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Factors Contributing to Treatment Default Across the Five States in Brazil with the Highest Tuberculosis Incident Rates (2011-2019)

Fatores que Contribuem para o Abandono do Tratamento nos Cinco Estados do Brasil com as Maiores Taxas de Incidência de Tuberculose (2011-2019)

Fernando Lopes[1], Júlia Fialho Cauduro[2], Maria Jacirema Ferreira Gonçalves[3].

[1] Undergraduated Student in Medicine. Universidade Federal do Amazonas. ORCID: 0000-0002-8218-3108 E-mail: fernandocamposlopes@hotmail.com

[2] Undergraduated Student in Medicine. Universidade Federal do Amazonas. ORCID: 0000-0003-1689-8161 E-mail: jfcauduro@gmail.com

[3] PhD in Epidemiology. Universidade Federal do Amazonas. ORCID: 0000-0002-8460-8501 E-mail: jaciremagoncalves@gmail.com

ABSTRACT

Objective: To identify the factors associated with tuberculosis treatment default in states with the highest incidence rates of the disease in Brazil and its large regions from 2011 to 2019. **Methods:** This cross-sectional study used secondary data of new tuberculosis cases reported by the National System for Notifiable Disease of Brazil. The annual distribution of tuberculosis incidence rate was analyzed by the Brazilian states. Pearson's chi-square test and logistic regression models were used to assess the associations between the predictor and outcome variables. **Results:** The states with the highest average incidence rates in their respective regions were Amazonas (North), Pernambuco (Northeast), Rio de Janeiro (Southeast), Rio Grande do Sul (South) and Mato Grosso (Central-West). The main factors associated with the tuberculosis treatment default were male sex, age group 15–40 years, black race/ethnicity, non-performance of directly observed treatment, HIV coinfection, pulmonary clinical form, and alcoholism. **Conclusion:** Despite public policies, tuberculosis treatment default remains a health problem in Brazil. Despite the similarities among default situations in the states, the profile of this indicator does not represent national data. Thus, knowing the factors associated with tuberculosis treatment default allows for individualized examination of each state according to their specificities.

Keywords: Tuberculosis. Epidemiological Profile. Treatment Adherence and Compliance. Patient Compliance.

RESUMO

Objetivo: Identificar os fatores associados ao abandono do tratamento da tuberculose nos estados com as maiores taxas de incidência da doença no Brasil e grandes regiões de 2011 a 2019. **Métodos:** Estudo transversal com casos novos de tuberculose notificados ao Sistema Nacional de Agravos de Notificação. A distribuição anual da taxa de incidência de tuberculose foi analisada. Para avaliar as associações entre as variáveis preditoras e o desfecho, utilizou-se o teste de qui-quadrado de Pearson a regressão logística multivariável. **Resultados:** Os estados com as maiores taxas médias de incidência em suas respectivas regiões foram Amazonas (Norte), Pernambuco (Nordeste), Rio de Janeiro (Sudeste), Rio Grande do Sul (Sul) e Mato Grosso (Centro-Oeste). Os principais fatores associados ao abandono do tratamento foram sexo masculino, faixa etária de 15 a 40 anos, raça/etnia negra, não realização de tratamento diretamente observado, coinfecção por HIV, forma clínica pulmonar e alcoolismo. **Conclusão:** Apesar das políticas públicas, o abandono do tratamento da tuberculose continua um problema no Brasil. Apesar das semelhanças entre os estados, o perfil de abandono não representa dados nacionais. Assim, conhecer os fatores associados ao abandono do tratamento da tuberculose permite uma análise individualizada de cada estado de acordo com suas especificidades.

Palavras-chave: Tuberculose. Perfil Epidemiológico. Cooperação e Adesão ao Tratamento. Adesão do Paciente.

1. INTRODUCTION

Tuberculosis is a public health problem that mostly affects the male population, mainly those aged from 30–49 years, in the economically active bracket. Although free treatment is available in Brazil, the low cure rate combined with the high proportion of tuberculosis treatment default hinders the established goals to control this disease[1-2]. In 2020, 66,819 new cases were registered in Brazil, of which only 67.4% were reported as cured and 12.9% as tuberculosis treatment default (a slight increase compared with that in 2019 [12.4%]), showing alarming epidemiological results with a constantly high proportion of treatment default. These indicators have lower rates than the global average and are far from the goals established by the World Health Organization[3]. Therefore, adequate treatment with case detection and follow-up strategies are fundamental for reversing the tuberculosis scenario in Brazil[2].

The tuberculosis treatment default favors drug resistance and negatively affects disease control. In Brazil, although the incidence of tuberculosis has been declining despite its high levels across the country, the trend is not reflected in tuberculosis treatment default rates[3]. High treatment noncompliance, especially in states with the highest tuberculosis incidence, is the main obstacle to achieving control goals in Brazil, as it is unevenly distributed across the country. Therefore, the identification of areas and associated factors allows the adoption of more specific and effective disease control measures[4]. In addition, multiple factors of negative influence on tuberculosis treatment persist in Brazil, making it difficult to comply with the milestones for reducing the incidence of tuberculosis established by the “End TB Strategy”[1]. Thus, this study aimed to identify the factors associated with tuberculosis treatment default in states with the highest incidence rates of the disease in Brazil and its large regions from 2011 to 2019.

2. METHODS

In this retrospective cross-sectional epidemiological study, secondary data on tuberculosis in Brazil, reported in the National System for Notifiable Disease (Sistema de Informação de Agravos de Notificações (SINAN), from January 2011 to December 2019, were used. As these data are freely available with no possibility of identifying patients, the study does not require submission to the Ethics Committee for Research with Human Beings according to Resolution 510/2016 of the National Health Council[5].

New cases of tuberculosis across the Brazilian states from 2011 to 2019 were filtered, and the states with the highest tuberculosis incidence rate per 100,000 inhabitants were subsequently selected in each Brazilian macro-region (North, Northeast, Southeast, Central-West, South). The recovered microdata files in the services tab, available at the DATASUS, which is the department of the Ministry of Health (MoH) responsible for publicizing health system databases[6] were analyzed using R statistical software (The R Foundation for Statistical Computing, Vienna, Austria)[7].

The study variables were incidence rates by 100,000 inhabitants, Brazilian states, sex, age groups, race or ethnicity, prisoners, schooling years, clinical form of the disease, associated comorbidities (HIV-AIDS, alcoholism, and other diseases, considering any disease reported to SINAN, such as hypertension and Alzheimer's disease), diagnose by sputum smear microscopy or molecular tests (Genexpert MTB/RIF assay), HIV test and results, directly observed treatment, and treatment outcome (tuberculosis treatment default yes/no and treatment default proportion).

This study included all cases of tuberculosis where the variable 'type of entry' was designated as either 'new case' or 'unknown' or 'transfer'. Cases where the 'type of entry' involved a diagnostic error, 'recurrence' and 're-entry after treatment default' and the variable 'outcome' was classified as 'change of diagnosis', 'unknown/blank outcome', 'transfer' were excluded. Additionally, cases with "undetermined" sex and ignored age (0.1%) were excluded. A total of 809,283 cases were identified in Brazil, of which 188,162 were excluded, leaving 621,121 cases. Considering the selected Brazilian states, a total of 207,646 (33.4%) cases were included in the analysis.

Categorical variables were evaluated according to percentages and tested using Pearson's chi-square test. Statistical significance was set at a P-value < 5%. Additionally, the adjusted standardized chi-square residuals (adjusted residuals = AR) were analyzed to specifically identify the category in which there was excess occurrence, with positive residuals greater than 1.96 being considered significant, corresponding to a significance level < 5% and 95% confidence interval.

Crude and adjusted automated stepwise backward logistic regression analysis was used to report the odds ratio (OR) as a measure of association. A regression analysis was tested for each Brazilian state and in Brazil as a whole. The criteria AIC was used in order to choose the best fitted model to explain the association. Thus, we present an analysis for Brazil, including the states as dummy variables in the model. The significance level for the

inclusion of the variable was 20%. In the final model, only variables with a significance < 5% were retained. Final model fit was evaluated using variance reduction analysis[8].

3. RESULTS

Table 1 shows the annual tuberculosis incidence rate in Brazil per 100,000 inhabitants in each state. The total column contains the average annual incidence of each state, from which the five with the highest incidence were selected for each region: Amazonas (AM) in the North, Pernambuco (PE) in the Northeast, Rio de Janeiro (RJ) in the Southeast, Rio Grande do Sul (RS) in the South and Mato Grosso (MT) in the Central-West. The Federal District had the lowest average incidence in the country, with 12.1 cases per 100,000 inhabitants. Amazonas had the highest national average incidence at 72.0 cases per 100,000 inhabitants, highlighting that this state was among the states with the highest annual incidence rate in Brazil from 2013 to 2019.

Table 1. Annual tuberculosis incidence rate per 100,000 inhabitants according to Brazilian states and macro-region (2011–2019).

Brazilian states and macro-region	2011	2012	2013	2014	2015	2016	2017	2018	2019	Average
North region	54.2	51.2	50.9	49.5	46.7	49.8	55.4	55.2	62.5	52.8
Rondônia	38.9	38.6	35.0	33.1	30.2	35.1	32.2	31.4	34.7	34.3
Acre	46.6	47.1	46.3	50.2	38.5	46.9	51.7	49.3	58.2	48.3
Amazonas	**65.4**	**69.0**	**70.0**	**70.6**	**72.7**	**69.2**	**76.3**	**76.4**	**78.0**	**72.0**
Roraima	34.5	26.4	31.9	26.5	30.8	28.0	37.6	42.6	50.3	34.3
Pará	51.5	44.7	45.6	43.3	38.4	42.1	46.6	47.6	54.5	46.0
Amapá	34.3	30.6	25.7	23.9	23.2	27.8	32.9	29.1	37.0	29.4
Northeast region	33.9	32.4	30.9	29.2	27.4	28.8	29.6	32.4	31.2	30.6
Tocantins	14.6	13.9	12.7	11.1	10.6	12.1	11.2	13.1	13.4	12.5
Maranhão	34.7	30.3	30.2	27.5	29.0	30.3	29.5	32.0	32.4	30.7
Piauí	26.4	24.3	23.4	21.1	19.2	20.5	21.0	22.5	20.1	22.1
Ceará	45.6	41.9	39.2	36.6	37.3	37.8	38.5	40.3	37.2	39.4
Rio Grande do Norte	32.0	31.6	31.8	29.9	27.5	28.8	32.1	39.2	33.7	31.9
Paraíba	30.8	30.8	28.7	24.9	16.4	22.3	23.7	28.0	27.3	25.9
Pernambuco	**50.7**	**53.8**	**49.2**	**49.1**	**49.8**	**48.8**	**52.5**	**51.4**	**52.2**	**50.8**
Alagoas	37.0	36.7	33.4	31.8	27.0	31.0	29.3	32.2	30.0	32.0
Sergipe	28.8	25.2	28.4	29.1	27.9	28.2	29.3	35.2	37.1	29.9
Bahia	38.9	35.6	32.1	31.6	29.4	28.7	29.5	30.6	28.9	31.7
Southeast region	42.2	40.5	37.8	37.2	36.7	36.7	38.1	40.2	39.6	38.8
Minas Gerais	20.3	18.7	17.8	17.8	16.4	16.4	16.7	17.2	17.6	17.7
Espírito Santo	36.1	35.8	30.8	29.7	30.5	27.5	29.1	35.0	33.8	32.0
Rio de Janeiro	**72.9**	**69.3**	**65.5**	**64.2**	**62.1**	**65.3**	**66.3**	**68.6**	**68.3**	**66.9**
São Paulo	39.5	38.2	37.4	37.4	37.8	37.9	40.4	40.0	38.8	38.6
South region	33.4	32.8	31.1	30.6	29.8	29.1	30.1	30.0	29.7	30.8
Paraná	23.0	21.5	21.4	20.4	19.7	19.3	18.4	21.1	20.3	20.6
Santa Catarina	29.8	30.4	28.7	28.6	27.2	27.2	26.9	25.8	24.4	27.7
Rio Grande do Sul	**47.6**	**46.7**	**43.3**	**43.0**	**42.7**	**40.9**	**45.0**	**43.1**	**44.4**	**44.1**
Central-West region	25.7	27.7	27.3	25.8	23.5	23.4	22.6	25.8	25.8	25.3
Mato Grosso do Sul	35.1	35.0	33.6	29.7	29.3	32.4	31.4	42.6	40.4	34.4
Mato Grosso	**39.9**	**45.2**	**49.0**	**47.0**	**37.7**	**36.7**	**34.7**	**34.0**	**37.2**	**40.2**
Goiás	15.3	15.6	14.8	13.4	14.9	13.8	15.0	15.1	14.3	14.7

Distrito Federal	12.8	15.2	12.0	13.3	12.4	11.0	9.5	11.6	11.5	12.1

Source: Prepared by the authors based on the study from Brazilian National System for Notifiable Disease for tuberculosis (SINAN).

Note: The five Brazilian states with the highest average incidence of tuberculosis per 100,000 inhabitants in their respective macroregions are highlighted in bold.

Table 2 presents the case profiles of the proportion of tuberculosis treatment default by the states with the highest incidence rate. Those that had an excess of occurrence with significant chi-squared AR > 1.96 were highlighted in bold. In all states, the following variables were significantly associated with tuberculosis treatment default: male sex, age group of 20–40 years, black race/ethnicity, schooling years of 5–10 years, HIV-AIDS, Alcoholism, and other diseases. Brown race/ethnicity and bacilliferous cases were significant in all states except Pernambuco. The age group 15 to < 20 years was significant in Amazonas, Rio de Janeiro, and Mato Grosso. The pulmonary clinical form was significant in Rio de Janeiro and Rio Grande do Sul, whereas the pulmonary + extrapulmonary form was significant in Pernambuco. The prisoner population was statistically significant for treatment default in Amazonas, Rio de Janeiro, and Rio Grande do Sul. tuberculosis treatment with no directly observed treatment strategy was significant in all states except Rio Grande do Sul. The state with the highest percentage of tuberculosis treatment default was Rio Grande do Sul.

Table 2. Epidemiologic tuberculosis profile associated to tuberculosis treatment default across the five selected states in Brazil with the highest average incidence rates per 100,000 inhabitants (2011–2019).

Variables	**Brazilian states**									
	Amazonas		Pernambuco		Rio de Janeiro		Rio Grande do Sul		Mato Grosso	
	n	%	n	%	n	%	n	%	n	%
New Cases of tuberculosis	24633		37386		93601		41591		10435	
Treatment default	3134	12.7	4374	11.7	**13787**	**14.7**	**6883**	**16.5**	1256	12.0
Sex										
Male	**2246**	**14.8**	**3140**	**12.2**	**10289**	**16.5**	**4922**	**17.6**	**907**	**12.9**
Female	888	9.3	1234	10.4	3498	11.1	1961	14.3	349	10.2
Age group (years)										
< 15	128	8.8	150	11.9	294	9.9	103	9.0	30	5.0
15 to < 20	**325**	**15.6**	255	12.5	**1179**	**17.4**	397	17.1	**70**	**15.1**
20 to < 40	**1758**	**16.3**	**2357**	**14.0**	**8035**	**19.3**	**3917**	**21.9**	**605**	**14.5**
40 to < 60	644	9.7	1264	10.6	3452	11.6	1943	14.1	402	12.1
60 or over	279	7.4	348	6.4	827	6.5	523	7.9	149	7.7
Race/ethnicity*										
White	231	9.0	748	9.9	3101	10.2	4217	14.5	217	9.9
Black	**131**	**16.3**	**600**	**15.3**	**3297**	**18.2**	**1497**	**22.8**	**209**	**16.3**
Yellow	19	13.9	65	14.4	96	14.9	23	15.4	11	14.6
Brown	**2506**	**13.1**	2389	11.1	**5683**	**16.0**	876	20.2	**740**	**12.9**
Indigenous	119	8.4	18	11.1	20	11.7	29	18.2	42	4.4
Ignored	**128**	**20.1**	**554**	**14.2**	**1590**	**17.5**	241	16.2	**37**	**16.8**

Schooling (years of study)										
< 5	714	12.1	1101	11.4	**2994**	**15.8**	1219	15.3	326	10.9
5 to <10	**860**	**10.2**	**914**	**13.2**	**4145**	**18.5**	**2862**	**19.9**	**328**	**13.4**
10 or over	811	15.4	586	8.6	2467	9.6	990	11.3	335	11.9
Ignored/not filled	**673**	**15.1**	**1683**	**12.5**	**4010**	**15.7**	**1762**	**17.5**	252	13.2
Not applicable (patients < 15 years old)	76	11.5	90	14.0	171	12.4	50	9.6	15	4.9
Clinical form										
Pulmonary	2692	13.2	3688	11.7	**12369**	**15.5**	**5716**	**17.4**	1131	12.0
Extrapulmonary	322	9.6	507	10.7	1059	9.5	802	12.1	96	11.1
Pulmonary+extrapulmonary	120	13.3	**179**	**15.7**	359	12.7	365	16.4	29	14.4
Condition										
Prisoners	**141**	**19.5**	290	6.7	**1335**	**21.9**	**873**	**19.2**	108	8.3
HIV-AIDS	**499**	**15.1**	**786**	**20.4**	**1445**	**17.2**	**1816**	**23.4**	**146**	**19.3**
Alcoholism	**542**	**21.1**	**1140**	**17.0**	**2558**	**22.1**	**1439**	**23.4**	**262**	**20.4**
Others diseases†	**1355**	**15.2**	**2393**	**14.3**	**6342**	**17.6**	**4473**	**19.5**	**573**	**14.8**
Pulmonary Bacilliferous										
Yes	**2048**	**14.4**	2186	10.9	**8231**	**15.8**	**4270**	**17.9**	**636**	**12.7**
No	1096	10.4	**2188**	**12.5**	5555	13.3	2613	14.6	620	11.3
Directly Observed Treatment										
Yes	597	9.4	1516	8.7	4679	12.7	1263	14.9	531	9.1
No	**2537**	**13.8**	**2858**	**14.2**	**9108**	**16.0**	**5626**	**16.9**	**725**	**15.6**

Source: Prepared by the authors based on the study from Brazilian National System for Notifiable Disease for tuberculosis (SINAN).

Note: Pearson's chi-square test was significant (P < 5%) for all variables tested in the Brazilian states.

Highlighted in bold are the variables that present standardized adjusted residuals to the chi-square greater than 1.96, which corresponds to the level of significance for excess occurrences between the categories.

Caption: HIV: Human Immunodeficiency Virus; AIDS: Acquired Immunodeficiency Syndrome.

*Classification based on Brazilian Institute of Geography and Statistics.

†Other diseases (diseases other than AIDS or alcoholism).

Table 3 shows the results of the crude and adjusted logistic regression analyses, in which the following factors most strongly associated with tuberculosis treatment default were identified: male sex, state of Rio Grande do Sul, age group 15 to < 40 years, black or unknown race/ethnicity, no directly observed treatment, pulmonary clinical form, HIV-AIDS, and alcoholism. Prisoner population emerged as a protective factor against tuberculosis treatment default (OR, 0.86; 95% CI, 0.82–0.90).

Table 3. Factors associated with tuberculosis treatment default across the five states in Brazil with the highest average incidence rates of the disease (2011–2019).

Variables	Crude OR	CI 95%	Adjusted OR	CI 95%
Sex				
Female	1.0	1.0	1.0	1.0
Male	1.44	1.40 - 1.48	1.34	1.30 - 1.38
Brazilian States				
Amazonas	1.10	1.05 - 1.16	1.07	1.01 - 1.12
Pernambuco	1.0	1.0	1.0	1.0
Rio de Janeiro	1.31	1.26 - 1.36	1.33	1.28 - 1.38
Rio Grande do Sul	1.52	1.46 - 1.58	1.63	1.56 - 1.71
Mato Grosso	1.03	0.96 - 1.10	1.21	1.13 - 1.29

Age groups (years)				
< 15	1.39	1.27 - 1.52	1.66	1.52 - 1.82
15 to < 20	2.58	2.43 - 2.75	2.79	2.62 - 2.98
20 to <40	2.97	2.83 - 3.11	2.90	2.76 - 3.04
40 to < 60	1.78	1.70 - 1.88	1.60	1.52 - 1.69
60 or over	1.0	1.0	1.0	1.0
Race/ethnicity*				
White	1.56	1.36 - 1.79	1.07	0.93 - 1.24
Black	2.65	2.32 - 3.06	1.77	1.54 - 2.05
Yellow	1.99	1.63 - 2.42	1.58	1.29 - 1.93
Brown	1.90	1.66 - 2.19	1.46	1.27 - 1.69
Indigenous	1.0	1.0	1.0	1.0
Ignored	2.30	2.00 - 2.66	1.68	1.45 - 1.95
Bacilliferous				
Yes	1.19	1.16 - 1.22	1.03	1.00 - 1.06
No	1.0	1.0	1.0	1.0
Directly Observed Treatment				
Yes	1.0	1.0	1.0	1.0
No	1.43	1.39 - 1.47	1.49	1.45 - 1.53
Clinical form				
Pulmonary	0.40	0.36 - 0.44	1.46	1.39 - 1.52
Extrapulmonary	1.0	1.0	1.0	1.0
Pulmonary+extrapulmonary	0.39	0.31 - 0.46	1.19	1.10 - 1.29
HIV-AIDS				
Yes	1.58	1.53 - 1.63	1.36	1.31 - 1.41
No	1.0	1.0	1.0	1.0
Prisoners				
Yes	1.17	1.12 - 1.22	0.86	0.82 - 0.90
No	1.0	1.0	1.0	1.0
Alcoholism				
Yes	1.78	1.72 - 1.84	1.71	1.65 - 1.77
No	1.0	1.0	1.0	1.0

Source: Prepared by the authors based on the study from Brazilian National System for Notifiable Disease for tuberculosis (SINAN).

Caption: OR: odds ratio; 95% CI: 95% confidence interval; HIV: Human Immunodeficiency Virus; AIDS: Acquired Immunodeficiency Syndrome.

*Classification based on the Brazilian Institute of Geography and Statistics.

4. DISCUSSION

The factors associated with tuberculosis treatment default differ across Brazilian states, indicating no uniform national pattern. Therefore, tuberculosis treatment default must be addressed differently in each state.

Most of the five selected states maintained a constant annual incidence rate, with slight fluctuations, which may indicate that despite the efforts made by the tuberculosis control program, they are not sufficient and do not reflect a reduction in the incidence rate of the disease or a successful treatment outcome. Nevertheless, a reduction in the incidence rate of tuberculosis was observed at the national level, with an average of 35.8 cases per 100 thousand inhabitants from 2011–2019[9]. Amazonas has consistently the highest tuberculosis incidence since 2013[9], and in 2020 and 2021[3], it continues to present a high disease burden. However, the state with the highest chance (OR, 1.63; 95% CI, 1.56–1.71) for tuberculosis

treatment default is Rio Grande do Sul, which has the highest proportion for treatment default in 2019[9], potentially representing difficulties in tuberculosis control in this state. This can be attributed to the increase in the incidence of the disease in the state since 1993 and the high prevalence of coinfection with HIV[10]. Conversely, the corresponding prevalence in Amazonas was 7.7% from 2001 to 2012[11], which increased morbidity and worsened treatment adherence[3,9-11]. The Brazilian states with the highest incidence rates are those that received contributions from the National Tuberculosis Control Program immediately after its creation[2] and present above-average tuberculosis treatment default percentages in Brazil.

In all the states studied, tuberculosis treatment default exceeded 10%, highlighting an alarming situation. This may reflect a lack of incentives and motivating schemes that can be extended to the patients or even thoroughly explained to them, as motivation to complete treatment is an extremely important factor in preventing tuberculosis treatment default[12].

The profiles of defaulter patients in terms of sex (male) and age groups (20–39 years) in these states are similar and do not differ from other regions with a lower incidence of the disease[4,13-14]. One of the reasons leading to tuberculosis treatment default by the male population, especially in the adult-young age group[4,13,15] is the inflexibility of lifestyle changes[16], which makes it difficult to comply with treatment schemes and outpatient follow-up.

The highest chance of tuberculosis treatment default is concentrated in the age group 20–39 years, corroborating with the results of other studies that tuberculosis mainly affects the adult-young populations[14-16]. There exists a need discuss the differences in the chance of treatment default in the age groups across the three states (Amazonas, Rio de Janeiro, and Mato Grosso). Notably, treatment default is also identified in the 15–19 years population, representing a factor that requires distinct approach in disease control effort, since it is an additional problem to be tackled. One reason for this may be the need for work and family support in this population; this requirement may results in individuals neglecting their own treatment and ultimately discontinuing it. Another explanation for treatment default may be the adverse effects of treatment or involvement in the workday, which does not allow going to health facilities at the scheduled time[12]. Conversely, treatment may be neglected based on the initial sense of recovery experienced by the patients at the commencement of treatment[12,17]. Additionally, it could be attributed to superheroes' mentality often observed in young individuals, characterized by the belief that nothing adverse will befall them[12].

Black patients warrant an important approach for tuberculosis treatment default. In a study conducted on a population aged between 18 and 24 years, it was found that the risk was almost twice as high as that of the indigenous population for treatment default, considering that tuberculosis in indigenous populations is also a major problem[18]. From 2015 to 2021, 65.7% of drug-resistant tuberculosis cases in Brazil was reported in black people[3], which could also be a consequence of tuberculosis treatment default. Furthermore, socioeconomic conditions and the quality of life of the population are important predictors of tuberculosis infection, complicating and abandoning disease treatment, wherein the black population predominates due to their vulnerability. Drawing attention to the strong association with tuberculosis treatment default found in cases of ignored race/ethnicity leads to questioning about the healthcare targeted to patients, given that the proper fulfillment of the information system is an indirect indicator of the quality of care provided to the patients[19]. Proper handling of notification forms allows the assessment of national epidemiological needs[14,19], which serve as research sources for studies on health situation of the population, improvement of treatment opportunities, and other strategies in dealing with tuberculosis problem[19]. Thus, when classifications such as “not applicable”, “ignored” or "missing data" are erroneously supplied in essential variables such as race/ethnicity, sex, and educational background, the proper interpretation of the population's health status may be affected, preventing improvements in public health policies to promote tuberculosis control.

The positive association between tuberculosis treatment default and positive bacilloscopy findings is concerning. Bacilliferous cases are potential sources of infection; therefore, tuberculosis treatment default in these cases poses increased risks for disease control and the likelihood of perpetuating the infectious cycle as well as developing multidrug-resistant strains[4,13-14.] Treatment default with positive bacilloscopy was significant in Amazonas, Rio de Janeiro, and Rio Grande do Sul, which should reinforce their control programs to prevent this outcome in all patients, especially those with bacilliferous cases. The pulmonary clinical form in Rio de Janeiro and Rio Grande do Sul showed a higher chance for treatment default, possibly owing to the fact that tuberculosis affects populations that are more vulnerable to the outcome[3,18].

Patients who did not undergo directly observed treatment were more likely to default from treatment, which was significant in all Brazilian states. Studies have indicated that directly observed treatment contributes to treatment adherence and success[20], and thus adequate investment, incentives, and direction of public policies are necessary to increase

directly observed treatment strategy coverage[18], as envisaged in the basic goals of the National Tuberculosis Control Program[2]. In Brazil, the Unified Health System (SUS) failed to meet the demand for directly observed treatment in some states, such as Amazonas, where only patients diagnosed using molecular tests are prioritized for this strategy[21]. Consequently, patient adherence to treatment poses additional challenge, with a greater risk of treatment abandonment or irregular use of medications. This may reflect an increase in multi-resistant bacterial species and in treatment costs, further weakening the Brazilian health system and population. Therefore, prioritizing directly observed treatment in states with high treatment default proportion improves healthcare quality and can reduce therapeutic failure rates.

HIV-AIDS coinfection was significantly associated with tuberculosis treatment default across all Brazilian states selected in this study. This coinfection serves as an alarming indicator of unfavorable outcomes, as HIV-AIDS alone contribute to unsuccessful tuberculosis treatment[20]. A systematic review in 2012 found that the concomitant use of therapeutic regimens against HIV and tuberculosis did not cause major side effects[22], different from the claim of a retrospective population-based study[23]. Considering this result, the main hypothesis for a high proportion of tuberculosis treatment default in this population may be linked to healthcare and the precariousness of adequate strategic planning to guarantee the effectiveness of health programs. The fragility of interdisciplinary relationships between health professionals and patients in the primary care network can, in theory, distance this vulnerable group and lead to a higher default rate[19].

The lower chance of tuberculosis treatment default by the prisoner population may be linked to the monitoring received by this population or a careful filling in of the information system, as we analyzed secondary data. However, an excess of treatment default was identified in this population from Amazonas, Rio de Janeiro, and Rio Grande do Sul. In this regard, it is considered that a thorough study of the prison issues in these states can clarify whether they are states with more prisoners or whether the tuberculosis control program activities in these places are effective; other factor contributes to more case detection; or even more records of abandonment due to issues on proper monitoring. A study using the directly observed treatment strategy in a Barcelona prison population for tuberculosis treatment showed good adherence, even among individuals living with HIV or using illicit drugs[24]. The fact that this proportion of patients is detained may signify that they undergo

stricter control of their health status, thus negating the previous assumption of a higher proportion of tuberculosis treatment default within the prisoner population[18].

Alcohol abuse was identified as an important risk factor for tuberculosis treatment default in other studies[18,20,25]. Here, alcohol consumption increased the chance of tuberculosis treatment default compared to non-alcoholic patients, which may be due to drug interaction with the substance that causes liver damage[14] and consequent adverse effects. Clinical research has revealed an association between alcoholism and the development of severe and even multidrug-resistant tuberculosis[20], characterizing alcoholism as a high-risk factor for treatment default or poor prognosis owing to the dynamics of treatment in these cases. A qualitative study indicated that one of the motivations for the default of alcoholic patients included the desire to continue consuming alcoholic beverages without the risk of developing side effects due to the interaction with the drugs[12], emphasizing the strong influence that addiction has on people and neglecting treatment to continue consuming alcohol.

The limitations of this study arose from the potentially inadequate or unsatisfactory completion of the notification forms; however, a shortcoming that did not compromise the analysis was the large volume of data. Notably, incomplete filling out of the field “other comorbidities” made it impossible to perform a detailed analysis of this variable, and thus it was impossible to discriminate the patients' other diseases. Consequently, the variable “other diseases” was not used in the multivariate analysis. The analysis of educational background used in the descriptive analysis was not included in the multivariate analysis due to the uncertainties inherent in filling out the notification. This is due to the fact that schooling does not apply for children; however, in the exploratory analysis, it was not possible to impute this variable as well as due to the excess of missing data. Despite these exclusions of variables from the multivariate analysis and the problems inherent in the use of secondary data, the large sample size allows for the reliability of the presented analysis.

5. CONCLUSION

Tuberculosis treatment default remains a problem in Brazil, which demands proper public health policies to mitigate this problem and achieve successful tuberculosis treatment. This study identified that although there are similarities in the characteristics of tuberculosis treatment default in the Brazilian states, the abandonment profile does not reflect national

data. The cases of the states of Rio Grande do Sul and Rio de Janeiro are more likely to default than are those with the highest tuberculosis incidence rates in Brazil. Men, those aged 20 to 39 years, black race/ethnicity, patients with HIV-AIDS, alcoholics, and those who did not undergo directly observed treatment showed the highest force of association with tuberculosis treatment default. A minimal difference in tuberculosis treatment default exists among bacilliferous cases (which proved to have negligible significance in the study), as well as in the clinical form of the disease.

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