Revista Contexto & Saúde
Editora Unijuí
Programa de Pós-Graduação em Atenção Integral à Saúde
ISSN 2176-7114 – v. 24, n. 48, 2024
http://dx.doi.org/10.21527/2176-7114.2024.48.14750
HOW TO CITE:
Ribeiro EA, Silva EMP, Volz LE, Sopran MA. Clinical and epidemiological overview of tuberculosis in a health region in the brazilian amazon. Rev. Contexto & Saúde, 2024;24(48): e14750

ORIGINAL ARTICLE

Clinical and Epidemiological Overview of Tuberculosis in a Health Region in the Brazilian Amazon

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Highlights:
1. The cases were concentrated in men, mixed race, low education and from urban areas.
2. Cases were detected in institutionalized population and co-infection with HIV/AIDS.
3. Low adherence to bacteriological culture, cases increased, and vaccination decreased.

ABSTRACT:

Introduction: Tuberculosis is one of the main global health problems, in addition to being one of the main causes of death by infectious agent. **Objectives:** To describe the clinical-epidemiological profile of tuberculosis and the relationship with the level of vaccination coverage among the municipalities of the 12th regional health center in the State of Pará. **Materials and Methods:** This is an ecological retrospective study, carried out with clinical data -epidemiological data from the Notifiable Diseases Information System. For data analysis, descriptive and inferential statistics were applied. **Results:** During the analyzed period (2012-2022), 1330 cases of tuberculosis were registered in the region. And considering the geographic distribution, only one municipality had most cases, Redenção with 34.8% (464/1330). In addition, considering sociodemographic analyses, it was noted that the cases were concentrated in brown individuals 52.1% (693/1330), men 64.2 (855/1330), aged between 20-59 years 64.3% (856 /1330) and incomplete primary education 56.3% (750/1330). Low adherence to performing bacteriological culture and resistance screening was evidenced. **Conclusions:** It was possible to delineate the global epidemiological profile of tuberculosis cases in the Araguaia health region. Regarding the geographic distribution, it was possible to evidence the centralization of notifications in a single municipality. Low adherence to complementary tests suggests the need to improve the autonomy of municipalities, aiming at assertive diagnosis and treatment and mitigation of damage to the health of affected patients.

Keywords: Disease Notification. Epidemiological Monitoring. Geographic Mapping. Health Strategies. Vaccination.

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INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* that mainly affects the lungs and can manifest clinically in numerous ways and in several organs[1]. The pathogenesis of the disease is studied by stage, beginning with the invasion, survival, and proliferation of macrophages, as this pathogen can prevent the formation of the phagolysosome[2].

Based on the knowledge of how the pathogen acts in the human body and the high rate of deaths that existed until the beginning of the twentieth century, a vaccine was created for TB prophylaxis, which should be administered soon after birth to ensure immunization against the severe form of the disease[3]. However, vaccination coverage across the country has decreased in the recent years, which has caused concern for health professionals because Bacillus of Calmette and Guérin (BCG) is one of the vaccines that has been reduced in coverage[4].

TB is one of the main health problems worldwide and a major cause of death due to infectious agents. This was evidenced in a report revealing that TB developed in approximately 10 million people in 2019, and the highest concentration of affected people lived in Southeast Asia (44%), Africa (25%), and the Western Pacific (18%), with lower percentages in the Eastern Mediterranean (8.2%), the Americas (2.9%), and Europe (2.5%)[5].

Although the incidence and mortality of TB have decreased, there is still a need to accelerate processes and improve mitigation strategies, as they are probably not occurring quickly enough for the WHO End TB targets to be met, given that there was a reduction of only 9% in incidence (2020 target = 20% reduction) and 14% reduction in the number of deaths (2020 target = 35% reduction) from 2015 to 2019[5].

In addition, the advent of the COVID-19 pandemic has had a direct impact on the epidemiological and clinical panorama of TB, contributing to the deceleration of mitigation processes[5]. In Brazil, 66,819 new cases and 4.5 thousand deaths were registered in 2020, and the highest diagnostic coefficients were recorded in the states of Amazonas (71.3%), Rio de Janeiro (67.4%), and Roraima (54.6%)[6].

It should be noted that, in addition to biological factors, the relationship between poverty and TB must be considered since the prevalence and number of TB-related deaths are higher in low-income countries. It is important to address poverty as a determinant through the interventions aimed at reducing socioeconomic inequality and improving the living conditions of the poorest populations[7].

Finally, it should be noted that antimicrobial resistance is an increasingly worrying threat to the treatment of bacterial infections, as it can result in therapeutic failures. This was corroborated in a study conducted in 2013 and 2014 in two hospitals in Rio de Janeiro and Paraná, which showed that approximately one-third of the samples collected were multidrug-resistant (MDR-TB), and a genetic variant associated with rifampicin resistance was identified[8]. Therefore, the early detection of MDR-TB strains is critical for the successful treatment of the disease, especially in countries, such as Brazil, where the rate of TB is high[8-9].

Based on the data presented, knowledge about the epidemiological distribution and local clinical characteristics associated with this pathology is of significant value because the region under study is remote and presents several structural and financial obstacles, especially regarding autonomy for the screening and mitigation of infectious pathologies. In addition, it is a disease with wide gaps that can cause biological, social, and economic damage, such as co-infection with the Human Immunodeficiency Virus (HIV), vulnerable socioeconomic conditions, and antimicrobial resistance. Thus, in view of this knowledge, it is possible to guide local, holistic, and assertive public health actions for the prevention, mitigation, and control of TB in this health region.

Therefore, the objective of this research was to describe the clinical-epidemiological profile of TB, as well as its relationship with the level of vaccination coverage (BCG) in the municipalities belonging to the 12th regional health center in the State of Pará.

MATERIALS AND METHODS

Type and place of study

This was a retrospective ecological study using a quantitative approach. It encompasses the health region of Araguaia in the State of Pará, composed of 15 Municipalities: Água Azul do Norte, Bannach, Conceição do Araguaia, Cumaru do Norte, Floresta do Araguaia, Ourilândia do Norte, Pau D'Arco, Redenção, Rio Maria, Santa Maria das Barreiras, Santana do Araguaia, São Félix do Xingú, Sapucaia, Tucumã, and Xinguara.

This region has a population of approximately 472,933 individuals with a population density of 2.64 inhabitants/km^2. This area has average temperatures of approximately 28º C per year between a minimum of 21.1ºC and a maximum of 35.2ºC. The annual relative humidity of the air in the region is an average of 40%, with a minimum of 20% and a maximum of 60%. These percentages suffer numerous oscillations due to the season, which is divided into rainy (November to May) and dry (June to October). The biome is Amazonian[10].

Hospital care of medium to high complexity is offered by a regional hospital in the municipality of Redenção, which is the sub-regional center of the other 15 municipalities of the Araguaia Region, located 906 km from the capital, Belém. Regarding basic sanitation in the total population of the Araguaia region, only 56,751 people had access to drinking water and garbage collection[10]. Additional important information is presented in Table 1.

Table 1. Sociodemographic data from the health region of Araguaia, Pará, Brazil.

	Sociodemographic and structural aspects					
Municipalities	**TMG**	**Sanitary sewage (%)**	**PIB per capita (R$)**	**IDHM**	**IDEB**	**Renda-SMM**
Água Azul do Norte	0.72	21.6	19.236.57	0.564	-	2.2
Bannach	0.87	1.8	30.851.86	0.594	-	2.0
Conceição do Araguaia	0.93	4.8	12.955.95	0.640	4.2	2.0
Cumaru do Norte	0.37	1.6	29.652.99	0.550	-	2.1
Floresta do Araguaia	0.24	1.4	20.176.54	0.583	4.1	2.1
Ourilândia do Norte	0.87	32.1	23.262.47	0.624	4.4	2.4
Pau D' arco	0.31	1.1	17.996.91	0.574	4.0	2.1
Redenção	12.71	10	23.710.97	0.672	4.4	2.0
Rio Maria	1.08	9.5	31.395.51	0.638	-	1.9
Santa Maria das Barreiras	-	15.8	33.661.09	0.544	-	2.1
Santana do Araguaia	0.04	15.0	14.967.72	0.602	3.2	2.3
São Félix do Xingu	1.18	22.5	11.939.09	0.594	-	2.5
Sapucaia	0.73	2.5	19.013.71	0.590	4.1	1.7
Tucumã	0.98	32.1	21.472.56	0.659	4.5	1.9
Xinguara	0.66	14.3	31.336.01	0.646	3.8	1.8
Regional Average:	***1.45***	***12.40***	***22.775.33***	***0.604***	***2.4***	***2.1***

Numerical data equal to zero not resulting from rounding. TMG: Overall mortality rate. PIB: Brute Interior Product. IDHM: Municipal Human Development Index. IDEB: Basic Education Development Index (Final years of elementary school- Public network). Renda-SMM: Average monthly wage of formal workers [2020]- minimum wages.

Source: Tabnet/DATASUS. Ministry of Health/SVS; Brazilian Institute of Geography and Statistics, 2023. -

Data collection and analysis

Secondary public clinical-epidemiological data on TB cases reported in Araguaia were obtained from the database of the Department of Informatics of the Unified Health System (Data-SUS-TABNET) through the virtual platform of the Notifiable Diseases Information System (SINAN). The data collected from the Ministry of Health platform were organized and tabulated using Microsoft Excel 2019 for further analysis. Logistic parameters were used to organize the data to complete the analysis and study of the results.

- The tables generated by SINAN were analyzed with respect to the annual frequency of TB cases in each municipality during the study period. An analysis of the available raw data was performed.
- The SINAN tables were evaluated by municipality, and the frequency of involvement in each year was analyzed by sex, age group, race, type of admission (new or recurrent cases), schooling, residency, institutionalized form, HIV/AIDS coinfection, laboratory confirmation, first sputum smear microscopy, culture test, antimicrobial resistance screening, evolution, and vaccination.
- The frequency of TB and vaccination rate over 10 years in the population of each municipality were evaluated, and an inferential statistical test was applied to demonstrate the relationship.
- Temporal trends were used to present the variations in the number of cases and vaccine doses applied during the research period.

Ethical aspects

As this is a study with public secondary data (SINAN), which does not allow the identification of individuals, this study was not submitted to the Research Ethics Committee in compliance with the resolution of the National Health Council No. 466 of December 12, 2012, and does not require signing of the Informed Consent Form (ICF).

Statistical analysis of the data

Descriptive analytics

The absolute frequency of cases from 2012 to 2022 in each of the 15 municipalities studied is described. In each municipality, the profile of cases was described using absolute (n) and relative (%) frequencies according to sex, age, race/skin color, type of entry, education, area of residence, and whether they were institutionalized. The relative frequencies were calculated based on the total number of cases in each municipality; some may not add up to 100% because of unknown or missing values. Clinical characteristics, including the form of the disease, presence of HIV/AIDS, disease progression, laboratory confirmation, results of the 1st bacilloscopy, bacteriological culture test, and resistance, were described in a similar manner using absolute and relative frequencies.

Trend and correlation analysis

A trend analysis was conducted to verify the trends in the number of cases of the disease and the number of vaccine doses (BCG) administered over the years. To estimate the trend of cases and vaccine doses, a multilevel linear regression model was adjusted, where the municipality represents level two and the year represents level one, to estimate the trend of cases and vaccine doses. These models generated a coefficient indicating the absolute mean annual change (VAMA) in the number of cases and vaccine doses administered. In addition to the coefficients, 95% confidence intervals were estimated. The correlation between the number of TB cases and the vaccine dose was evaluated for each municipality. Pearson's correlation coefficient was estimated, and the respective p-values were calculated.

All analyses were conducted using the Stata 17.0 software (StataCorp LLC, College Station, TX, USA). All analyses were considered to have a significance level of 5%.

It is notable that some factors should be considered when analyzing data on vaccination coverage above 100% in some regions, such as the occurrence of newborn records in locations other than the mother's residence, especially in small municipalities without maternity hospitals, which may affect the calculation of vaccination coverage. In addition, the greater ease of access to vaccination rooms in neighboring municipalities results in a number of vaccinated people beyond the target population of the respective municipality[11].

RESULTS

During the analyzed period (2012-2022), 1330 cases of TB were registered in the 12th regional health center (Araguaia region), of which 93.7% (1.247/1.330) were characterized as having the pulmonary form. A temporal analysis revealed that 2021 had the highest rate of TB diagnoses with 13.2% (175/1.330), and the lowest percentage of cases occurred in 2016 (5.9% (79/1.330)). In addition, considering the frequency of vaccination, it was noted that 2013 had the highest number of doses applied (10.3%) (8.568/82.866), whereas 2020 had the lowest frequency (7.4%) (6.160/82.866).

Regarding the spatial distribution, the municipalities with the highest vaccination coverage for the analyzed period were Sapucaia with 118%, Bannach with 115.8%, and Tucumã with 111.7%, and the municipality with the lowest vaccination coverage was Cumaru do Norte with 69.2%. Regarding the distribution of cases, the municipality with the highest frequency was Redenção with 34.8% (464/1.330) followed by São Félix do Xingu 15% (200/1.330) and Ourilândia do Norte 10% (134/1.330), the lowest frequency was evidenced in Bannach with 0.4% (6/1.330) of the cases (Table 2).

An analysis of the sociodemographic variables revealed that the cases were concentrated among brown individuals, 52.1% (693/1.330); males, 64.2% (855/1.330); aged between 20 and 59 years, 64.3% (856/1.330); and incomplete elementary education, 56.3% (750/1.330). In relation to housing, there was a high rate of unknown/blank data (63% (838/1.330), and among the cases registered, urban areas prevailed (24.2% (323/1.330) (Table 2).

Regarding the clinical characteristics, most TB cases were cured in 53.3% (709/1.330), followed by abandonment in 10.4% (139/1.330) and death in 3% (40/1.330). A complementary diagnosis was confirmed in 55.3% (736/1.330) of the cases, and positive sputum smear microscopy results were observed in 57.8% (770/1.330) of the records (Table 3).

However, there was low adherence to the culture test, which was not performed in 86.2% (1.147/1.330) of patients. Thus, the municipalities with the worst associated rates were Pau D'arco and Santa Maria das Barreiras, both with 92.0% (11/12) each, followed by Redenção and Ourilândia do Norte with 90.0% (417/464) and 90% (120/134), respectively (Table 3).

In addition, screening for bacterial resistance to antimicrobials was ignored in 90% (1.196/1.330) of the global reports. The municipalities with the lowest rates were Banach (100%, 6/6), Xinguara (97%, 94/97), Redenção (94%, 436/464), and Ourilândia do Norte (93%; 125/134) (Table 3).

Tables 2 and 3 describe the number of TB cases in the 15 municipalities of interest between 2012 and 2022. Just below the number of cases, each table describes the profiles of these cases using absolute and relative frequencies. As reported in the Methodology section, some relative frequencies may not add up to 100% of the cases due to the lack of information or ignored values.

Table 2. Epidemiological profile of tuberculosis cases in a health region in southeastern Pará, Brazil, 2012 to 2022.

Variables	Municipalities n (%)														
	AAN n=16	B n=6	CA n=85	CN n=35	FA n=51	ON n=134	PD n=12	R n=464	RM n=26	SA n=68	SFX n=200	S n=23	SMB n=12	T n=101	X n=97
Sex															
Female	3 (19)	3 (50)	33 (39)	15 (43)	23 (45)	56 (41.8)	6 (50)	169 (36)	6 (23)	11 (16)	81 (40)	8 (34.8)	1 (8.3)	28 (27.7)	32 (33)
Male	13 (81)	3 (50)	52 (61)	20 (57)	28 (55)	78 (58.2)	6 (50)	295 (64)	20 (77)	57 (84)	119 (60)	15 (65)	11 (91.7)	73 (72.3)	65 (67)
Age (years)															
0-14	-	1 (17)	3 (3.5)	11 (31)	2 (4.0)	17 (13)	-	35 (8.0)	2 (8.0)	-	28 (14)	2 (9.0)	1 (8.3)	9 (9.0)	5 (5.0)
15-19	-	-	2 (2.4)	4 (11)	-	15 (11)	-	43 (9.0)	2 (8.0)	3 (4.0)	14 (7.0)	2 (9.0)	-	9 (9.0)	3 (3.0)
20-59	13 (81)	4 (66)	54 (63.5)	15 (43)	37 (73)	79 (59)	7 (58)	319 (69)	18 (69)	48 (71)	121 (61)	15 (65)	4 (33.3)	60 (59)	62 (64)
≥ 60	3 (19)	1 (17)	26 (30.6)	5 (14)	12 (24)	23 (17)	5 (42)	67 (14)	4 (15)	17 (25)	9 (18)	4 (17)	7 (58.3)	23 (23)	27 (28)
Race/color															
White	-	1 (16.7)	10 (12)	-	12 (24)	19 (14)	3 (25)	46 (10)	5 (19.2)	12 (18)	29 (15)	2 (9.0)	-	16 (16)	17 (17)
Black	3 (19)	1 (16.7)	11 (13)	2 (6.0)	9 (18)	31 (23)	3 (25)	51 (11)	2 (7.7)	13 (19)	16 (8)	6 (26)	-	14 (14)	9 (9.0)
Indigenous	1 (6.0)	-	-	25 (71)	-	42 (31)	3 (25)	104 (22)	-	1 (1.5)	69 (35)	-	-	25 (25)	0 (0)
Brown	11 (69)	4 (66.7)	60 (71)	8 (23)	30 (59)	39 (29)	3 (25)	260 (56)	19 (73)	41 (60)	82 (41)	12 (52)	12 (100)	41 (40)	71 (73)
Ticket Type															
New Case	14 (88)	5 (83)	63 (74)	27 (77)	43 (84)	111 (83)	9 (75)	386 (83)	24 (92)	57 (84)	175 (88)	16 (70)	9 (75)	85 (84)	78 (80)
Recidivism	-	-	9 (11)	2 (6,0)	5 (10)	4 (3.0)	1 (8.0)	32 (7.0)	1 (4.0)	1 (2.0)	9 (5.0)	2 (9.0)	-	8 (8.0)	5 (5.0)
Reentry	-	-	7 (8.0)	2 (6,0)	1 (2)	7 (5.0)	1 (8.0)	37 (8.0)	-	5 (7.0)	10 (5.0)	2 (9.0)	2 (17)	3 (3.0)	3 (3.0)
Transfer	1 (6.0)	-	6 (7.0)	4 (11)	2 (3.9)	10 (8.0)	1 (8.0)	9 (2.0)	1 (4.0)	5 (7.0)	6 (3.0)	2 (9.0)	-	5 (5.0)	11 (11.0)
Schooling															
Incomplete elementary school	4 (25)	5 (83)	34 (40)	21 (60)	25 (49)	73 (55)	6 (50)	289 (62)	14 (54)	46 (68)	120 (60)	6 (26)	4 (33)	44 (44)	59 (61)
Complete Elementary	3 (19)	-	3 (4.0)	2 (6.0)	2 (4.0)	1 (1.0)	1 (8.0)	32 (7.0)	1 (4.0)	4 (6.0)	9 (4.5)	-	-	3 (3.0)	2 (2.0)
Incomplete high school	-	1 (17)	6 (7.1)	-	4 (8.0)	2 (2.0)	1 (8.0)	37 (8.0)	3 (12)	4 (6.0)	10 (5.0)	-	-	1 (1.0)	6 (6.0)
High school or higher education	3 (19)	-	9 (11)	3 (9.0)	9 (18)	8 (6)	1 (8.0)	32 (7.0)	6 (23)	5 (7.0)	9 (4.5)	1 (4.0)	-	4 (4.0)	12 (12)
Area of residence															
Urban	6 (38)	1 (17)	32 (38)	2 (6.0)	11 (22)	23 (17)	2 (17)	135 (29)	1 (4.0)	23 (34)	18 (9)	6 (26)	-	23 (23)	40 (41)
Rural	2 (13)	1 (17)	4 (5.0)	1 (3.0)	4 (8.0)	28 (21)	4 (33)	52 (11)	-	6 (9.0)	40 (20)	-	3 (25)	14 (14)	9 (9.0)
Institutionalized cases															
Non-institutionalized	3 (19)	2 (33)	11 (13)	1 (3.0)	-	24 (18)	1 (8.0)	96 (21)	-	11 (16)	9 (5.0)	3 (13)	-	6 (6.0)	-
Prison/Asylum	-	-	-	-	-	2 (1.5)	-	4 (1.0)	-	-	2 (1.0)	-	-	1 (1.0)	-
Other	1 (6.0)	-	2 (2.0)	-	1 (2.0)	3 (2.2)	1 (8.0)	19 (4.0)	-	2 (3.0)	22 (11)	2 (9.0)	1 (8.0)	1 (1.0)	-

( ) Numerical data shown as a percentage, representing the geographic distribution of cases, resulting from rounding. - Numerical data equal to zero not resulting from rounding. AAN=Água Azul do Norte B=Bannach CA=Conceição do Araguaia CN=Cumaru do Norte ON=Ourilândia do Norte PD=Pau D´arco R=Redenção RM=Rio Maria SMB=Santa Maria das Barreiras SA=Santana do Araguaia SFX=São Félix do Xingu S=Sapucaia T= Tucumã X=Xinguara FA=Floresta do Araguaia. Sometimes, cases don't close 100% due to cases being ignored in the records.

Source: Tabnet/DATASUS. Ministry of Health/SVS.

Table 3. Clinical overview of leprosy cases in a health region in southeastern Pará, Brazil, 2012 to 2022.

	Municipalities n (%)														
Variables	**AAN n=16**	**B n=6**	**CA n=85**	**CN n=35**	**FA n=51**	**ON n=134**	**PD n=12**	**R n=464**	**RM n=26**	**SA n=68**	**SFX n=200**	**S n=23**	**SMB n=12**	**T n=101**	**X n=97**
Form															
Pulmonary	15 (94)	6 (100)	73 (86)	34 (97)	50 (98)	125 (93)	11 (92)	435 (94)	23 (89)	65 (96)	194 (97)	22 (96)	11 (92)	96 (95)	87 (90)
Extra pulmonary	1 (6.0)	-	10 (12)	-	1 (2)	9 (7.0)	-	27 (5.8)	1 (4.0)	3 (4.0)	4 (2)	-	1 (8.0)	5 (5)	8 (8.0)
Pulmonary + extrapulmonary	-	-	2 (2.0)	1 (2.9)	-	-	1 (8.0)	2 (0.4)	2 (7.0)	-	2 (1)	1 (4.0)	-	-	2 (2.0)
HIV/AIDS co-infection															
Yes	-	-	4 (5,0)	-	1 (2)	4 (3)	-	16 (3.0)	2 (7.0)	3 (4.0)	6 (3)	1 (4.0)	-	2 (2)	4 (4.0)
No	12 (75)	5 (83)	42 (49)	33 (94)	31 (61)	109 (81)	10 (83)	429 (93)	21 (81)	63 (93)	155 (77)	16 (70)	7 (58)	81 (80)	82 (85)
Ignored	-	1 (17)	39 (46)	2 (6.0)	19 (37)	21 (16)	2 (17)	19 (4)	3 (12)	2 (3.0)	39 (19.5)	6 (26)	5 (42)	18 (18)	11 (11)
Laboratory confirmation															
Yes	12 (75)	4 (67)	32 (38)	15 (43)	39 (76)	80 (60)	6 (50)	222 (48)	16 (62)	47 (69)	114 (57)	10 (44)	11 (92)	70 (69)	58 (60)
No	4 (25)	2 (33)	53 (62)	20 (57)	12 (24)	54 (40)	6 (50)	242 (52)	10 (39)	21 (31)	86 (43)	13 (56)	1 (8,0)	31 (31)	39 (40)
Result 1st sputum smear microscopy															
Positive	11 (69)	3 (50)	34 (40)	15 (43)	42 (82)	89 (66.4)	8 (66.7)	231 (50)	14 (54)	49 (72)	121 (60)	9 (39)	10 (83)	75 (74)	59 (61)
Negative	1 (6.0)	1 (17)	25 (29)	3 (8.0)	4 (8.0)	26 (19.4)	2 (16.7)	155 (33)	6 (23)	8 (12)	35 (18)	3 (13)	0 (0)	9 (9.0)	15 (16)
Not carried out	4 (25)	2 (33)	26 (31)	17 (49)	5 (10)	19 (14,2)	2 (16.7)	78 (17)	6 (23)	11 (16)	44 (22)	11 (48)	2 (17)	17 (17)	22 (23)
Culture Test Result															
Positive	3 (19)	-	9 (11)	3 (8.0)	12 (23)	9 (7.0)	1 (8,0)	14 (3)	4 (15)	-	22 (11)	2 (9.0)	-	22 (22)	3 (3.0)
Negative	-	1 (17)	4 (5.0)	2 (6.0)	-	3 (2.0)	-	18 (4.0)	-	3 (4.0)	6 (3.0)	1 (4.0)	-	4 (4.0)	5 (5.0)
In progress	-	-	3 (3.0)	2 (6.0)	-	2 (1.0)	-	15 (3.0)	-	-	3 (1.0)	3 (13)	1 (8.0)	-	3 (3.0)
Not carried out	13 (81)	5 (83)	69 (81)	28 (80)	39 (77)	120 (90)	11 (92)	417 (90)	22 (85)	65 (96)	169 (84)	17 (74)	11 (92)	75 (74)	86 (89)
Resistance															
Isoniazid	-	-	-	-	-	-	-	-	-	-	-	-	1 (8.0)	-	-
Isoniazid and rifampicin	-	-	-	-	-	-	-	1 (0.2)	-	-	-	-	-	-	-
Drug resistance 1st line	-	-	1 (1.0)	-	-	1 (1.0)	-	-	-	-	-	-	-	-	-
Sensitive strain	-	-	2 (2.0)	-	3 (6.0)	-	-	1 (0.2)	-	-	2 (1)	-	-	-	-
In progress	-	-	-	-	2 (4.0)	-	-	1 (0.2)	-	-	-	-	-	-	1 (1.0)
Not carried out	3 (19)	-	7 (8.0)	12 (34)	7 (14)	8 (6.0)	1 (8.0)	25 (5.4)	3 (12)	10 (15)	17 (9.0)	-	2 (17)	21 (21)	2 (2.0)
Ignored	13 (81)	6 (100)	75 (88)	23 (66)	39 (76)	125 (93)	11 (92)	436 (94)	23 (88)	58 (85)	181 (90)	23 (100)	9 (75)	80 (79)	94 (97)
Disease course															
Cure	7 (44)	6 (100)	44 (52)	24 (69)	35 (69)	79 (59)	8 (67)	288 (62)	17 (65)	38 (56)	26 (13)	6 (26)	4 (33)	64 (63)	63 (65)
Abandonment	1 (6.0)	-	14 (17)	3 (8.0)	2 (4.0)	18 (13)	2 (17)	55 (12)	2 (8.0)	12 (18)	20 (10)	6 (26)	-	8 (8.0)	7 (7.0)
Death	-	-	9 (10)	2 (6.0)	2 (4.0)	6 (4.0)	1 (8.0)	24 (5.0)	3 (11)	8 (12)	10 (5)	2 (9.0)	1 (8.0)	8 (8.0)	9 (9.0)
Transfer	4 (25)	-	12 (14)	1 (3.0)	2 (4.0)	15 (11)	1 (8.0)	54 (12)	-	5 (7.0)	21 (10)	1 (4.0)	2 (17)	7 (7.0)	14 (14.0)
TB-DR	-	-	-	-	-	-	-	4 (1.0)	-	-	-	1 (4.0)	1 (8.0)	-	-
Schema change	1 (6.0)	-	-	1 (3.0)	1 (2.0)	-	-	1 (0.2)	-	-	-	-	-	1 (1.0)	-
Bankruptcy	-	-	-	-	-	2 (1.0)	-	1 (0.2)	-	-	-	-	-	-	-
Ignored	3 (19)	-	6 (7.0)	4 (11)	9 (18.0)	14 (10)	-	37 (8.0)	4 (15)	5 (7.0)	123 (62)	7 (30)	4 (33)	13 (13)	4 (4.0)

( ) Numerical data demonstrated as percentages, representing the geographic distribution of cases. - Numerical data equal to zero not resulting from rounding. AAN=Água Azul do Norte B=Bannach CA=Conceição do Araguaia CN=Cumaru do Norte ON=Ourilândia do Norte PD=Pau D´arco R=Redenção RM=Rio Maria SMB=Santa Maria das Barreiras SA=Santana do Araguaia SFX=São Félix do Xingu S=Sapucaia T=Tucumã X=Xinguara FA=Floresta do Araguaia. TB-DR: Drug-resistant tuberculosis

Source: Tabnet/DATASUS. Ministry of Health/SVS.

Inferences (trend and correlation) were also performed, and the trends in the mean number of cases and doses of the TB vaccine are described in Table 4. For each year, the average number of cases and vaccines were estimated, along with their 95% confidence intervals. The VAMA statistic indicated that, on average, there was a statistically significant increase of 0.4 TB cases (95%CI = 0.1; 0.6) per year between 2012 and 2022. Conversely, it was estimated that there will be an average decrease in 6.8 vaccine doses (95%CI = -13.5; -0.1) administered per year between 2012 and 2022, with a statistically significant decrease.

Table 4. Estimate of the average number of cases and doses of vaccines administered per year in a health region in southeastern Pará, Brazil, between 2012 and 2022.

Year	Number of cases		Number of vaccinations	
	Average	**IC95%**	**Average**	**IC95%**
2012	6.2	0.8; 11.6	536.2	302.1; 770.3
2013	6.6	1.3; 11.9	529.4	296.2; 762.6
2014	6.9	1.7; 12.2	522.6	290.0; 755.2
2015	7.3	2.1; 12.5	515.8	283.7; 747.9
2016	7.7	2.5; 12.9	509.0	277.2; 740.8
2017	8.1	2.9; 13.3	502.2	270.5; 733.9
2018	8.4	3.2; 13.7	495.4	263.6; 727.2
2019	8.8	3.6; 14.0	488.6	256.5; 720.7
2020	9.2	3.9; 14.4	481.8	249.3; 714.4
2021	9.6	4.2; 14.9	475.0	241.8; 708.3
2022	9.9	4.6; 15.3	468.2	234.1; 702.3
VAMA	0.4	0.1; 0.6	-6.8	-13.5; -0.1

VAMA: Mean Absolute Annual Change; IC: Confidence interval. Source: Own authorship.

Figure 1 shows the relationship between the number of cases and the number of vaccines administered per year. The line indicates a gradual increase in the number of cases and a reduction in the number of doses in each graph.

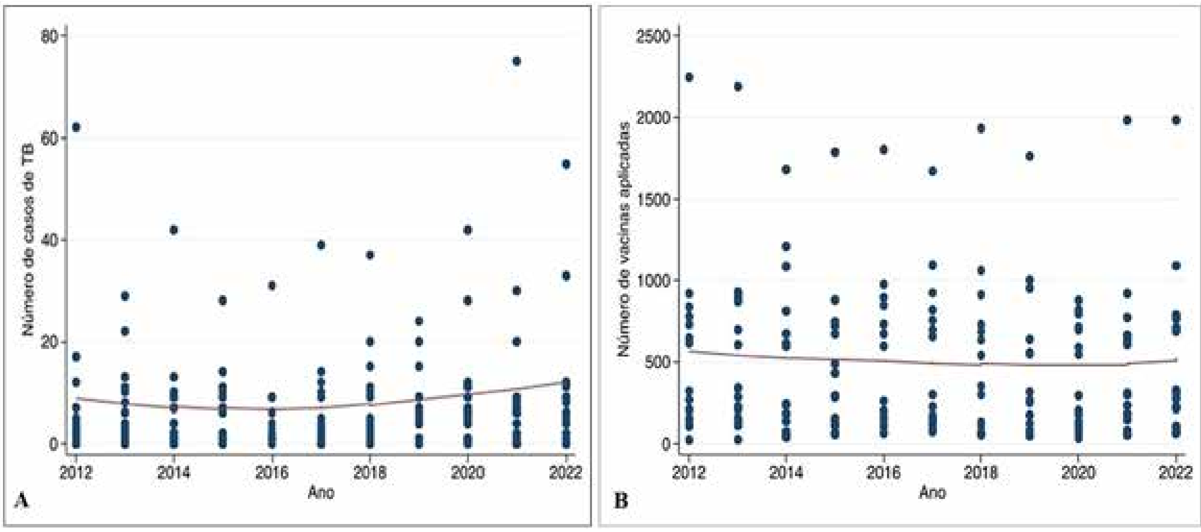

Figure 1. Relationship between the number of TB cases and vaccines administered per year, respectively, in a health region in southeastern Pará, Brazil, 2012 to 2022. In **A**, the number of TB cases per year and the trend curve over the years are verified. Figure **B** shows the number of TB vaccine doses administered per year and the trend curve over the years.
Source: Own authorship.

The correlation between the number of TB cases and number of vaccines administered was evaluated for each municipality. The correlation coefficients (r) and p-values are presented in Table 5. Five of the 15 correlation coefficients (33%) were negative, indicating an inverse relationship between the number of cases and the vaccines administered. However, no statistically significant correlations were observed for any of the 15 coefficients (all $p > 0.05$).

Table 5. Correlation between the number of cases and number of TB vaccine doses in each municipality with respective p-values, in Southeastern Pará, Brazil from 2012 to 2022.

Municipalities	Correlation between number of cases and vaccines	
	r	p-value
Água Azul do Norte	0.428	0.189
Bannach	0.011	0.974
Conceição do Araguaia	0.089	0.795
Cumaru do Norte	-0.416	0.203
Floresta do Araguaia	-0.131	0.702
Ourilândia do Norte	0.468	0.146
Pau D’arco	0.273	0.471
Redenção	0.197	0.561
Rio Maria	0.298	0.374
Santana do Araguaia	0.279	0.406
São Félix do Xingu	-0.451	0.164
Sapucaia	-0.019	0.956
Santa Maria das Barreiras	0.187	0.581
Tucumã	-0.381	0.248
Xinguara	0.356	0.282

Source: Authored by the authors, 2023.

DISCUSSION

The present study outlined the clinical-epidemiological profile of TB and its relationship with the level of vaccination coverage among the municipalities of the 12th Regional Health Center in the state of Pará. The results showed a predominance of men, adults, brown skin color, those with low schooling, and those living in urban areas. Another relevant finding was the occurrence of HIV/AIDS co-infection in the general population. This highlights the importance of local screening for the holistic mapping of the disease spread.

Therefore, it is essential to emphasize that it is a disease with a global impact and high morbidity and mortality rates. In Brazil, TB is endemic, and its incidence varies over time[12]. Importantly, TB is intrinsically related to unfavorable socioeconomic conditions, such as poverty, lack of access to health services, precarious housing, and social inequality[12-13].

Thus, an epidemiological analysis is of paramount importance for equitable access aimed at successful TB treatment[14]. The CDC (*Centers For Disease Control And Prevention*, 2020) [15] highlights that programs aimed at TB control and mitigation can benefit from research participation, either by working with local students or by participating in national and international studies. The benefits include improving of population health, early identification of cases, reduction of the spread of TB, prevention of outbreaks, equity, equitable access to health services, and reduction of TB-related costs[15].

Based on the epidemiological data obtained in the present study, it was possible to draw an epidemiological profile of TB in the study region. The results revealed a higher proportion of males than females. This disparity can be attributed to several factors, including biological and behavioral differences[16].

Regarding other sociodemographic variables, TB mainly affected individuals with an incomplete primary education. Similarly, a study carried out on the island of Marajó (PA) revealed that most of the new TB cases identified were in the age group between 20 and 39 years (334; 45%), male (487; 65%), brown (611; 82%), and with schooling between the 1st and 4th grades of elementary school (201; 27%)[17].

In addition, TB is prevalent in prison populations due to overcrowding, lack of adequate ventilation, precarious health systems, malnutrition, and immunodeficiency. There are also barriers associated with diagnosis and treatment, due to the lack of access to adequate health services, and lack of medications, as well as problems, such as a low adherence to treatment related to prisoner transfers, lack of continuity of health care after release, and social stigma. These findings reinforce the importance of assertive preventive measures[13].

Thus, when analyzing the global trends for the study period, it was evident that there was a significant increase in the number of overall TB cases, which was inversely proportional to the number of doses administered. Therefore, it is important to emphasize that vaccination is essential for mitigating the cases and complications associated with TB[3].

Although childhood BCG is effective for the prevention of severe and extrapulmonary forms of TB in children, several clinical trials have shown varying efficacies in preventing TB in adolescents and adults, highlighting the importance of developing modern techniques[18].

In this context, it is relevant to note that there are new *insights* into this issue, such as the underlying protective immune responses, including the potential functions for 'trained' innate immunity and CD4+ (and CD8+) Th1/Th17 T cells. There is also evidence of a potential new use of BCG for the prevention of high-risk populations in *M. tuberculosis* infections and a new adjuvanted recombinant protein vaccine candidate (M72/AS01 E) for the prevention of disease in adults who are already infected[19-20]. Therefore, due to the global morbidity and mortality associated with TB, it is time to accelerate processes and innovations[21].

However, the current survey revealed that 2020 had the lowest vaccination rates. This can be explained by the advent of the COVID-19 pandemic, which affected the prevention, diagnosis, and treatment of this disease as attention and resources were directed toward it. In addition, COVID-19 can increase the risk of developing TB because both diseases can cause lung damage and compromise the immune function of patients[6].

Thus, it is important to maintain TB surveillance, emphasizing the need for prevention, diagnosis, and treatment in parallel with measures to combat COVID-19[6]. In this study, we observed the occurrence of TB co-infections with HIV/AIDS, revealing the importance of screening and monitoring these cases. This fact was corroborated in an epidemiological study showing that for People Living with HIV (PLHIV) without evidence of TB, the mortality rates were 26.2 per 1,000 person-years, and for those with HIV/TB co-infection it was 57.8 per 1,000 person-years. Thus, PLHIV with TB coinfection had a 40% higher mortality rate than those without TB[22].

Another important finding demonstrated in the current study is that the city of Redenção had the highest number of TB cases, which raises questions about the possible factors that contribute to this situation. When analyzing the local reality, it is evident that the presence of a TB and Leprosy

Health Center may have contributed to the migration of patients from the neighboring municipalities in search of effective detection, diagnosis, and treatment.

Thus, there is a need to implement decentralization strategies to improve the quality of healthcare services. Some strategies include management autonomy for local institutions, community participation, training of local health authorities, decentralization of financial resources, and the integration of services[23].

Regarding the records associated with the laboratory diagnosis analyzed in the present study, it was noted that despite the clinical and epidemiological relevance, bacteriological culture and consequently antimicrobial resistance screening were highly ignored or not performed at all.

This may be associated with a lack of autonomy in the infrastructure and microbiology laboratories. A systematic review demonstrated that serious data gaps exist in several low-income settings, emphasizing the need to expand the capacity of microbiology laboratories and data collection systems to improve our understanding of this important threat to human health[24].

Corroborating these data, according to the World Health Organization[25], it was estimated that in 2018, there were approximately half a million new cases of rifampicin-resistant TB (RR-TB), the majority of which were MDR-TB, with a high proportion of underreported cases. Less than 60% of the patients treated for MDR/RR-TB have been successfully cured[25]. Therefore, it is crucial that the screening and diagnostic system be expanded to reliably reflect the susceptibility profiles of strains detected using sputum smear microscopy.

Another crucial fact is that bacteriological culture is more sensitive than the common sputum smear microscopy and is highly recommended, especially in low-income regions where molecular testing is not feasible[26]. A study conducted in Brazil revealed that approximately one-third of isolates had phenotypic resistance to second-line anti-TB drugs (31%). Death is a frequent outcome in these individuals and is associated with resistance. This reinforces the need for improvements in the tracing and reporting flows of such cases[9,27].

Other weaknesses may contribute to treatment failure, such as high costs of transportation, food, and medications, and loss of income due to the impossibility of working during treatment[28]. Thus, there is a need for intervention measures to reduce the costs of TB treatment, and consequently alleviate the impact of the disease associated with poverty. Notably, there is evidence of the benefits inherent in the inclusion of patients in government social programs[28-29].

Thus, it is well-known that the fight against TB is a global challenge. Therefore, the WHO Health Organization has set ambitious targets, including the elimination of TB by 2030, through integrated approaches that encompass an early diagnosis, appropriate treatment considering resistant strains, and large-scale prevention actions, such as a more effective vaccine. To achieve these goals, it is necessary to strengthen the health systems, promote a patient-centered approach, invest in research and innovation, and coordinate actions globally[30].

As this is an ecological study, it has some limitations, such as the use of secondary data, which do not allow full control of the recovered data. In addition, the relationships between the population and health variables at the group level were examined. Thus, it is recommended that the results be applied at the population level to mitigate the ecological fallacies and confounding biases. This finding suggests the need for additional research, such as cohort studies and clinical trials, to confirm the observed associations and establish more solid causal relationships.

CONCLUSIONS

Based on the data presented, it was possible to delineate the global epidemiological profile of TB cases in the Araguaia health region comprising men, adults, browns, those with low schooling, and those living in urban areas. In addition, the institutionalized population was affected, as was the occurrence of HIV/AIDS coinfection in the general population. It should be noted that there was a low adherence to bacteriological culture and screening of antimicrobial-resistant strains, and considering the geographical distribution, only one municipality had the most cases. This reveals the need to improve the autonomy of municipalities, aiming at an assertive diagnosis and treatment and mitigation of damage to the health of affected patients.

According to a temporal analysis, the overall number of cases increased over the years, and in relation to vaccination, the rates were inversely proportional; that is, the number of doses decreased over the course of the study. However, some municipalities in the region show a negative correlation, while others show a positive correlation. Therefore, it is necessary to conduct further studies on this correlation to improve public databases.

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Submitted: March 7, 2023

Accepted: August 23, 2023

Published: February 22, 2024

Authors' contributions:

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All authors approved the final version of the text.

Conflict of interest: There is no conflict of interest.

Financing: Does not have financing.

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Associate Editor: Dra. Amanda Silva dos Santos Aliança
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