









Temporal trend of the incidence of TB/HIV coinfection and HIV testing of the old Brazilian population from 2008 to 2018

Janderson Diego Pimenta da Silva¹ 
Rosemeiry Capriata de Souza Azevedo¹ 
Annelita Almeida Oliveira Reiners¹ 
Aenne Zandonadi Rodrigues Santana¹ 
Amanda Cristina de Souza Andrade² 
Ana Carolina Macri Gaspar Vendramini¹ 

Abstract

Objective: Analyze the temporal trend of the incidence of TB/HIV coinfection and the ratio of HIV testing in the Brazilian old population and its regions from 2008 to 2018. **Method:** Ecological, time-series study carried out with all new cases of old people with TB/HIV coinfection. The data were extracted from SINAN-TB and analyzed using the *Prais-Winsten* method. **Results:** In the temporal analysis of the incidence, Brazil showed a stable trend (VPA 2.1), and regarding the regions: Southeast, decreasing trend (VPA -2.15); Northeast and North, increasing trends (VPA 9.92; VPA 10.18, respectively); and South and Midwest, stable trends (VPA 0.17; VPA 4.81, respectively). In Brazil and its regions, the ratio of HIV testing showed growing trends: Brazil (VPA 12.82), North (VPA 20.46), Northeast (VPA 17.85), Southeast (VPA 10.29), South (VPA 7.11), and Midwest (VPA 6.10). Of the 3213 new cases of TB/HIV coinfection reported during the study period, most (68.66%) were male, 78.74% in the age group from 60 to 69. As for the clinical form, the majority (72.70%) was of the pulmonary type. **Conclusion:** Given the magnitude and implications of TB/HIV coinfection in the old population for health care services, these findings may support health professionals and managers in adopting effective measures to control these diseases.

Keywords: Coinfection. Tuberculosis. HIV. Time Series Studies. Health of the Elderly.

¹ Universidade Federal de Mato Grosso, Faculdade de Enfermagem, Programa de Pós-Graduação em Enfermagem. Cuiabá, MT, Brasil.

² Universidade Federal de Mato Grosso, Instituto de Saúde Coletiva, Programa de Pós-Graduação em Saúde Coletiva. Cuiabá, MT, Brasil.

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Correspondence
Janderson Diego Pimenta da Silva
jandersonpimenta@hotmail.com

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INTRODUCTION

Tuberculosis (TB)/HIV coinfection has been a major challenge for global health. In 2017, among the 10 million people with TB in the world, 9% had TB/HIV coinfection¹. In Brazil, the percentage of new coinfection cases varied from 11.5% in 2009 to 12.4% in 2014, and in 2017 it was 11.4% being the 19th position in the ranking of the 30 countries with high TB / HIV coinfection load².

The TB/HIV association causes complications of the clinical condition and treatment such as mental confusion, hepatotoxicity, and nephrotoxicity, as well as drug resistance³. Also, it causes modification of both infections, which impacts the sexual, work, social, and behavioral lives of people living with HIV (PVHIV)⁴.

Studies on TB/HIV coinfection show that the disease is more frequent in adults^{5,6}, and temporal trend studies conducted with the general population show an increase in prevalence, incidence, and mortality in the age group of 60 years and over^{7,8}. In Brazil, there was an increase in the incidence of TB/HIV coinfection in this population from 0.32/100,000 inhabitants in 2002 to 0.99/100,000 inhabitants in 2012, with a total variation of 209.38%⁷, as well as increased mortality⁸.

TB/HIV coinfection in the old population is the result of increased HIV³ and vulnerability to TB. Older people living with HIV are more susceptible not only because of the disease⁹ but also due to the alterations inherent to aging¹⁰.

In the old population, TB/HIV coinfection is worrying since TB increases the possibility of association with other chronic diseases and unfavorable events¹¹, and HIV promotes increased comorbidity and frailty in old people¹². Besides, the economic burden of TB/HIV coinfection is high due to the increased demand for the health system¹³.

The knowledge of TB/HIV coinfection by temporal distribution allows identifying the magnitude of the disease. In Brazil, the literature has so far investigated this outcome through secondary data considering the general population and focusing on the mortality and incidence of this coinfection^{7,8}. In the international context, a study

focusing only on incidence was carried out in the Xinjiang Province, China¹⁴.

Considering the magnitude of TB/HIV coinfection, the increasing frequency of this disease in older people, population aging, and the ratio that TB/HIV coinfection can achieve in this population, the objective of the present study was to analyze the temporal trend of TB/HIV coinfection, and the ratio of HIV testing in the old population of Brazil and its regions from 2008 to 2018.

METHOD

This is a population-based, ecological, time-series study carried out in Brazil and its geographic regions from 2008 to 2018. All new cases of TB/HIV coinfection in the age group of 60 years or over were included.

TB/HIV coinfection was defined as new TB cases (comprising new, unknown, and post-mortem cases) covering all forms and types of diagnosis whose *status* of the HIV variable was “positive”¹⁵. A new case includes any patient who has never been treated for TB or has been for up to 30 days; unknown are those identified at the time of or after death, considering the individuals when the possibilities for investigating previous entries and post-death are exhausted¹⁶.

Data on the annual incidence of TB/HIV coinfection were obtained from the Notifiable Diseases Information System (SINAN-TB) on Tuberculosis available on the website of the SUS Department of Informatics (DATASUS). Population data were obtained through intercensus estimates made available by the Brazilian Institute of Geography and Statistics (IBGE) available at DATASUS.

The sociodemographic variables investigated in the study were gender (male, age group - 60 to 69 years, 70 to 79 years, 80 years and over), period in years (2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017 and 2018), and regions (North, Northeast, Southeast, South, and Midwest). The clinical variables were clinical form (pulmonary, extrapulmonary, pulmonary + extrapulmonary), and use of antiretroviral (ignored/white, yes, no).

The data were organized in a database with the aid of the program *Excel* and analyzed with the statistical program *Stata* version 12.0. Absolute and relative frequencies were used for the descriptive analysis from 2008 to 2018.

Incidence rates of TB/HIV coinfection were calculated per 100,000 inhabitants. Subsequently, the incidence rates adjusted by age were directly standardized using as reference the Brazilian population from intercensus projections (2000 - 2030) available in DATASUS, to nullify the effect of the unequal demographic distribution of the population. The testing ratio was obtained by dividing the number of positive, negative, and ongoing cases of the HIV variable by the total number of new TB cases, by year of study and geographic region.

The regression of *Prais-Winsten*¹⁷ was used to calculate the annual percentage change (APC). The increasing, decreasing, and stable trends were expressed as APC with the respective confidence intervals (95%). An increasing trend was considered when the APC was positive, negative decreasing, and stable when there was no significant difference between its value and the zero number ($p < 0.05$):

$$APC = [-1 + 10^{b1}] * 100\%$$

$$CI_{95\%} = [-1 + 10^{b1min}] * 100\%; [-1 + 10^{b1max}] * 100\%$$

RESULTS

In Brazil, 3,213 new cases of TB/HIV coinfection were reported in the elderly population

from 2008 to 2018. Table 1 shows the number and percentage of new cases and the trend in the incidence rates of TB/HIV coinfection in Brazil and its regions. Although the Southeast region had a higher ratio of cases (TB/HIV) (41.70%), it was the region with one of the lowest rates (1.17/100,000 inhabitants), and a decreasing trend of TB/HIV coinfection (APC -2,15%). The northern region had the highest average rate of TB/HIV coinfection (2.50/100,000 inhabitants), and an increasing trend (APC 10.18%), as well as the Northeast region (APC 9.92%).

In some regions, long confidence intervals are observed due to the lower case records in these regions. The historical series of the incidence rates of TB/HIV coinfection in Brazil and its geographic regions is shown in Figure 1.

Table 2 shows the characterization by gender, age group, clinical form, and antiretroviral. Most of the cases were male aged between 60 and 69 years old and clinical form of pulmonary type. Less than 40% of antiretroviral information has been completed.

Table 3 shows the percentage and trend of cases tested for HIV. The trend in the testing ratio increased both in Brazil and in its regions, and a higher APC was observed in the North and Northeast regions, which showed lower testing ratios of 55.95% and 54.36%, respectively.

Figure 2 shows the representation of the historical series of HIV testing ratios in Brazil and its geographic regions.

Table 1. Number and percentage of new cases in the old population, average coefficient per 100,000 inhabitants, and the trend in the incidence rates of TB/HIV coinfection in Brazil and its geographic regions. 2008 – 2018.

Region	Cases N (%)	Average coefficient*	APC**	95% CI**	Interpretation
North	318 (9.90)	2.50	10.18	1.09 - 20.08	Increasing
Northeast	758 (23.59)	1.28	9.92	1.11 - 19.50	Increasing
Southeast	1.340 (41.70)	1.17	- 2.15	- 4.14 - -0.12	Decreasing
South	648 (20.17)	1.60	0.17	- 7.36 - 8.32	Stable
Central-West	149 (4.64)	0.96	4.81	- 4.39 - 14.91	Stable
Brazil	3.213 (100.00)	1.32	2.10	- 0.24 - 4.52	Stable

*Standardized rates for the population of Brazil; **Annual percentage variation; ***Confidence Interval of APC.

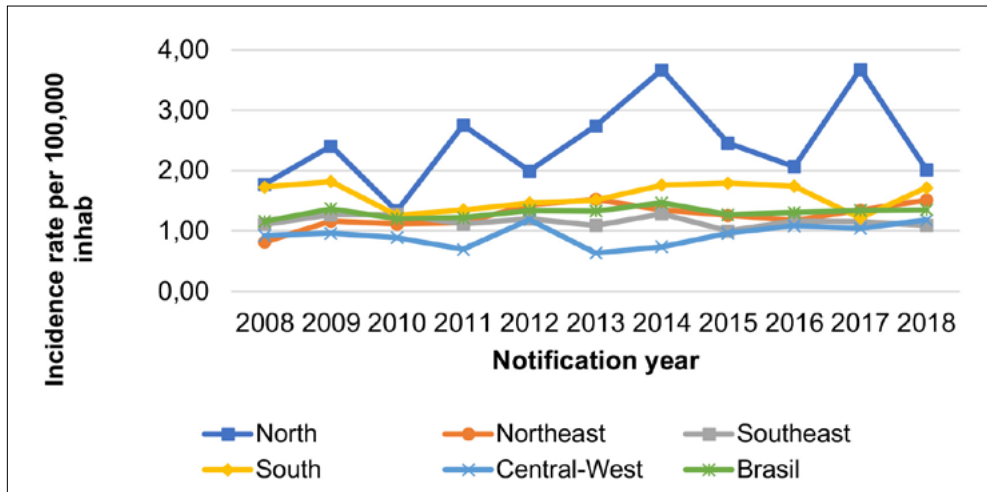


Figure 1. Historical series of standardized incidence rates of TB/HIV coinfection in old people in Brazil and its geographic regions. 2008 – 2018.

Table 2. Distribution of new cases of TB/HIV coinfection by sociodemographic and clinical variables in the old population in Brazil and its geographic regions. 2008 – 2018.

Variables	North		Northeast		Southeast		South		Central-West		Brasil																																																																																																																																																																																							
	n*	%**	n*	%**	n*	%**	n*	%**	n*	%**	n*	%**																																																																																																																																																																																						
Gender													Male	211	66.35	561	74.01	911	67.99	421	64.97	102	68.46	2206	68.66	Female	107	33.65	197	25.99	429	32.01	227	35.03	47	31.54	1007	31.34	Age group (years)													60 – 69	231	72.64	563	74.27	1078	80.45	540	83.33	118	79.19	2530	78.74	70 – 79	69	21.70	148	19.53	231	17.24	93	14.35	26	17.45	567	17.65	80 and over	18	5.66	47	6.20	31	2.31	15	2.31	5	3.36	116	3.61	Clinical form													Pulmonary	238	74.84	622	82.06	961	71.72	401	61.88	114	76.51	2336	72.70	Extrapulmonary	56	17.61	103	13.59	275	20.52	177	27.31	24	16.11	635	19.80	Pulmonary+ Extrapulmonary	24	7.55	33	4.35	103	7.69	70	10.80	11	7.38	241	7.50	Antiretroviral													Ignored/Blank	234	73.58	561	74.01	1010	75.37	395	60.96	100	67.11	2300	71.59	Yes	60	18.87	132	17.41	216	16.12	168	25.93	41	27.52	617	19.20	No	24	7.55	65	8.58	114	8.51	85	13.12	8	5.37	296	9.21
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*Absolute frequency; **Relative frequency; Source: SINAN.

Table 3. Number and percentage of tests carried out in the old population, average coefficient, and trend in the HIV testing ratio in Brazil and its geographic regions. 2008 – 2018.

Region	Cases N (%)	Average coefficient*	APC**	95% CI***	Interpretation
North	6.905 (9.55)	55.93	20.46	11.42; 30.23	Increasing
Northeast	19.105 (26.41)	54.36	17.85	12.59; 23.35	Increasing
Southeast	32.223 (44.55)	70.26	10.29	7.39; 13.27	Increasing
South	10.362 (14.32)	75.93	7.11	3.50; 10.85	Increasing
Central-West	3.736 (5.17)	61.57	6.10	2.25; 10.09	Increasing
Brazil	72.331 (100.00)	63.89	12.82	9.01; 16.75	Increasing

*Average testing rates; **Annual percentage variation; ***APC confidence interval.

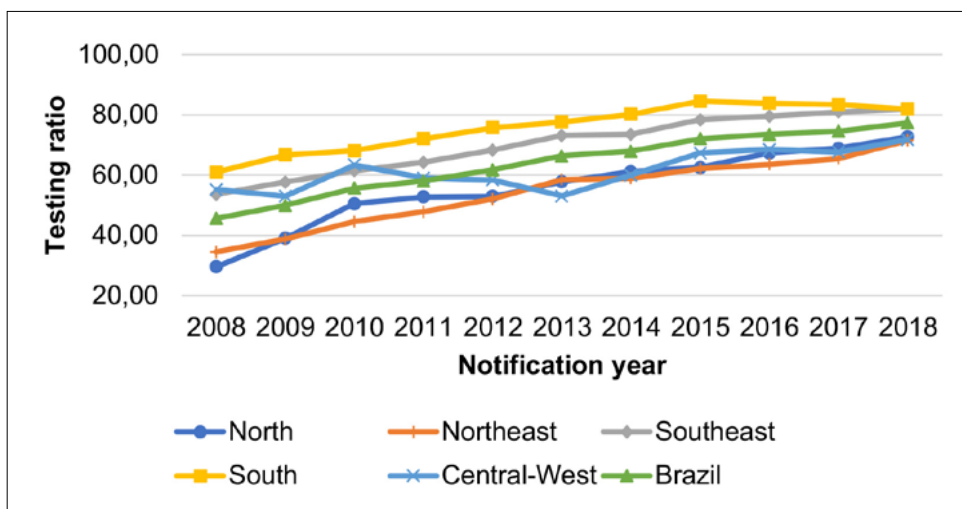


Figure 2. Historical series of the HIV testing ratio in the old people in Brazil and its geographic regions. 2008 – 2018.

DISCUSSION

The present study allowed to know the profile and the time trend of TB/HIV coinfection in the Brazilian old population, as well as the HIV testing. These findings enable the development of strategies to control these outcomes, reduce morbidity and mortality in this population, as well as contribute to the maintenance of sexuality and healthy aging.

The stable trend of TB/HIV coinfection in the old population found in Brazil in the period studied

is a different finding from that found in the study by Gaspar et al.⁷ evaluating the progression of TB and TB/HIV coinfection in Brazil in the period from 2002 to 2012 with the general population. During the period under analysis, the trend of this condition was increasing in all age groups, including those aged 60 and over.

The trend towards the stability of TB/HIV coinfection may be due to the combined treatment (therapy for TB and HIV) that was more effective in reducing TB/HIV coinfection by proposing a

deterministic model for the transmission of the coinfection including the use of both treatments as ideal control strategies¹⁸.

The difference in time trend among the Brazilian regions analyzed in the present study was coincident with the findings of the study by Gaspar et al.⁷ in which there was growth in the North, Northeast, and Central-West regions, whereas the South did not present significant differences, and differently from other regions in the Southeast region there was a reduction in rates.

In the present study, both the growing trend of TB/HIV coinfection observed in the North and Northeast regions and the decreasing trend of cases in the Southeast region may be related to health, education, and income indicators in these regions¹⁹. Brazil is a large country with distinct regional characteristics, in particular regarding social and economic characteristics.

The regional difference in terms of trends in the incidence of TB/HIV coinfection may be related to the quality of health care services resulting from socioeconomic inequalities that in turn influence the control of TB/HIV coinfection. A study analyzing the epidemiological aspects of co-infection in Northeastern Brazil showed that the region is an important endemic area for TB/HIV coinfection. Furthermore, the low percentage of cure, high percentage of non-adherence, occurrence of severe forms of extrapulmonary TB, and high lethality rate reflect the challenge to control TB/HIV coinfection in the Northeast region²⁰.

Another research aimed to verify the epidemiological aspects of TB/HIV coinfection in the state of Mato Grosso do Sul, and its association with the HDI showed that the cases of coinfection were associated with the HDI in areas with a higher population density, showing the need to adopt specific strategies²¹.

An integrative review analyzed the relation between TB and social inequalities and showed that age, income, education, professional training, poverty, unemployment, access to health care services, and basic sanitation are factors that can interfere in the

control of the disease²². Therefore, socioeconomic vulnerabilities can determine unfavorable results in the treatment of TB/HIV coinfection.

On the other hand, a study analyzing the quality and management of care for TB/HIV coinfection in the state of São Paulo showed that in the municipalities where quality was satisfactory there was a low ratio of TB/HIV coinfection, and a low AIDS incidence rate. In the municipalities where quality was unsatisfactory, there was a high ratio of TB/HIV coinfection, and a high AIDS incidence rate²³.

The higher frequency of TB/HIV coinfection in males is a similar finding to that found in another study carried out with a population aged 20 to 60 years or more in Brazil²⁴. It seems likely that these results are because men are more likely to deny their vulnerability to diseases and exempt themselves from responsibility for self-care²⁵. Regarding vulnerability to HIV, the old population cannot understand they are at risk of having the disease. Therefore, they usually do not use condoms during sexual intercourse²⁶.

Regarding age group, the incidence of TB/HIV coinfection in the younger age group is a result corroborated by studies analyzing the trend in the incidence and mortality of TB/HIV coinfection^{7,8} in the general population. Both found higher rates in the younger old population. When compared to previous generations, people in this age group are more sexually free, and they are generally single or divorced, have more casual relationships²⁷, and do not use condoms²⁸ which makes them more vulnerable to HIV and consequently to TB.

The predominance of the clinical pulmonary form of TB is probably because this form is the most frequent one and the main infectious source for the disease spread²⁹. Its incidence is similar to that found in the general population^{5,6}.

Comparing the percentage of those making use or not of antiretroviral therapy (ART), most of them are being treated. This is probably due to the early treatment of PLHIV with active TB to reduce mortality³. The importance of using ART

in co-infected people has been emphasized in some studies. A study in Ethiopia showed that ART had a protective effect against TB³⁰. Similarly, a Chinese study found that not using ART was a risk factor for TB³¹. Other studies have shown that late-onset of ART³² or not doing it³³ were risk factors for mortality in cases of coinfection.

The significant absence of national records regarding the use of antiretroviral drugs is a result that draws attention. This high percentage may be because the records regarding ART were included in SINAN only from the year 2014, and in the State of São Paulo only in the second half of 2016. Underreporting also contributes to the incompleteness of data, reflecting the result of organizational and structural problems on epidemiological surveillance systems, such as lack of notification by health professionals, late notification, manual or bureaucratic systems, extensive or inadequate forms requiring more time to complete, and notification of only a few diseases depending on the severity³⁴, which reinforces the need to improve data on coinfection.

The time trend of HIV testing in the old population with increasing TB in Brazil and all its regions is a relevant result. This increase in the testing ratio possibly results from the recommendation of testing all people with active TB for HIV, for which the use of the rapid HIV test is recommended since 2015³. WHO data show that of the 4.3 million TB cases reported in the general population in 2018, 64% were tested for HIV, representing a 27-fold increase in the number of people with TB tested for HIV when compared to 2004⁹.

The early diagnosis of HIV in old people does not reduce the incidence of the disease, but promotes the timely onset of treatment with ART, and contributes to the improvement of health conditions and reduction of mortality³⁵.

The trends observed regionally must be analyzed with caution due to the inequalities of the data record in SINAN-TB, since the increased trends may reflect more an improvement in the quality of the information system than an increase in incidence.

Although the present study allows knowing the movement of measures of interest in health - in this case, TB/HIV coinfection -, it has some limitations. The population is old, therefore their results may be subject to survival bias. Other limitations were the use of secondary data from SINAN-TB and IBGE, the operational difficulties of this system such as underreporting, incorrect, incomplete, and duplicate filling of the variables, which can interfere in the interpretation of the data. Therefore, we recommend the linkage between databases and the HIV/AIDS Notifiable Diseases Information System (SINAN-Aids), Tuberculosis Mortality Information System (SIM-TB), and the HIV/AIDS Mortality Information System (SIM-AIDS) to improve data analysis in future studies.

Further studies on aging, sexuality, and prevention of TB/HIV coinfection in older people should be developed. Follow-up studies are recommended to analyze the impact of TB/HIV coinfection in the old population, as well as intervention research to control these diseases in this population.

CONCLUSION

The incidence of TB/HIV coinfection showed a stable trend in Brazil. However, it was decreasing in the Southeast, and increasing in the North and Northeast. The occurrence of an increasing trend in the HIV testing ratio in Brazil and its regions is emphasized.

Given the magnitude and implications of TB/HIV coinfection in the old population for health care services, these findings may support health professionals and managers in adopting effective measures to control these diseases.

As the population ages, new challenges in the health care sector appear. Therefore, the epidemiological knowledge and the behavior of these diseases over time allow to outline strategies aimed at the prevention and control of these diseases in this population, contributing to healthy aging.

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