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ORIGINAL ARTICLE

Spatial technologies for identifying critical areas of TB-HIV coinfection: Application of Getis-Ord Gi*

*Tecnologias espaciais para identificação de áreas críticas da coinfecção TB-HIV: aplicação do Getis-Ord Gi**

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ABSTRACT This work aims to evaluate the spatial pattern and identify municipalities with greater vulnerability to the occurrence of tuberculosis and human immunodeficiency virus coinfection in the state of Mato Grosso, Brazil. This is an ecological study of reported cases of coinfection from 2012 to 2021 in the state. The data were collected by the Notifiable Diseases Information System, subsequently carrying out a descriptive analysis of the sociodemographic and clinical data, and the spatial distribution of the incidence obtained for Getis-Ord Gi* analysis. 1,407 cases of coinfection were reported, the majority of which were men, mixed race, aged between 20 and 39 years old, and with low education. The spatial analysis identified municipalities with a higher association with the occurrence of the disease and its indicators, such as Cuiabá, which had an incidence of 10.93 cases per 100,000 inhabitants. The presence of hot spots indicating emerging territories for coinfection was identified, with reliability testing between 90% and 99%. The findings in this work can serve as an alert to identify the most vulnerable populations and areas at risk, in addition to supporting the implementation of public policies aimed at strategies for controlling coinfection in the state of Mato Grosso.

KEYWORDS Epidemiology. Cluster analysis. Mycobacterium tuberculosis. HIV.

RESUMO *Este trabalho objetivou avaliar o padrão espacial e identificar municípios com maior vulnerabilidade para ocorrência da coinfecção tuberculose e Vírus da Imunodeficiência Humana no estado de Mato Grosso. Trata-se de um estudo ecológico dos casos notificados de coinfecção no período de 2012 a 2021 no estado. Os dados foram coletados pelo Sistema de Informação de Agravos de Notificação, posteriormente realizadas a análise descritiva dos dados sociodemográficos e clínicos e a distribuição espacial da incidência obtida para análise Getis-Ord Gi*. Foram notificados 1.407 casos de coinfecção, sendo a maioria homens, de cor parda, com idade entre 20 e 39 anos, e de baixa escolaridade. A análise espacial identificou municípios de maior associação à ocorrência da doença e seus indicadores, como Cuiabá, com incidência de 10,93 casos por 100 mil habitantes. Foi identificada a presença de hot spots que indicam territórios emergentes para coinfecção, com teste de confiabilidade entre 90% e 99%. Os achados neste trabalho podem colaborar como um alerta para identificação de populações mais vulneráveis e áreas de risco, além de subsidiar a implementação de políticas públicas de visem estratégias para o controle da coinfecção no estado de Mato Grosso.*

PALAVRAS-CHAVE *Epidemiologia. Análise por conglomerados. Mycobacterium tuberculosis. HIV.*

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Introduction

Tuberculosis (TB) is a disease caused by Mycobacterium tuberculosis. Despite being preventable and curable, TB is the second leading cause of death worldwide and the leading cause of death among people living with the Human Immunodeficiency Virus (HIV)[1]. In 2023, approximately 10,8 million people contracted TB, with 1,09 million deaths recorded, including 161,000 deaths among People Living with HIV/AIDS (PLWHA)[2].

Coinfection between TB and HIV poses a significant public health challenge, as these diseases have a highly complex interaction and can mutually aggravate the progression and severity of both. TB can cause an increase in viral load and a reduction in CD4+ T lymphocytes in PLWHA, while HIV can modify the pathogenesis of TB, thus generating negative smear microscopies, further complicating its diagnosis[3].

TB-HIV coinfection is a public health problem that leads to increased healthcare costs due to the large number of new diagnoses. The World Health Organization (WHO) has established intermediate milestones to reduce the number of deaths by 35%, 75%, and 90%, and the incidence rate by 20%, 50%, and 80% for the years 2020, 2025, and 2030[4].

Brazil is one of the priority countries with a high burden of TB-HIV coinfection that has been included in a global list. Therefore, for the country to achieve the goals proposed by the WHO in the End TB strategy, it is essential to invest in actions aimed at populations that are more vulnerable, such as PLWHA[5].

Among the challenges to be overcome are issues related to the territory, which hinder access to health services and timely diagnosis of both TB and HIV[6]. Understanding local contexts and emerging regions can foster the development of collaborative activities between TB and HIV services to reduce both health problems[7].

In this context, considering the epidemiological importance of territories in TB-HIV coinfection, studies using spatial technologies to understand the dynamics of this coinfection are still scarce, particularly in the state of Mato Grosso, in the Central-West region of Brazil. Studies previously conducted in the state using this approach have only included the capital, Cuiabá, and have not yet included TB-HIV cases, which understanding is essential for achieving the TB elimination goals[8,9]. Therefore, studies covering the entire state, including municipalities in the interior, could provide valuable evidence for addressing TB in Mato Grosso, particularly with regard to TB-HIV coinfection.

Thus, the present study aimed to evaluate the spatial pattern and identify municipalities with greater vulnerability to the occurrence of TB-HIV coinfection in the state of Mato Grosso.

Material and methods

This is an ecological study of reported cases of TB with HIV coinfection in the state of Mato Grosso. The state is located in the Central-West region, composed of 141 municipalities, has an area of 903,208.361 km^2, and a population of 3,658,813 people[10]. In this context, the following cases were included in the study: cases registered between 2012 and 2021.

Data were collected through the Notifiable Diseases Information System (Sinan) platform, as well as from the Data Repository of the Information Systems of the Mato Grosso State Health Department (DwWeb/SES-MT). Population information was obtained from the 2022 Demographic Census of the Brazilian Institute of Geography and Statistics (IBGE)[10]. The data were separated into two groups and tabulated in Microsoft Excel® spreadsheets for better visualization. The first group consisted of sociodemographic variables (sex, age, race/color, and education), and the second, clinical characteristics (sputum smear microscopy, form, tuberculin skin test, sputum culture, histopathological examination, form of admission, and case outcome). The geographic network with the municipalities of the state of Mato Grosso was obtained through the IBGE[11].

The data were tabulated, and descriptive statistics were performed, presenting the results using absolute and relative frequencies. The calculation of the incidence of TB-HIV cases during the study period for the 141 municipalities was obtained using the following formula:

$$\text{TB-HIV Incidence} \quad \frac{\textit{Number os cases during the study period}}{\textit{Population number of each municipality}} \times 100.000/10$$

Incidence rates per year were expressed using a graph that included the entire study period.

After the incidence calculations were carried out, thematic maps were created with the spatial distribution of the rates obtained for each of the municipalities in Mato Grosso, in which the hottest colors represent the most critical areas in relation to TB-HIV.

The spatial technology called Getis-Ord Gi*[12] was used to verify the spatial association of the incidence. This technique provides detailed spatial patterns by identifying clusters and analyzes spatial association locally, based on a spatial concentration indicator and a neighborhood matrix for each location (each municipality). The Getis-Ord Gi* is given by the following formula[12]:

$$G_i^* = \frac{\sum_{j=1}^{n} w_{i,j} x_j - \overline{X} \sum_{j=1}^{n} w_{i,j}}{s\sqrt{\frac{\left[n \sum_{j=1}^{n} w_{i,j}^2 - \left(\sum_{j=1}^{n} w_{i,j}\right)^2\right]}{n-1}}}$$

Where: *Gi** is the spatial autocorrelation statistic of an event *i* over *n* events (total number of components); *xj* characterizes the magnitude of the variable *x* in events *j* over all *n*; and *w* is the spatial weight between components *i* and *j*. The inference for the significance of *Gi** is based on a standardized distribution[12].

Where x is the mean, and S, the variance:

$$\overline{X} = \frac{\sum_{j=1}^{n} x_j}{n}$$

$$S = \sqrt{\frac{\sum_{j=1}^{n} x_j^2}{n} - \left(\overline{X}\right)^2}$$

The interpretation of this statistic is based on the Z sign (z-score) and significance level values (α). A positive Z value with statistical evidence indicates a spatial cluster of higher occurrence of the event (hot spot), while a negative Z value and statistical evidence indicate a cluster of lower occurrence of the event (cold spot). Confidence levels 90%, 95% e 99% were adopted[12]. To apply the Getis-Ord Gi* spatial statistics, a neighborhood matrix based on a fixed distance with a radius of 120 km between the centroids of the municipalities was used, in order to capture the most relevant regional interactions between the territories of Mato Grosso. The use of the fixed distance matrix allows capturing clustering patterns considering the spatial dispersion of cases even in less densely populated areas. For all spatial analyses and map preparation, the matrix was constructed in the environment using ArcGIS® software version 10.6, with standardization by weighting the number of neighbors, ensuring comparability between areas with different neighborhood densities[13].

This study was approved by the Research Ethics Committee of the Federal University of Mato Grosso – UFMT (CAAE: 32128820.3.0000.5587 and Opinion No. 4,062,429), in accordance with the Guidelines and Regulatory Standards for Research involving Human Beings[14,15].

Results

From 2012 to 2021, there were 1,407 confirmed cases of TB-HIV coinfection in the state of Mato Grosso. From the coinfection assessments, it can be observed that the male sex (n = 1,018; 72.35%), aged between 20 and 39 years (n = 711; 50.53%), of mixed race/brown skin color (n = 887; 63.04%) and with incomplete elementary education (n = 507; 36.03%) was the epidemiological profile that predominated (*table 1*).

Table 1. Sociodemographic profile. Mato Grosso, Brazil (2012 to 2021)

Variables	**n**	**%**
Sex		
Masculine	1.018	72.35
Feminine	388	27.58
Ignored	1	0.07
Race/color		
Brown	887	63.04
White	256	18.19
Black	205	14.57
Indigenous	10	0.71
Yellow	7	0.50
Blank/ignored	42	2.99
Age		
0 to 19 years old	42	2.99
20 to 39 years old	711	50.53
40 to 59 years old	571	40.58
60+	83	5.90
Education		
Blank/ignored	348	24.73
Incomplete elementary education	507	36.03
No education	46	3.28
Complete higher education	48	3.41
Incomplete higher education	31	2.20
Complete elementary education	109	7.75
Complete high school	190	13.50
Incomplete high school	106	7.53
Not applicable	22	1.57

Source: Prepared by the authors themselves based on data from Sinan (2012-2021).

Regarding the clinical presentation, the pulmonary form accounted for the highest number of cases (n = 1,086; 77.19%), with the majority being new cases (n = 1,046; 74.34%). Regarding diagnostic tests, sputum smear microscopy (n = 968; 68.80%), sputum culture (n = 1,191; 84.65%), and histopathology (n = 1,170; 83.16%) were mostly not performed. Regarding the tuberculin skin test, most cases were blank (n = 1,094; 77.75%). Regarding the outcome of the cases, 37.95% evolved to cure (*table 2*).

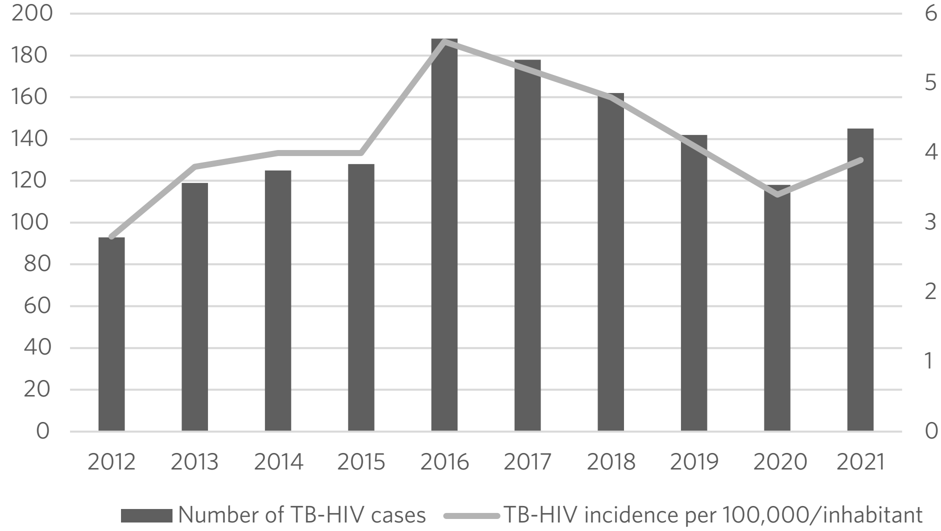
Table 2. Clinical characteristics. Mato Grosso, Brazil (2012 to 2021)

Variables	n	%
Clinical form		
Pulmonary	1,086	77.19
Extrapulmonary	247	17.55
Pulmonary + extrapulmonary	74	5.26
Sputum smear microscopy		
No	968	68.80
Yes	439	31.20
Sputum culture		
Unrealized	1,191	84.65
Negative	100	7.11
Positive	91	6.47
In progress	25	1.78
Histopathological		
Unrealized	1,170	83.16
Positive Baar	95	6.75
In progress	56	3.98
Suggestive of TB	49	3.48
Blank	28	1.99
Non-suggestive TB	9	0.64
Tuberculin skin test		
Blank	1,094	77.75
Unrealized	223	15.85
Strong reactor	46	3.27
Non-reactor	36	2.56
Weak reactor	8	0.57
Input type		
New case	1,046	74.34
Transfer	157	11.16
Re-entry after abandonment	108	7.68
Relapse	78	5.54
Don't know	11	0.78
Death	7	0.50
Case evolution		
Cure	534	37.95
Transfer	251	17.84
Death from other causes	220	15.64
Abandonment	207	14.71
Death from TB	53	3.77
Change of diagnosis	53	3.77
Primary abandonment	40	2.84
Blank	40	2.84
Multidrug-resistant TB	5	0.36
Scheme change	3	0.21
Bankruptcy	1	0.07

Source: Prepared by the authors themselves based on data from Sinan (2012-2021).

The state incidence of TB-HIV in the period 2012-2021 showed an average of 5.6 cases/100,000 inhabitants, with marked temporal variation. A three-year epidemic period (2016-2018) was observed with annual peaks of, respectively, 7.1, 6.9 and 6.5 cases/100,000, values higher than the average for the period investigated (*graph 1*).

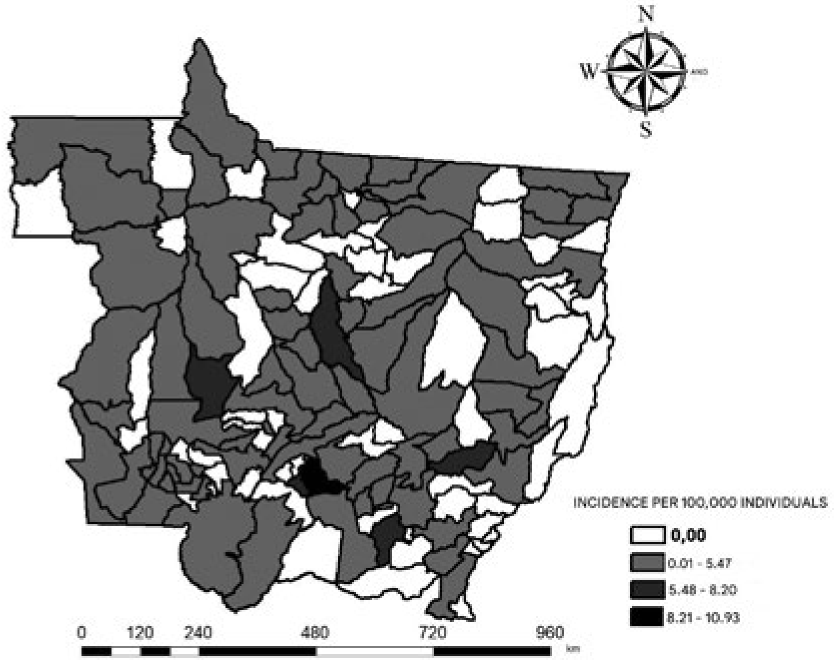
Graph 1. Number of reported cases of TB-HIV coinfection and incidence rate per 100,000 inhabitants over a decade in the state of Mato Grosso, Brazil (2012 to 2021)



Source: Prepared by the authors.

The geographic distribution revealed clusters of high incidence in the Cuiabá-Várzea Grande axis (10.93 and 8.20 cases/100,000 respectively), with a decreasing gradient towards the interior (*figure 1*). Rondonópolis (7.15 cases/100,000) and Sorriso (6.88 cases/100,000) emerged as secondary hot spots, configuring a pattern of radial dispersion from the capital.

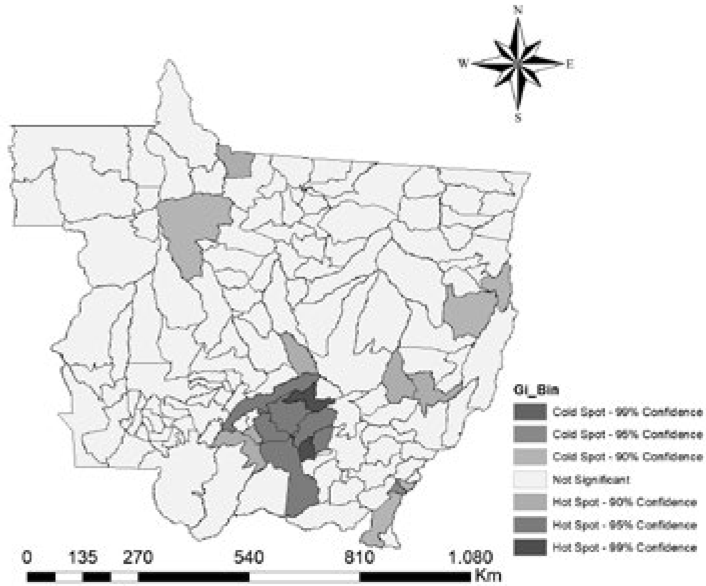
Figure 1. Spatial distribution of TB-HIV coinfection incidence rates in Mato Grosso state, Brazil (2012-2021)



Source: Prepared by the authors.

The spatial analysis (Getis-Ord Gi*) identified statistically significant hot spots (z-score > 2.58; $p < 0.01$), including the municipalities of Cuiabá, Nova Brasilândia, Jaciara, Rosario do Oeste, Chapada dos Guimaraes, Campo Verde, Santo Antônio do Leverger and Dom Aquino, with confidence level between 90% and 99% (*figure 2*). Additionally, cold spots (z-score < -1.96; $p < 0.05$) were detected in regions of low population density, such as Araguainha, Juara, Novo Santo Antônio, Ribeirão Cascalheira and Alto Araguaia, with confidence levels between 90% and 99% (*figure 2*).

Figure 2. Getis Ordis* analysis of areas with spatial association for TB-HIV coinfection in Mato Grosso state, Brazil (2012 a 2021)



Source: Prepared by the authors.

Discussion

This study aimed to investigate the spatial pattern and critical areas for TB-HIV coinfection. The results showed that there are emerging areas in the state that require priority intervention regarding strategic actions to combat TB, especially among PLWHA.

The state of Mato Grosso is among those with the highest percentage of Antiretroviral Therapy (ART) implementation, which consequently has an impact on the total number of TB-HIV coinfection cases in the state. Over the years studied, there were declines in reported cases in some years. This may be related to changes in TB control strategies in Primary Health Care (PHC), which reduced consultation times and facilitated treatment, making diagnosis and therapy more accessible to these most affected populations, resulting in increased population coverage[16,17].

Therefore, PHC activities, such as the provision of rapid HIV tests, scheduling appointments with specialists by the medical team, and responding to spontaneous demands, play a crucial role in improving the detection of TB-HIV coinfection. These actions are intrinsically linked to increasing the sensitivity of the surveillance system, enabling the active identification of TB cases in the general population. Furthermore, they allow the provision of culture tests for *Mycobaterium*. Therefore, this scenario illustrates how detection combined with notification can drive strategies aimed at expanding health coverage for the population[18].

According to sociodemographic results, the most impacted population was male. This is due, according to recent studies, to a combination of factors. Among them are behavioral factors, such as a higher level of exposure to the pathogen, factors related to the immune response, and genetic predisposition, since the construction of masculinity in society discourages self-care, thus hindering treatment adherence[19,20].

Regarding race/color, the most prevalent for coinfection was brown, which is also observed in other studies carried out in Brazil, which show a higher prevalence of coinfection in this group[21]. This is possibly due to the major characteristics that make up the Brazilian population[22].

The most prevalent age group is young adults aged 20 to 39. This may be due to their economically active status, as people in this age group are at the peak of their work capacity and productivity. However, this concentration may also be related to greater exposure to risk factors, both in terms of health and socioeconomic factors[23,24].

Regarding education, most data were blank or missing, followed by incomplete primary education. Education level has a direct impact on self-care, as it can make a person more susceptible to risky behaviors and, at the same time, reduce their ability to fully understand their health condition. Furthermore, it consequently reduces the number of people seeking health services, thus hindering early diagnosis and successful TB-HIV treatment[25,26].

It is important to emphasize that social vulnerability is one of the factors contributing to low educational attainment, which in turn increases the risk of both TB and HIV infection. Policies aimed at improving education level tend to have a significant impact on the population's health, thus reducing the risk of complications from these diseases[27].

Regarding the clinical characteristics presented in this study, the most prevalent form is pulmonary, which can be explained by the pathogen's natural affinity for the lung parenchyma. Therefore, respiratory problems are among the most frequent complications in PLWHA, as the virus weakens the immune system and makes the body more susceptible to opportunistic infections, which are the main causes of hospitalizations in this population segment. Therefore, the importance of coinfection control and appropriate treatment is highlighted[28]. Furthermore, some studies indicate that the extrapulmonary form of TB is more common in cases of coinfection, highlighting the fragility of the immune system and the ease with which the TB bacillus spreads throughout the body through the bloodstream[29].

Despite the availability in the market of more accurate tests for diagnosing TB, smear microscopy is still considered a valuable resource due to its simplicity and relatively low cost. However, in this study, we observed that there were a significant number of cases in which the test was not performed, which is consistent with other studies conducted in other regions[30,31].

It was noted that, across all the years analyzed, the most common clinical outcome was patients' cure. This suggests that treatment and monitoring of affected individuals are being carried out, even in the face of challenges in the context of health services[32].

Studies show that the cure rate for TB with HIV coinfection occurs in at most 50% of cases, as it is related to the immunodeficiency caused by the virus in these patients, due to the time of diagnosis and initiation of treatment. Although treatments are provided free of charge by the Unified Health System (SUS), difficulties with dispensing medications and following treatment are still evident, as the long duration and side effects contribute to non-adherence[33].

Recognizing the scenarios that require more urgent intervention may be key to accelerating actions aimed at reducing TB-HIV cases. Understanding the spatial pattern and geographic areas most vulnerable to this coinfection can therefore contribute to strategic planning by health managers and professionals. Thus, the use of spatial analysis techniques enables a dialogue between geographic and epidemiological statistics and dynamic aspects of the population, such as migration processes, population flow, and socioeconomic conditions, since the analyses consider the population of each specific region[34].

In this investigation, the use of these tools allowed us to segment municipalities into high-risk areas (hot spots) based on the visualization of spatial clusters and the demarcation of areas for TB-HIV coinfection, encompassing the 141 municipalities of Mato Grosso. The capital, Cuiabá, was highlighted as a priority area at high risk for the development of coinfection, possibly due to its larger population. This may also be related to the migratory flow due to the need for improved quality of life, job searches, and treatment, which ultimately lead individuals to urban centers for better living conditions[35,36].

It is known that the social determinants of health have a great influence on the health-disease process[37]. Analyzing data from IBGE Cities on municipalities located in high-risk areas, it was observed that most of them have low rankings in education, economy, and labor compared to other municipalities in the state, such as Nova Brasilândia, which ranks 110th out of 141 in education and 106th out of 141 in economy. Next, Jaciara ranks 81st out of 141 in economy, Chapada dos Guimarães 105th in education, and Dom Aquino 71st in labor/employment. These rankings may explain why these municipalities are considered priority areas[38].

Thus, the analysis of the municipalities identified as hotspots in this study, such as Cuiabá, Nova Brasilândia, Jaciara, Chapada dos Guimarães, and Dom Aquino, reveals a confluence of social determinants that deepen vulnerability to TB-HIV coinfection. For example, Nova Brasilândia and Chapada dos Guimarães face high rates of informal employment and significant dependence on income transfer programs, reflecting the precarious local economic conditions[11].

Another relevant aspect is the precarious housing conditions present in several identified critical areas, where there is overcrowding, lack of basic sanitation, and limited access to drinking water. These conditions favor TB transmission, especially in immunosuppressed groups, such as PLWHA. In municipalities such as Santo Antônio do Leverger and Rosário Oeste, IBGE data indicate that more than 30% of households in urban areas lack adequate sanitation, which compromises the environmental determinants of health and worsens the epidemiological situation[10]. The association between poverty, poor housing conditions and a higher incidence of TB has been well documented in the literature, reinforcing the need for intersectional policies that integrate health, housing and social development[37].

Furthermore, internal migration dynamics, driven by the search for work in regional economic hubs, such as Cuiabá, Rondonópolis, and Sorriso, generate unstable population flows and increase the risk of spreading TB and HIV. This mobility hinders continuity of care and contact tracing, especially among seasonal workers, such as those in farms and meatpacking plants. Recent studies indicate that workers in labor-intensive production sectors, such as agribusiness and the meatpacking industry, have a higher prevalence of respiratory infections and face barriers to adherence to TB-HIV treatment, whether due to long working hours or a lack of support from occupational health services[39,40].

In addition, the concentration of rural settlements and indigenous communities in some of these locations increases barriers to access health services, especially diagnostic and treatment services for TB and HIV. This territorial and economic marginalization increases the risk of exposure and delays in starting ART, as demonstrated in studies that associate low levels of human development with higher TB mortality rate. These findings reinforce the importance of integrating health surveillance with specific strategies targeting vulnerable working populations[9].

A key risk factor for TB infection that should be mentioned is the contact with people with active disease. Individuals who live or work in environments with high disease burdens are at greater risk of exposure to the bacillus. Therefore, knowing areas with a high incidence of TB can contribute to the active search for cases and breaking the chain of transmission, especially in the case of higher-risk populations, such as PLWHA, which becomes even more essential[40].

In this context, it is crucial to emphasize the importance of promoting closer collaboration between services dealing with TB-HIV and providing continuous education to health professionals at all levels of the health system, especially in Health Care Services specialized in HIV/AIDS. This involves the regular implementation of preventive, diagnostic, and treatment measures for TB and HIV/AIDS. It is essential that professionals promote access to diagnostic testing for both conditions and ensure that diagnosed individuals are appropriately referred to treatment, with a focus on ART[41,42].

It is essential to emphasize that treatment of latent *Mycobacterium tuberculosis* infection (LTBI) represents one of the main strategies for controlling TB and achieving agreed-upon goals. This treatment is particularly recommended for PLWHA, as it not only reduces the incidence of active TB but also significantly contributes to reducing mortality in this specific group[43].

In this sense, it is important to consider the inequities linked to the local health context, lack of resources and access to health care, education, income and sanitation, which ultimately influence situations of vulnerability, favoring the exposure and illness from TB-HIV[40].

The evidence demonstrated in this study regarding spatial patterns can be valuable for the implementation of new TB-HIV control strategies, so that the goals already established by the WHO can be achieved. Furthermore, strengthening and investing in PHC in these municipalities is of paramount importance for public health.

Conclusions

The findings obtained in relation to sociodemographic profiles and clinical aspects together with spatial technologies, can collaborate as an alert for identifying populations that are more vulnerable and risk areas, in addition to subsidizing the implementation of public policies aimed at strategies for controlling TB cases, especially among those diagnosed with HIV in the state of Mato Grosso.

Collaborators

Alves JD (0000-0001-9771-9123)* contributed to the conception and design of the research, data acquisition, analysis and interpretation of data, statistical analysis, writing and critical review of the manuscript for important intellectual content. Kunrath D (0000-0002-5570-4668)* contributed to the conception and design of the research, data acquisition, analysis and interpretation of data, statistical analysis and writing of the manuscript. Barros NS (0009-0008-1691-1577)* contributed to data acquisition, analysis and interpretation of data, writing and critical review of the manuscript for intellectual content. Rodrigues GVS (0000-0001-5779-9296)* contributed to data acquisition, statistical analysis and writing of the manuscript. Oliveira Júnior JS (0000-0002-5771-5854)* contributed to data acquisition, statistical analysis and writing of the manuscript. Scholze AR (0000-0003-4045-3584)* contributed to data acquisition, analysis and interpretation, and critical review of the manuscript for important intellectual content. Abade AS (0000-0001-9771-9123)* contributed to the definition of the methodology and the review of results. ■

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