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# **EPIDEMIOLOGICAL ANALYSIS OF TUBERCULOSIS/HIV COINFECTION**

Layze Braz de Oliveira<sup>1</sup>, Christefany Régia Braz Costar<sup>1</sup>, Artur Acelino Francisco Luz Nunes Queiroz<sup>2</sup>, Telma Maria Evangelista de Araújo<sup>3</sup>, Karinna Alves Amorim de Sousa<sup>4</sup>, Renata Karina Reis<sup>5</sup>

**ABSTRACT:** Objective: analyze the epidemiological profile of coinfection by tuberculosis and the immunodeficiency virus. Method: descriptive study, developed based on a survey in the database of the Disease Notification System in the State of Piauí between 2007 and 2016. The data were collected through an instrument with sociodemographic characteristics and data related to the coinfection by tuberculosis and the immunodeficiency virus. Simple descriptive analysis was applied. Results: The prevalence of coinfection by tuberculosis and the immunodeficiency virus amounted to 6.1% of the patients (n=619). The data show the predominance of male individuals (n=467/75.4%), adults between 20 and 49 years old (n=492/79.5%) and mulattos (n=457/ 73.8%). The most identified clinical form of tuberculosis was the pulmonary with n=412 (66.6%) cases. These patients' cure percentage corresponded to 60.8%. Conclusion: The results appointed a high prevalence of this coinfection and a high detection of the infection by the immunodeficiency virus in tuberculosis patients.

**DESCRIPTORS:** Tuberculosis; HIV; Prevalence; Epidemiology; Coinfection.

# ANÁLISE EPIDEMIOLÓGICA DA COINFECÇÃO TUBERCULOSE/HIV

**RESUMO:** Objetivo: analisar o perfil epidemiológico da coinfecção tuberculose e o vírus da imunodeficiência. Método: estudo descritivo, realizado com levantamento na base de dados do Sistema de Informação de Agravos de Notificação no estado do Piauí, no período de 2007 a 2016. A coleta ocorreu por meio de instrumento contendo características sociodemográficas e relacionadas à coinfecção Tuberculose/vírus da imunodeficiência. Realizou-se análise descritiva simples. Resultados: A prevalência da coinfecção tuberculose e vírus da imunodeficiência foi de 6,1% pacientes (n=619). Os dados mostram a predominância de indivíduos do sexo masculino (n=467/75,4%), adultos com faixa etária entre 20 a 49 anos (n=492/79,5%) e pardos (n=457/73,8%). A forma clínica da tuberculose mais encontrada foi a pulmonar com n=412 (66,6%) casos. O percentual de cura dos destes pacientes foi de 60,8%. Conclusão: Os resultados apontaram uma alta prevalência dessa coinfecção e uma elevada detecção da infecção do vírus da imunodeficiência em pacientes com tuberculose.

**DESCRITORES:** Tuberculose; HIV; Prevalência; Epidemiologia; Coinfecção.

#### ANÁLISIS EPIDEMIOLÓGICO DE LA COINFECCIÓN TUBERCULOSIS/VIH

**RESUMEN:** Objetivo: analizar el perfil epidemiológico de la coinfección por la tuberculosis y el virus de la inmunodeficiencia. Método: estudio descriptivo con búsqueda en la base de datos del Sistema de Información de Agravios de Notificación en el estado de Piauí, en el período de 2007 a 2016. Los datos fueron recolectados mediante instrumento con características sociodemográficas y relacionadas a la coinfección Tuberculosis/virus de la inmunodeficiencia. Fue aplicado análisis descriptivo simple. Resultados: La prevalencia de la coinfección tuberculosis y virus de la inmunodeficiencia correspondió al 6,1% de los pacientes (n=619). Los datos muestran la predominancia de individuos del sexo masculino (n=467/75,4%), adultos con rango de edad entre 20 y 49 años (n=492/79,5%) y pardos (n=457/73,8%). La forma clínica de la tuberculosis más encontrada fue la pulmonar con n=412 (66,6%) casos. El porcentaje de cura de estos pacientes fue del 60,8%. Conclusión: Los resultados indicaron alta prevalencia de esa coinfección y alta detección de la coinfección por el virus de la inmunodeficiencia en pacientes con tuberculosis.

**DESCRIPTORES:** Tuberculosis; VIH; Prevalencia; Epidemiología; Coinfección.

Corresponding author: Layze Braz de Oliveira

Universidade de São Paulo

Av. dos Bandeirantes, 3900 - 14040-902 - Ribeirão Preto, SP, Brasil

E-mail: layzebraz@usp.br

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<sup>&</sup>lt;sup>1</sup>RN. Master's student in Nursing. University of São Paulo. Ribeirão Preto, SP, Brazil.

<sup>&</sup>lt;sup>2</sup>RN. Master's student in Nursing. University of São Paulo. Ribeirão Preto, SP, Brazil.

<sup>&</sup>lt;sup>3</sup>RN. Ph.D. in Nursing. Professor, Federal University of Piauí. Teresina, PI, Brazil.

<sup>&</sup>lt;sup>4</sup>RN. Management Specialist in Tuberculosis control programs. Transmissible Disease Coordinator, Piauí State Health Department. Teresina, PI, Brazil.

<sup>&</sup>lt;sup>5</sup>RN. Ph.D. in Nursing. Nursing Professor, University of São Paulo. Ribeirão Preto, SP, Brazil.

#### INTRODUCTION

Tuberculosis (TB) is considered a resurging disease, due to the gradual increase in the number of cases in recent years. The main factors predisposing to TB acquisition follow the causal model of the epidemiological triad, which shows that the interaction among the bacillus, the host and environmental factors increases the probability of catching TB<sup>(1)</sup>.

Although part of the deaths caused by tuberculosis is preventable, this is the second largest cause of deaths by infectious disease in the world, behind the human immunodeficiency virus (HIV) only. In 2015, the World Health Organization (WHO) estimated that there were 9.6 million new TB cases worldwide and about one-third of these patients may never have been diagnosed or treated. Among the new cases, 1.2 million were coinfected with the HIV virus and 0.4% of the deaths occurred associated with HIV-TB coinfection<sup>(2)</sup>.

Tuberculosis, caused by Mycobacterium tuberculosis (MTB), is an opportunistic infection that causes exacerbation of the viral load and a decrease in CD4 counts in HIV-positive individuals. HIV infection can also alter the pathogenesis of MTB, leading to negative sputum smear microscopy, atypical radiographic manifestations and extrapulmonary manifestations, making the diagnosis of this disease difficult<sup>(3)</sup>.

People living with HIV are approximately 30 times more likely to develop TB when compared to those who are not infected with HIV, so HIV testing is a standard recommendation for all individuals with TB.

HIV testing coverage among tuberculosis patients remains low in health services. In Brazil, rapid HIV testing for these patients performed well in the Center-West, although it is assumed that there are performance disparities among the different regions of the country<sup>(4-5)</sup>.

The proposal of the Joint United Nations Program on HIV/AIDS (UNAIDS) was that 90% of people who had the HIV virus would know their serostatus by 2010. Although HIV testing has become widely available, barriers remain for its implementation. Countries with high epidemics, such as African nations, still underestimate the actual magnitude of this infection. The main barriers that interfere in this implementation are the lack of guidance, low adherence by health workers, lack of HIV kits and inappropriate supervision by both TB and HIV programs<sup>(4,6-7)</sup>.

Therefore, this study aims to characterize the epidemiological profile of TB/HIV co-infection, in order to promote the discussion about care by health services and provide support to implement measures aimed at preventing this coinfection.

## METHOD

This is a descriptive, epidemiological study, carried out based on the data available in DATASUS, through the SINAN Information System on Notifiable Diseases in the state of Piauí. The data were collected in March 2017 and refer to the years 2007 till 2016.

Existing instruments were used to collect the data: SINANNET notification sheets describing the epidemiological profile of TB/HIV coinfection. Information is provided on the sociodemographic profile of the individuals, the closure situation of TB cases and the performance of a serological test for HIV detection. The researchers themselves carried out the research, who are part of the State Health Care Management.

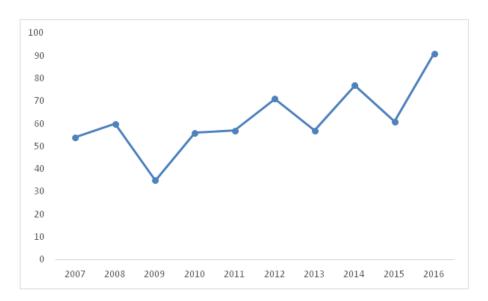
SINAN data mainly come from the reporting and investigation of cases of diseases that figure on the national list of notifiable conditions<sup>(8)</sup>.

After the data collection, the data was tabulated in the program Excel. A simple descriptive analysis was performed. TABNET software was used for the analysis of the SINAN data. The most significant findings were presented in tables. The discussion of the data was based on the scientific production on the subject. The study was submitted and approved by the Ethics Committee of the Federal University

of Piauí, under opinion 1.576.964.

## RESULTS

Of the 10,154 reported TB cases in the state of Piauí between 2007 and 2016, 619 (6.1%) were coinfected with HIV / TB. The largest number of individuals was diagnosed in 2016 with a total of 91 cases, and the smallest in 2009 with 35 cases, representing a heterogeneous increase in the prevalence of this coinfection (Graph 1).



Graph 1 – Distribution of HIV in cases of Tuberculosis per year in-2007 till 2016 (n=619). Teresina, PI, Brazil, 2017

As regards the subjects' profile, men were predominant (75.4%; n=467). Ages ranged between under one year old and over 80 years old. A higher frequency of coinfected patients was observed in the age range 35-49 years (41.5%; n=257), followed by the group 20-34 years with 38% (n=235). Lower percentages were found in children and adolescents.

Table 1 – Distribution of HIV in cases of Tuberculosis per sex, age range and clinical form in Piauí-2007 till 2016 (n=619). Teresina, PI, Brazil, 2017 (continues)

Variables	N	%
Sex		
Female	152	25.6
Male	467	75.4
Age range (years)		
<1 year	2	0.3
1-4	6	1
5-9	3	0.5
10-14	5	0.8
15-19	6	1
20-34	235	38
35-49	257	41.5
50-64	89	14.3

65-79	13	2.1				
80 e +	3	0.5				
Ethnic origin						
Mulatto	457	73.8				
White	60	9.7				
Yellow	5	0.8				
African descendant	81	13.1				
Unknown/White	16	2.6				
Clinical form						
Pulmonary	412	66.6				
Extrapulmonary	157	25.4				
Pulmonary+Extrapulmonary	50	8				

What the ethnic origin is concerned, 73.8% (n=457) of the individuals were mulatto, followed by white and African descendants 9.7% (n=60) and 13.1% (n=81), respectively. The pulmonary clinical form was predominant with 66.6% (n=412) of the reports, followed by extrapulmonary TB 25.4% (n=157) and 8% (n=50) of the cases presented both forms of the disease (pulmonary and extrapulmonary).

Table 2 – Closure situation of Tuberculosis cases in the State of Piauí - 2007 till 2016 (n=10154). Teresina, PI, Brazil, 2017

Closure situation	N	%
Cure	6178	60.8
Abandonment	484	4.8
Death by Tuberculosis	351	3.5
Death by other causes	385	3.8
Transfer	2031	20
Drug resistant tuberculosis (TB/DR)	43	0.4
Change in scheme	6	0.06
Primary default	5	0.04
Unknown/Blank	671	6.6

The analysis of the results of the closure situation of TB cases in the state revealed a cure rate of 60.8% (n=6178) and a significant number of cases of default (4.8%; n=484), death (3.5%; n=351) and unknown/blank (6.6%; n=671).

Table 3 – Serological test for the detection of HIV in tuberculosis cases. 2007 till 2016 (n=10154). Teresina, PI, Brazil, 2017 (continues)

Year	Positive		Negative		In progress		Not executed		Total
Diagnosis	n	%	n	%	n	%	n	%	
2007	54	4.0	337	24.9	177	13.0	789	58.1	1357
2008	60	4.9	373	30.5	256	20.9	535	43.7	1224
2009	35	3.2	383	34.5	201	18.1	490	44.2	1109
2010	56	5.6	478	48.1	42	4.2	418	42.1	994

2011	57	5.7	451	45.1	56	5.6	436	43.6	1000
2012	71	7.7	492	53.4	36	4.1	321	34.8	920
2013	57	5.9	561	58.3	38	3.9	307	31.9	963
2014	77	8.7	564	63.4	22	2.5	226	25.4	889
2015	61	7.4	583	70.4	19	2.3	164	19.8	828
2016	91	10.5	493	56.7	92	10.5	194	22.3	870
Total	619	6.1	4715	46.4	939	9.2	3880	38.2	10154

Table 3 represents the percentage of patients with a request for serological testing for HIV in relation to the total number of tuberculosis cases per year studied. In this time series, the percentage of tuberculosis patients not tested for HIV infection has declined over the years. Similarly, the percentage of patients with a known serostatus in relation to the total number of tuberculosis cases increased from 28.9% in 2007 to 67.1% in 2016 and only 0.1% (n = 1) of the notifications in 2015 it was blank/unknown.

The main limitations of the study involve the absence of the outcome for the TB/HIV coinfected patients, thus not presenting the case closure situation. In the course of this time series, there was a rise in the number of coinfected patients, which increased heterogeneously (Graph 1). In contrast, the number of notified tuberculosis patients dropped over the years (Table 3).

#### DISCUSSION

The World Health Organization (WHO) reported advances in the treatment of tuberculosis, with a 47% reduction in mortality between 1990 and 2015. The incidence of TB has decreased by 1.4% per year since 2000, but the number of notifications increased to an incidence of 10.4 million cases in 2015, 11% of which were infected with HIV. The main regions hosting these two infections are Sub-Saharan Africa and the countries of the former Soviet Union<sup>(9)</sup>.

TB has altered the prospects of control in the world due to the increase in the number of cases. In Brazil, the Northeast is the most endemic region for TB/HIV coinfection, with incidence and mortality rates that surpass other regions, such as the Midwest and South<sup>(10)</sup>.

In this study, the scenario of TB-HIV coinfection is appointed. In addition, the approach was presented to identify the HIV diagnosis in patients who were initially detected for TB treatment by means of screening.

Concerning the sociodemographic characteristics of people with TB coinfected with HIV, the predominance of male adults between 20 and 49 years old (79.5%) stands out. The results corroborate a study carried out in a developing country, which indicates that the large majority of this coinfection is concentrated in the economically productive age group (between 25 and 49 years). This fact can be justified by greater exposure to the activities performed in this stage of life, such as sexual intercourse, blood transfusions with syringes and contaminated needles, and intravenous drug use<sup>(11)</sup>.

Although the factors that determine the higher frequency of the disease in men remain unclear, but this fact may be related to several conditions, both biological, related to self-care for one's health, and low diagnosis in women<sup>(12)</sup>.

Regarding the clinical form, the predominance of pulmonary tuberculosis was identified, in line with other studies on TB and HIV co-infection. This clinical form is characterized by its high infectivity, so it is urgent to confirm infection by tuberculosis early, with a view to interrupting the transmission chain of this disease<sup>(13-15)</sup>.

One of the main factors predisposing to the high prevalence of this clinical form is the preference of the pathogen for the pulmonary parenchyma. Thus, respiratory problems figure among the most frequent complications in people infected with HIV and tuberculosis becomes the most common opportunistic infection and one of the main causes of hospitalization in this population segment<sup>(16-17)</sup>.

The diagnosis of pulmonary tuberculosis in immunodepressed patients is characterized by the presence of chronic cough for at least two to three weeks, with evening fever, weight loss, anorexia, asthenia and night sweating<sup>(17)</sup>.

Regarding the reasons for the closure of TB cases, the cure rates were still lower than those agreed upon by WHO, which aims to cure 85% of new cases. It follows that patient monitoring through the consultations favors the treatment success and consequent cure, especially due to the clarification of doubts about the disease, the treatment and the transmission. The absence of the patient from the scheduled appointments is a sign of possible intention to abandon treatment<sup>(18-19)</sup>.

Although the percentage of TB treatment abandonment is close to WHO recommendations (5%), it should be highlighted that this problem needs emphasis, being one of the main limitations to cure this infection, besides entailing implications for society, such as the increased development of multidrugresistant tuberculosis, mortality and relapses<sup>(16,18)</sup>.

TB-HIV coinfection is a factor that predisposes to the abandonment of tuberculosis treatment, as adverse reactions and drug interactions are more intense in seropositive patients, often causing the patient to opt for the priority use of antiretrovirals instead of the TB drug. In this perspective, the implementation of Directly Observed Treatment (DOTS) was proposed as a goal, with the purpose of minimizing or even eliminating cases of treatment abandonment and stimulating the correct use of the drug<sup>(18)</sup>.

Regarding the prevalence of coinfected patients, the results found reveal that the findings in this time series do not accurately reflect the actual magnitude of this coinfection, as more than half of the files were completed as "not performed" or "in progress". The delay in the release of the results and the lack of updating of the data by the Municipal Health Department can favor this high percentage of completion as "in progress".

It is deducted that there are structural failures in health services, such as loss of examinations, delay in receiving the result, difficulty to access the laboratory and even lack of updating of the information system. In this perspective, the early diagnosis of TB-HIV coinfection is characterized by deficiencies in the information flow in the care network and lack of suitable infrastructure.

TB-HIV coinfection still poses a major challenge to global health, especially in countries with limited resources and large populations of individuals such as Africa and Asia, posing diagnostic and therapeutic challenges and exerting enormous pressure on health systems<sup>(20)</sup>.

Despite the proposal of the National Plan for Tuberculosis Control, which establishes that all patients with tuberculosis be submitted to the anti-HIV test, in practice, the request and execution rates of this serology test are low. The main implication for this practice is the uncertainty about the true dimension of this problem<sup>(17,21)</sup>.

There are several recommendations to support TB control, such as strengthening the decentralization of control actions to Health Units, and building a search routine in other information systems to improve the quality of information on the closures of TB cases and assess the tuberculosis surveillance system in the city, in order to set the guidelines and priorities for improving the cure, abandonment and incidence indicators of the disease<sup>(22)</sup>.

Although this goes beyond the scope of this study, it is important to highlight that the main challenge is the improvement of SINAN-TB, the main goal being the completeness of the information, which in turn will support the analysis of the diseases and will permit appropriate evaluation, offering new findings of epidemiological value.

The study presented as a limitation the cross-sectional design that did not permit the establishment of causal relationships and the follow-up of the patients. In addition, its findings cover the epidemiological characteristics of tuberculosis coinfection and the immunodeficiency virus of patients diagnosed in a state in the Northeast of Brazil.

## CONCLUSION

In this study, it was observed that most individuals coinfected with TB/HIV were male, in the age group of 35 to 49 years and mulatto. Pulmonary tuberculosis was the most prevalent form. The distribution of coinfected individuals throughout the study period was heterogeneous.

The outcome of the tuberculosis treatment is mostly characterized by cure. Nevertheless, despite the access to the treatment of these two infections and the expansion of rapid HIV testing, there is an urgent need to implement interventions appropriate to the multiple circumstances, with a view to achieving high cure rates of TB patients and high detection rates of patients coinfected with TB and HIV.

Although the detection of HIV based on the cases of tuberculosis infection is not recommended, this reality is in fact present. In this context, it is relevant to identify this infection early, as well as to implement rapid tests to detect HIV cases prior to the onset of opportunistic diseases and AIDS.

Despite the efforts health teams make, coinfection still poses a severe problem, as people contaminated by both infections are potent sources to spread the disease. In this perspective, it is important that the State takes into account the local reality and seeks measures to reduce and combat these diseases.

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