28 (1.14-1.43)	1.01 (0.92-1.11)	0.86 (0.79-0.94)
	Other	1.22 (0.88-1.69)	0.97 (0.73-1.28)	0.59 (0.43-0.80)
	Years of education			
	No education	Reference	Reference	Reference
	Up to 4	0.94 (0.82-1.07)	0.85 (0.76-0.95)	0.91 (0.82-1.03)
	5 to 8	1.00(0.84-1.20)	0.76 (0.65-0.89)	0.80 (0.69-0.93)
	≥ 8	0.83 (0.65-1.08)	0.62 (0.49-0.78)	0.60 (0.48-0.74)
	Population experiencing homelessness			
	No	Reference	Reference	Reference
2[d]	Yes	4.14(3.17-5.41)	1.78 (1.28-2.48)	1.35 (0.92-1.99)
	Healthcare worker			
	No	Reference	Reference	Reference
	Yes	0.49 (0.26-0.91)	0.66 (0.39-1.13)	0.39 (0.21-0.73)
	HIV[g] status			
	Negative	Reference	Reference	Reference
	Positive	2.18 (1.96-2.41)	2.10 (1.93-2.30)	1.88 (1.67-1.99)
	Alcoholism			
	No	Reference	Reference	Reference
	Sim	1.49 (1.30-1.72)	1.69 (1.50-1.91)	1.26 (1.11-1.43)
	Smoking			
	No	Reference	Reference	Reference
3[e]	Yes	1.27 (1.13-1.43)	1.49 (1.35-1.66)	1.28 (1.16-1.42)
	Other drugs			
	No	Reference	Reference	Reference
	Yes	2.01 (1.52-2.65)	1.58 (1.20-2.09)	1.26 (0.91-1.74)
	Diabetes			
	No	Reference	Reference	Reference
	Yes	0.85 (0.75-0.98)	1.04 (0.93-1.16)	1.11 (1.01-1.23)
	Mental illness			
	No	Reference	Reference	Reference
	Yes	1.39 (1.03-1.88)	1.73 (1.35-2.21)	1.09 (0.82-1.45)

to be continued

Continuation of Table 2

Level	Variables	Cure-loss to follow-up OR[a] (95% CI[b])	Cure-tuberculosis-related mortality OR (95% IC)	Cure-mortality from other causes OR (95% CI)
	Types of hospitalization			
	New case	Reference	Reference	Reference
	Relapse	1.40 (1.18-1.65)	1.11 (0.95-1.30)	0.93 (0.80-1.09)
	Re-entry after	4.98 (4.21-5.89)	1.74 (1.40-2.16)	1.32 (1.05-1.66)
	Unknown	1.06 (0.30-3.71)	3.04 (1.35-6.84)	3.21 (1.49-6.92)
	Transfer	1.23 (0.90-1.70)	1.42 (1.10-1.83)	1.01 (0.77-1.32)
	Clinical form of tuberculosis			
	Pulmonary	Reference	Reference	Reference
	Extrapulmonary	0.88 (0.74-1.05)	0.84 (0.72-0.99)	1.11 (0.97-1.26)
	Pulmonary + Extrapulmonary	0.88 (0.61-1.26)	2.19 (1.76-2.73)	1.71 (1.37-2.12)
4[f]	Sputum bacilloscopy			
	Negative	Reference	Reference	Reference
	Positive	0.68 (0.60-0.77)	1.76(0.95-1.20)	0.55 (0.49-0.61)
	Not performed	0.99 (0.86-1.13)	1.32(1.17-1.50)	0.85 (0.77-0.95)
	Chest X-ray			
	Normal	Reference	Reference	Reference
	Suspected	1.04 (0.82-1.32)	1.71 (1.33-2.20)	1.20 (0.99-1.45)
	Other pathology	1.54 (1.03-2.32)	2.28 (1.56-3.34)	1.68 (1.24-2.28)
	Not performed	1.19 (0.93-1.54)	1.20 (0.91-1.57)	0.96 (0.78-1.18)
	Culture			
	Negative	Reference	Reference	Reference
	Positive	1.23 (1.01-1.50)	1.17 (0.97-1.41)	0.99 (0.84-1.17)
	in progress	1.15 (0.74-1.79)	1.71 (1.21-2.41)	1.31 (0.92-1.85)
	Not performed	1.48 (1.25-1.76)	1.68 (1.44-1.97)	1.52 (1.33-1.74)

a. Odds ratio; b. Confidence interval; c. Individual characteristics; d. Contextual characteristics; e. Comorbidity-related characteristics; f. Tuberculosis-related characteristics; g. Human Immunodeficiency Virus.

DISCUSSION

The results of this study revealed that the characteristics related to the three axes of vulnerability had a significant association with the occurrence of unfavorable TB outcomes in older adults. In the individual axis, advanced age, self-reported race, female sex, and level of education were highlighted. In the social axis, comorbidities, use of licit and illicit drugs, as well as homelessness, emerged as important determinants. Finally, in the programmatic axis, the mode of entry into treatment, type of TB, and performance of diagnostic tests also significantly influenced unfavorable outcomes. These findings highlight the complex interaction of individual, social, and programmatic factors in the experience of TB in older adults.

Primarily, investigating individual vulnerability in TB provides insight into the various characteristics that influence treatment outcomes. Aspects such as advanced age, race, sex, and educational level are key elements that underscore the interaction among individual factors in the disease experience[9].

Advanced age, for instance, is a vulnerability factor associated with unfavorable TB outcomes due to immunosenescence, characterized by the diminished capacity of the immune system to respond due to aging. These immunological

alterations are exacerbated by the presence of other preexisting health conditions, rendering older adults more vulnerable to a fatal outcome from TB or related causes[7,10]. Furthermore, there is a highlighted association between advanced age and an increased risk of adverse events during TB treatment due to polypharmacy, which can complicate therapeutic management and lead to severe adverse reactions, necessitating personalized strategies to ensure the safety and efficacy of treatment in older adults[11].

Similarly, racial disparities contribute to the occurrence of unfavorable outcomes, as black and mixed-race individuals often face structural and socioeconomic barriers that hinder access to healthcare and treatment continuity[10,12].

Sex also plays a crucial role in individual vulnerability, as differences in treatment outcomes between sex are related to biological, behavioral, and even differences in healthcare-seeking behavior, given that the majority of individuals accessing healthcare services are female[13,14].

Moreover, educational level serves as a significant determinant of treatment outcomes, as individuals with higher levels of education possess greater knowledge about the disease, its modes of transmission, and the importance of treatment adherence[15,16]. It is noteworthy that education is associated with better access to healthcare services, greater ability to make informed decisions about one's health, and a higher likelihood of adhering to medical recommendations[12,15,16].

Regarding the social vulnerabilities of TB, various contextual and behavioral factors significantly influence treatment outcomes. Aspects such as comorbidities, HIV co-infection, substance abuse, and homelessness stand out as key elements that exacerbate the social vulnerability of patients[9].

Comorbidities, for instance, can both protect and increase an individual's vulnerability. While diabetes mellitus may be associated with a lower likelihood of loss to follow-up due to regular monitoring and proximity to healthcare services[17,18], mental disorders tend to increase vulnerability, impairing treatment adherence and the ability to cope with challenges associated with TB[19-21].

HIV coinfection also represents a significant risk factor for unfavorable treatment outcomes in TB, given the immunological suppression caused, combined with immunosenescence. HIV increases patients' susceptibility to opportunistic infections like TB, favoring the occurrence of unfavorable outcomes[22]. Moreover, the interaction between HIV and TB can be complex, with both diseases mutually exacerbating, resulting in a poorer prognosis and additional challenges in treatment[23-25].

The harmful use of alcohol, tobacco, and illicit drugs is also strongly associated with unfavorable treatment outcomes in TB. These substances increase the risk of developing active TB and also interfere with treatment adherence, impairing regular healthcare seeking and compromising therapeutic efficacy[26-28].

The condition of being homeless also showed a strong association with unfavorable outcomes in older adults, presenting a fourfold higher likelihood of treatment abandonment and a greater chance of progressing to TB-related mortality. The poor housing conditions, lack of financial resources and social support, as well as the presence of physical and mental comorbidities, are some of the challenges faced by these individuals, resulting in a 56-fold higher risk of TB illness[29], and negatively affecting their treatment adherence and consequently the outcomes[29-31].

Finally, the analysis of programmatic vulnerabilities in TB reveals the importance of considering aspects related to health programs in the treatment and management of the disease[9], especially in older populations. Various elements such as treatment entry type, TB clinical form, and diagnostic methods play significant roles in determining treatment outcomes and the effectiveness of interventions.

Regarding treatment entry types, cases of relapse and returns after abandonment among older adults stand out as specific challenges that require targeted strategies. The fragility of the immune system related to age and the presence of comorbidities increase the vulnerability of these patients, requiring frequent monitoring and continuous support to ensure treatment continuity and improve outcomes[32,33].

The analysis of TB clinical forms also highlights the importance of a personalized approach for older adults. Both the pulmonary and extrapulmonary forms of the disease are associated with a higher risk of TB-related mortality and other causes, reflecting the fragility of the immune system and the presence of frequent comorbidities in this age group[32-35].

Regarding diagnostic methods, still within the programmatic axis, it was identified that positive bacilloscopy was associated with a lower likelihood of loss to follow-up and death from other causes. Conversely, failure to perform bacilloscopy increased the likelihood of death from TB. These findings underscore the importance of conducting appropriate diagnostic tests to ensure effective and timely TB treatment, as positive bacilloscopy is associated with early diagnosis and consequently, prompt and suitable treatment, which can reduce disease progression and thus TB-related mortality[31,34,35]. However, that older adults may encounter difficulties in providing a high-quality sample, yet confirmation through this diagnostic method is not inferior when compared to younger individuals[4].

Culture is considered the gold standard for identifying drug-resistant TB strains and monitoring treatment, and the absence of this test can lead to delayed diagnoses, inadequate treatments, and more negative prognoses[31,34]. Furthermore, studies have demonstrated that there are no significant differences in the outcomes of this test between older adults and younger individuals, thus reinforcing its importance across all age groups for accurate and effective TB diagnosis[10,18,31].

Lastly, it is worth noting that radiographic presentation in older adults may be atypical[10], emphasizing the crucial need for proper interpretation of imaging exams and a comprehensive approach in evaluating patients suspected of TB[31,34].

In Brazil, the Unified Health System (SUS) relies on the technology of molecular rapid testing for TB diagnosis, providing a more sensitive and specific approach[2]. This technology is crucial as it enables early detection of cases, thereby contributing to more effective and timely treatment. Furthermore, molecular rapid testing is also capable of identifying cases of resistance to rifampicin, one of the primary medications in TB treatment, thus enabling more targeted and effective actions in combating the disease[1-3].

The findings presented point to the need for the development of comprehensive and integrated strategies to improve TB treatment outcomes among older adults in the country. This includes strengthening access to healthcare services, implementing approaches sensitive to gender and race issues, promoting education and awareness about TB, establishing social support networks for vulnerable groups, providing specialized care for individuals with comorbidities, and implementing harm reduction measures for the use of psychoactive substances in this population.

However, it is important to acknowledge the limitations of this study, as it was based on secondary data subject to inherent limitations in the notification system, such as possible underreporting of TB cases, which may affect the representativeness of the sample used in the study. Furthermore, inconsistencies in records or filling errors can compromise the data quality and introduce bias into the analyses. It should be added that generalizing the results to other populations and contexts should be done cautiously, considering the particularities of each location.

CONCLUSION

The results of this study have highlighted the influence of factors spanning individual, social, and programmatic axes on unfavorable treatment outcomes of tuberculosis (TB) in older adults. In the individual axis, advanced age, self-reported race, and female sex were prominent factors, along with educational level. In the social axis, aspects such as homelessness were identified as important determinants of unfavorable outcomes. In the programmatic axis, comorbidities such as diabetes mellitus and mental disorders, as well as coinfection with the human immunodeficiency virus, proved to be relevant. These findings underscore the complexity of factors involved in TB treatment in older adults and the need for integrated approaches to improve outcomes.

Therefore, a specific, integrated, and comprehensive approach, considering medical, social, and psychosocial aspects, is essential to address the challenges and improve treatment outcomes of TB in older adults, leading to favorable outcomes.

AUTHORSHIP

- Letícia do Nascimento Rodrigues Moraes: conception and design of the study, analysis and interpretation of data, drafting and critical revision of the manuscript, approval of the version to be published, agreement to be accountable for all aspects of the work.
- Fernanda Mattos de Souza: conception and design of the study, analysis and interpretation of data, critical revision of the manuscript, approval of the version to be published, agreement to be accountable for all aspects of the work.
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- Thiago Nascimento do Prado: conception and design of the study, analysis and interpretation of data, critical revision of the manuscript, approval of the version to be published, agreement to be accountable for all aspects of the work.

Edited by: Isac Davidson S. F. Pimenta

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