

Coinfection of Tuberculosis-HIV in Midwest region of Brazil: an epidemiologic study

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Abstract

*Tuberculosis is a major health problem in Brazil and worldwide, being considered the main cause of infection by a single agent (*Mycobacterium tuberculosis*). In individuals without comorbidities, tuberculosis already has the potential to be a serious and disabling disease, however, among people living with HIV, the risk of lethality is even greater. In this immunodepressed population, there is a vaster chance of therapeutic failure, resistance to drugs, serious adverse reactions and of extrapulmonary and disseminated forms of tuberculosis. The objective of this work was to analyze the epidemiological aspects of TB-HIV coinfection in the Midwest of Brazil between the years 2010 to 2019. It is a longitudinal study, with retrospective character, a descriptive and quantitative approach, using DATASUS database. The results of the study presented that, in the last 10 years, 4,122 people had TB/HIV coinfection, from which 139 died, with a lethality of 3.37%. A reduction in lethality was observed during the years studied. In addition, the analysis of the data in this*

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study showed an insufficient amount of anti-HIV tests in patients tested positive for tuberculosis, in which less than half (40.76%) of TB/HIV coinfecting patients were discharged after being cured and 15.33% abandoned treatment. It is concluded, therefore, that the present study can contribute to information on the longitudinal epidemiology of TB/HIV in the Midwest, which can be used to develop control strategies, favoring the improvement of health services, reducing morbidity and mortality by TB/HIV, and to ensure a better quality of life for the population.

Keywords: Tuberculosis; HIV Infections; Coinfection; Acquired Immunodeficiency Syndrome; Public Health; Brazil; Epidemiology; Disease Notification.

INTRODUCTION AND OBJECTIVE:

Tuberculosis (TB) is a major health problem in Brazil, being registered 200 new cases per day across the country (BRASIL, 2019). This is a curable disease, but it is considered serious and it is among the 10 leading causes of death worldwide, with 10 million cases and more than 1 million deaths per year (WHO, 2019).

TB is the main cause of infection by a single agent (*Mycobacterium tuberculosis*), surpassing even HIV/AIDS and can infect anyone anywhere (WHO, 2019). By 2022, it is estimated that 13 billion dollars will be spent annually on TB prevention and treatment, aiming to benefit 40 million people worldwide (WHO, 2019).

The transmission of TB occurs by air, through a bacilliferous person, who excretes bacilli in secretions from speech, coughing or sneezing. When in contact with healthy individuals, the bacterium is able to reach the alveoli, where it can multiply and cause what is called the primo-infection (BRASIL, 2019).

Infection by the human immunodeficiency virus (HIV) is a potent risk factor for TB, seeing as *Mycobacterium tuberculosis* is an opportunistic microorganism that most commonly affects people with advanced disease, making TB the leading cause of death among people living with HIV (PLHIV) (CORBETT et al., 2003; TRINH et al.,

2015). In 2013, there were 1.1 million new cases of TB-HIV co-infection worldwide, representing 12% of the incident of TB cases and 360 thousand deaths (TRINH et al., 2015).

Due to immunosuppression, HIV infection increases the risk of activating latent Mycobacterium tuberculosis infection (KERAMAT et al., 2020). PLHIV has a 28 times greater risk of illness from TB, compared to the general population (BRAZIL, 2019).

When compared to the general population, PLHIV patients with TB also more frequently present the occurrence of therapeutic failure, resistance to drugs, serious adverse reactions and of the extrapulmonary and disseminated forms of TB (BRASIL, 2019). As a consequence, such individuals have mortality rates 2.4 to 19.0 times higher than those without coinfection (BARBOSA; COSTA, 2014).

Brazil is among the 30 countries with high incidence for TB and TB-HIV considered priority by WHO for the control of the disease in the world. In that manner, the World Health Assembly, in 2014, approved what is called the “Strategy for the End of Tuberculosis”, with Brazil as the main proponent (BRASIL, 2019; WHO, 2014). The Strategy aims to end the global epidemic of the disease, by the means of goals to be met by 2035. Among these goals, it is highlighted the reduction of the incidence rate to less than 10 cases per 100 thousand inhabitants and the number of deaths by TB reduced by 95% (WHO, 2014).

The Midwest region of Brazil consists of the states of Goiás (GO), Mato Grosso (MT) and Mato Grosso do Sul (MS), besides the Federal District (DF), covering an area of 1 606 403.506 km² and it has an estimated population of 16.085 million inhabitants, with a population density of 10.01 inhab./km² (IBGE, 2010).

Regarding TB, the Midwest region has a coefficient of disease incidence of 19.7 new cases per 100 thousand inhabitants (BRASIL, 2016). The proportional distribution of HIV cases in the region corresponds to 6.1% of the total cases in the country (BRASIL, 2016). Observing the number of cases of TB-HIV coinfection, the region occupies the third place among the most prevalent, presenting a rate of 9.4% (BRASIL, 2016).

Considering the magnitude that the problem of TB-HIV coinfection represents, the knowledge of the different aspects related

to the occurrence of this coinfection favors the development of control strategies in the different spheres of health management, increasing the reinforcement for areas with greater risk to the community or for those in which the program's operational situation falls short of the established objectives.

The objective of this study, conclusively, was to analyze the epidemiological aspects of TB-HIV coinfection in the Midwest of Brazil.

METHODOLOGY:

This article is a longitudinal, retrospective study with a descriptive and quantitative approach. All new cases of diagnosis of infections by *Mycobacterium tuberculosis* in the Midwest region of Brazil, between 2010 and 2019, were included. The database used in the research was made available by the Information System for Notifiable Diseases (SINAN) and DATASUS until May 2019. It was chosen an approach of the period between 2010 and 2019 because it is a long period that allows a broad view of the disease's progression in the region's population. The elaboration of the TB- HIV coinfection profile considered the following clinical and epidemiological variables:

Sociodemographic variables	Clinical variables
Sex	Clinical form
Age group	Diagnostic tests
Institutionalized	Complications
	Disclosure

The presentation of the information was carried out by means of graphs and tables and discussion of the findings made by the specific literature on the subject. As this is a study carried out using data from secondary sources, approval by the Research Ethics Committee was not necessary.

RESULTS:

41,716 cases of tuberculosis were reported in the Midwest (MW) of Brazil in the years 2010 to 2019. Of these, 11,160 did not undergo the HIV test and 30,556 did. Regarding those who performed, 25,101 had a negative result; 1,217 had an ongoing serology and in 116 ignored this information. 4,122 HIV positive cases were registered among those infected with TB, thus characterizing in this region a percentage of 9.88% of TB/HIV coinfection in the last 10 years.

Related to deaths from coinfection, there were 139 in total, which makes a lethality rate of 3.37%. Between the studied years, 2010 had the highest number of deaths and the highest mortality rate of 20% and 5.68% respectively. Table 1 shows, during the years from 2010 to 2019, the results of the performance of anti-HIV serology and the deaths from TB-HIV coinfection in the Midwest.

Year Diagnosis	Ign/White	HIV Positive	Death TB-HIV	HIV Negative	Processing	Unperformed	Total
2010	1	352	20	2195	136	1073	3757
2011	1	382	11	2153	153	1207	3896
2012	2	420	16	2268	194	1424	4308
2013	91	405	11	2387	139	1507	4529
2014	7	427	12	2359	77	1425	4295
2015	1	416	16	2555	57	989	4018
2016	4	437	16	2514	71	1026	4052
2017	7	473	16	2672	65	953	4170
2018	-	445	11	3193	79	830	4547
2019	2	365	10	2805	246	726	4144
Total	116	4122	139	25101	1217	11160	41716

Table 1: Sorography HIV and deaths by TB-HIV coinfection in the Midwest 2010-2019.

Source: Notifiable Diseases Information System. Datasus, 2020.

Regarding the mortality rate of TB-HIV coinfection, the tendency during the years studied was regressive. From year 2015 to 2018 there was a progressive reduction in mortality, however in 2019, it was shown again an increase in comparison to the previous year. The year 2010 was the one that obtained the highest fatality rate, while the 2018, the smallest. The Figure 1 shows the evolution of the mortality rate of TB-HIV coinfection in the Midwest in the past 10 years.

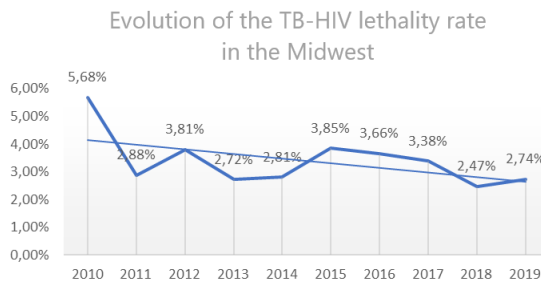


Figure 1 TB-HIV lethality rate. Source: Notifiable Diseases Information System. Datasus, 2020.

The Table 2 shows the analysis of epidemiological variables related to cases of coinfection by TB-HIV in the Midwest of Brazil through the years 2010-2019. The male sex was the most affected, with a total of 74.92%. The most prevalent age group was between 15-39 years (54.60%), followed by 40-59 years (39.85%). 5.9% of coinfecting individuals were institutionalized. Regarding the disclosure, 40.76% of coinfecting patients were cured of tuberculosis, 15.33% abandoned treatment, 0.49% developed drug-resistant TB and 3.37% died from TB. The most frequent clinical form was pulmonary type, presented in 70.11% of coinfecting, followed by extrapulmonary in 20.57%; the double clinical scenarios of pulmonary and extrapulmonary forms were present in 9.32% of the analyzed population. In the case of extrapulmonary forms, the peripheral ganglion was the most frequent (39.86%), followed by meningoencephalic and miliary, with 26.42% and 26.30%, respectively; the pleural form also had a considerable incidence, with 24.17%. Of the patients coinfecting with TB-HIV, 92.24% showed clinical manifestations of acquired immunodeficiency

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syndrome (AIDS); 65.38% underwent microscopic sputum smear and 32.05% were positive on the 1st trial/test.

Variable	N° of cases	Percentage (%)
SEX		
Male	3088	74,92%
Female	1033	25,06%
Ignored	1	0,02%
AGE GROUP		
<15 years old	37	0,90%
15-39 years old	2.251	54,60%
40-59 years old	1.643	39,85%
> 60 years old	191	4,63%
INSTITUTIONALIZED		
Ign/White	2304	55,90%
No	1575	38,21%
Yes	243	5,90%
DISCLOSURE		
Ign/White	429	10,41%
Cured	1680	40,76%
Abandonment	632	15,33%
Death by tuberculosis	139	3,37%
Death by other causes	683	16,57%
Transference	453	10,99%
TB-DR	20	0,49%
Treatment Change	47	1,14%

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Bankruptcy	1	0,02%
Primary Abandonment	38	0,92%
CLINICAL FORM		
Pulmonary	2890	70,11%
Extrapulmonary	848	20,57%
Pulmonary+Extrapulmonary	384	9,32%
IF EXTRAPULMONARY		
Pleural	205	24,17%
Peripheral ganglionar	338	39,86%
Genitourinary	10	1,18%
Bone	26	3,07%
Miliary	223	26,30%
Meningoencephalic	224	26,42%
Other	203	23,94%
AIDS		
Ign/White	114	2,77%
Yes	3802	92,24%
No	206	5,00%
1st SPARROW BACILLOSCOPY		
Positive	1321	32,05%
Negative	1374	33,33%
Unperformed	1288	31,25%
Doesn't apply	139	3,37%
SPUTUM CULTURE		

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Positive	709	17,20%
Negative	591	14,34%
In Progress	226	5,48%
Unperformed	2596	62,98%

Table 2 epidemiological and clinical variables of cases of coinfection TB-HIV in the Midwest of Brazil in the years 2010-2019.

Source: Notifiable Diseases Information System. Datasus, 2020.

DISCUSSION:

HIV seropositivity is often discovered during the diagnosis of tuberculosis. The advent of the HIV/AIDS epidemic in Brazil, a country endemic for tuberculosis, has resulted in a significant increase in tuberculosis cases with more complications and a higher incidence of death (BRASIL, 2011).

Although the Midwest has the lowest TB incidence coefficient (/100 thousand inhab.) of the Federation Units in Brazil (19.7/100 thousand inhab.), it is still considerably far from reaching the goals of the “Strategy for the End of Tuberculosis” defined by the WHO in 2014 (BRASIL, 2016). According to WHO, reaching the goal of reducing the tuberculosis incidence coefficient to less than 10 cases per 100 thousand inhabitants would represent the end of tuberculosis as a public health problem (WHO, 2014).

In this study, the percentage of people diagnosed with TB-HIV coinfection was 9.88% in the Midwest for the last 10 years. A value slightly higher than that found in a previous study (9.4%) (BRASIL, 2016). For other states and countries, the percent of the coinfection TB-HIV in the Midwest was higher than in the Northeast region (4.86%) (Barbosa; Costa, 2014), Minas Gerais (8.3%) (Augusto et al., 2013) and Vietnam (7.2%) (TRINH et al., 2015), however it was lower than in the Southern (17.3%) and Northern (9.9%) regions (BRAZIL, 2016) and in Thailand (15%) (TRINH et al., 2015).

The early diagnosis of HIV infection in people with TB has an important impact on the clinical course of the disease. Therefore,

every patient diagnosed with tuberculosis should be tested for HIV as early as possible, allowing early initiation of antiretroviral therapy and prophylaxis of opportunistic infections (BRAZIL, 2019). However, in the present study, it was noticed a percentage of diagnosed TB cases in which the anti-HIV test was not performed (n = 11,160) (26.75%), which is considered high.

In the epidemiological study in Brazil (2016), the percentage of people diagnosed with TB who did not undergo anti-HIV testing in the Midwest was 33.5%. Therefore, it is understood that there has been an improvement in this region in recent years, that is, more people performed the test considered routine in confirmed TB cases. These high percentages of people who have not been tested for HIV may indicate the need for greater efforts by health professionals and managers, so that everyone has access to early and adequate diagnosis and treatment.

From all the analyzed cases of TB-HIV coinfection, there was a predominance in males (74.92%). This predominance is in accordance with studies by Junior, Rocha and Soares (2019) in the state of Alagoas, Rossetto et al. (2019) in the city of Porto Alegre (RS) and van der Werf et al. (2016) in 20 countries of the European Union. The factors that interfere in the higher occurrence of cases in men have not been fully clarified yet, however, they may be related to several conditions, both biological and self-care for health and even underdiagnosis in women (BALDAN; FERRAUDO; ANDRADE, 2017; BARBOSA; COSTA, 2014).

This study showed that there is a greater number of cases of TB-HIV coinfection in individuals aged 15 to 39 years, which reflects a higher incidence of TB in this group or more frequent HIV testing in this age group. A similar conclusion was found in other studies (NETO et al., 2012; ROSSETTO et al., 2019). The lifestyle of the population with vulnerable behaviors in this age group, can result in greater exposure to HIV and M. tuberculosis (BALDAN; FERRAUDO; ANDRADE, 2017). In addition, as it is a predominantly young adult population, it can result in serious social implications, as this group should be inserted in the labor market and helping to support their families (BARBOSA; COSTA, 2014).

For groups of people living in institutions such as orphanages, shelters, nursing homes and, especially, in prisons, tuberculosis has always been a serious health problem, as environmental conditions favor not only its transmission but also illness (BRASIL, 2019). In this study, the percentage of TB-HIV coinfection cases in institutionalized people was 5.9%. This amount follows the same as that observed in other studies in Brazil (BARBOSA; COSTA, 2014; JUNIOR; ROCHA; SOARES, 2019).

Sputum collection for sputum smear, culture, species identification and sensitivity testing should be insistently performed as a routine investigation of suspected TB cases, using, when necessary, induced sputum or bronchoscopy (BRASIL, 2011). In this research, however, there was a high number of cases in which the bacilloscopic examination was not performed (31.25%) and neither was the sputum culture (62.98%). An epidemiological study in Brazil in 2016, also shows a high number of cases in which these diagnostic tests were not carried out (BRASIL, 2016).

Regarding the clinical characteristics observed in this study, the pulmonary form was the one with the highest number of cases. This finding is corroborated by several studies carried out in Brazil (BALDAN; FERRAUDO; ANDRADE, 2017; JUNIOR; ROCHA; SOARES, 2019; NETO et al., 2012). The extrapulmonary form is not considered a risk factor regarding the transmission of the disease, but there has been an increase in its incidence, a fact linked to the HIV epidemic (BRASIL, 2019). The percentage of extrapulmonary forms found was 20.57%, similar to the studies by Baldan, Ferraudo and Andrade (2017) and Barbosa and Costa (2014).

In cases of the extrapulmonary form of TB in those coinfecting with HIV, the most frequent presentation was the peripheral ganglion (39.86%), followed by meningoencephalic (26.42%). Regarding the peripheral ganglionic form, a similar result was found in the Northeast of Brazil in the study by Barbosa and Costa (2014), being the main form of extrapulmonary involvement. However, Barros et al. (2014), in the municipality of Campina Grande (PB), had the pleural form as the most incident in coinfecting TB/HIV in their study.

The Ministry of Health has set a goal of at least 85% cure and less than 5% abandonment for tuberculosis cases. To achieve this

goal, directly observed treatment (DOT) is used, aiming to strengthen the patient's adherence to treatment and to prevent the appearance of drug-resistant strains, reducing cases of abandonment and increasing the likelihood of cure (BRASIL, 2011). The analysis of the data in this study showed that less than half (40.76%) of TB/HIV coinfecting patients were discharged after being cured. A similar result was found in the studies by Baldan, Ferraudo and Andrade (2017) and Junior, Rocha and Soares (2019). However, in the studies by van der Werf et al. (2016), with European Union countries, and de Neto et al. (2012), in Maranhão, more than half of the cases of TB/HIV coinfection were cured and successful with treatment.

The effectiveness of the service was also shown to be insufficient due to the rate of treatment abandonment, which was 15.33%, far exceeding the goal below 5% of the Ministry of Health (BRASIL, 2011). In other studies, an average rate of 12.6% was found in Campina Grande (PB) (BARROS et al., 2014), 17.4% in Alagoas (JUNIOR; ROCHA; SOARES, 2019) and 35.6% in Porto Alegre (RS) (ROSSETTO et al., 2019).

Regarding the death rate, 3.37% of the analyzed TB/HIV coinfecting died of tuberculosis. This result was inferior to several other studies (BALDAN; FERRAUDO; ANDRADE, 2017; ROSSETTO et al., 2019; VAN DER WERF et al., 2016), demonstrating the evolution of the Midwest Region in the face of this disease.

Importantly, during the study, it was found the presence of limitations, such as the bad filling of some fields of the notification form and underreporting caused by it. According to Santos' research (2014), the proportion of AIDS underreporting based on SINAN TB records during the years 2001 to 2010 for the state of Pernambuco was 38%.

Despite these limitations, the results presented here fulfill the role of providing an overview of the clinical and epidemiological aspects of TB/HIV coinfection in the region under analysis, since they were based on an official database provided by the Ministry of Health.

CONCLUSION:

From the analysis of the results obtained, it is evident that, during the investigated period, 9.8% cases of TB had coinfection with HIV, however, among the reported cases, 26.7% did not perform the anti-HIV test and 2, 9% of those performed, serology was in progress.

The results express significant attenuation after the first year investigated and greater stability in the years 2015 to 2018, the latter being the year with the lowest rates of TB lethality cases in HIV seropositive population in the Midwest of Brazil, however in 2019 it again presented an increase in relation to the previous year.

Patients with TB-HIV coinfection in this region were found to be the majority male, at an economically productive age, between 15-39 years old, with a significant percentage of non-institutionalized individuals and with high evolution for cure. Pulmonary tuberculosis was the most prevalent clinical form, looking closely to the extrapulmonary form, with a greater number of peripheral ganglia involvement, followed by meningoencephalic. From the patients with TB-HIV coinfection, the majority had clinical manifestations of the acquired immunodeficiency syndrome (AIDS), and a considerable portion of this group had a positive result in the first smear performed.

Finally, this study may contribute to information about longitudinal epidemiology of TB/HIV in the Midwest, which might be used to the creation of control strategies, favoring the improvement of health services, reducing morbidity and mortality from TB/HIV, and thus ensure a better quality of life for the population.

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