

## FACTORS ASSOCIATED WITH ABANDONMENT OF PULMONARY TUBERCULOSIS TREATMENT

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### ABSTRACT

**Objective:** to analyze the factors associated with the abandonment of pulmonary tuberculosis treatment in Rondonópolis, Mato Grosso, Brazil, from 2008 to 2017.

**Method:** a quantitative, cross-sectional and descriptive study, of historical series. The data were collected from the Notifiable Diseases Information System. A descriptive analysis was carried out and, in order to verify associations, the Chi-square and Fisher's Exact tests were used in cases with frequencies below five. The Odds Ratio and 95% confidence intervals were estimated.

**Results:** there were 584 cases of pulmonary tuberculosis, of which 8.56% abandoned the treatment. The profile of the abandonment cases was as follows: male (62%), adults (94%), brown-skinned (54%), elementary school (48%), urban area (90%), and who underwent Directly Observed Treatment (56%). Age group and DOT were factors associated with treatment abandonment.

**Conclusion:** this study will be able to contribute to the planning of health actions with prevention strategies, aiming to ensure adherence to the treatment.

**DESCRIPTORS:** Tuberculosis; Therapeutics; Epidemiology; Quantitative Analysis; Primary Health Care.

### FACTORES ASOCIADOS AL ABANDONO DEL TRATAMIENTO DE LA TUBERCULOSIS PULMONAR

#### RESUMEN:

**Objetivo:** analizar los factores asociados al abandono del tratamiento de los casos de tuberculosis pulmonar en Rondonópolis, Mato Grosso, Brasil, de 2008 a 2017. **Método:** estudio cuantitativo, transversal, descriptivo y de series de casos. Los datos fueron recolectados en el Sistema de Información de Enfermedades de Notificación Obligatoria. Se realizó un análisis descriptivo y, para verificar asociaciones, se utilizaron las pruebas de Chi-cuadrado y Exacto de Fisher en los casos con frecuencias menores a cinco. Las razones de probabilidad y los intervalos de confianza se estimaron en 95%. **Resultados:** se registraron 584 casos de tuberculosis pulmonar, de los cuales el 8.56% abandonó el tratamiento. El perfil de los casos de deserción fue: sexo masculino (62%), adultos (94%), de piel morena (54%), escuela primaria (48%), zona urbana (90%) y sometidos a Tratamiento Directamente Observado (56%). El rango de edad y el TDO fueron factores asociados al abandono del tratamiento. **Conclusión:** este estudio puede contribuir a la planificación de acciones de salud con estrategias de prevención para garantizar la adherencia al tratamiento.

**DESCRIPTORES:** Tuberculosis; Tratamiento; Epidemiología; Análisis Cuantitativo; Atención Básica de la Salud.

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## INTRODUCTION

Tuberculosis is an infectious and communicable disease, caused by *Mycobacterium tuberculosis*, of mandatory notification, and which affects mainly the lungs (pulmonary form), with the possibility of spreading to other organs and systems (extrapulmonary form)<sup>(1)</sup>. The spread of its bacteria occurs through respiratory droplets in the air. The susceptible individual inhales particles expelled by the infected person, evolving to an active or latent infection. Active infection is characterized by the bacterial migration to the alveoli<sup>(2)</sup>. As for latent infection, it occurs when the organism finds itself in metabolically unfavorable situations for the bacillus, with a slow multiplication during days or years, with the possibility of leading to illness<sup>(1)</sup>.

According to world statistics, in 2016, 10.4 million people fell ill from tuberculosis and nearly 1.3 million evolved to death<sup>(3)</sup>. A total of 69,569 new cases were notified in Brazil in 2017, as well as 4,426 deaths from tuberculosis. The incidence and mortality coefficients presented a mean annual reduction of 1.6% (2008 to 2017) and 2.0% (2007 to 2016)<sup>(4)</sup>.

In 1993, the World Health Organization (WHO) launched the Directly Observed Treatment strategy, in Brazil named *Tratamento Diretamente Observado* (TDO) and, in 1999, the Ministry of Health ratified this strategy in the country. The DOT has as objective the patient's adherence to the treatment, reducing the number of abandonment cases and increasing cure probability. In it, the health professional observes the intake of medications from the beginning until the end of the drug therapy<sup>(5-6)</sup>.

Treatment abandonment is defined when the patients do not attend the reference unit for more than 30 days consecutively, after the expected return date, and in DOT cases, this deadline is accounted for from the last medication intake<sup>(6)</sup>. These abandonment cases are as important as new tuberculosis cases, given that, in addition to causing bacillus resistance, they generate costs with human and material resources which need to be made available by the health services each time treatment is initiated<sup>(7)</sup>.

The main factors associated with the difficulty in adhering to the treatment are related to lack of information on the disease by the patient and the family, use of alcoholic beverages and illicit drugs, social barriers, schooling, and adverse reactions to the medication and the DOT. In addition to altering the daily routine, applying this treatment can cause embarrassment when performed in the health unit<sup>(8)</sup>.

By carrying the therapy scheme within the deadline delimited by the Ministry of Health, the transmission chain is interrupted and notifications of new cases are avoided. In this sense, the importance of epidemiological studies is justified by the lack of publications on this theme, and it is expected that the results to subsidize the municipal health management into intervening with the prevention of this disease and avoiding treatment abandonment.

Consequently, this study had as objective to analyze the factors associated with the treatment abandonment rates of new pulmonary tuberculosis cases in the city of Rondonópolis, Mato Grosso, Brazil, from 2008 to 2017.

## METHOD

This is a quantitative, cross-sectional and descriptive study, of historical series of the factors associated with the abandonment of tuberculosis treatment, notified in Rondonópolis-MT, between 2008 and 2017.

The state of Mato Grosso is located in the Brazilian Midwest region and has an estimated population of 3,441,998 inhabitants. Rondonópolis is located in the South region of Mato Grosso, and is approximately 215 km from the capital, with an estimated population of 228,857 inhabitants<sup>(9)</sup>. It has 44 Primary Health Units, six Specialized Outpatient Clinics, and six health service facilities, distributed for outpatient care according to the National Registry of Health Institutions. These units are responsible for the notification of tuberculosis cases.

The medication scheme for the treatment of tuberculosis is made available for free in the Specialized Care Service (*Serviço de Atenção Especializada*, SAE) in Rondonópolis, which also performs an active search of new cases, exams, referrals, vaccination, and chemoprophylaxis. Cases that need hospitalization are referred to the state's reference hospital.

To outline the study population, all new cases of tuberculosis that were notified between 2008 and 2017 were included, which presented a situation of treatment conclusion by discharge, cure, or abandonment and positive bacilloscopy exam. As exclusion criteria, re-entry after abandonment and transfer, relapse entry type, conclusion situation due to death, change of diagnosis, and resistant tuberculosis.

Data collection occurred through a secondary source, by means of the Notifiable Diseases Information System, available in the Statistics Department of the Unified Health System; and the data were stored in the Tabwin application, version 3. The following variables were selected: conclusion situation (discharge, cure, and abandonment); gender (male and female); age range (<14, 15-59 and >60); race (white, black, brown, and indigenous); schooling (illiterate, incomplete and complete elementary/high school or higher education); area of residence (urban, peri-urban and rural); test for Human Immunodeficiency Virus (HIV) (positive, negative and not taken); diabetes (no and yes); alcoholism (no and yes); illicit drugs (no and yes); mental illness (no and yes); and having comorbidities (no and yes).

The statistical analyses were performed in the R program. IN the first place, descriptive analysis was performed. To verify possible associations between variables, the Chi-square and Fisher's Exact tests were used in the cases in which the expected frequencies were below five. Odds Ratio (OR) and respective 95% confidence intervals (95% CI) were estimated. The reference categories were assigned an OR of 1.00.

Despite dealing with secondary and public domain data, this study respects the ethical aspects of research with human beings, according to Resolution 466/2012, and was approved by the Research Ethics Committee of the Júlio Muller Hospital, under opinion No. 1,571,782.

## RESULTS

Between 2008 and 2017, 584 pulmonary tuberculosis cases were notified in the municipality under study; among these cases, 50 (8.56%) abandoned the treatment. The year 2016 stands out, when the notifications were more prevalent (n=71; 12.84%), as well as 2010, with the greatest prevalence of treatment abandonment cases (n=13; 26%) (Table 1).

Table 1 - Cases of notified pulmonary tuberculosis and cases of pulmonary tuberculosis treatment abandonment in Rondonópolis, from 2008 to 2017. Rondonópolis, MT, Brazil, 2019

Year of the Notification	Tuberculosis Cases		Treatment Abandonment Cases		Qui-square (p-value)
	n	%	n	%	
2008	47	8,05	1	2	4.57 (0,003)
2009	40	6,85	4	8	
2010	49	8,39	13	26	
2011	52	8,9	1	2	
2012	65	11,13	5	10	
2013	55	9,41	5	10	
2014	62	10,62	3	6	
2015	71	12,16	6	12	
2016	75	12,84	6	12	
2017	68	11,65	6	12	

Source: The authors (2019).

According to the sociodemographic data, it is observed that the profile of tuberculosis treatment abandonment cases consisted in male individuals (n=31; 62%), aged from 15 to 59 years old (n=47; 94%), brown-skinned (n=27; 54%), complete and/or incomplete elementary school (n=24; 48%) and living in the urban area (n=45; 90%) (Table 2).

Table 2 - Distribution of pulmonary tuberculosis treatment abandonment cases according to sociodemographic variables. Rondonópolis, Mato Grosso, Brazil, 2019 (continues)

	Tuberculosis Treatment Abandonment				OR	95% IC	p-value
	Yes		No				
	n	%	n	%			
Abandonment							
2008 – 2012	24	48	229	42,88	1	-	
2013 – 2017	26	52	305	57,12	1,23	[0,68; 2,20]	0,485
Gender							
Male	31	62	377	70,6	1	-	
Female	19	38	156	29,21	0,67	[0,37; 1,25]	0,198
Unknown	-	-	1	0,19			
Age group							
Over 60 years old	3	6	94	17,6	1	-	
15-59	47	94	423	79,22	<b>3,32</b>	[1,17; 14,32]	<b>0,029</b>

0-14	-	-	17	3,18			
Race							
White	13	26	153	28,65	1	-	
Brown	27	54	269	50,37	1,17	[0,59; 2,42]	0,636
Others (Indigenous, Black and Asian)	9	18	92	17,23	1,15	[0,45; 2,81]	0,756
Unknown/White	1	2	20	3,75	-	-	-
Schooling							
Illiterate	3	6	35	6,55	1	-	
Elementary School (Complete and/or Incomplete)	24	48	261	48,88	1,28	[0,55; 3,88]	0,546
High School (Complete and/or Incomplete)	7	14	88	16,48	1,18	[0,46; 4,27]	0,759
Higher Education (Complete and/or Incomplete)	3	6	25	4,68	0,59	[0,20; 2,63]	0,737
Unknown/ Blank/ Does not apply	13	26	125	23,41	-	-	-
Area of Residence							
Urban	45	90	466	87,27	1		
Peri-urban, Rural and Blank	5	10	68	12,73	1,27	[0,53; 3,85]	0,576

Source: The authors (2019).

In the association analysis of these cases with gender, there was not statistical significance ( $p=0.1977$ ). Regarding the age range, an Odds Ratio value of 3.32 was observed, which means that individuals in the age range from 15 to 59 years old have 3.32 times more risk of abandoning the treatment than the others, as well as  $p=0.0289$  indicates that this reason is significant in relation to these variables. In the studied cases, race ( $p=0.6360$ ), schooling ( $p=0.5455$ ), and area of residence ( $p=0.5762$ ) did not show statistical significance as for the association with treatment abandonment (Table 2).

In relation to the clinical characteristics, the profile of the treatment abandonment cases was as follows: negative HIV test ( $n=36$ ; 72%), non-alcoholics ( $n=34$ ; 68%), non-smokers ( $n=9$ ; 18%), non-diabetics ( $n=45$ ; 90%), with no mental disorder ( $n=46$ ; 92%), not using illicit drugs ( $n=8$ ; 16%), without any other pathologies ( $n=39$ ; 78%) and having undergone DOT ( $n=28$ ; 56%). High unknown or blank data are observed in the smoking ( $n=34$ ; 68%) and illicit drugs ( $n=36$ ; 72%) variables (Table 3).

Table 3 - Distribution of the pulmonary tuberculosis treatment abandonment cases according to the clinical characteristics. Rondonópolis, Mato Grosso, Brazil, 2019

	Tuberculosis Treatment Abandonment						
	Yes		No		OR	95% CI	p-value
	n	%	n	%			
Treatment Abandonment							
2008 – 2012	24	48	229	42,88	1	-	
2013 – 2017	26	52	305	57,12	1,23	[0,68; 2,20]	0,485
HIV test							
Negative	36	72	365	68,35	1	-	
Positive	8	16	61	11,43	0,74	[0,34; 1,80]	0,491
In progress/ Not taken	6	12	108	20,22	-	-	-
Alcoholism							
No	34	68	428	80,15	1	-	-
Yes	13	26	69	12,92	1,38	[0,51; 1,15]	0,145
Unknown/Blank	3	6	37	6,93	-	-	-
Smoking							
No	9	18	453	84,83	1	-	-
Yes	7	14	75	14,05	1,56	[0,87; 1,23]	0,454
Unknown/Blank	34	68	6	1,12	-	-	-
Diabetes							
No	45	90	470	88,02	1	-	-
Yes	3	6	32	5,99	0,97	[0,33; 4,35]	0,973
Unknown/Blank	2	4	32	5,99	-	-	-
Mental Illness							
No	46	92	471	88,2	-	-	-
Yes	1	2	29	5,43	-	-	-
Unknown/ Blank	3	6	34	6,37	-	-	-
Illicit Drugs							
No	8	16	159	29,78	1	-	-
Yes	6	12	22	4,12	1,02	[0,23; 3,02]	0,626
Unknown/ Blank	36	72	353	66,1	-	-	-
Other Disease							
No	39	78	423	79,22	1	-	-
Yes	3	6	25	4,68	0,73	[0,24; 3,03]	0,677
Unknown/ Blank	8	16	86	16,1	-	-	-
DOT performed							
No	10	20	83	15,54	1	-	-
Yes	28	56	346	64,8	<b>1,80</b>	[1,25; 3,46]	<b>0,034</b>
Unknown/ Blank	12	24	105	19,66	-	-	-

Source: The authors (2019).

Regarding the HIV test ( $p=0.4908$ ), alcoholism ( $p=0.1453$ ), smoking, ( $p=0.4538$ ), diabetes mellitus ( $p=0.9730$ ), illicit drugs ( $p=0.6261$ ), and other disease ( $p=0.6765$ ), there has been a statistically significant absence between these variables and treatment abandonment. When analyzed if the DOT was performed, those who underwent it have 1.80 times more chances of abandonment than the individuals who did not.  $p=0.0342$  reveals statistical significance between DOT performed and treatment abandonment (Table 3).

## DISCUSSION

In this study, the minority of the cases (8.56%) abandoned the pulmonary tuberculosis treatment. A finding similar to studies carried out in the Hospital do Rio de Janeiro-RJ from 2007 to 2013 (4.8%)<sup>(10)</sup>; in the state of Alagoas, from 2008 to 2017 (12.27%)<sup>(11)</sup>; and in Pernambuco (11.3%), from 2011 to 2014<sup>(12)</sup>. In general, treatment abandonment is related to a bad prognosis<sup>(13)</sup>.

Despite few treatment abandonment cases notified, the year 2010 presented significant prevalence in relation to other study years (26%). This fact can be related to the management of the tuberculosis cases, with the intensification of follow-up and notification, performed in that year by the health professionals working in the municipality.

In Rondonópolis-MT, most of the treatment abandonment cases (62%) were males. A study in Buenos Aires (Argentina) reveals that there is greater risk for hospitalized men not to adhere to the treatment<sup>(14)</sup>.

As for the age range, most cases were adults (97%). The age range from 20 to 39 years old corresponded to 12.7% of the cases in Pernambuco, from 2011 to 2014<sup>(12)</sup>. In Rio de Janeiro, being 50 years old or older showed an association with the lowest risk of abandoning treatment in relation to the cases of tuberculosis carriers aged 15-29 years old<sup>(15)</sup>. A similar fact in Recife-PE: 20 to 59-year-old individuals generated 85.6% of the notifications between 2005 and 2010<sup>(16)</sup>.

There was a statistical association between age range and abandonment cases in this study. This population from 15 to 59 years old affected by tuberculosis is also affected by economic issues, given that they are inserted in the labor market and are responsible for the family income<sup>(11)</sup>. Another reason for this abandonment is the difficulty in accessing the health services, due to the incompatibility with the workload of the professional occupation<sup>(17)</sup>.

According to the analysis of race in this study, there were more notifications of brown-skinned individuals (54%); corroborating with cases of non-white-skinned individuals (86.5%) in Maranhão, between 2001 and 2010<sup>(18)</sup>. Regardless of race, social and economic inequalities reflect the persistence of tuberculosis in the world, which leads to an impact on morbidity and mortality, including the most vulnerable population<sup>(19)</sup>.

In the schooling variable, complete and/or incomplete elementary school prevailed (48%), corroborating cases in Recife-PE, where there was a greater chance of abandonment in those with no schooling and education levels below incomplete elementary school<sup>(16)</sup>. In Pernambuco, between 2001 and 2014, 12.1% of the cases had low schooling<sup>(12)</sup>.

Low schooling also occurs in the capital of Peru, where patients who are more prone to abandoning treatment are those with less than six years of study<sup>(13)</sup>. A study conducted in Rio de Janeiro-RJ with patients presented a greater risk of abandoning the treatment<sup>(15)</sup>.

In this study, most of the cases (90%) lived in the urban area. Among the notifications of new tuberculosis cases (2008 to 2017), the urban area corresponded to 80.63%<sup>(11)</sup>. In

Belo Horizonte-MG, 86% of the patients hospitalized due to tuberculosis were living in the metropolitan region, a fact related to housing conditions, socioeconomic level, and greater population density<sup>(20)</sup>, which facilitates transmission of the bacillus.

As for HIV tests, 72% presented negative results. Taking this test is established by the Ministry of Health, as individuals with HIV/AIDS have a greater risk of falling ill from tuberculosis, for it is an immunosuppressive disease<sup>(1)</sup>. In 2017, there were 91,000 new tuberculosis cases with HIV in Brazil, and treatment coverage was approximately 87%<sup>(21)</sup>. In Niterói-RJ, it is noted that HIV co-infections take place in central regions, where prostitution areas are concentrated<sup>(22)</sup>.

When the alcoholism variable is analyzed, non-alcoholics total 68% of the cases. In Maranhão, non-alcoholics prevailed (83.8%)<sup>(18)</sup>. Chronic alcoholism is a risk factor for tuberculosis, due to a decline in the immune system, exposure to risky situations, and social fragility<sup>(23)</sup>. Regarding smoking, non-smokers totaled 18%. It is highlighted that smokers with tuberculosis must be informed about the harms that this practice can cause to them and to other individuals, especially to the contacts with greater risk of contracting active tuberculosis<sup>(24)</sup>.

In relation to diabetes mellitus, non-carriers (90%) stand out, a fact that can be justified by the more frequent search for the health service due to the association between diabetes and tuberculosis, the treatment control measures thus being more intensified<sup>(18)</sup>. The importance of providing the diabetes diagnosis to tuberculosis carriers is emphasized, due to the influences caused during the infection<sup>(20)</sup>.

Non-mentally ill individuals accounted for 92% of the abandonment cases. A review study points out that there are high proportions of common mental disorders, anxiety, and/or depression among tuberculosis carriers; however, it did not present statistical data that confirm the association between them<sup>(24)</sup>.

In relation to other diseases, non-carriers accounted for 78% of the study. The relevance of the death cases due to tuberculosis can be related to other comorbidities, such as diseases of the circulatory and digestive systems and neoplasms, which can delay the diagnosis and fail in the treatment of the cases<sup>(25)</sup>.

Analyzing the illicit drugs variable, non-users prevailed (16%). Likewise, in Rio de Janeiro-RJ, between 2007 and 2014, non-users of illicit drugs accounted for 41.7% of treatment abandonment cases<sup>(26)</sup>. Due to the complexity of tuberculosis with the use of illicit drugs, it is necessary for health authorities and professionals to create strategies to evaluate the behavior of the health service users, as well as to establish intervention policies to control the pathology<sup>(27)</sup>.

There was a statistical association between DOT and tuberculosis treatment abandonment, with 56% of the cases. An international review study points out that there is a minimal difference in treatment conclusion when comparing the DOT performed by health professionals self-administration of the medication<sup>(28)</sup>.

This strategy alters the daily routine and generates constraints to the patients when it is carried out in the health unity, one of the factors associated with the difficulty in adhering to the treatment<sup>(8)</sup>. In São Paulo-SP, the need for the patients to attend the consultations in the units caused wear out due to long distance, as well as to inappropriate conditions of public transportation, physical impairment because of the pathology, and extensive waiting time until the consultation<sup>(29)</sup>.

It is up to the municipality to operationalize the DOT and monitor the prevention measures. This is an important tool for controlling the disease; however, it is necessary to reinforce that it is more than just supervising the medication intake so that treatment effectiveness increases<sup>(30)</sup>.

A high number of notifications in blank and/or filled out as unknown is observed, with

the smoking (68%) and illicit drugs (72%) variables standing out. Mandatory notifications of tuberculosis are important for local epidemiological data and are relevant to carry out an active search of new cases and following-up the patients during treatment. In this context, incorrect and/or incomplete filling out of the notification in primary health care reflects a failure of the team and of the health service.

The analysis of this study presented limitations for using a secondary database and due to the lack of important data in the notification. Despite the limitations, the results allowed for a diagnosis of tuberculosis treatment abandonment cases in the municipality in question. Thus, this study is expected to contribute to planning the health actions and to serve as a basis for more studies on this theme.

## CONCLUSION

The adult age range and performing the DOT presented statistical relevance, being factors associated with the tuberculosis treatment abandonment cases in Rondonópolis-MT. In this setting, it is up to the health professionals to carry out prevention strategies aiming to ensure adherence to the treatment of this disease, such as welcoming, following-up the DOT and monitoring adherence, singular therapeutic project, consultation focused on adherence, and conversation circles.

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