ORIGINAL ARTICLE

SPATIAL RISK AREAS FOR DRUG-RESISTANT TUBERCULOSIS (DR-TB) IN PARANÁ / BRAZIL: ITS RELATIONSHIP WITH THE BORDER REGION

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Highlights: (1) Risk areas for DR-TB were identified in the state of Paraná, involving cities in the North, East, and West macroregions of the state. (2) There was a decline in DR-TB cases starting in 2020, which may be related to decreased diagnostic investigation due to the COVID-19 pandemic. (3) The occurrence of DR-TB showed no direct relationship with the border region, suggesting that health care related to the diagnosis and treatment of DR-TB presents a certain uniformity throughout the state.

PRE-PROOF
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ABSTRACT:

Objective: to analyze the spatial distribution and behavior of drug-resistant tuberculosis in the state of Paraná, from the perspective of incidence, temporal trends, and its relationship with Brazil's border region with other countries. **Method:** ecological study with spatial and temporal analysis. Data were collected from the Special Tuberculosis Treatment Information System and the Department of Informatics of the Unified Health System. New cases of drug-resistant tuberculosis reported in Paraná between 2013 and 2020 were included. The incidence rate was calculated, followed by the Spatial and Space-Time Scan Statistics technique, and temporal regression analysis using the Joinpoint technique. **Results:** 515 cases of drug-resistant tuberculosis were reported during the study period, with an incidence of 15.76 cases/100,000 inhabitants, identifying risk areas in the North, East, and West regions of the state. Space-time analysis identified, in the East region, a cluster with the highest relative risk (RR = 9.89) for the period from 2013 to 2016. In the temporal trend, it was found that drug-resistant tuberculosis cases decreased from 2020 onwards. **Conclusion:** it is interesting to note that, in this study, drug-resistant tuberculosis did not demonstrate a direct relationship with this region. However, spatial analysis of incidence and the identification of clusters with high rates and risks provided an overview of cases in the state. Given this scenario, it is essential to invest in prevention, diagnosis, and treatment strategies to reduce the burden of resistant bacilli and achieve the proposed goals for tuberculosis eradication.

Keywords: Pulmonary Tuberculosis. Drug Resistance. Epidemiology. Spatial Analysis. Border Health.

SPATIAL RISK AREAS FOR DRUG-RESISTANT TUBERCULOSIS (DR-TB) IN PARANÁ / BRAZIL: ITS RELATIONSHIP WITH THE BORDER REGION

INTRODUCTION

Tuberculosis (TB) is a priority issue on the global agenda and is among the leading causes of death. Its infectious agent is Mycobacterium tuberculosis, which primarily affects the lungs. In 2022, 10 million people fell ill with TB worldwide, of whom 1.3 million died from the disease[1]. Angola, Bangladesh, and Brazil are among the 30 countries with the highest TB burden in the world[1]. In Brazil, in 2022, 78,057 thousand new TB cases were diagnosed[2], corresponding to an incidence rate of 36.3 cases/100,000 inhabitants and 5,072 deaths, equivalent to a mortality rate of 2.38 deaths/100,000 inhabitants[2].

The COVID-19 pandemic had a negative impact on access to TB diagnosis and treatment. Data indicate that, on a global scale, approximately 10.1 million individuals developed the disease, but only 5.8 million were diagnosed and reported. This scenario may result in increased community transmission, with an anticipated rise in the number of cases in the coming years, as well as an increase in mortality rates[4].

In 2022, in the state of Paraná, 2,302 TB cases were reported, representing an incidence rate of 19.7 cases per 100,000 inhabitants. Additionally, 126 deaths related to the disease occurred, resulting in a mortality rate of 1.3 deaths per 100,000 inhabitants[2].

In addition to the number of cases and deaths, there is another aggravating factor: Drug-Resistant Tuberculosis (DR-TB), which occurs when M. tuberculosis exhibits resistance to one or more antimicrobial drugs, making treatment limited and expensive. Drug resistance in TB has become a major public health problem, threatening progress in the fight against the disease worldwide[3]. In 2022, an estimated total of 410 thousand cases were reported globally[1], with 1,104 cases notified in Brazil[2].

There are various causes for the development of DR-TB, among which the interruption and/or irregular use of medications stand out; there is also the situation in which patients acquire the disease through an already resistant strain and the natural emergence of resistance during the bacillus multiplication process[3]. Moreover, some population groups have a higher chance of developing DR-TB, including the Incarcerated Population, Homeless Population, and People with Alcohol and Other Drug Use Disorders[4,5].

Research indicates that factors such as being male, being under 40 years old, and having low educational level are associated with a higher risk of treatment abandonment.

Conversely, higher levels of education increase the likelihood of treatment adherence, due to better understanding and greater access to information about the disease[6,7].

Thus, when a patient develops DR-TB, treatment is conducted with more toxic medications that are up to 100 times more expensive, in addition to having a longer period, approximately two years, until the end of treatment. This is a complicating factor for treatment success, as it can strengthen resistance if the patient does not use the medications continuously and correctly[8].

In general, TB transmission and illness are related to demographic, social, and economic factors, resulting from increasing and disorganized urbanization, inequality in income distribution, precarious housing, overcrowding, food insecurity, low educational level, and difficulty accessing health services[3]. Such factors can be identified as social determinants of health in relation to TB and DR-TB, especially in border regions, which present complexities and peculiarities different from other regions within the same national territory[9].

Studies indicate a growing volume of floating population in these regions due to tourism, commerce, and education. Human mobility is a very strong characteristic in these locations, where ethnic, cultural, and religious diversity is also observed, resulting from the presence of immigrants[10–12]. Migration does not represent a health threat; however, it contributes to the vulnerability of individuals in these regions, considering the different characteristics of populations and the health systems in place in their countries of origin[13].

DR-TB presents itself as a priority problem in some countries. Although this is not yet the case in Brazil, this problem has impacts on incidence, treatment, and mortality. In the Brazilian context, such impacts may be aggravated by socioeconomic factors, difficulties in accessing healthcare, and increased population mobility in border areas, such as in the state of Paraná, where immigration dynamics and floating population create additional challenges for TB control.

This study is justified by the need to understand the spatial distribution of DR-TB in Paraná, especially in border regions, in order to guide more effective public health policies for disease control. Given the above, the objective of this study was to analyze the spatial distribution and behavior of drug-resistant tuberculosis in the state of Paraná, from the perspective of incidence, temporal trends, and its relationship with Brazil's border region with other countries.

METHOD

Study design

Ecological study using spatial and temporal analysis techniques.

Study setting

The study setting comprises the state of Paraná, located in the Southern Region of Brazil, which in 2020 had an estimated population of 11.52 million inhabitants, distributed across 399 municipalities, with a territorial extension of 199,298.982 km^2[14]. The state is divided into four Health Macroregions: East, West, North, and Northwest; which, in turn, are subdivided into 22 Health Regions[15].

A characteristic feature of the state of Paraná is its western border with Paraguay and southwestern border with Argentina. At this meeting point of countries, the western point is constituted, forming the triple border region. According to IBGE[14], 139 municipalities are located in the border strip and on the border line of the state of Paraná, constituting approximately 35% of the total municipalities in Paraná (n = 399 municipalities). It is worth noting that Brazil considers the Border Strip as an internal area 150 km wide, parallel to the terrestrial dividing line of the national territory[16].

Study period and population

All cases notified as DR-TB in the Special Tuberculosis Treatment Information System (SITE-TB) were considered as the population of this study. The study period was from 2013 to 2020, with 2013 being the year in which the state began reporting DR-TB cases in this system.

Data referring to 2021 and 2022 were collected via the Department of Informatics of the Unified Health System (DATASUS), a public domain platform of the Ministry of Health. However, as these data are preliminary, they were used only to update information and to perform temporal regression in the identified clusters.

Data source and study variables

Data referring to SITE-TB were provided by the State Health Department of Paraná (SESA-PR) in the first half of 2021.

For this study, variables referring to the municipality of residence and its relationship with the border strip were considered. We chose to collect data from SITE-TB, as this is an important tool for surveillance of cases with resistance to medications used in TB treatment in Brazil.

SITE-TB is an online system that allows notification, monitoring, and closure of cases of individuals with DR-TB, being considered a complementary system to the Notifiable Diseases Information System (SINAN)[17]. All confirmed TB cases must be notified first in SINAN and, when diagnosed as DR-TB, must be closed as such and then notified in SITE-TB for more detailed monitoring.

As inclusion criteria, all cases notified in SITE-TB as DR-TB from 2013 to 2020 were considered. As exclusion criteria, cases in which the place of residence was absent in the SITE-TB notification and duplicate records were removed. For the years 2021 and 2022, the inclusion criterion was being in SINAN/DATASUS as DR-TB in municipalities of Paraná.

Data analysis

Initially, the incidence rate was calculated for each municipality in Paraná for the period from 2013 to 2020, according to the following formula:

$$\text{Incidence rate} = [(NC / PP) \times 100{,}000]/T$$

*where NC is the number of new cases in the period; PP is the population of the period, considering the 2010 census count, official data without estimation; and T is the analyzed period.

Incidence rates were calculated using Microsoft Excel® software. For descriptive statistics, median, standard deviation, maximum and minimum values, proportion of zero, and normality were calculated, with the latter parameter analyzed by the Kolmogorov-Smirnov test.

To compare DR-TB incidence rates, two groups were analyzed: municipalities in the border strip and municipalities outside this strip. The border group consisted of 139 municipalities in Paraná, while the others formed the non-border group. The comparison was performed using the Mann-Whitney U test, due to the indication of non-normality of incidence rates by the Kolmogorov-Smirnov test. Descriptive analysis and normality and U tests were performed using Jamovi software (version 2.3.21).

The merging of cases and disease rates with the shapefile of the state of Paraná made it possible to identify the distribution of cases in municipalities. Based on shapefile information and the 2010 Census, three spreadsheets (centroid, population, and cases) were constructed using Microsoft Excel® software, which were used to search for clusters and calculate relative risk, using SaTScan™ software version 9.3.

The Spatial and Space-Time Scan Statistics technique was applied, which searched only for high-risk clusters, with calculation of spatial Relative Risk (RR) and their respective 95% confidence intervals (95% CI).

The scan analysis began with the purely spatial technique, using default parameters for the scan, which consider up to 50% of the exposed population. Subsequently, the GINI command was applied to determine the ideal probe size, considering the event and the population evaluated. The GINI command indicated a value of 10%, which was adopted in all tests as the probe size applied for analysis.

This detail prevents cluster overlap and improves their observation. Also as a technique parameter, circular-shaped clusters and 999 replications in Monte Carlo simulation were applied[18].

After identifying risk clusters, we performed an update in these municipalities with partial data from 2021 and 2022, with the purpose of conducting a temporal regression analysis. The analytical method used was Joinpoint, which allows identifying not only a single line as a regression model, but also recognizing the points at which significant changes occur that alter the pace of growth or decrease.

The benefit of this technique is to detect points that indicate abrupt changes in the evaluated time series and suggest more than one model, if necessary and possible, according to statistical parameters[19].

The *Joinpoint Regression Program* is a Windows-based statistical software package that analyzes *Joinpoint* models. The software allows the user to test whether an apparent change in trend is statistically significant or not[20].

It is not always reasonable to expect that a single APC (*Annual Percent Change*) can accurately characterize the trend throughout an entire data series. The *Joinpoint* model uses statistical criteria to determine when and how often the APC changes. For rare events, it is appropriate to use joined log-linear segments, so that each segment can be characterized using an APC[20].

Joinpoint fits the selected trend data to the simplest model that the data allow. The resulting graph shows several different lines connected at "joinpoints"[21].

The model that offers the best fit is determined by the lowest BIC (Schwarz Bayesian Criterion or Bayesian Information Criterion), which assumes the existence of a "true model" that describes the relationship between the dependent variable and independent variable among the various models under selection. The criterion for BIC is defined as the statistic that maximizes the probability of identifying the true model among those evaluated[21].

For temporal regression analysis, the free software Joinpoint Regression Program, version 5.0.1, provided by the Statistical Research and Applications Branch, National Cancer Institute, USA, was used[19].

For all tests performed in the study, the significance level α was set at 5%, that is, < 0.05.

Ethical aspects

This work meets the recommendations of Resolution 466/12 of the National Health Council, with approval from the Research Ethics Committee of the State University of Western Paraná (UNIOESTE), according to detailed opinion No. 4,737,272, approved in May 2021. Furthermore, this research was conducted following the ethical precepts established in the Declaration of Helsinki.

RESULTS AND DISCUSSION

In the first evaluated period (2013 to 2020), 515 DR-TB cases were recorded, with 78 (19.55%) municipalities presenting DR-TB cases, while 321 (80.45%) municipalities did not register drug resistance cases during the study period, indicating that the scenario presents zero inflation, which hinders linear analyses based on municipal rates.

Descriptive statistics revealed that the highest incidence rate for DR-TB was 15.79 cases/100,000 inhabitants, with a mean of 0.29 cases/100,000 inhabitants, median equal to zero, and standard deviation of 1.07 cases/100,000 inhabitants. The same parameters were evaluated for the sets of municipalities belonging to the border strip (n = 139), compared to municipalities outside the border strip (n = 260), according to Table 1.

The Kolmogorov-Smirnov test indicated that municipal DR-TB rates do not present normal distribution (KS = 0.385; $p < 0.001$). Subsequently, the Mann-Whitney U test was performed to compare the means of the two groups, and it was found that there was no statistical difference in the mean DR-TB (Municipalities in the border strip x Municipalities outside the border strip; U = 16685, p = 0.068).

Table 1 - Comparison between municipalities in the border strip and outside the border strip in the state of Paraná, regarding the DR-TB rate, from 2013 to 2020 (n = 399)

Parameters	Overall DR-TB Rate	Border strip mun. rate*	Rate mun. outside border strip
N	399	139	260
Mean	0.29	0.20	0.34
Standard deviation	1.07	0.64	1.24
Median	0	0	0
Minimum	0	0	0
Maximum	15.79	4.19	15.79

Legend: Units per hundred thousand inhabitants. *Border line municipalities were considered as border strip. ł Mun.=Municipalities.
Source: Prepared by the authors.

With scan statistics, it was possible to identify purely spatial and space-time risk clusters. These clusters indicate regions where evidence of increased spatial Relative Risk (RR) of DR-TB was confirmed, compared to other municipalities in the state.

With purely spatial scanning, it was possible to identify eight risk clusters, three in the North region, two in the East region, and three in the West region of the state of Paraná (Figure 1). Some municipalities draw attention, as they are characterized as a risk area and are close to another cluster, which occurs with Londrina (cluster 4) and Jataizinho (cluster 5), representing the risk areas for DR-TB throughout the state of Paraná, with RR variation between 2.45 and 26.26.

This means that the population of cluster 8 is 2.45 times more likely to have DR-TB than residents of the rest of the state.

According to Figure 1, risk clusters were recorded in all macroregions of Paraná, BR. Noteworthy is cluster 8 (RR = 2.45; 95% CI = 1.81 – 3.30) in the West macroregion, as it involves the largest number of municipalities (11 municipalities). However, the North macroregion presented 3 agglomerated risk clusters (clusters 2, 4, and 5), also being the region where the highest RR was recorded (Jataizinho - cluster 5; RR = 26.26; 95% CI = 15.77 – 44.04).

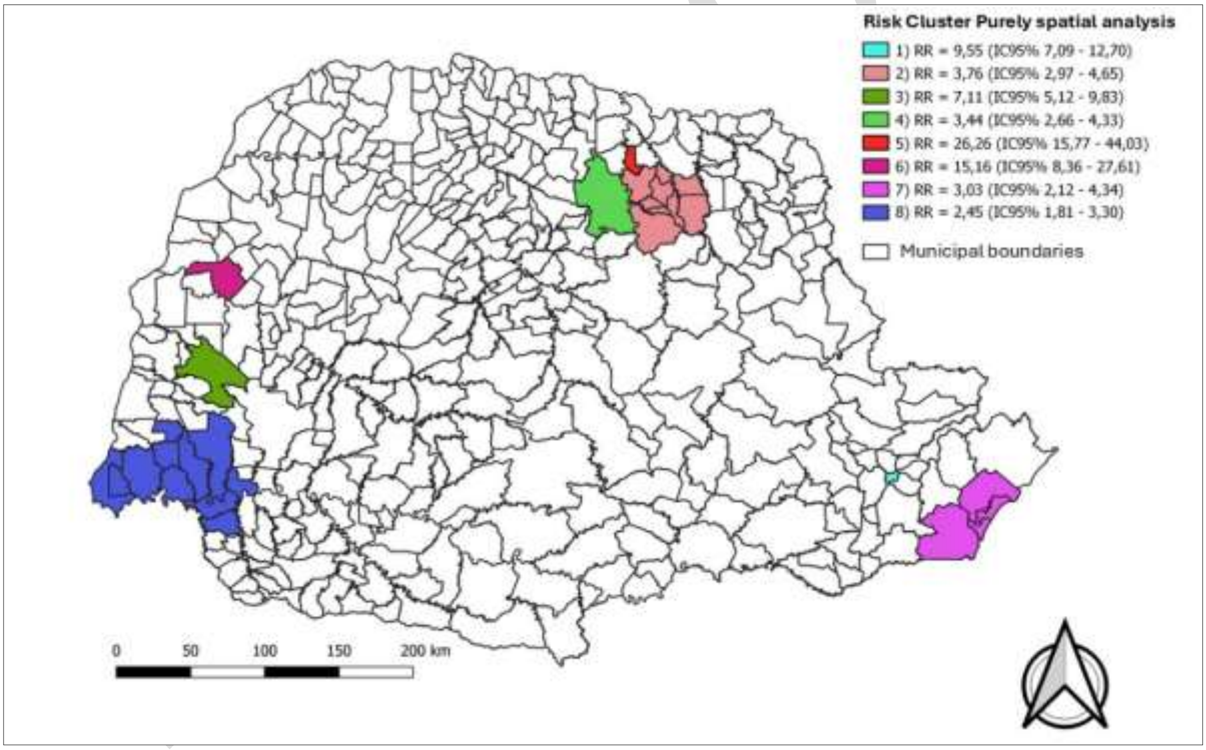

Figure 1 -Spatial Risk Analysis for New Cases of DR-TB in Paraná, Brazil, 2013 to 2020.

Source: Prepared by the authors.

Figure 2 shows the details of the space-time scan analysis, which seeks to identify the variation of spatial risk over time. It was possible to identify four space-time risk areas, with one area (cluster 3) having increased RR (RR = 9.89) in the period from 2013 to 2016. Meanwhile, clusters 1 (RR = 5.43), 2 (RR = 3.99), and 4 (RR = 5.60) identified began with RR in 2017 and remained until the end of the studied period. Noteworthy is cluster 2, which encompasses municipalities from two macroregions of the state of Paraná (West and Northwest).

Still according to Figure 2, four clusters are verified, with clusters 1 and 2 composed of 11 and 34 municipalities, respectively, and clusters 3 and 4 with only 1 municipality each. Cluster 1 involves the cities of Londrina, Jataizinho, and other surrounding cities that are part of the North Macroregion.

Cluster 2 is the largest grouping and is concentrated in the West Macroregion, encompassing from Foz do Iguaçu to Guaíra and Iporã, covering municipalities from four Health Regions (9th, 10th, 20th of the West Macroregion; and 12th of the Northwest Macroregion). The other clusters are isolated municipalities, namely Pinhais (cluster 3) and Almirante Tamandaré (cluster 4), both from the East Macroregion and part of the 2nd Health Region.

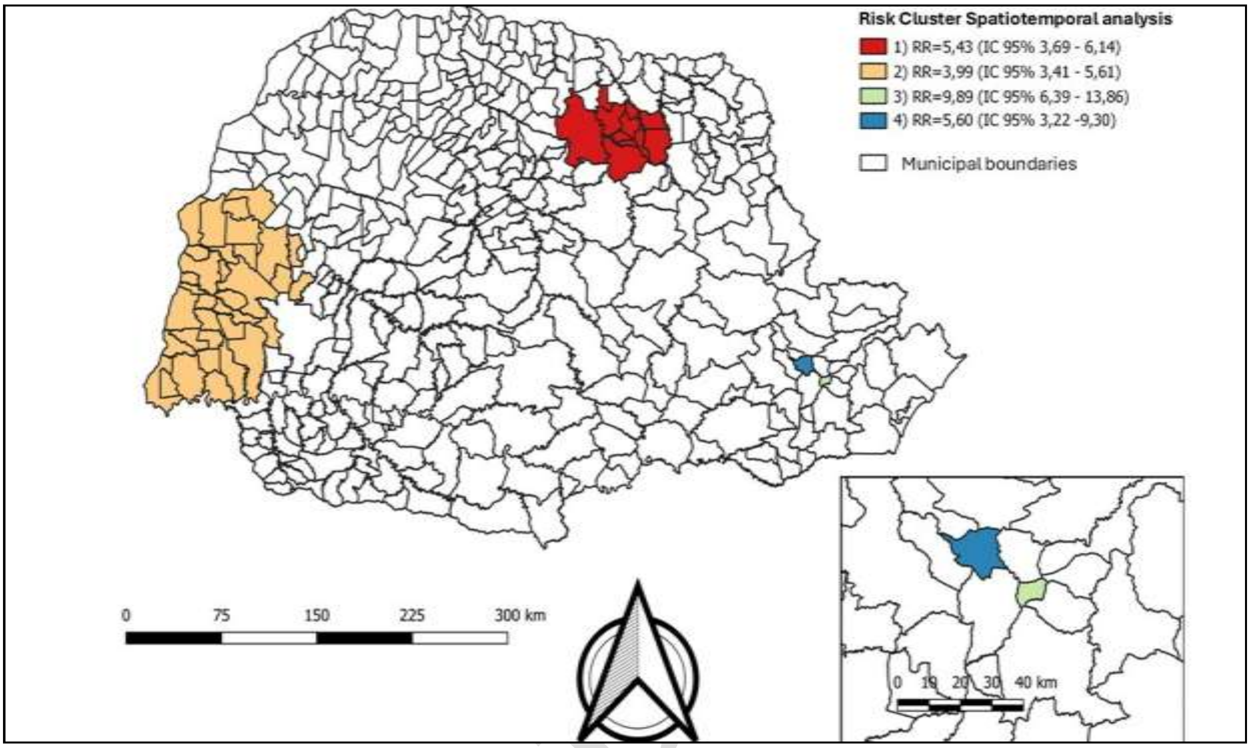

Figure 2 - Relative Risk Clusters from Space-Time Analysis for DR-TB in Paraná, Brazil, 2013 to 2020

Source: Prepared by the authors.

Subsequently, to expand the analysis of the clusters, a temporal regression of DR-TB cases was performed in the municipalities of the clusters identified in the space-time scan. For this analysis, DR-TB cases recorded in 2021 and 2022 were included. The state of Paraná added 145 new DR-TB cases in these two years, with 52 cases belonging to the already identified risk clusters, which means that 35.9% of cases occurred within risk areas.

According to the temporal regression analysis of the state of Paraná, it is possible to verify growth in the number of cases until 2019 (APC = 33.5%; $p = 0.030$) followed by a decline (APC = -10.9%; $p = 0.268$) in cases since the first year of the COVID-19 pandemic (2020), allowing an inflection in the trend curve. In the following period, a continuous decline was observed. According to Figure 3, it is possible to verify that case diagnosis had its trend directly influenced by the COVID-19 pandemic.

It should be noted that non-significant values ($p > 0.05$) for trend analysis are influenced by the small number of years observed and their oscillations. Therefore, to confirm the downward trend, it is necessary to obtain more annual observations, that is, include years in the analysis. These data demonstrate how the COVID-19 pandemic interfered with DR-TB diagnostic services in the studied region and in all temporal clusters identified in the previous technique.

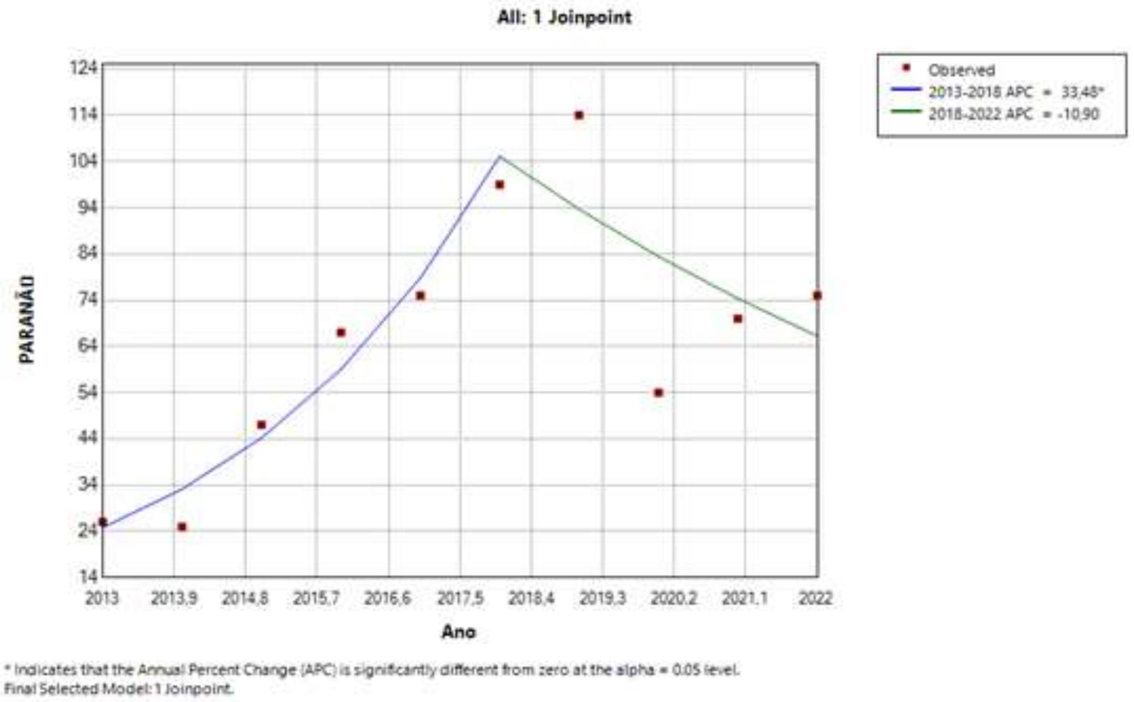

Figure 3 - Trend of DR-TB cases distributed annually in the state of Paraná, Brazil, 2013 to 2022 Source: Prepared by the authors.

However, when observing temporal trends in the identified risk clusters, it is possible to notice distinct behaviors. Based on Figure 1, we performed the temporal analysis presented in Figure 4, in which the cluster numbers correspond between the figures.

Thus, it is observed that, of the four clusters analyzed, only No. 1 shows a growth trend (APC = 17.0%; p = 0.010) throughout the entire period. Cluster No. 2 shows a downward trend from 2020 (APC = -24.9; p = 0.313). While clusters 3 and 4 showed oscillations before the COVID-19 pandemic and a downward trend from 2020.

All models presented met the BIC criterion, although they cannot reach the value of p <0.05 due to the number of years evaluated in each segment and, in some cases, presenting data oscillation, resulting in stationary segments, that is, segments that do not confirm a specific trend. Thus, the graphic form is what best helps to understand the trend, and the parameters of the models found for each cluster demonstrate the "measurement" of the trend.

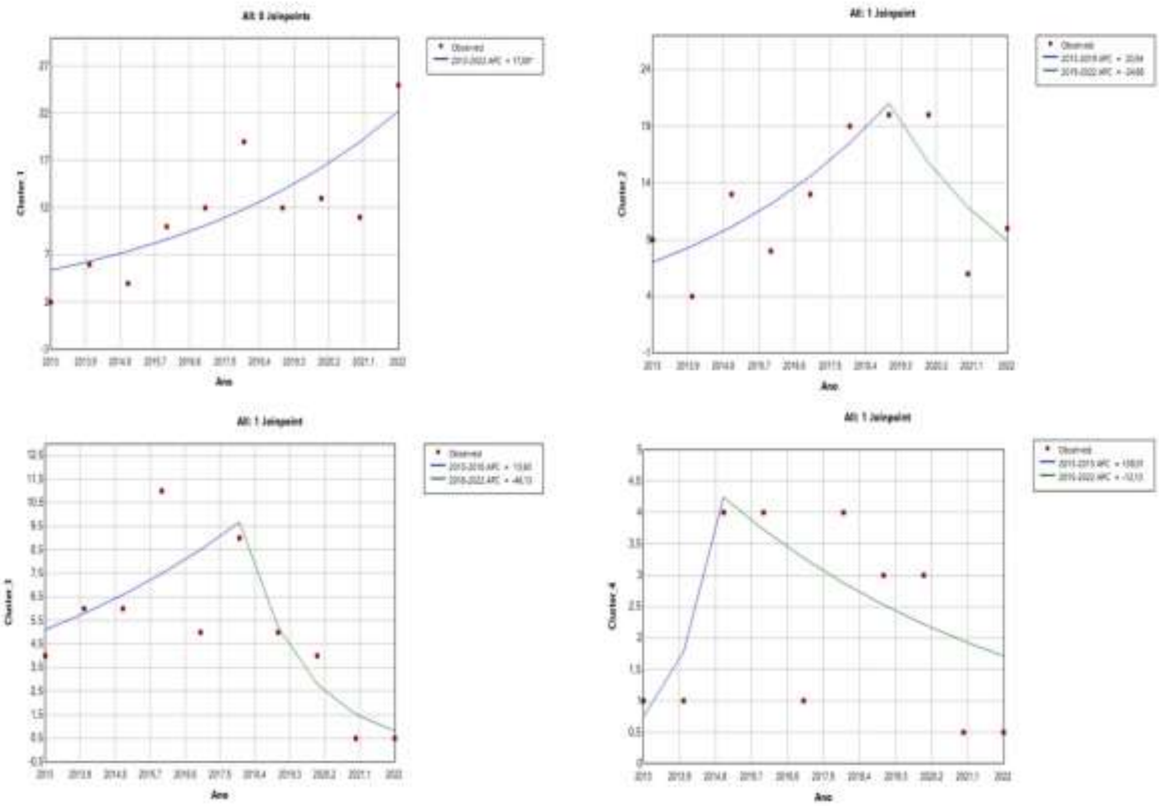

Figure 4 - Trend of DR-TB cases distributed annually in the state of Paraná, Brazil, according to risk cluster, 2013 to 2022

Source: Prepared by the authors.

Based on the objectives of this study and considering the geographical situation of the state of Paraná, it was possible to verify through spatial analysis the formation of high-risk clusters for DR-TB in some specific regions of the state. It is also noteworthy that DR-TB was present in all health regions of the state.

In the present study, the DR-TB incidence rate was lower in border strip municipalities, unlike the study conducted by Marques et al.[22], which showed a higher DR-TB rate in the border region between Brazil, Paraguay, and Bolivia, compared to the rest of the state. This difference may be related to the fact that the state of Paraná, located in the Southern Region of Brazil, has a more comprehensive health system compared to the states in the Central-West Region, where the study by Marques et al.[22] was conducted, which may contribute to reducing inequalities in the indicator evaluated in this study.

The temporal trend analysis deserves special mention, which revealed a decrease in DR-TB diagnoses in the state of Paraná during the COVID-19 pandemic period. However, the study points out that this reduction did not occur equally throughout the state. One of the areas with high RR for DR-TB showed a growth trend even during the COVID-19 pandemic period.

It is worth noting that important actions must be implemented, such as the expansion and strengthening of Primary Health Care (PHC), in addition to investment in the qualification of professionals involved with the program[23].

A study conducted by Santos et al.[24], using spatial and temporal analyses to investigate DR-TB cases in the incarcerated population in the state of Paraná, revealed that the North, West, and East regions of the state presented themselves as risk areas for the condition in the studied population. These results are similar to those found in the present study, where the same regions of the state presented high-risk clusters for DR-TB, indicating that these areas need greater attention from managers.

Another integrative review study conducted by Germano, Esteves, and Garrido[25] on guidance and monitoring of people with DR-TB reported that, among the guidance provided by PHC, there is information about diagnosis, treatment adherence, emotional support, TB transmission prevention, side effects, among others. Furthermore, the monitoring and treatment of these people are carried out in PHC, including contact tracing, medication provision, promotion of the importance of health care, among others.

It is observed that, despite the various actions carried out by PHC to guide and monitor people with TB, some regions still persist as high-risk areas, as evidenced in this study. Moreover, studies indicate that DR-TB is also related to socioeconomic factors, such as low education, low income, precarious housing, unemployment, among others[26].

The success of DR-TB treatment, in addition to treatment regimens, depends on the access of sick people to health services. It is the responsibility of management to offer alternatives to overcome the difficulties faced by these people and facilitate communication between the various health services involved in care, mainly on the part of PHC, which must monitor the person with TB[25].

Another valuable supervision strategy is Directly Observed Treatment (DOT), as it links the individual to care and services, monitors treatment adherence, ensures the complete dose, monitors treatment progress, prevents TB transmission, in addition to providing support and health education to patients[3].

With the aim of assisting in TB prevention, care, and control, the use of Information and Communication Technologies (ICT) has been intensifying, especially with the use of mobile applications, such as "Care TB," "Tuberculosis Cure & Treatment," "Nursing DRTB guide," among others[27].

Although PHC is recognized as the gateway and considered a priority for the control and care of people with TB, more than 25% of DR-TB cases in a study conducted in the state of São Paulo were diagnosed in other types of services. According to Arroyo et al.[23], this gap highlights PHC's difficulty in making timely diagnosis of the disease, in addition to both individual and community factors, as well as access to health services, which were associated with the occurrence of DR-TB cases.

The study demonstrated that the state of Paraná has concerning regions (East, Northeast, and West) with several risk clusters for DR-TB. Knowledge about the risk of contracting TB and developing drug resistance is crucial to dealing with this serious public health issue, which is growing worldwide, according to WHO[1].

The space-time scan analysis identified four space-time risk areas, with the cluster in the East region showing increased RR in the period from 2013 to 2016. Clusters 1 (North), 2 (West and Northeast), and 4 (East) began with changes in RR in 2017 and remained until the end of the studied period, even indicating a decline in annual incidence (clusters No. 2 and 4) in the years related to the COVID-19 pandemic. However, the time these areas remain as risk zones is uncertain, and it is possible that they are still at risk. Although they present small transformations over time, such areas will only cease to present risk for DR-TB infection when they manage to drastically reduce the incidence in these locations.

It should be noted that some municipalities indicated as at risk in the space-time analysis remain at risk in the purely spatial analysis. This may mean that, throughout the entire period, these municipalities had DR-TB cases, but at some point they were more concentrated, which allows these space-time clusters to be identified.

Studies conducted in India[28], China[29], and Portugal[30] identified formations of risk clusters for DR-TB. These studies emphasized the importance of monitoring people with TB from these areas, with active surveillance focused on social determinants and risk factors associated with DR-TB. Although this study did not identify the factors and determinants present in these risk areas, additional studies can be conducted for better care planning.

Alene et al.[29] describe in their study that understanding the spatial distribution of DR-TB and identifying areas with higher incidence and risk are the first steps to reducing the disease burden, and suggest that specific actions and interventions should be directed to these locations. Therefore, identifying areas with higher disease occurrence can function as a guiding instrument for public policy managers, which contributes to the development of strategies and interventions for TB and DR-TB prevention and control.

Regarding migratory movement and border regions, WHO recommends systematic testing and treatment for latent tuberculosis for international migrants from countries with high TB burden[31]. However, in Brazil, Ministry of Health recommendations indicate requesting tests for this group only if they present cough, regardless of symptom duration.

Although TB and DR-TB are subject to mandatory notification in Brazil, underreporting of cases can be considered a limitation for this study. Additionally, the use of secondary data from SITE-TB may present limitations due to the lack of uniformity and completeness of recorded data. Even so, methodological rigor and robust statistical analyses were used with the aim of minimizing possible biases.

This study contributes to the advancement of knowledge, as by applying spatial analysis techniques, it was possible to highlight risk areas for DR-TB in the state of Paraná, data that become valuable tools for health managers, allowing actions to be defined to address drug resistance, given that DR-TB treatment has a higher cost for the state.

The authors highlight the need for new studies that can map risk areas for DR-TB in other regions of Brazil. These studies can assist in combating the disease and achieving the goals proposed by the 2030 Sustainable Development Agenda, which aims to end epidemics, which also includes TB.

CONCLUSION

Considering that TB illness may be related to demographic, social, and economic factors, and that the border region could intensify this situation, it is interesting to observe that, in this study, DR-TB did not demonstrate a direct relationship with this region. This suggests that TB-related health care has been occurring similarly throughout the state of Paraná.

The spatial analysis of incidence and the identification of clusters with high rates and risks provided a comprehensive view of DR-TB cases in the state. This allows health managers to develop specific strategies that can be intensified, especially in regions with high rates. Furthermore, there is the possibility of implementing a TB control program more efficiently, with the aim of interrupting the transmission chain of the resistant bacillus, which is present in all regions of the state of Paraná, Brazil.

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SPATIAL RISK AREAS FOR DRUG-RESISTANT TUBERCULOSIS (DR-TB) IN PARANÁ / BRAZIL: ITS RELATIONSHIP WITH THE BORDER REGION

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