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Fatores de risco associados ao abandono do tratamento de tuberculose no estado do Rio de Janeiro, Brasil, 2015-2019

| Risk factors associated with abandonment of tuberculosis treatment in the state of Rio de Janeiro, Brazil, 2015-2019

RESUMO | Introdução: *O abandono do tratamento da tuberculose é um dos principais obstáculos para o controle da doença no Brasil e no mundo. Em 2018, o estado do Rio de Janeiro registrou 15,5% de abandono do tratamento nos casos novos, superior ao recomendado.* **Objetivos:** *Investigar os fatores associados ao abandono do tratamento segundo características sociodemográficas e clínico-epidemiológicas dos casos novos de tuberculose no estado do Rio de Janeiro, Brasil.* **Métodos:** *Foram utilizados dados do Sistema de Informação de Agravos de Notificação de 2015 a 2019. A associação das variáveis explicativas com o abandono do tratamento foi explorada por meio de modelos de regressão logística binária univariada e multivariada.* **Resultados:** *Dos 14.831 indivíduos com tuberculose incluídos no estudo, 1.852 abandonaram o tratamento, o que representa 12,5% da amostra. Homens jovens, com baixa escolaridade, não brancos, fumantes e usuários de drogas ilícitas apresentaram predisposição ao abandono, com a população de rua apresentando maior chance de abandono do tratamento para tuberculose.* **Conclusão:** *O estudo mostra a importância de acompanhar o perfil dos pacientes com tuberculose para desenvolver estratégias que aumentem a cooperação e adesão do paciente.*

Palavras-chave | *Tuberculose; Aderência ao Medicamento; Adesão do Paciente; Epidemiologia.*

ABSTRACT | Introduction: Abandonment of tuberculosis treatment is one of the main obstacles to control the disease in Brazil and in the world. In 2018, the state of Rio de Janeiro registered a 15.5% treatment abandonment rate in new cases, which is above the recommended by WHO. **Objectives:** Investigating factors associated with the abandonment of treatment according to sociodemographic and clinical-epidemiological characteristics of new tuberculosis cases in the state of Rio de Janeiro, Brazil. **Methods:** Data from the Health Notification Information System for the period 2015-2019 were used. The association of explanatory variables with treatment abandonment was explored through univariate and multivariate binary logistic regression models. **Results:** Out of the 14,831 individuals with tuberculosis included in the study, 1,852 abandoned treatment, representing 12.5% of the sample. Young males, with low schooling, of non-white color, smokers, and illicit drug users showed a predisposition to abandon treatment; the homeless population presented the highest chance of abandoning treatment. **Conclusion:** The study shows the importance of following these patient profiles to develop strategies that increase patient compliance to tuberculosis treatment.

Keywords | Tuberculosis; Medication Adherence; Patient Compliance; Epidemiology.

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INTRODUCTION |

Tuberculosis (TB) is a worldwide disease and a serious public health problem, representing one of the top 10 causes of death in the world. The disease is caused by the bacillus *Mycobacterium tuberculosis*, whose transmission occurs through the air. It usually affects the lungs (pulmonary TB), but it can also affect other locations (extrapulmonary TB). In 2019, 10 million people became ill with TB and 1.4 million died of the disease, despite being curable and preventable[1].

According to the World Health Organization (WHO), Brazil is part of a group of 30 countries responsible for about 87% of the TB cases in the world[1]. In 2020, around 67,000 new cases of TB were reported in the country and more than 4,000 cases evolved to death in 2019[2].

Despite the reduction in the TB incidence rate in Brazil (from 51.8 cases of TB/100,000 in 1990[3] to 31.6/100,000 in 2019[2]), it was not possible to observe an improvement in other TB control related data, such as treatment results. Cure percentages of new cases remained low (70.4% in 2001 and 70.1% in 2019), while follow-up losses persisted at high levels (10.7% in 2001 and 12.0% in 2019)[2,4]. WHO recommends detecting at least 70% and curing 85% of cases to reverse the TB situation, and treatment abandonment should not exceed 5%[4]. As observed, these values have not been reached in recent years.

Abandonment of treatment occurs when the individual does not attend the health unit for more than 30 consecutive days, after the defined date for follow-up[5]. Several individual socioeconomic and behavioral factors, besides the side effects of drugs, have been reported as the main reasons for non-adherence to anti-tuberculosis treatment[6-9].

The WHO has established the strategy of Directly Observed Treatment Short-Course (DOTS) to ensure drug adherence and disease control; however, treatment abandonment is still one of the main difficulties in achieving therapeutic success[10]. When patients abandon treatment, in addition to causing individual harm (such as not healing), they become a source of contagion and develop possible resistance to individual drugs[6], which puts public health at risk as resistance to TB drugs threatens the progress made in TB treatment and control worldwide.

In the state of Rio de Janeiro, more than 10,000 new cases were reported in 2020, with over 600 deaths due to TB registered in 2019[2]. In the same year, the state had the third highest TB mortality rate (3.8 deaths per 100,000 population) and its capital city had the third highest TB incidence rate (84.9 cases per 100,000 population), losing only to Manaus (90.1 cases per 100,000 population) and being equivalent to Recife (85.0 cases per 100,000 population)[2]. In 2018, the state of Rio de Janeiro registered a 15.9% treatment abandonment rate of new laboratory confirmed cases[2], avalue above the WHO recommendations.

Knowing the profile of TB patients that are likely to abandon the treatment and the factors that can trigger such outcome is an essential strategy to identify the main obstacles of therapeutic success, as well as to establish actions aimed at adherence and disease control. Thus, this study aimed to identify the risk factors for abandonment of TB treatment in the state of Rio de Janeiro – the third highest abandonment rate in Brazil.

METHODS |

This is a descriptive epidemiological study, of a quantitative nature, using secondary data, collected indirectly. The source of data on TB patients was the Notifiable Diseases Information System (SINAN), available on the Unified Health System (SUS) Information Technology Department (Datasus).

The target population of the study were TB cases reported in the state of Rio de Janeiro, in the period from January 2015 to December 2019. The collection of electronic data was carried out in October 2020. The data were entered into an electronic spreadsheet of the Microsoft Excel 2013 program (Microsoft Corporation, United States).

Only cases labeled as new and with a defined status of abandonment or cure were selected for the study. New cases represent every patient who has never undergone TB treatment or has done so for up to 30 days. Abandonment is when the patient does not show up at the health unit, after the beginning of treatment, for at least 30 consecutive days after the established follow-up date; cure is when two smears tests of the patient are negative: one in the follow-up phase and another at the end of treatment[5].

Observations that presented incoherent categories, incomplete or missing values were excluded from the study to avoid confusion due to lack of data. After the

pre-processing stages, the data totaled 14,831 observations –12,979 cure cases and 1,852 abandonment cases.

The variables selected for the study were case status (cure and abandonment); age group (in full years: less than or equal to 19, 20 to 39, 40 to 59, 60 or more);sex (male, female);race (white and not-white); education (in full years: no schooling, 1 to 8 years, over 8 years); deprived of liberty (yes or no);homeless (yes or no); health professional (yes or no); immigrant (yes or no); beneficiary of a government cash transfer program (yes or no); illicit drug use (yes or no); alcohol consumption (yes or no); smoking (yes or no); diabetes (yes or no); mental illness (yes or no); other diseases (yes or no); clinical form of TB (pulmonary, extrapulmonary, pulmonary + extrapulmonary); HIV serology (negative, positive, ongoing, not performed); and DOTS (yes or no).

Initially, descriptive statistical analysis was performed, calculating the absolute and percentage frequencies for the categorical variables. Then, Pearson's chi-square test was used to determine the association between the outcomes (cure or abandonment) and the predictors included in the study. The association of sociodemographic, behavioral and clinical characteristics with TB treatment abandonment was explored using univariate and multivariate binary logistic regression models. Variables with a p-value < 0.20 in the univariate analysis were included in multivariate logistic regression models. The stepwise selection process with backward elimination of variables was used to select the variables of the final model. Odds ratio (OR) and 95% confidence interval (95%CI) were reported. The value p < 0.05 was considered statistically significant. All statistical analyses were performed in R software (version 4.0.2, R Foundation for Statistical Computing, Vienna, Austria)[11].

This study complies with the ethical principles of Resolution 466/2012, of the National Health Council, and the data used were accessed in official and freely accessible databases, which justifies the absence of an opinion by the Research Ethics Committee.

RESULTS|

Of the total of 14,831 individuals with TB included in the study, 1,852 cases were abandoned - 12.5% of the sample. The abandonment rates per year were close to 11.7% between 2015 and 2017, with the highest rate recorded in 2018 (14.0%). In 2019, 13.1% of new cases notified abandoned treatment.

Among the cases of cure, 61.1% were male, 44.9% were between 20 and 39 years old, 63.5% were non-white and 49.1% had less than 8 years of schooling. Most of the cured patients were not deprived of liberty (98.8%), were not in a homeless situation (98.8%), were not health professionals (97.9%), were not immigrants (99.5%) and did not receive a government help (92.4%). Ninety per cent of the patients did not use illegal drugs, 89.2% were not alcohol dependent and 82.6% did not smoke. Regarding comorbidities, 92.3% were not diabetic, 97.6% were not mentally ill and 91.0% did not have other diseases. The pulmonary form was the predominant one (85.3%); 84.2% tested negative for HIV and 61.9% were under DOTS (Table 1).

Table 1 – Distribution of tuberculosis (TB) cases according to sociodemographic, clinical and epidemiological characteristics and the outcome of cure or abandonment, reported in the state of Rio de Janeiro, 2015 to 2019

	Cure (n = 12.979)		Abandonment (n = 1.852)	
Variables	**n**	**%**	**n**	**%**
Sex				
Female	5,053	39.8	519	28.0
Male	7,926	61.1	1,333	72.0
Age group (years)				
<=19	1,421	10.9	217	11.7
20-39	5,824	44.9	1,073	57.9
40-59	3,938	30.3	442	23.9
60+	1,796	13.8	120	6.5
Race				
White	4,735	36.5	435	23.5
Non-white	8,244	63.5	1,417	76.5

*to be continued.

*continuation.

Schooling (years)				
No schooling	808	6.2	106	5.7
<=8 years	6,369	49.1	1,221	65.9
>8 years	5,802	44.7	525	28.3
Population deprived of liberty				
Yes	491	1.2	111	6.9
No	12,488	98.8	1,741	93.1
Homeless population				
Yes	157	1.2	128	6.9
No	12,822	98.8	1,724	93.1
Health professional				
Yes	278	2.1	17	0.9
No	12,701	97.9	1,835	99.1
Immigrant				
Yes	61	0.5	16	0.9
No	12,918	99.5	1,836	99.1
Beneficiary of government cash transfer program				
Yes	983	7.6	141	7.6
No	11,996	92.4	1,711	92.4
Use of illicit drugs				
Yes	1,293	10.0	578	31.2
No	11,686	90.0	1,274	68.8
Alcoholism				
Yes	1,405	10.8	382	20.6
No	11,574	89.2	1,470	79.4
Smoking				
Yes	2,263	17.4	631	34.1
No	10,716	82.6	1,221	65.9
Diabetes				
Yes	1,004	7.7	79	4.3
No	11,975	92.3	1,773	95.7
Mental Illness				
Yes	313	2.4	83	4.5
No	12,666	97.6	1,769	95.5
Other diseases				
Yes	1,165	9.0	115	6.2
No	11,814	91.0	1,737	93.8
Clinical form of TB				
Pulmonary	11,071	85.3	1,671	90.2
Extrapulmonary	1,644	12.7	142	7.7
Pulmonary + Extrapulmonary	264	2.0	39	2.1
HIV serology				
Positive	763	5.9	168	9.1
Negative	10,930	84.2	1,412	76.2
In progress/Unrealized	1,286	9.9	272	14.7
DOTS[a]				
Yes	8,035	61.9	979	52.9
No	4,944	38.1	873	47.1

DOTS: Directly Observed Treatment Short-Course. Source: Authors.

Among those who abandoned treatment, 72.0% were male, 57.9% were in the 20-39 age group, 76.5% were non-white, and 65.9% had less than 8 years of schooling. Most of them were not deprived of freedom (93.1%), were not in a homelessness situation (93.1%), were not health professionals (99.1%), were not immigrants (99.1%) and did not receive a government help (92.4%). Two thirds (68.8%) of the patients did not use illegal drugs, 79.4% were not alcohol dependent, and 65.9% did not smoke. Regarding comorbidities, 95.7% were not diabetic, 95.5% were not mentally ill, and 93.8% did not have other diseases. The pulmonary form was predominant (90.2%), 76.2% tested negative for HIV and 52.9% were under DOTS (Table 1).

In the bivariate analysis, it was observed that males under 60 years of age, of non-white color, and with less than 8 years of schooling were associated with abandonment of TB treatment (p < 0.001). Patients deprived of their liberty and homeless patients were also associated with this outcome (p < 0.001), as well as immigrants (p = 0.030). In turn, health professionals were more successful than non-professionals (p = 0.002). Illicit drug users, alcoholics, smokers, mentally ill, and patients living with HIV also presented a treatment abandonment profile (p < 0.001). On the other hand, diabetics and patients with other diseases had a lower chance of abandoning treatment (p < 0.001). The extrapulmonary clinical form and being under DOTS presented themselves as a protection factor (p < 0.001). The only variable thatdid notpresent any significant association was whetherthe patient was a beneficiary of a government cash transfer program (p = 0.952) (Table 2).

Table 2 – Bivariate analysis of factors associated with the abandonment of tuberculosis treatment, in the period from 2015 to 2019. Rio de Janeiro, Brazil, 2020

Variables	Abandonment (%)	Unadjusted OR (95%CI)	p-value
Sex			
Female	9.3	1.0	
Male	14.4	1.64 (1.47-1.82)	**< 0.001**
Age group (years)			
<=19	6.3	1.00	
20-39	10.1	1.68 (1.37-2.08)	**<0.001**
40-59	15.6	2.76 (2.28-3.37)	**<0.001**
60+	13.2	2.29 (1.81-2.89)	**<0.001**
Race			
White	8.4	1.00	
Non-white	14.7	1.87 (1.67-2.10)	**<0.001**
Schooling (years)			
>8 years	8.3	1.00	
<=8 years	16.1	2.12 (1.90-2.36)	**<0.001**
No schooling	11.6	1.45 (1.16-1.80)	**0.001**
Population deprived of liberty			
No	12.1	1.00	
Yes	18.4	1.62 (1.31-2.00)	**<0.001**
Homeless population			
No	11.9	1.00	
Yes	44.9	6.06 (4.77-7.69)	**<0.001**
Health professional			
No	12.6	1.00	
Yes	5.8	0.42 (0.25-0.67)	**0.001**
Immigrant			
No	12.4	1.00	
Yes	20.8	1.85 (1.03-3.13)	**0.030**

*to be continued.

*continuation.

Beneficiary of government cash transfer program			
No	12.5	1.00	
Yes	12.5	1.01 (0.83-1.20)	0.952
Use of illicit drugs			
No	9.8	1.00	
Yes	30.9	4.10 (3.66-4.59)	**<0.001**
Alcoholism			
No	11.3	1.00	
Yes	21.4	2.14 (1.89-2.42)	**<0.001**
Smoking			
No	10.2	1.00	
Yes	21.8	2.45 (2.20-2.72)	**<0.001**
Diabetes			
No	12.9	1.00	
Yes	7.3	0.53 (0.42-0.67)	**<0.001**
Mental Illness			
No	12.3	1.00	
Yes	21.0	1.90 (1.47-2.42)	**<0.001**
Other diseases			
No	12.8	1.00	
Yes	9.0	0.67 (0.55-0.81)	**<0.001**
Clinical form of TB			
Pulmonary	13.1	1.00	
Extrapulmonary	8.0	0.57 (0.48-0.68)	**<0.001**
Pulmonary + Extrapulmonary	12.9	0.98 (0.69-1.36)	0.901
HIV serology			
Negative	11.4	1.00	
Positive	18.0	1.70 (1.43-2.03)	**<0.001**
In progress/Unrealized	17.5	1.64 (1.42-1.88)	**<0.001**
DOTS			
No	15.0	1.00	
Yes	10.9	0.69 (0.63-0.76)	**<0.001**

DOTS: Directly Observed Treatment Short-Course; 95%CI: 95% confidence interval; OR: odds ratio. Source: Authors.

In the multivariate analysis, represented in Table 3, it was found that males under 60 years of age, of non-white color and less than 8 years of schooling were still associated with abandonment of TB treatment. Patients belonging to the age groups ≤19 and 20-39 years were the most related to such outcome (OR = 2.38; 95%CI: 1.86-3.04; p < 0.001 and OR = 2.38; 95%CI: 1.94-2.94; p < 0.001). Those without schooling were 44% (OR = 1.44; 95%CI: 1.14-1.81, p = 0.002) more likely to abandon treatment; patients of non-white color were 50% (OR = 1.50; 95%CI: 1.34-1.70; p < 0.001) more likely to abandon treatment.

Being deprived of liberty decreased the risk of abandoning treatment (OR = 0.73; 95%CI: 0.57-0.93; p = 0.011);while being part of the homeless population was the risk factor that increased the chances of abandoning treatment the most—almost 3.5 times higher (OR = 3.49; 95%CI: 2.67-4.55; p < 0.001).

Smokers and illicit drug users showed a profile of abandonment of treatment, increasing this chance by 1.47 (95%CI: 1.29-1.67; p < 0.001) and 2.28 (95%CI: 1.98-2.62; p < 0.001) times, respectively. Patients living with HIV presented 53% higher chance of abandoningtreatment (OR= 1.53; 95%CI: 1.26-1.84; p < 0.001) compared with those with a negative serology. Being clinically extrapulmonary and under DOTS reduced the chances of abandoning treatment in around 20% (OR = 0.78; 95%CI: 0.64-0.93; p = 0.008) and 40% (OR = 0.60; 95%CI: 0.54-0.67; p < 0.001).

Table 3 – Multivariate analysis of the factors associated with abandonment of tuberculosis treatment included in the model, in the period from 2015 to 2019. Rio de Janeiro, Brazil, 2020

Variables	Adjusted OR (95%CI)	p-value
Sex		
Female	1.0	
Male	1.28 (1.14-1.44)	**< 0.001**
Age group (years)		
<=19	1.00	
20-39	1.41 (1.14-1.76)	**0.002**
40-59	2.38 (1.94-2.94)	**<0.001**
60+	2.38 (1.86-3.04)	**<0.001**
Race		
White	1.00	
Non-white	1.50 (1.34-1.70)	**<0.001**
Schooling (years)		
>8 years	1.00	
<=8 years	1.72 (1.53-1.93)	**<0.001**
No schooling	1.44 (1.14-1.81)	**0.002**
Population deprived of liberty		
No	1.00	
Yes	0.73 (0.57-0.93)	**0.011**
Homeless population		
No	1.00	
Yes	3.49 (2.67-4.55)	**<0.001**
Health professional		
No	1.00	
Yes	0.67 (0.38-1.09)	0.126
Use of illicit drugs		
No	1.00	
Yes	2.28 (1.98-2.62)	**<0.001**
Smoking		
No	1.00	
Yes	1.47 (1.29-1.67)	**<0.001**
Diabetes		
No	1.00	
Yes	0.79 (0.61-1.01)	0.061
Clinical form of TB		
Pulmonary	1.00	
Extrapulmonary	0.78 (0.64-0.93)	**0.008**
Pulmonary + Extrapulmonary	1.03 (0.71-1.46)	0.870
HIV serology		
Negative	1.00	
Positive	1.53 (1.26-1.84)	**<0.001**
In progress/Unrealized	1.63 (1.39-1.91)	**<0.001**
DOTS		
No	1.00	
Yes	0.60 (0.54-0.67)	**<0.001**

DOTS: Directly Observed Treatment Short-Course; 95%CI: 95% confidence interval; OR: odds ratio. Source: Authors.

DISCUSSION |

This study sought to identify the main risk factors associated with abandonment of TB treatment among patients living in the state of Rio de Janeiro. Between 2015 and 2019, the abandonment rate was 12.5% – well above the 5% rate determined by WHO. Today, Rio de Janeiro ranks third among the Brazilian states with the highest rates of TB treatment abandonment.

Regarding sociodemographic characteristics, men who were less 39 years old, of non-white color and with less than 8 years of schooling presented the highest chances of abandoning treatment. Soares et al.[13] also observed a similar pattern in patients from Pernambuco, between 2001-2014.

The male sex has been identified as a risk factor for abandonment in several other studies[14-17]. A possible explanation of this behavior is the social pressure suffered by men, characterizing them as strong enough not to be sick or dependent on medical treatment[18].

In their findings, Viana, Redner and Ramos[19] observed that the age group of 50 years or more was associated with a lower risk of treatment abandonment when compared with cases in the age group of 15 to 29 years. In our study, young adults tended to abandon treatment, which is similar to the results of other studies on the same theme[15,16]. Since this age group is more prone to use drugs and alcohol, it is possible that treatment abandonment is linked to such behaviors[13].

The use of illicit drugs and smoking are also associated with abandonment of TB treatment in the multivariate model. This pattern has also been observed in previous studies[13,19-21]. It is harder to prevent TB infection among illicit drugs users, they are prone to develop the active form of the disease and likely to present comorbidities—such as hepatitis B, hepatitis C and HIV—in addition to carrying a heavy burden of stigma, due to both TB and consumption of illegal drugs[22].

The low schooling showed association with the outcome, a similar result to the writings of Arruda[14], Harling et al.[16], and Viana, Redner and Ramos[19]. Possible explanations refer to the fact that the patient with lower school level often cannot understand what is prescribed or the health professional does not try to convey the information in a less formal way, leading to disinterest and consequent abandonment[23]. Communication between professionals and patients is of

fundamental importance to avoid treatment abandonment and maintain regular attendance at the health unit.

Non-white skin has been associated with treatment abandonment in relation to self-declared whites. This result was also found in other evaluation studies on the aspects of abandonment of TB treatment[14,16]. However, this association is not a racial predisposition to TB, but a reflection of the ethnic demographic structure of the state of Rio de Janeiro[14].

Patients living with TB-HIV co-infection also presented more chances of abandoning TB treatment, a result that agrees with other studies[16,24-26]. This may be due to drug interactions between antiretroviral and TB treatments. Often, these patients choose to continue only the HIV treatment due to the high number of pills they must take per day, in addition to the side effects of undergoing both treatments[27,28]. The care of co-infected TB/HIV patients must include close attention to adherence to tuberculosis regimens and antiretroviral treatment. Without both treatments, HIV infection can amplify and accelerate the development of TB from infection to the advanced stages of the disease, and can reactivate a previous TB infection. Tuberculosis, in turn, may lead to a reduction in CD4 T lymphocytes, intensifying the immunodepressive effect of HIV and possibly resulting in increased viral activity.

Similar to the findings of other authors[16,17,24,29], diabetes decreased the chances of abandoning TB treatment. Abreu et al.[29] concluded that diabetics show have a greater link with the Basic Health Units due to the treatment of this comorbidity.

Regarding the homeless population, the result was as expected, since this population is considered a highly vulnerable group by the Ministry of Health. Ranzani and collaborators[30] also observed that the lack of housing led to a sharp reduction in the successful treatment of recently-diagnosed pulmonary TB in the state of São Paulo.

The extrapulmonary form of tuberculosis was considered a protection factor against treatment abandonment, similar to Gomes et al.[17] and Harling et al.[16]. This result may occur because this type of TB is associated with less resistance to the medication. However, in the study by Soares et al.[13], abandonment was more frequent among pulmonary TB cases associated with extrapulmonary, different from what we observed in our study.

With respect to DOTS, patients who were under this condition during therapy had less chance of abandonment. As in other findings, those who did not complete this strategy presented higher abandonment rates, which reflects the need for effective implementation, in addition to the completeness, of this method for TB treatment[14,16].

Despite the limitations of our study, such as high incompleteness of some variables and lack of important information, such as income, the study identified the main factors associated with tuberculosis treatment abandonment in the state of Rio de Janeiro, between 2015 and 2019.

CONCLUSION |

In this study, a high abandonment rate of TB treatment was observed in the state of Rio de Janeiro (12.5%) from 2015 to 2019. Young males, with low schooling, of non-white color, smokers and illicit drug users may be contribute to this increase. The homeless population is the most likely to abandon treatment. It is important to always evaluate the approaches of patient profile monitoring, as to develop different strategies aimed at increasing patient compliance to TB treatment.

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