

Spatiotemporal Dynamics of TB-HIV Coinfection in Health Regions Of The Brazilian Amazon

Dinâmica Espaço-Temporal da Coinfecção TB-HIV em Regiões de Saúde da Amazônia Brasileira

Dinámica Espaciotemporal de la Coinfección TB-VIH e n Regiones de Salud de la Amazonia Brasileña

RESUMO

Objetivo: A coinfecção tuberculose-HIV (TB-HIV) permanece como importante problema de saúde pública na Amazônia brasileira, especialmente em áreas com vulnerabilidade socioeconômica e limitações no acesso aos serviços de saúde. **Método:** Este estudo ecológico retrospectivo analisou casos notificados entre 2010 e 2024, agregados por regiões de saúde. A incidência anual foi calculada por 100.000 habitantes, enquanto a tendência temporal foi avaliada por regressão binomial negativa e mínimos quadrados generalizados. A análise espacial incluiu índice de Moran global, autocorrelação espacial local e modelo autorregressivo espacial. **Resultados:** Observou-se tendência crescente da incidência ao longo do período, com intensificação após 2018, redução em 2020 e retomada subsequente. A análise espacial revelou autocorrelação significativa, com concentração de áreas de maior risco nas regiões oeste e central da Amazônia e menor risco na porção leste. **Conclusão:** Os achados evidenciam crescimento sustentado e distribuição heterogênea da coinfecção, reforçando a necessidade de estratégias integradas de vigilância e controle.

DESCRIPTORES: *Tuberculose; HIV; Análise Espacial.*

ABSTRACT

Objective: Tuberculosis-HIV (TB-HIV) coinfection remains a major public health problem in the Brazilian Amazon, particularly in areas marked by socioeconomic vulnerability and limited access to healthcare services. **Methods:** This retrospective ecological study analyzed reported cases between 2010 and 2024 aggregated by health regions. Annual incidence rates were calculated per 100,000 inhabitants, while temporal trends were assessed using negative binomial regression and generalized least squares models. Spatial analysis included Global Moran's Index, local spatial autocorrelation, and spatial autoregressive modeling. **Results:** A progressive increase in incidence was observed throughout the study period, with intensification after 2018, reduction in 2020, and subsequent recovery. Spatial analysis revealed significant autocorrelation, with higher-risk clusters concentrated in the western and central Amazon and lower-risk areas in the eastern portion. **Conclusion:** These findings demonstrate sustained growth and heterogeneous distribution of TB-HIV coinfection, highlighting the need for integrated surveillance and control strategies in priority regions.

DESCRIPTORS: Tuberculosis; HIV; Spatial Analysis.

RESUMEN

Objetivo: La coinfección tuberculosis-VIH (TB-VIH) continúa siendo un importante problema de salud pública en la Amazonia brasileña, especialmente en áreas con vulnerabilidad socioeconómica y limitaciones en el acceso a los servicios de salud. Este estudio ecológico retrospectivo analizó casos notificados entre 2010 y 2024, agregados por regiones de salud. **Método:** La incidencia anual fue calculada por 100.000 habitantes y la tendencia temporal fue evaluada mediante regresión binomial negativa y mínimos cuadrados generalizados. El análisis espacial incluyó índice de Moran global, autocorrelación espacial local y modelo autorregresivo espacial. **Resultados:** Se observó una tendencia creciente de la incidencia durante el período analizado, con intensificación después de 2018, reducción en 2020 y posterior recuperación. El análisis espacial mostró

autocorrelación significativa, con concentración de áreas de mayor riesgo en las regiones occidental y central de la Amazonia y menor riesgo en la porción oriental. **Conclusión:** Los hallazgos evidencian crecimiento sostenido y distribución heterogénea de la coinfección, reforzando la necesidad de estrategias integradas de vigilancia y control.

DESCRIPTORES: Tuberculosis; VIH; Análisis Espacial.

RECEIVED: 05/15/2026 **APPROVED:** 06/19/2026

How to cite this article: Macedo GP, Coelho JMR, Amaral MHM, Santos MAS, Simeone D. Spatiotemporal Dynamics of TB-HIV Coinfection in Health Regions Of The Brazilian Amazon. *Saúde Coletiva (Brazilian Edition)* [Internet]. 2026 [cited year month day];18 (111):20540-20553. Available from: DOI: 10.36489/saudecoletiva.2026v18i11p20540-20553

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INTRODUCTION

Communicable infectious diseases constitute complex systems in which biological interactions and the organization of health care systems influence the dynamics of their occurrence and spread⁽¹⁾. In this context, tuberculosis (TB), caused by bacteria of the *Mycobacterium tuberculosis* complex, remains one of the leading causes of morbidity and mortality worldwide, especially in low- and middle-income countries, where inequalities in access to diagnosis and timely treatment persist⁽²⁾. Transmission occurs predominantly through the air, via inhalation of aerosols containing bacilli shed by infected individuals, with the pulmonary form being primarily responsible for sustaining the chain of transmission⁽³⁾.

The epidemiological dynamics of TB are significantly altered in the presence of human immunodeficiency

virus (HIV) infection, creating a syndemic system in which the two pathogens interact synergistically⁽⁴⁾. HIV-induced immunosuppression substantially increases the risk of progression from latent infection to active TB, making this disease one of the leading opportunistic infections in people living with HIV/AIDS⁽⁵⁾. It is estimated that HIV-positive individuals are up to 30 times more likely to develop active TB compared to the general population, underscoring the magnitude of this interaction⁽⁶⁾. In this context, TB-HIV coinfection is a major public health problem, associated with greater clinical severity, a higher risk of treatment failure, and increased mortality, as well as a greater burden on health care systems⁽⁷⁾.

In Brazil, the distribution of TB-HIV coinfection exhibits high spatial heterogeneity, reflecting regional inequalities in health infrastructure

and living conditions⁽⁸⁾. The Brazilian Amazon represents a particularly relevant scenario, characterized by vast territorial areas, geographic barriers to access to health services, and operational challenges for epidemiological surveillance⁽⁹⁾. Furthermore, the organization of the healthcare network into health regions—which often have varying levels of installed capacity—can influence the detection, registration, and management of cases⁽¹⁰⁾. These factors reflect the complexity of TB-HIV coinfection in contexts marked by social inequality and fragmented care, which tends to hinder integrated disease control^(1,11).

Despite the epidemiological relevance of coinfection, studies that comprehensively assess its temporal and spatial dynamics in the Brazilian Amazon remain limited, especially when considering territorial units aligned with the organization

of health services. Spatiotemporal analysis has proven to be a valuable approach for identifying distribution patterns, detecting high-risk areas, and understanding the persistence of coinfection in different territorial contexts⁽¹²⁾. In this regard, investigating TB-HIV coinfection from an integrated perspective allows for the identification of trends over time and spatial patterns of risk, providing more robust evidence for the planning and organization of health surveillance activities.

The present study aims to analyze the spatiotemporal dynamics of TB-HIV coinfection in the Brazilian Amazon from 2010 to 2024, seeking to assess the temporal trend in incidence and identify spatial distribution patterns by detecting clusters and high-risk areas across health regions. Understanding these patterns can contribute to strengthening surveillance and control strategies, especially in regional contexts marked by high vulnerability and territorial complexity.

METHOD

STUDY DESIGN

The study was conducted in the Brazilian Legal Amazon, a macroregion covering approximately 5.2 million km², corresponding to about 61% of the national territory. This region comprises nine states—Acre, Amapá, Amazonas, Maranhão, Mato Grosso, Pará, Rondônia, Roraima, and Tocantins—and exhibits high socio-environmental heterogeneity, with an uneven population distribution between established urban centers and extensive rural and peri-urban areas⁽¹³⁾. The total population is estimated to exceed 28 million inhabitants, characterized by marked socioeconomic and structural inequalities.

This is an ecological and retrospective study based on secondary data from the Notifiable Diseases Infor-

mation System (SINAN), provided by the Information Technology Department of the Unified Health System (DataSUS) of the Brazilian Ministry of Health⁽¹⁴⁾. Annual figures for confirmed cases of tuberculosis (TB) with information on HIV status were extracted. Based on this dataset, cases of TB-HIV coinfection were identified, defined as those in which there is a positive HIV test result among the reported tuberculosis cases. All available records from January 2010 through December 2024 were included.

The data were initially extracted at the municipality of residence level and subsequently aggregated by health regions and by year to ensure compatibility between the territorial units used in the spatial and temporal analyses. The database included information on the number of cases per geographic unit and period, as well as corresponding population data, enabling the construction of standardized epidemiological indicators.

Annual population data were obtained from DataSUS, enabling the standardization of incidence rates and the adjustment of statistical models according to population size. For census years, official demographic totals were used, while intercensal estimates were adopted for the remaining periods, ensuring the continuity of the time series.

Only records with valid information on municipality of residence, health region, year of notification, and HIV status were included in the analysis. Records with inconsistencies in these variables or lacking essential information for calculating incidence were excluded. This procedure aimed to ensure the quality, consistency, and comparability of the data used in the temporal and spatial analyses.

DATA ANALYSIS

All analyses were conducted using the GNU R statistical environment,

version 4.4.1⁽¹⁵⁾. Initially, the databases of TB-HIV coinfection cases and the general population were standardized, allowing for the integration of information by health region and year. Next, the data were aggregated by spatiotemporal unit, calculating the total num of cases and the corresponding population. The annual incidence was estimated as the number of cases divided by the population, multiplied by 100,000 inhabitants.

The temporal analysis was conducted based on the annual aggregation of the data, allowing for the construction of a time series of incidence. To model the temporal dynamics of TB-HIV coinfection, negative binomial regression models were fitted, which are appropriate for count data with potential overdispersion. The number of cases was used as the dependent variable, the year as the independent variable, and the logarithm of the population was included as an offset term, allowing for the direct modeling of incidence rates. The estimated coefficients were transformed into incidence rate ratios (IRR) by raising the parameters to the power of 1 and are presented with their respective 95% confidence intervals (95% CI). As a sensitivity analysis, a generalized least squares (GLS) model was fitted, with the logarithm of annual incidence as the outcome. In this model, a first-order autoregressive (AR1) correlation structure was incorporated to control for temporal autocorrelation and refine the trend estimate over the analyzed period.

The data were then integrated into a cartographic database of health regions using spatial joining. The average incidence was calculated for the period from 2010 to 2024, allowing for the characterization of the spatial pattern of coinfection. The spatial dependency structure was defined using a contiguity-based neighborhood matrix, which was subsequently converted into a standardized spatial weight

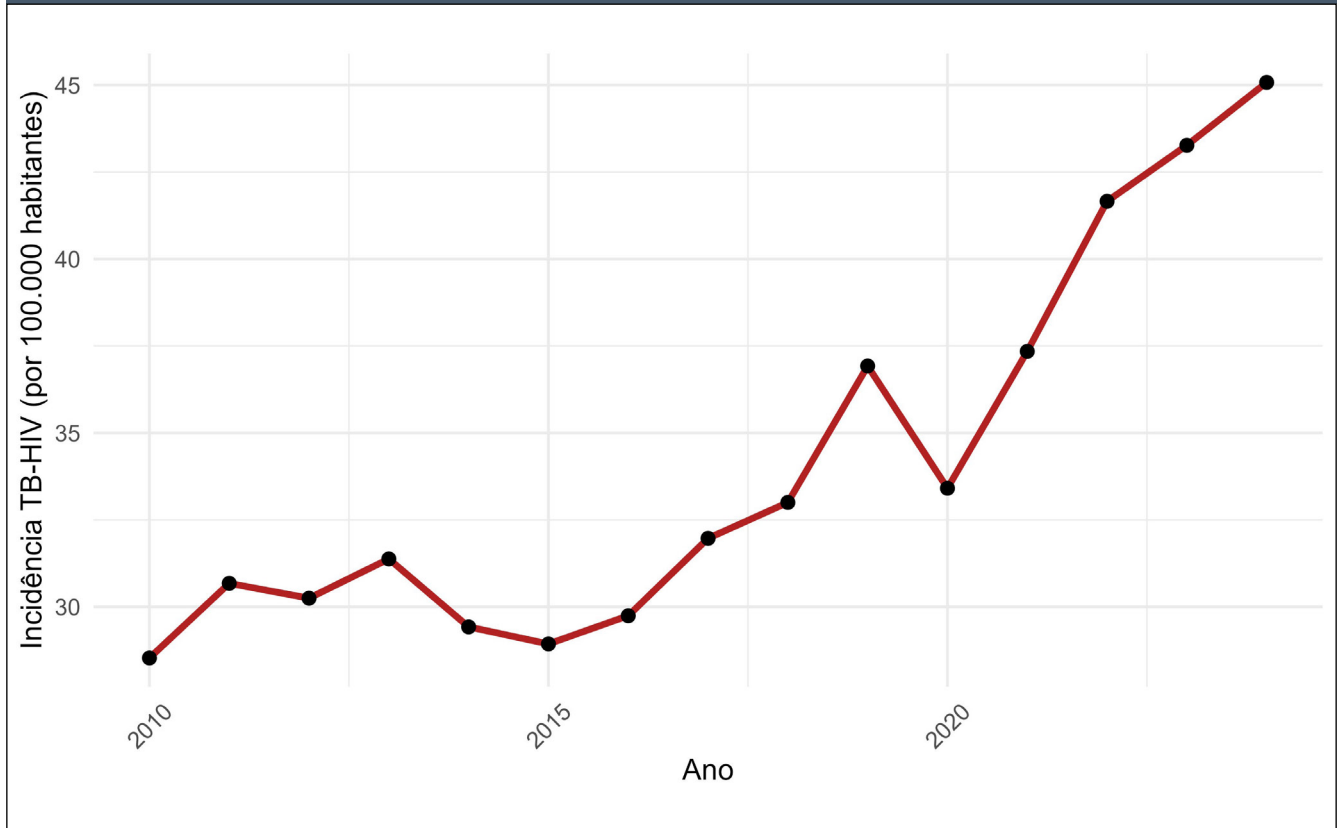
matrix. Global spatial autocorrelation was assessed using Moran's index to verify the presence of non-random spatial patterns. Next, a local autocorrelation analysis (LISA) was conducted to identify spatial clusters of incidence. To classify spatial patterns, statistical significance ($p < 0.10$) was combined with the distribution of incidence values and their respective spatial lags, using the 25th and 75th quantiles as cutoff points. The regions were classified into the following categories: high-high (hotspots), low-low

(coldspots), high-low, low-high, and non-significant areas. Additionally, a spatial autoregressive (SAR) model was fitted, considering the average incidence as the dependent variable and incorporating the previously defined spatial weight matrix. Model fit was assessed through spatial autocorrelation analysis of the residuals, using Moran's index, to verify whether spatial dependence had been adequately captured.

RESULTS

Examination of the time series of TB-HIV incidence (Figure 1) revealed an upward trend over time, with moderate interannual variations. Notably, there was a more pronounced increase beginning in 2018, followed by a slight decrease in 2020 and a resumption of growth through 2024, when incidence reached its peak in the series. This pattern suggests a positive temporal trend, with a recent increase in the incidence of coinfection in the region.

Figure 1. Time series of TB-HIV coinfection incidence (per 100,000 inhabitants) in the Brazilian Amazon from 2010 to 2024.



Negative binomial regression analysis confirmed the increasing trend over time, with a statistically significant association between year and number of cases ($\beta = 0.03$; $p < 0.001$). The estimated incidence rate ratio (IRR) was 1.03 (95% CI: 1.02–1.04),

indicating an increase in the incidence of TB-HIV coinfection. The GLS model also indicated a positive and statistically significant temporal trend ($\beta = 0.03$; $p = 0.02$). The autocorrelation parameter ($\phi = 0.89$) revealed strong temporal dependence

in the time series, indicating that incidence values in consecutive years are highly correlated. These results reinforce the consistency of the observed upward trend, even after controlling for autocorrelation.

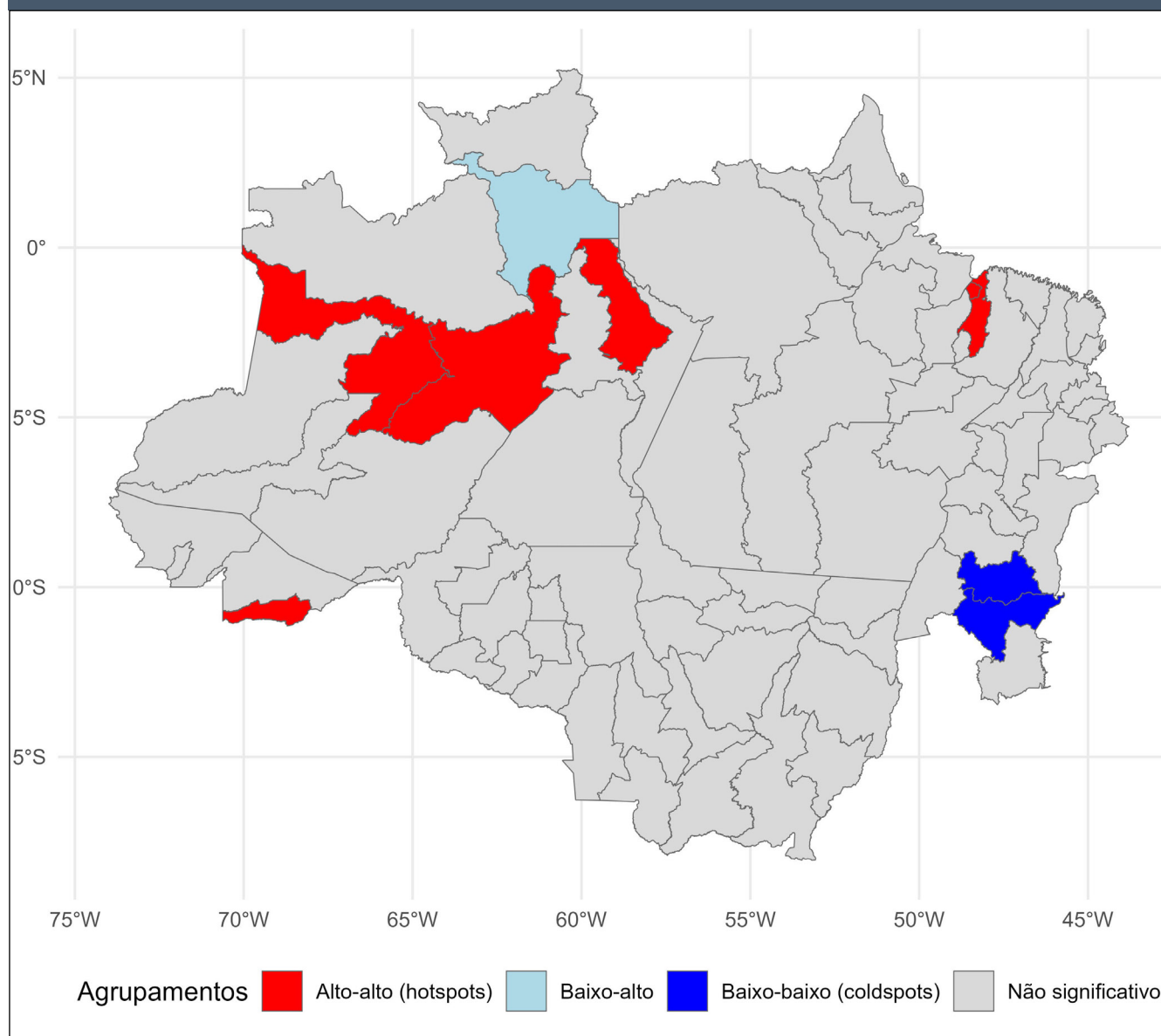
The global autocorrelation analy-

sis revealed a non-random spatial pattern in the average incidence of TB-HIV (Moran's $I = 0.30$; $p < 0.001$), indicating the presence of spatial clusters. Local analysis (LISA) identified specific clustering patterns (Figure 2),

with “high-high” clusters (hotspots) concentrated mainly in regions of the western and central Amazon. On the other hand, “low-low” clusters (coldspots) were identified in areas of the eastern portion, indicating regions

with lower incidence and similar neighboring areas. “Low-high” patterns were also observed, characterizing transition zones or spatial outliers, although less frequently.

Figure 2. Spatial distribution of clusters of average TB-HIV coinfection incidence by health regions in the Brazilian Amazon, based on local spatial autocorrelation analysis (LISA), classifying areas as high-high (hotspots), low-low (coldspots), high-low, low-high, and non-significant.



Spatial modeling using the autoregressive model (SAR) confirmed the presence of significant spatial depen-

dence in the distribution of incidence ($\rho = 0.47$; $p < 0.001$), indicating that incidence values in a given region

are associated with those observed in neighboring regions. The model showed a better fit compared to the

simple linear model (AIC = 584.23 vs. 593.77), reinforcing the importance of incorporating spatial structure into the analysis. Residual analysis did not indicate significant spatial autocorrelation (Moran's $I = -0.0096$; $p = 0.47$), suggesting that the model was adequate for capturing the spatial dependence present in the data.

DISCUSSION

The dynamics of TB-HIV coinfection in the Brazilian Amazon show a consistent pattern of intensification over time. This trend indicates that coinfection persists in the region, with incidence levels tending to accumulate over the years, suggesting difficulty in reducing the disease burden at the population level. Among health regions, the distribution of coinfection reveals a clearly heterogeneous pattern, with areas of higher risk concentrated in the western and central portions of the Amazon. These clusters of high incidence indicate the presence of territories where coinfection occurs more intensely and continuously, constituting priority areas for surveillance⁽⁸⁾. In contrast, regions in the eastern portion exhibit patterns of lower incidence, forming areas of lower relative risk.

Areas classified as hotspots represent regions where coinfection is consistently concentrated within the territory, suggesting contexts in which the disease burden is higher and more persistent. These spatial patterns are consistent with scenarios characterized by greater socioeconomic vulnerability, including limited access to health services, lower healthcare coverage, and difficulties in ensuring continuity of care^(11,16). In the Amazon, these conditions are often associated with more remote areas, characterized by sparse infrastructure and greater geographical inaccessibility⁽¹⁷⁾. On the other hand, areas with lower incidence tend to be concentrated

in regions with a better-organized healthcare network and improved access to health services, which may be associated with greater capacity for diagnosis and case management. Although these differences cannot be interpreted causally, the observed spatial pattern is consistent with the unequal distribution of resources and infrastructure across the region⁽¹⁾.

The presence of spatial dependence reinforces the fact that high-risk areas are not isolated but organized into continuous territorial blocks. This pattern indicates that neighboring regions tend to share similar incidence levels, forming zones of heightened risk. In practice, this means that coinfection is distributed across interconnected territories, rather than in isolated pockets, which has direct implications for epidemiological surveillance⁽¹⁸⁾. The transition areas identified in the spatial analysis indicate regions that do not follow the dominant pattern of their surroundings and may represent territories undergoing epidemiological change. These areas are particularly relevant, as they may reflect processes of expansion or contraction of coinfection and should be monitored with greater attention⁽¹⁹⁾.

In the Amazon, these spatial patterns must be interpreted in light of historical and structural socioeconomic inequalities⁽²⁰⁾. The region faces significant limitations related to health infrastructure, geographic access, service distribution, and the population's living conditions. These inequalities are directly reflected in the organization of the healthcare network and the responsiveness of services, contributing to the persistence of high-risk areas⁽¹⁾. Furthermore, the territorial structure based on health regions may exhibit heterogeneity in care capacity, which tends to be reflected in the distribution of coinfection. Regions with lower avail-

ability of specialized services and less integration between primary care and referral services may face greater difficulties in early diagnosis and case follow-up, contributing to the persistence of the disease^(11,7).

These findings reinforce the fact that TB-HIV coinfection in the Brazilian Amazon is not distributed homogeneously but follows well-defined territorial patterns associated with socioeconomic and structural inequalities. The identification of high-risk areas and consistent spatial patterns highlights the importance of targeted surveillance strategies, focusing on priority regions and employing an integrated territorial approach.

CONCLUSION

TB-HIV coinfection in the Brazilian Amazon exhibits an increasing temporal trend associated with a heterogeneous and structured spatial distribution. The consistency of incidence levels over time and the presence of geographic clusters suggest that the disease dynamics are related to structural and territorial characteristics that persist over time. The results indicate that coinfection is unevenly distributed across the territory, with regions exhibiting higher incidence levels in association with neighboring areas, highlighting patterns of spatial interdependence. This behavior reinforces the importance of considering the territory as an integrated unit in epidemiological surveillance. Understanding these spatiotemporal patterns contributes to a more comprehensive view of the distribution of TB-HIV coinfection, providing insights for planning surveillance strategies and organizing health services in complex regional contexts.

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