Publication status: Not informed by the submitting author

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https://doi.org/10.1590/SciELOPreprints.12636

Submitted on: 2025-07-17
Posted on: 2025-07-22 (version 1)
(YYYY-MM-DD)

Impact of the COVID-19 Pandemic on Mortality among Patients with TB–HIV Coinfection in the Brazilian Amazon: A Case–Control Study

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Abstract

Background: The COVID-19 pandemic disrupted healthcare services worldwide, potentially worsening outcomes for individuals with chronic infectious diseases, including tuberculosis (TB) and HIV.

Objective: To identify factors associated with mortality among patients with TB–HIV co-infection, and to assess the impact of the COVID-19 pandemic on these outcomes.

Methods: Methods: We analyzed 3,352 TB-HIV cases treated at a referral center in Amazonas, Brazil (2014-2022). Two case-control analyses compared TB-related and non-TB-related deaths with cured TB patients. Multivariate logistic regression was used to identify independent risk factors

Results: In TB-related death group, predictors included diagnosis during the COVID-19 pandemic, rural residence, disseminated TB, prior TB treatment, CD4+ <200, and HAART initiation at or after TB diagnosis. Non-TB deaths were associated with age >60, homelessness, disseminated TB, prior treatment, low CD4+, high viral load, and delayed or absent HAART. Both groups reflected advanced disease, immunosuppression, and poor treatment access.

Conclusions: The pandemic increased TB-related mortality but not non-TB deaths. Mortality was also driven by disease severity, delayed care, and social vulnerability, with rural residence highlighting healthcare barriers. Tackling the TB–HIV–COVID-19 syndemic demands integrated, context-sensitive strategies targeting biological, social, and structural determinants to reduce mortality and improve outcomes in high-burden, resource-limited settings

Key words: TB-HIV-Covid-19 syndemic; Mortality; Brazilian Amazon; Case-Control

Introduction

Tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis* (MTB), primarily transmitted through respiratory droplets and capable of infecting phagocytic cells. Although pulmonary disease is the most common presentation, the pathogen may spread hematogenously, resulting in extrapulmonary or disseminated (miliary) tuberculosis — severe systemic forms associated with poor prognosis. [1-3]

In immunocompetent individuals, most infections remain latent. However, people living with HIV (PLHIV), especially those not receiving highly active antiretroviral therapy (HAART), have a markedly increased risk of developing active TB due to impaired cellular immunity. [4,5] TB remains a leading cause of morbidity and mortality among PLHIV. [6,7]

According to data from the Brazilian Unified Health System (DataSUS/TabNet), between 2008 and 2024, 1,556,426 TB cases were reported in Brazil, with 58,048 attributed deaths—an overall case fatality rate (CFR) of 3.7%. When stratified by HIV status and outcome, CFR was 3.99% (6,334/159,567) among HIV-positive individuals and 3.15% (30,103/952,675) among HIV-negative individuals, yielding an odds ratio (OR) of 1.27 (95% CI: 1.24–1.31), underscoring the substantial impact of HIV coinfection on TB-related mortality.

In 2023, TB incidence in Brazil was 39.8 cases per 100,000 population—significantly exceeding the WHO target. [8] The state of Amazonas reported 81.6 cases per 100,000, the second-highest national rate. Concurrently, Amazonas and its capital, Manaus, registered the second-highest HIV/AIDS

detection rates nationwide (32/100,000 and 48.3/100,000, respectively), highlighting a critical syndemic interface.

The TB–HIV burden in the Amazon is compounded by structural and socioenvironmental determinants, including rapid urbanization, expansion of informal settlements, and migration from remote areas under conditions of extreme poverty. These processes elevate exposure to known vulnerability factors such as unemployment, substance use (notably crack cocaine), homelessness, and transactional sex. [9] Additionally, TB remains endemic among several Indigenous communities in Amazonas, where limited access to health services and low treatment adherence contribute to frequent hospitalizations in tertiary centers. [10,11]

The COVID-19 pandemic profoundly disrupted healthcare delivery in the state of Amazonas. In early 2021, the region faced acute oxygen shortages and a near-total collapse of its healthcare system, exacerbated by geographic isolation and significant logistical challenges. [12] Official records report 12,506 COVID-19 deaths in Amazonas during the first 16 epidemiological weeks of 2021, corresponding to a mortality rate of 172.8 per 100,000 population — the second highest in Brazil.

Health service disruptions during the pandemic compromised TB and HIV care, particularly in high-burden settings. Studies have identified triple infection with TB, HIV, and SARS-CoV-2 as a risk factor for severe disease and elevated mortality. [13-15]

The present study aims to identify risk factors associated with mortality among patients with TB–HIV coinfection in Amazonas between 2014 and 2022, with a focus on assessing the impact of the COVID-19 pandemic on patient outcomes.

Patients and Methods

Study Setting. The state of Amazonas, located in the North region of Brazil, has a population of 4,269,995 inhabitants, of which 2,279,686 reside in the capital, Manaus **(Figure 1)**. According to the 2022 census by the Brazilian Institute of Geography and Statistics - IBGE[16] 1,368,098 people – approximately 60% of the state's population – live in urban areas with low levels of sanitation, predominantly in Manaus - reflecting significant social and health vulnerabilities. The state is home to numerous Indigenous territories with diverse ethnic groups and Brazil´s largest riverine population, both facing barriers to healthcare access. The Dr. Heitor Vieira Dourado Tropical Medicine Foundation (FMT-HVD), located in Manaus, is a regional referral center for infectious and tropical diseases. As part of the Brazilian Unified Health System (SUS), FMT-HVD offers free and universal access and is also a leading institution for malaria treatment in this hyperendemic region. [17] It also offers specialized care for people living with HIV, tuberculosis, and other infectious diseases.

Study Design, Population, and Statistical Analysis. This was a nested case-control study within a retrospective cohort of patients diagnosed and treated for TB–HIV coinfection at FMT-HVD between January 2014 and December 2022. A total of 3,352 cases were identified, of which 1,777 (53.0%) resulted in cure, 757 (22.6%) in treatment abandonment, 156 (4.7%) in TB-related death, and 662 (19.7%) in death from other causes. Cause of death was classified using the Brazilian Mortality Information System (SIM), which relies on official death certificates. Deaths were attributed to TB when it was listed as the immediate cause of death (i.e., the final disease or condition directly leading to death). These cases were recorded among 2,808 PLHIV, 2,413 (86%) of whom had a single TB episode; the remainder had two or more distinct TB episodes during the study period. Annual case fatality rates for TB-related and non-TB-related deaths were calculated. Two nested case-control studies were conducted: Case group 1: TB-related deaths; Case group 2: deaths from other causes; Control group: TB–HIV cases that achieved cure **(Figure 2).** The following independent variables were evaluated: period of diagnosis (pre-pandemic [2014–2019] vs. pandemic [2020–2022]), age group, sex, illicit drug use, alcohol use, residence (urban vs. rural), homelessness, educational level, incarceration, healthcare worker status, clinical form of TB (pulmonary, extrapulmonary, or both), CD4+ T-cell count, HIV viral load, and HAART status. Statistical analysis

included bivariate and multivariate logistic regression. Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Statistical significance was defined as $p < 0.05$, assessed using Fisher's exact test. Data were analyzed with the IBM SPSS Statistics® version 25 (IBM Corp, Armonk, NY, USA).

Tuberculosis diagnostic criteria: Laboratory confirmation methods included Ziehl–Neelsen staining for acid-fast bacilli (AFB), mycobacterial culture, nucleic acid amplification testing (Xpert MTB/RIF), and line probe assays (LPA), performed on both sputum and extrapulmonary specimens. For extrapulmonary or disseminated disease, histopathological examination was conducted when appropriate. Among the 3,352 cases analyzed, 1,948 (58.1%) had laboratory-confirmed TB. The remaining diagnoses were based on clinical and radiological criteria, evaluated by experienced physicians. Laboratory confirmation rates by clinical outcome were Cure: 1,017/1,777 (57.2%), TB-related deaths: 101/156 (64.7%), Deaths from other causes: 344/662 (52.0%), Treatment abandonment: 486/757 (64.2%)**. Table 1** presents laboratory confirmation rates by clinical form and period (pre-pandemic vs. pandemic).

Ethical Considerations. This study was approved by the Research Ethics Committee of the Dr. Heitor Vieira Dourado Tropical Medicine Foundation (protocol no. 5777896).

Results

As shown in **Figure 3**, the annual case fatality rate among patients with TB–HIV coinfection treated at the FMT-HVD ranged from 2% to 6% between 2014 and 2020, peaking at 10% in 2021, coinciding with the peak of the COVID-19 pandemic. In contrast, the annual fatality rate from non-TB causes ranged from 16% to 22.5% over the same period, with no discernible increase during the pandemic.

In the first case-control analysis (**Table 2**), which compared TB-related deaths to cured cases, the following variables were independently associated with increased risk of death due to TB in the multivariate logistic regression model: diagnosis during the COVID-19 pandemic (OR = 1.99, 95% CI: 1.36–2.90, $p < 0.001$); residence in rural areas (OR = 2.11, 95% CI: 1.13–3.90, $p = 0.018$); disseminated TB (pulmonary and extrapulmonary) (OR = 1.78, 95% CI: 1.20–2.66, $p = 0.004$); history of previous TB treatment (OR = 1.91, 95% CI: 1.25–2.91, $p = 0.002$); CD4+ count <200 cells/mm³ (OR = 4.74, 95% CI: 1.69–13.28, $p = 0.003$); initiation of HAART at or after TB diagnosis (OR = 1.86, 95% CI: 1.03–3.37, $p = 0.039$)

In the second case-control analysis (**Table 3**), which compared deaths from non-TB causes to cured cases, the following factors were independently associated with increased risk: age >60 years (OR = 2.16, 95% CI: 1.27–3.69, $p = 0.004$); homelessness (OR = 1.62, 95% CI: 1.02–2.56, $p = 0.039$); disseminated TB (OR = 1.41, 95% CI: 1.02–1.94, $p = 0.037$); history of previous TB treatment (OR = 1.29, 95% CI: 1.00–1.68, $p = 0.049$); CD4+ count <200 cells/mm³ (OR = 2.15, 95% CI: 1.52–3.05, $p < 0.001$); CD4+ count between 200 and 350 cells/mm³ (OR = 1.63, 95% CI: 1.03–2.56, $p = 0.034$); HIV viral load 1,001–10,000 copies/mm³ (OR = 1.63, 95% CI: 1.03–2.56, $p = 0.034$); HIV viral load >10,000 copies/mm³ (OR = 2.15, 95% CI: 1.52–3.05, $p < 0.001$); Initiation of HAART at or after TB diagnosis (OR = 1.78, 95% CI: 1.26–2.50, $p < 0.001$); never having initiated HAART (OR = 1.42, 95% CI: 1.10–1.83, $p = 0.007$). Additionally, two variables showed a protective effect against mortality from non-TB causes: being younger than 19 years (adjusted OR = 0.21; 95% CI: 0.06–0.67; $p = 0.009$) and being a health care worker (adjusted OR = 0.31; 95% CI: 0.11–0.88; $p = 0.028$).

Discussion

This study identified factors associated with mortality in patients with TB–HIV coinfection. The case fatality rate attributed specifically to TB was higher than the rate reported for the general population of the Amazonas state during the same period (DataSUS/TabNet). This discrepancy likely reflects the more severe clinical profile of the study population, most of whom were hospitalized.

Among the study, deaths from causes not directly attributed to TB outnumbered those where TB was recorded as the immediate cause. However, TB likely contributed to many of these deaths as an underlying or associated condition. In the context of advanced HIV disease, fatal outcomes often result from a sequence of interconnected clinical events. Therefore, attributing mortality based solely on the immediate cause of death may underestimate the true impact of TB on overall mortality.

Immunosuppression, as measured by CD4+ T-cell count and HIV viral load, demonstrated distinct patterns of association with mortality. A CD4+ count below 200 cells/mm³ emerged as the strongest independent predictor of TB-related death. In contrast, for non-TB-related deaths, the risk extended to patients with CD4+ counts between 200 and 350 cells/mm³, suggesting that even moderate immunological decline increases vulnerability to other fatal outcomes. HIV viral load further reinforced this pattern, displaying a dose–response gradient in which higher copy counts were progressively associated with increased risk of non-TB-related mortality. These observations support the notion that non-TB mortality among coinfected patients may be more broadly sensitive to degrees of immunosuppression, beyond the thresholds traditionally linked to TB progression.

In TB-related deaths, severe immunodeficiency contributes to extensive pulmonary damage, acute respiratory failure, TB sepsis with multiorgan failure, and cachexia, leading to TB being recorded as the immediate cause of death. In contrast, non-TB-related deaths were often due to opportunistic infections (e.g., cerebral toxoplasmosis, *Pneumocystis jirovecii* pneumonia, disseminated histoplasmosis, cryptococcosis, atypical mycobacteriosis) or AIDS-related malignancies (e.g., Kaposi's sarcoma), frequently observed in this study. Additional causes included bacterial sepsis, fungemia, renal failure, pulmonary embolism, stroke, non-COVID viral pneumonia, and COVID-19.

AIDS-defining illnesses remain a leading cause of death in Brazil's North and Northeast regions, diverging from trends in the South and Southeast, where mortality is more frequently associated with cardiovascular disease and non-AIDS-related cancers. [18]

A key finding was the strong association between TB-related deaths and TB–HIV diagnoses made during the COVID-19 pandemic, particularly in 2021—a year marked by health system collapse in Amazonas due to critical shortages in hospital beds and oxygen supply. This pattern aligns with findings from India, where lockdown measures disrupted TB diagnostic and treatment services. [19] In Amazonas, the pandemic's impact was compounded by the emergence of the P.1 SARS-CoV-2 variant, structural vulnerabilities, and the burden of preexisting endemic diseases. [20,21] During this period, outpatient clinics in Manaus were either closed or operating at reduced capacity, severely compromising continuity of care. [22]

The clinical overlap between TB and COVID-19—particularly respiratory symptoms—also likely contributed to delayed TB diagnosis and treatment, worsening outcomes. [23-26] Immunologically, co-infection with TB and COVID-19 has been associated with overexpression of inflammatory cytokines (e.g., TNF-α, IL-9, GM-CSF) and dysregulated immune responses, including lymphopenia and altered IL-2 signaling, which may predispose to respiratory failure. [27] Multinational studies have confirmed increased mortality in patients co-infected with TB and COVID-19. [28]

Interestingly, the pandemic period was associated with TB-related deaths but not with deaths from other causes. This distinction may reflect the hospital crisis: patients with severe TB-induced respiratory failure may have died without receiving appropriate support, whereas patients dying from non-TB causes followed different clinical trajectories. The proportion of laboratory-confirmed TB cases also increased during the pandemic, potentially reflecting more intensive diagnostic efforts in hospitalized patients. This may have influenced the documentation of TB as the immediate cause of death.

Patterns of HAART use were distinctly associated with mortality depending on the cause of death. In the comparison between non-TB-related deaths and cured cases, two patterns were independently associated with increased mortality: initiating HAART concomitantly with TB treatment and never having used HAART. These findings suggest that delayed or absent initiation of antiretroviral therapy contributes significantly to mortality from causes other than TB in coinfected individuals.

In contrast, in the comparison between TB-related deaths and cured cases, only HAART initiation during TB treatment was associated with increased mortality, whereas never having used HAART did not reach statistical significance. These results reinforce the importance of early and sustained

antiretroviral therapy as a protective strategy in both settings, while also suggesting that delayed initiation may be particularly detrimental in the context of active TB disease, consistent with the established role of antiretroviral therapy in restoring immune competence and reducing HIV-associated morbidity and mortality.

In the comparison between non-TB-related deaths and cured cases, being older than 60 years was independently associated with increased mortality, while individuals younger than 19 years exhibited a protective effect. Although similar trends were observed in the comparison involving TB-related deaths, these did not reach statistical significance, possibly due to the smaller number of cases in extreme age groups. Contrary to what is widely reported in the literature, advanced age in this cohort was more strongly associated with death from non-TB causes than from tuberculosis itself. Advanced age is a well-established predictor of adverse TB outcomes, often attributed to immunosenescence, the burden of comorbidities, and impaired pulmonary reserve. However, in the context of HIV coinfection, it is plausible that older individuals may succumb to other opportunistic infections or chronic complications before TB becomes the leading cause of death. This underscores the need to interpret age-related vulnerability within the broader clinical spectrum of HIV-associated morbidity. [29,30] Prior TB treatment was another predictor of mortality. This variable reflects various factors—treatment failure, drug resistance, non-adherence, and reactivation in the context of immunosuppression—all of which contribute to more severe or chronic disease. [31]

Living in rural areas was associated with TB-related death. Amazonas is geographically vast, and many remote communities are accessible only by river transport. This geographic barrier hinders timely diagnosis, continuity of care, and treatment adherence. Additionally, many rural cases occur among Indigenous populations, where adherence to TB treatment is often suboptimal. The clinical form of TB also impacted outcomes: patients with disseminated TB (i.e., concurrent pulmonary and extrapulmonary disease) had nearly twice the risk of death, consistent with previous studies indicating that disseminated forms are more severe and associated with higher mortality. Finally, homelessness was significantly associated with non-TB deaths. Homeless individuals often face barriers to healthcare access and are at increased risk for treatment non-adherence and opportunistic infections.

The protective effect observed among health care workers and individuals under 19 years of age may reflect earlier access to care, better treatment adherence, and fewer comorbidities. In the case of adolescents, biological resilience and structured follow-up—particularly in vertically infected individuals—could contribute to more favorable outcomes. For health workers, greater health literacy and access to timely diagnosis and ART initiation may offer a survival advantage.

In the state of Amazonas and its capital, Manaus, the high detection rates of HIV/AIDS and tuberculosis—both the second highest in the country—associated with the high burden of COVID-19 have created a critical syndemic. The interaction between these epidemics has resulted in a significant impact on both the individual burden of the disease, especially among the most vulnerable, and on local public health. In this context, the emergence of COVID-19 has added complexity to the epidemiological landscape, exacerbating the already heightened immunological vulnerability of individuals with TB and HIV, and likely intensifying the risks of morbidity and mortality. Furthermore, the pandemic has further strained health systems, already challenged by TB-HIV coinfection, reducing the provision of care and access to diagnostic and treatment services, and worsening the health status of the coinfected population.

This study has limitations inherent to the use of secondary data from health information systems. The incompleteness and variable quality of records, as well as the potential for underreporting or inconsistencies in the databases, may have affected the accuracy of the analyses and the interpretation of the results. It is important to note that these limitations reflect operational challenges common to surveillance systems, particularly in settings with high demand and logistical constraints. Nevertheless, the findings provide valuable insights into the phenomenon under study and underscore the importance of ongoing efforts to improve the quality of public health data.

Conclusion

This study demonstrates that the COVID-19 pandemic had a significant impact on TB-related mortality among individuals with TB–HIV coinfection. However, the data analyzed did not reveal an association between the pandemic and mortality from other causes. Beyond the pandemic, mortality was driven by clinical indicators of disease severity, such as disseminated TB, prior TB treatment, severe immunosuppression (low CD4+ count and high HIV viral load), and delayed or absent initiation of HAART. Non-TB deaths were also influenced by sociodemographic factors including older age and homelessness. Residence in rural areas emerged as a specific predictor of TB-related death, likely due to limited access to specialized healthcare. Improved access to antiretroviral therapy and targeted follow-up strategies are essential to reduce mortality in TB–HIV coinfected individuals in high-burden, resource-limited settings. Interpreting these results through a syndemic lens underscores how the convergence of TB, HIV, and COVID-19 exacerbates vulnerabilities, intensifies individual and public health burdens, and overwhelms healthcare systems. Addressing this triple syndemic requires integrated, context-specific public health approaches that simultaneously target the biological, social, and structural factors driving these intertwined epidemics.

Conflict of interests

The authors declare no conflicts of interest.

Authors' contributions

LO-S conceived and designed the study, collected and compiled patient data, constructed the database, and drafted the manuscript. FAC-C contributed to study design, performed data analysis, and drafted the manuscript. MGFSA, MSGS, and VSA collected clinical and sociodemographic data. NCSN reviewed the data and contributed to manuscript writing. FEM-E and MCS-M supervised the study, contributed to its design, and revised the manuscript.

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Figure 1. Map showing the location of the city of Manaus in the state of Amazonas and in the Amazon biome, in Brazil

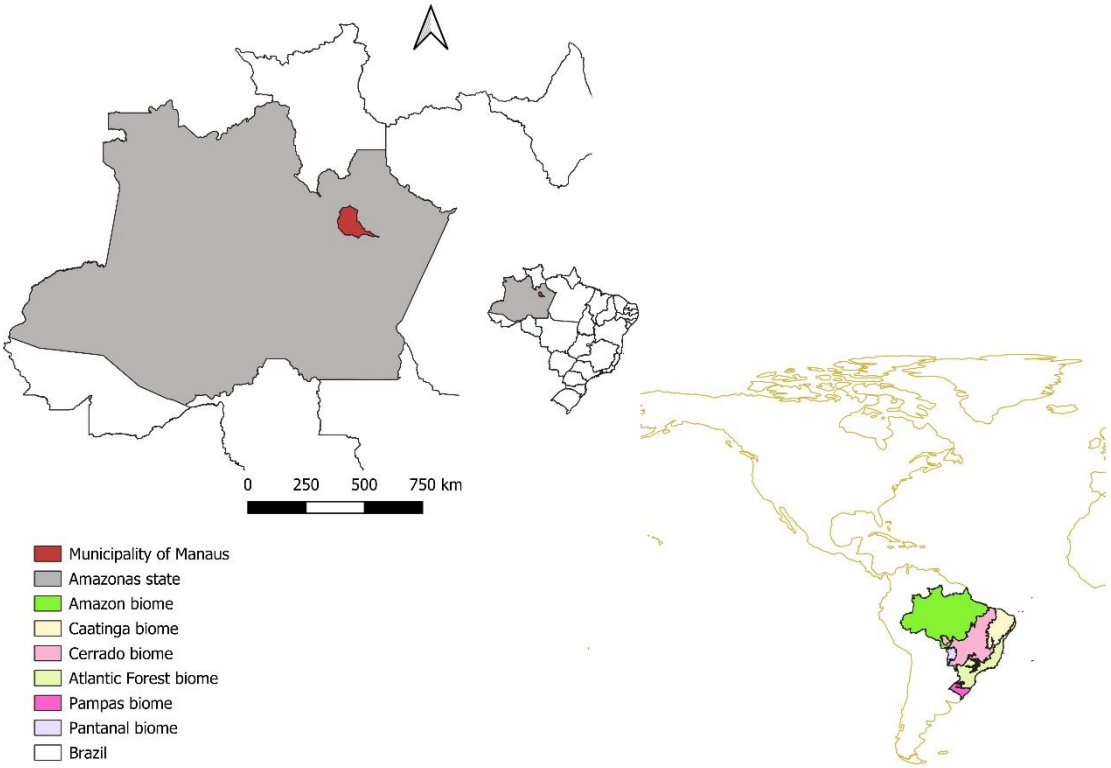

Figure 2. Flowchart of the study design

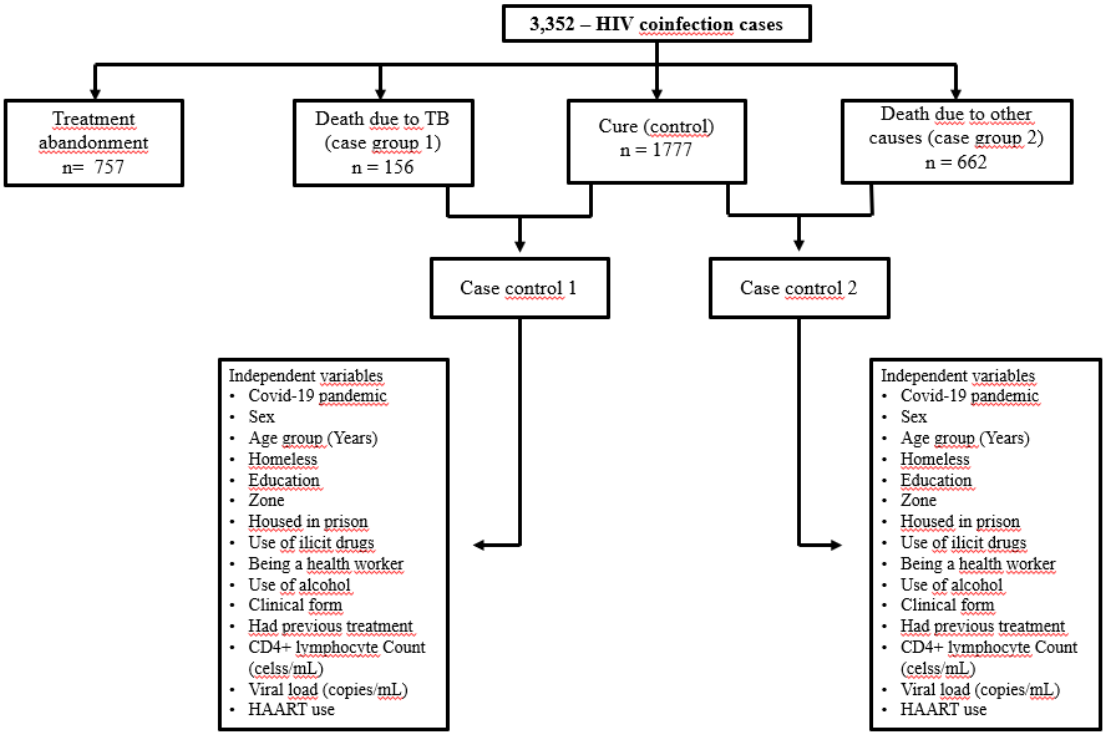

Figure 3. Non-lethal outcomes, annual number of deaths from tuberculosis and other causes, and case fatality rates among 3,352 cases of tuberculosis–HIV co-infection at a specialized hospital in the state of Amazonas, Brazil, from 2014 to 2022

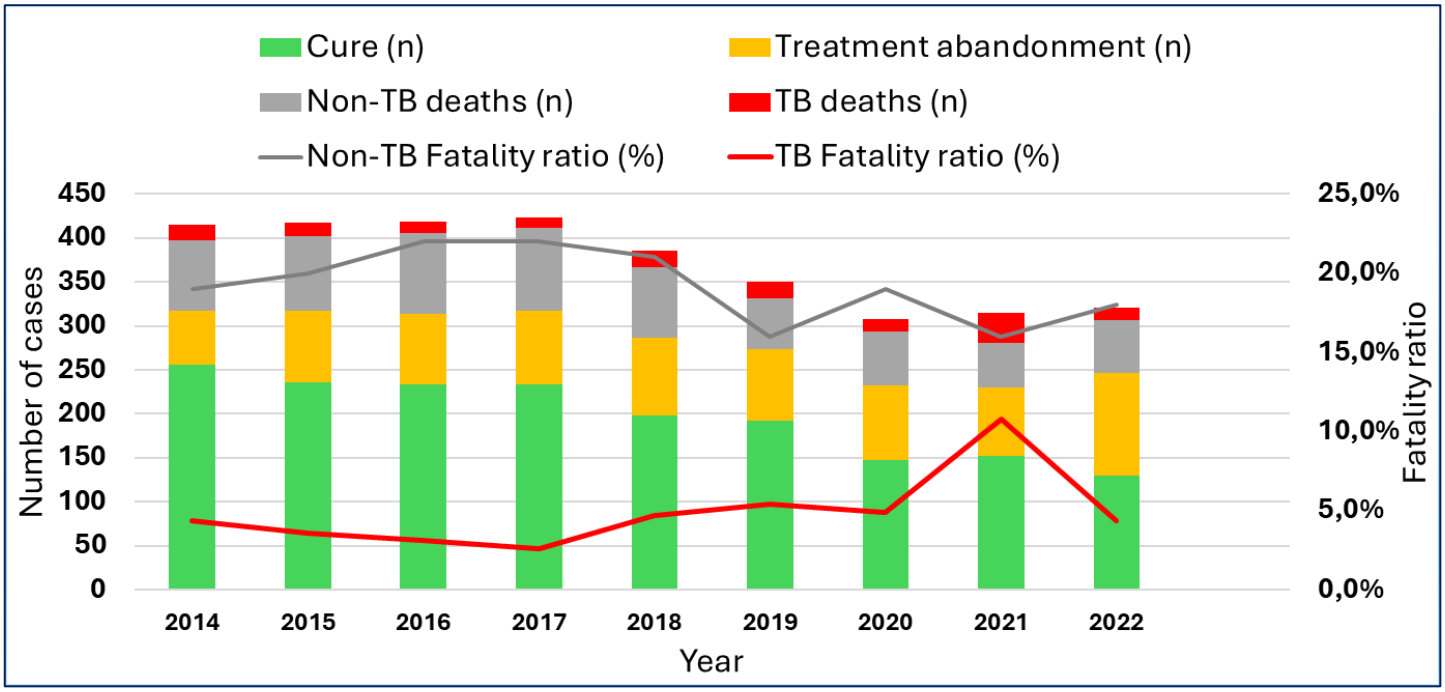

Table 1. Laboratory methods used to confirm tuberculosis in different clinical forms in 3352 patients treated by the Dr. Heitor Vieira Dourado Tropical Medicine Foundation before and during the COVID-19 pandemic, from 2014 to 2022.

Clinical Form / Method	Pre-pandemic (2014–2019) N=2408	Pandemic (2020–2022) N=944
Pulmonary (N=1497 / N=553)		
Laboratory confirmation	590 (39.3%)	407 (73.6%)
Positive sputum microscopy	445 (29.7%)	262 (47.4%)
Positive sputum culture	357 (23.8%)	245 (44.3%)
Xpert MTB/RIF rifampicin-sensitive	348 (23.2%)	337 (60.9%)
Xpert MTB/RIF rifampicin-resistant	23 (1.5%)	19 (3.4%)
LPA rifampicin/isoniazid-sensitive	2 (0.1%)	48 (8.7%)
LPA rifampicin-resistant	0	1 (0.2%)
LPA isoniazid-resistant	0	4 (0.7%)
LPA rifampicin/isoniazid-resistant	0	2 (0.4%)
Extrapulmonary (N=289 / N=95)		
Laboratory confirmation	220 (76.1%)	76 (80.0%)
Positive sputum microscopy	2 (0.7%)	1 (1.1%)
Positive sputum culture	3 (1.0%)	4 (4.2%)
Xpert MTB/RIF rifampicin-sensitive	1 (0.3%)	2 (2.1%)
Xpert MTB/RIF rifampicin-resistant	1 (0.3%)	2 (2.1%)
Extrapulmonary microscopy	58 (20.1%)	32 (33.7%)
Extrapulmonary culture	38 (13.1%)	21 (22.1%)
Extrapulmonary Xpert rifampicin-sensitive	31 (10.7%)	21 (22.1%)
Extrapulmonary Xpert rifampicin-resistant	1 (0.3%)	0
Positive histopathology	26 (9.0%)	10 (10.5%)
Disseminated (N=622 / N=296)		
Laboratory confirmation	407 (65.4%)	248 (83.8%)

Positive sputum microscopy	167 (26.8%)	108 (36.5%)
Positive sputum culture	184 (29.6%)	144 (48.6%)
Xpert MTB/RIF rifampicin-sensitive	130 (20.9%)	152 (51.4%)
Xpert MTB/RIF rifampicin-resistant	8 (1.3%)	8 (2.7%)
LPA rifampicin/isoniazid-sensitive	0	25 (8.4%)
LPA rifampicin-resistant	2 (0.3%)	1 (0.3%)
LPA isoniazid-resistant	0	4 (1.4%)
LPA rifampicin/isoniazid-resistant	0	2 (0.7%)
Extrapulmonary microscopy	130 (20.9%)	78 (26.4%)
Extrapulmonary culture	90 (14.5%)	80 (27.0%)
Extrapulmonary Xpert rifampicin-sensitive	61 (9.8%)	69 (23.3%)
Extrapulmonary Xpert rifampicin-resistant	8 (1.3%)	4 (1.4%)
Positive histopathology	60 (9.6%)	45 (15.2%)

Table 2. Factors associated with death due to tuberculosis among patients with HIV–tuberculosis coinfection admitted from 2014 to 2022 in the Dr. Heitor Vieira Dourado Tropical Medicine Foundation, Amazonas state, Manaus

Variable	Cases (N=156)	Controls (N=1777)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Covid-19 pandemic period						
Yes (2020–2022)	40.4%	24.1%	2.12 (1.51 – 2.98)	<0.001	1.99 (1.36 – 2.90)	<0.001
No (2014–2019)	59.6%	75.9%	1		1	
Sex						
Male	75%	74.3%	1		NP	NP
Female	25%	25.7%	0.96 (0.66 – 1.40)	0.471	NP	NP
Age group (years)						
0–19	1.3%	2.9%	0.50 (0.12 – 2.08)	0.580	0.35 (0.04 – 2.58)	0.300
20–39	55.8%	62.2%	1		1	
40–59	38.5%	32%	1.34 (0.95 – 1.89)	0.103	1.23 (0.83 – 1.82)	0.295
> 60	4.5%	3%	1.67 (0.74 – 3.80)	0.207	2.01 (0.79 – 5.11)	0.140
Homelessness						
Yes	6.4%	3.9%	1.67 (0.84 – 3.30)	0.105	1.23 (0.83 – 1.82)	0.295
No	93.6%	92.1%	1		1	
Education						
Illiteracy or elementary	52.9%	39.5%	1		1	
Intermediate to university	47.1%	60.5%	0.58 (0.41 – 0.82)	0.002	0.71 (0.41 – 1.04)	0.082
Zone						
Urban	89.1%	94.4%	1		1	

Rural	10.9%	5.6%	2.07 (1.20 – 3.56)	0.013	2.11 (1.13 – 3.90)	0.018
Housed in prison						
Yes	3.8%	2.4%	1.61 (0.67 – 3.85)	0.282	NP	NP
No	96.2%	97.6%	1		NP	NP
Use of illicit drugs						
Yes	12.8%	14%	0.90 (0.55 – 1.47)	0.401	NP	NP
No	87.2%	86%	1			
Being a health worker						
Yes	0%	2.1%	undefined	undefined	undefined	undefined
No	100%	97.9%				
Use of alcohol						
Yes	35.9%	33.1%	1.13 (0.80 – 1.59)	0.269	NP	NP
No	64.1%	66.9%	1			
Clinical form						
Pulmonary	49.7%	62.1%	1		1	
Extrapulmonary	11.5%	12.2%	1.19 (0.70 – 2.03)	0.478	1.49 (0.82 - 2.69)	0.182
Both	39.1%	25.8%	1.90 (1.34 – 2.71)	<0.001	1.78 (1.20 - 2.66)	0.004
Had previous treatment						
Yes	31.4%	18%	2.08 (1.45 – 2.98)	<0.001	1.91 (1.25 - 2.91)	0.002
No	68.6%	82%	1			
CD4+ lymphocyte count (cells / mL)						
< 200	82%	63.3%	4.13 (1.66 – 10.24)	<0.001	4.74 (1.69 - 13.28)	0.003
200 – 350	12.7%	16.1%	2.51 (0.92 – 6.85)	0.084	2.67 (0.86 - 8.23)	0.086
351 - 500	2%	10.1%	0.63 (0.14 – 2.69)	0.724	0.82 (0.18 - 3.79)	0.806

> 500	3.3%	10.6%	1			
Viral load (copies / mL)						
< 50	10.2%	10.3%	1			
50 – 1000	8.8%	10.2%	0.87 (0.40 – 1.89)	0.845	NP	NP
1001 – 10000	65.3%	57.6%	1.14 (0.64 – 2.01)	0.780	NP	NP
> 10000	15.6%	22%	0.71 (0.36 – 1.40)	0.370	NP	NP
HAART use						
Regular, consistent, previous to TB	24.4%	30.3%	1		1	
Started along with TB treatment	19.2%	10.5%	2.27 (1.36 – 3.77)	0.002	1.86 (1.03 – 3.37)	0.039
Previous irregular use	5.8%	11.8%	0.60 (0.28 – 1.28)	0.238	0.71 (0.32 – 1.60)	0.411
Never used	50.6%	47.4%	1.32 (0.88 – 1.98)	0.198	1.59 (1.00 – 2.56)	0.052

Table 3. Factors associated with death due to non-tuberculosis conditions among patients with HIV – tuberculosis coinfection admitted from 2014 to 2022 in the Dr. Heitor Vieira Dourado Tropical Medicine Foundation, Amazonas state, Manaus

Variable	Cases (N=662)	Controls (N=1777)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Covid-19 pandemic period						
Yes (2020–2022)	26%	24.1%	1.10 (0.89 – 1.35)	0.369	NP	NP
No (2014–2019)	74%	75.9%	1			
Sex						
Male	74.3%	74.3%	1			
Female	25.7%	25.7%	0.95 (0.77 – 1.17)	0.347	NP	NP
Age group (years)						
0–19	0.5%	2.9%	0.16 (0.05 – 0.51)	<0.001	0.21 (0.06 – 0.67)	0.009
20–39	61%	62.2%	1		1	
40–59	33.5%	32%	1.06 (0.88 – 1.29)	0.521	1.17 (0.93 – 1.45)	0.164
> 60	5%	3%	1.70 (1.08 – 2.66)	0.024	2.16 (1.27 – 3.69)	0.004
Homelessness						
Yes	6.2%	3.9%	1.61 (1.08 – 2.39)	0.024	1.62 (1.02 – 2.56)	0.039
No	93.8%	92.1%	1		1	
Education						
Illiteracy or elementary	44%	39.5%	1.20 (1.00 – 1.45)	0.059	0.92 (0.74 – 1.14)	0.455
Intermediate to university	56%	60.5%	1		1	
Zone						
Urban	93.1%	94.4%	1			
Rural	6.9%	5.6%	0.79 (0.55 – 1.13)	0.211	NP	NP
Housed in prison						

Yes	2%	2.4%	0.80 (0.43 – 1.51)	0.309	NP	NP
No	98%	97.6%	1			
Use of illicit drugs						
Yes	11.9%	14%	0.835 (0.63 – 1.09)	0.205	NP	NP
No	88.1%	86%	1			
Being a health worker						
Yes	1.2%	2.1%	0.56 (0.26 – 1.20)	0.179	0.31 (0.11 – 0.88)	0.028
No	98.8%	97.9%	1			
Use of alcohol						
Yes	36.7%	33.1%	1.17 (0.97 – 1.40)	0.103	1.08 (0.88 – 1.34)	0.440
No	63.3%	66.9%	1		1	
Clinical form						
Pulmonary	59.5%	62.1%	1		1	
Extrapulmonary	11.8%	12.2%	1.01 (0.76 – 1.34)	0.942	1.12 (0.89 – 1.42)	0.312
Both	28.7%	25.8%	1.16 (0.94 – 1.42)	0.154	1.41 (1.02 – 1.94)	0.037
Had previous treatment						
Yes	21.1%	18%	1.22 (0.98 – 1.52)	0.080	1.29 (1.00 – 1.68)	0.049
No	78.9%	82%	1			
CD4+ lymphocyte count (cells / mL)						
< 200	86.1%	63.3%	8.83 (4.63 – 16.83)	< 0.001	2.15 (1.52 – 3.05)	< 0.001
200 – 350	8.7%	16.1%	3.50 (1.74 – 7.06)	< 0.001	1.63 (1.03 – 2.56)	0.034
351 - 500	3.6%	10.1%	2.32 (1.07 – 5.04)	0.041	1.11 (0.68 – 1.81)	0.662
> 500	1.6%	10.6%	1		1	
Viral load (copies / mL)						
< 50	6.6%	10.3%	1		1	

50 – 1000	9.1%	10.2%	1.39 (0.88 – 2.19)	0.167	1.11 (0.68 – 1.81)	0.662
1001 – 10000	74.8%	57.6%	2.01 (1.40 – 2.88)	< 0.001	1.63 (1.03 – 2.56)	0.034
> 10000	9.4%	22%	0.66 (0.42 – 1.03)	0.079	2.15 (1.52 – 3.05)	< 0.001
HAART use						
Regular, consistent, previous to TB	31%	30.3%	1			
Started along with TB treatment	15%	10.5%	1.38 (1.03 – 1.86)	0.032	1.78 (1.26 – 2.50)	< 0.001
Previous irregular use	11.5%	11.8%	0.95 (0.70 – 1.29)	0.814	1.19 (0.83 – 1.69)	0.329
Never used	42.6%	47.4%	0.87 (0.71 – 1.08)	0.236	1.42 (1.10 – 1.83)	0.007

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