



Space and space-temporary clusters of tuberculosis in a Northeast Brazilian municipality

Aglomerados espaciais e espaço-temporais de tuberculose em município do Nordeste Brasileiro

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ABSTRACT

The objective was to detect spatial and spatiotemporal clusters of tuberculosis in a municipality in northeastern Brazil that is a priority for disease control. This is an ecological study, in which new cases of tuberculosis that occurred in Imperatriz (MA), between 2009 and 2018, were collected from the Notifiable Diseases Information System. Scanning statistics was used to detect the spatial and spatiotemporal clusters of the cases. Three spatial clusters of high relative risk (RR) were identified: cluster 1 (RR = 2.10), cluster 2 (RR = 2.20) and cluster 3 (RR = 2.70). The spatiotemporal analysis showed two spatiotemporal clusters of high relative risk, cluster 1 (RR = 2.80) that occurred between 01/01/2009 and 12/31/2013 and cluster 2 (RR = 3.40) occurring between 01/01/2009 and 12/31/2010. Such findings point to the need to elaborate procedures for combating and controlling risk areas, considering the evident socio-spatial inequalities present in the municipality under investigation.

Keywords: Geographic information systems. Notifiable diseases information system. Spatial analysis. Tuberculosis.

RESUMO

Objetivou-se detectar aglomerados espaciais e espaço-temporais de tuberculose em município do nordeste brasileiro prioritário para o controle da doença. Trata-se de um estudo ecológico, no qual foram considerados os casos novos de tuberculose ocorridos em Imperatriz (MA), entre 2009 e 2018, coletados juntos ao Sistema de Informação de Agravos de Notificação. Utilizou-se da técnica de estatística de varredura para a detecção dos aglomerados espaciais e espaço-temporais dos casos. Foram identificados três aglomerados espaciais de alto risco relativo (RR): aglomerado 1 (RR=2,10), aglomerado 2 (RR= 2,20) e aglomerado 3 (RR=2,70). A análise espaço-temporal evidenciou dois aglomerados de alto risco relativo, o aglomerado 1 (RR=2,80) que ocorreu entre 01/01/2009 a 31/12/2013 e o aglomerado 2 (RR= 3,40) com ocorrência entre 01/01/2009 a 31/12/2010. Tais achados apontam para a necessidade da elaboração de estratégias para o combate e controle nas áreas de risco, considerando as evidentes desigualdades socioespaciais presentes no município sob investigação.

Palavras-chave: Análise espacial. Sistemas de informação geográfica. Sistema de informações de agravos de notificação. Tuberculose.

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INTRODUCTION

Considered a neglected and endemic disease in several countries, tuberculosis is an infectious disease, caused by *Mycobacterium tuberculosis*, and transmitted through the respiratory tract by inhaling aerosols containing bacilli expelled by coughing, speaking or sneezing in a patient with active pulmonary or laryngeal tuberculosis¹. This disease mainly affects the lungs and can also be spread to other parts of the body (extrapulmonary tuberculosis) depending on endogenous factors, especially the integrity of the immune system¹. Worldwide, it is estimated that a quarter of the population is infected with the bacillus, at risk of developing the disease, and approximately 95.0% of cases of illness occur in developing countries¹.

Despite the reduction in tuberculosis morbidity and mortality over the last few decades, in 2018, about 1.5 million people died worldwide, and even with the tendency to decrease the incidence of the disease, its burden remains high among low-income populations and in situation of social vulnerability, since about 10 million people were affected by it that same year².

In Brazil, in 2018, 72,788 new cases of tuberculosis were diagnosed and registered, corresponding to an incidence rate of 34.8 cases/100 thousand inhabitants. Specifically in Maranhão, in that same year, 2,132 cases were diagnosed and recorded, with an incidence rate of 30.3 cases/100 thousand inhabitants³, representing an important epidemiological panorama in terms of public health, requiring new research approaches.

Aiming to reduce its incidence rates in Brazil, scenarios were defined with characteristics to be worked on in the coming years in priority municipalities for this disease control. For example, Imperatriz-MA is located in scenario 2, characterized by disadvantaged operational and socioeconomic indicators, with a higher AIDS incidence rate, in addition to having a higher tuberculosis mortality rate.

Such subscenario presents epidemiological challenges to be overcome, as well as social determinants understood as social, economic or behavioral factors, which influence health, positively or negatively, and can be influenced by political, economic and/or individual decisions⁴, in addition to increasing the risk of tuberculosis occurrence⁵.

Scientific investigations related to the geographical distribution of tuberculosis have been stimulated over the years in order to characterize its spatial and spatiotemporal behavior in different locations⁶⁻⁸. Such studies pointed out that this disease is essentially urban and brought subsidies for the formulation of hypotheses about risk factors at a social and environmental level. Thus, tuberculosis also needs to be studied from the perspective of analyzing spatial and spatiotemporal distribution in priority scenarios, allowing quick access to the necessary information to carry out case surveillance⁹.

In this perspective, the identification of spatial and spatiotemporal clusters performed by means of scanning statistics in other scenarios^{10,11} made it possible to observe the areas that present the greatest relative risk for the occurrence of tuberculosis, and, in turn, facilitated the work of epidemiological surveillance in order to reduce morbidity and mortality due to it and to know its distribution and trend over time, providing subsidies for the implementation of control actions.

Considering the magnitude and complexity involved in the occurrence of tuberculosis cases, circumscribed to the need to understand its distribution in space and space-time, in a disaggregated way in different scenarios that did not make use of scanning statistics as a method of geospatial analysis, this study aimed to detect spatial and spatiotemporal clusters of tuberculosis in a municipality in northeastern Brazil that is a priority for disease control.

METHODOLOGY

DESIGN AND LOCATION OF STUDY

This is an ecological study, whose units of analysis were the census sectors of Imperatriz (MA). Data from the 2010 IBGE Census and records

of tuberculosis cases obtained from the National Notifiable Diseases Information System (SINAN) were used. The study was carried out in Imperatriz (Figure 1), which has an estimated population of 258,682 inhabitants, a territorial area of 1,368.98 km² and 102 health establishments registered in the Unified Health System (SUS)¹².

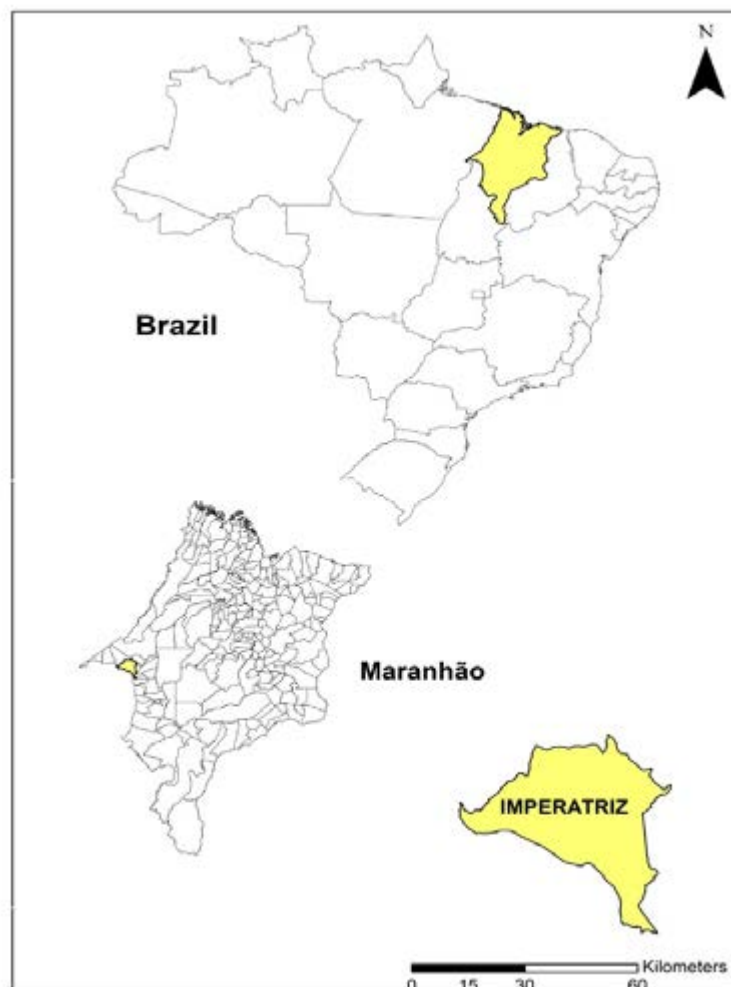


Figure 1. Brazil map, highlighting the State of Maranhão and the city of Imperatriz. Adapted from geographic bases

According to the results of the last census, conducted in 2010, the city of Imperatriz is divided into 246 census sectors, 218 urban and 28 rural, distributed in 160 neighborhoods¹³.

Located 626 km away from the capital city São Luís, the municipality is considered the second largest population, economic, political and cultural center of Maranhão and has 48.3% of adequate sanitation, and

86% of drinking water supply and 98.4% of schooling rate from six to 14 years old¹².

DATA COLLECTION

All confirmed reported new cases were included, based on the SINAN tuberculosis notification forms, from January 2009 to December

2018. The survey data were collected by the proposal coordinator in June 2019, together with the Health Surveillance Service (SVS) of the Regional Health Management Unit of Imperatriz (UGRSI), after specific training to define the variables to be obtained from SINAN.

DATA ANALYSIS

Standardization and matching of addresses in the urban and rural areas of Imperatriz was carried out with the cartographic base of the municipality, with UTM/WGS84 projection, Shapefile format. Then, with the help of TerraView software version 4.2.2, geocoding was carried out, when there was an address linear interpolation, to a point in the corresponding street segment, being possible, from then on, to elaborate point patterns of events. Additionally, the Batch Geocode tool (available at <http://batchgeo.com/br/>) and on-site searches using the Global Positioning System (GPS) were used.

To detect spatial and spatiotemporal clusters of tuberculosis cases, the census sector was used as an ecological analysis unit, based on the fact that it is the most disaggregated level of population and socioeconomic groups, collected in a systematic, periodic and standardized way nationally covered¹⁴.

The Scan statistic¹⁵ was used in order to detect the clusters of tuberculosis cases in space and in space-time. Three files were created, the first containing cases with data on the number of the census sector where the event occurred, date of occurrence, sex and age of the people notified; the second file with the geographical coordinates of the centroids of the census sectors; the third with population data from the census sectors followed a connotation with sex and age according to the data from the Results of the Universe¹³.

Taking into account the identification of essentially spatial clusters, in which the distribution is heterogeneous and events are rare in relation to the population, the Poisson discrete model was used,

and required conditions such as the non-geographical overlap of clusters, the maximum size of the agglomerate equal to 50% of the exposed population, with a circular shape and 999 replications¹⁵.

To detect spatiotemporal clusters, the Poisson discrete model was again considered with similar analysis conditions, however, meeting the criteria of maximum size of the temporal cluster equal to 50% of the study period¹⁵, accuracy of time in day, month and year and time period between January 2009 and December 2018.

Together with it, space and space-time detections were carried out by controlling the occurrence of tuberculosis cases by the size of the population in the census sectors, by their age distribution and according to sex, in addition to attempts to detect clusters of high and low relative risks.

Thematic maps of the scan analyzes containing the relative risk (RR) of the clusters were built. The relative risk, on this occasion, allowed comparing information from different areas, standardizing them and removing the effect of different populations, in order to portray the intensity of the occurrence of the phenomenon in relation to all study regions¹⁵. All cluster detection analyzes were processed using SaTScan™ software, version 9.2 and thematic maps were generated using ArcGis 10.5 software.

ETHICAL ASPECTS

In accordance with the precepts of Resolution No. 466/2012, in order to carry out this study, the project was previously submitted to the Research Ethics Committee involving human beings at the Federal University of Maranhão (UFMA) (CAAE 55982316.2.0000.5087) and approved under No. 1,627.931 issued on July 7, 2016.

RESULTS

Between 2009 and 2018, 800 new cases of tuberculosis were registered, mostly referring to male

gender (63.0%), brown race/color (60.0%), with a predominance of education from first to fourth grade incomplete (39.4%). Of these, 761 were geocoded, which corresponds to approximately 95.0% of the total, with 700 cases (92%) using the TerraView software, 50 cases (6.6%) using the Batch Geocode tool and 11 cases (1.4%) performing searches of addresses using GPS. The geocoding of 39 (5.0%) of the cases was

not possible, as they presented inconsistencies and/or inconsistencies in the provided addresses, even with the use of several strategies for the geocoding of events under study.

The spatial scanning analysis allowed the detection of three spatial clusters of high relative risk, statistically significant (Figure 2).

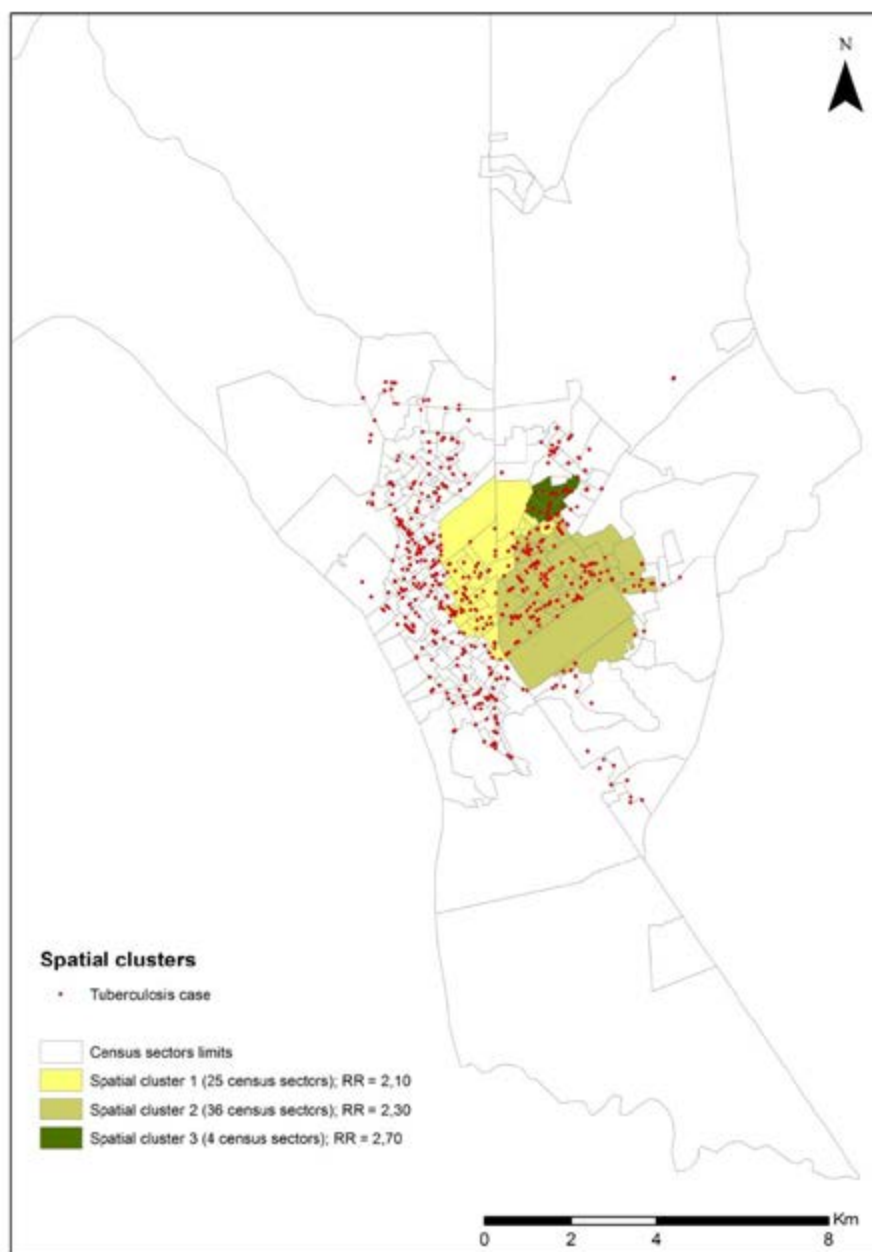


Figure 2. Spatial clusters of tuberculosis cases, controlled by the population of the census sectors and their distribution by sex and age, Imperatriz-MA (2009 to 2018)

Characteristics such as number of cases, number of census sectors, population, incidence, RR (95% CI) and neighborhoods involved in the detected spatial clusters are shown in Table 1.

Table 1. Characterization of spatial clusters of tuberculosis cases, controlled by the population of the census sectors and according to their distribution by sex and age, Imperatriz-MA (2009 to 2018)

Spatial clusters	Nº of census sectors	Nº of cases	Population (inhab)	RR (95% CI)	<i>p</i> value	Incidence/100,000 inhab-year	Neighborhoods
1	25	86	15,495	2.10 (1.60 – 2.80)	$p < 0.001$	56.6	Downtown, Mercadinho, Bacuri, Parque Anhanguera, Nova Imperatriz, Vila Lobão, Santa Rita.
2	36	202	29,990	2.20 (1.75 – 3.10)	$p < 0.001$	58.8	Vila Lobão, Santa Rita and São José, Entrocamento, Vila Nova, Bom Sucesso, Vila Ipiranga, Vila Redenção, Parque Alvorada, Santa Lúcia and Parque Sanharol.
3	4	39	5,300	2,70 (1,91 – 2,92)	$p < 0.002$	79.7	Vila Cafeteira, Vila Ipiranga, Vila Redenção, Santa Lúcia and Vila Lobão,

RR, relative risk; CI, confidence interval.

Spatial cluster 1 (RR = 2.10; 95% CI = 1.60 - 2.80; $p < 0.001$) encompassed 25 census sectors and had an incidence rate equal to 56.5 cases/100,000 inhabitants-year, involving neighborhoods Downtown, Mercadinho, Bacuri, Parque Anhanguera, Nova Imperatriz, Vila Lobão, Santa Rita.

Spatial cluster 2 (RR = 2.20; 95% CI = 1.75 - 3.10; $p < 0.001$) involved 36 census sectors belonging to the neighborhoods Vila Lobão, Santa Rita, São José, Entrocamento, Vila Nova, Bom Sucesso, Vila Ipiranga, Vila Redenção, Parque Alvorada, Santa Lúcia, Parque Sanharol, and presented an incidence rate equal to 58.8 cases/100,000 inhabitants-year.

Spatial cluster 3 (RR 2.70; 95% CI = 1.91 - 2.92; $p < 0.002$) included four census sectors belonging to the neighborhoods Vila Cafeteira, Vila Ipiranga, Vila Redenção, Santa Lúcia, Vila Lobão, with population of 5,300 inhabitants, and an incidence rate equal to 79.7 cases/100,000 inhabitants-year.

Regarding the analysis of space-time scanning of cases, two clusters of high relative risk were identified, statistically significant. The description of the characteristics of the spatiotemporal clusters is shown in Table 2 and presented in Figure 3.

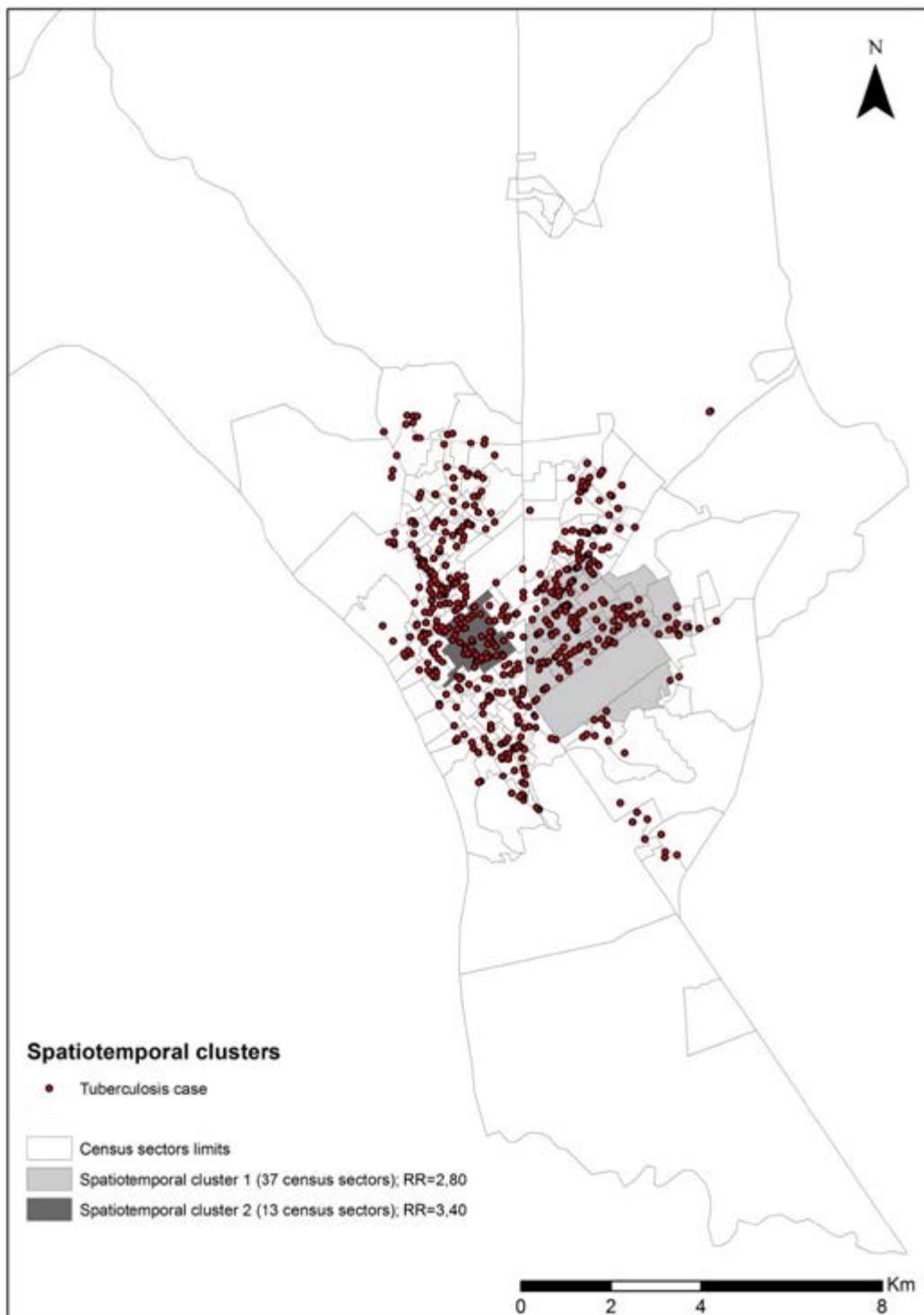


Figure 3. Spatiotemporal clusters of tuberculosis cases, controlled by the population of the census sectors according to their distribution by sex and age, Imperatriz-MA (2009 to 2018)

Table 2. Characterization of spatiotemporal clusters of tuberculosis cases, controlled by the population of the census sectors according to their distribution by sex and age, Imperatriz-MA (2009 to 2018)

Spatiotemporal clusters and detection period	Nº of census sectors	Nº of cases	Population (inhab)	RR (95% CI)	Pvalue	Incidence/100,000 inhab-year	Neighborhoods
1 01/11/2009 and 31/12/2013	37	203	41,110	2.80 (1.92 – 3.73)	p<0.001	76.4	Vila Lobão, Santa Rita, São José, Entrocamento, Vila Nova, Bom Sucesso, Vila Ipiranga, Vila Redenção, Parque Alvorada and Santa Lúcia
2 01/01/2009 and 31/12/2010	13	63	11,629	3.40 (2.26 – 4.33)	p<0.007	102.2	Downtown, Mercadinho, Santa Rita, Nova Imperatriz and Bacuri

RR, relative risk; IC, confidence interval.

Encompassing 37 census sectors, the spatiotemporal cluster 1 ($p < 0.001$) had an incidence rate of 76.4 cases/100.00 inhabitants-year, with the census sectors belonging to the neighborhoods Vila Lobão, Santa Rita, São José, Entrocamento, Vila Nova, Bom Sucesso, Vila Ipiranga, Vila Redenção, Parque Alvorada, Santa Lucia, between 11/01/2009 and 12/31/2013. The risk for tuberculosis for the inhabitants of this cluster was 2.80; 95% CI = 1.92 - 3.73.

The spatiotemporal cluster 2 ($p < 0.007$) involved 13 census sectors and had an incidence rate equal to 102.2 cases/100,000 inhabitants-year, with census sectors belonging to the neighborhoods Downtown, Mercadinho, Santa Rita, Nova Imperatriz, Bacuri, between 01/01/2009 and 12/31/2010. The risk for tuberculosis for the inhabitants of this cluster was 3.40; 95% CI = 2.26– 4.33.

Both spatial and spatiotemporal clusters were detected in census sectors in the urban area of the municipality.

DISCUSSION

This investigation aimed to detect spatial and spatiotemporal clusters of tuberculosis cases in Imperatriz-MA, a municipality in northeastern

Brazil that is a disease control priority. With regard to the geocoding of the cases under investigation, the percentage of approximately 95% of the cases is shown to be a relevant and highly valuable rate when carrying out spatial analyzes, in studies using database addressing¹⁶. Investigations carried out in several locations¹⁷⁻²⁰, working with geocoding in health and addressing the notification of tuberculosis cases, obtained a geocoding rate similar to that of this study, ranging from 82% to 98% of georeferencing of events for the application of the proposed spatial analyzes.

In this investigation, the main reasons for the non-geocoding of 5% of cases are attributed to failures in the registration of information, such as the registration of addresses that do not exist or are incompatible with the cartographic base, failure to fill in addresses and, still, areas of irregular occupation such as subnormal agglomerates, adversity also identified in other studies conducted in the country^{18,20,21}. It is also worth mentioning that, despite having a Human Development Index (HDI) of 0.731, considered high and the second highest in the federative unit¹², the municipality of Imperatriz, at the end of 2018, had population coverage estimated by the Family Health Strategy (FHS) teams of 60.99%²², a fact that can contribute to the underreporting of cases.

Studies have shown that health services are not evenly organized across territories, especially Primary

Health Care (PHC), leading to the suspicion that intervention for tuberculosis control and surveillance is not occurring in a geographically balanced manner. Based on that, it is assumed that there are risk areas for these events that are not assisted, pointing out the need for detailed investigation^{8,23,24}.

Using scan statistics, it was possible to identify spatial and spatiotemporal clusters that present a high relative risk for the occurrence of tuberculosis in Imperatriz-MA, with an incidence ranging from 56.5 to 102 cases/100,000 inhabitants, higher than those presented in national studies^{25,26}. In these locations, a more detailed investigation would be essential to be able to identify the factors associated with greater detection of cases in these clusters, in relation to the territories that have the protection factor because they do not have a high risk of illness⁷.

When using census sectors as a unit of ecological analysis, there are two important points for reflection, since at the same time that it results in problems related to the statistical instability of incidence rates due to small populations, it leads to the possibility of working with more homogeneous populations than neighborhoods, for example²⁷. Thus, the scan analysis allowed to segment the municipality in high-risk areas by visualizing spatial and spatiotemporal clusters capable of demarcating homogeneous areas⁸.

The lack of planning in the scenario under investigation in the initial urban growth phase is pointed out as the cause of inextinguishable marks, evident aspects nowadays. The expansion of the city's urban framework has not been accompanied by adequate care by public managers, and there is no interest from the government to guide and organize the urban growth of Imperatriz. Such expansion, without prior planning, resulted in the appearance of areas considered subnormal, mostly lacking essential public services^{28,29}.

People residing in census sectors, belonging to the Bacuri neighborhood, had a high risk for tuberculosis, both in space and in space-time. This

neighborhood, located in the Southwest region of the municipality, is one of the oldest in the city whose large part is the result of a disorderly residential wastewater and suffers from the presence of areas that serve only as waste receptors thrown by the local inhabitants, and problems caused by floods as a result of the overflow of the Bacuri stream, such as those that normally occur during periods of rain^{30,31}, favoring the proliferation of diseases, including tuberculosis.

Similar problems are faced in the Parque Anhanguera neighborhood, related to the accumulation of garbage and in periods of rain with the overflow of the Cacau and Capivara streams that cut through the referred neighborhood³¹.

The populations living in the census sectors, belonging to Downtown and Nova Imperatriz neighborhoods, were inserted in spatial and space-time clusters of high risk for tuberculosis; such areas have better living conditions and are located in the central region of the city. Studies point out that the higher number of cases in the Central region may be related to the greater underreporting in the city outskirts^{7,19}, and may justify the lower demand for health services in the outskirts, as well as the increased population agglomeration in the Central region, resulting in the greatest number of tuberculosis cases and high incidence.

It is worth noting that the greater concentration of people favors the circulation of the bacillus that causes tuberculosis¹⁷. Imperatriz has several areas focused on retail trade, represented by fairs/free markets in the neighborhoods Downtown, Mercadinho, Bacuri, Nova Imperatriz and Vila Lobão, areas with high relative risk for the occurrence of tuberculosis, in addition to being favorable spaces to have higher rates of tuberculosis by the greater population concentration, and intense flow of people coming from different locations³⁰.

The disorderly, regular and irregular growth gave rise to several Imperatriz neighborhoods, such as Santa Rita, and occupations in the Vila Lobão neighborhood that extended to Vila Redenção and Vila

Ipiranga. To the east, in contiguity with Vila Nova, a large population contingent occupied the areas where Vila Cafeteira is currently located, and infrastructure problems are present³². The result of this scenario is the production of a segmented and dual urban space, characterized by intense socio-spatial inequalities, without the care of public administration³⁰.

In this sense, it is worth mentioning that the greater number of tuberculosis cases in less favored regions, from a social point of view, implies and justifies the intensification of activities related to the search for respiratory symptoms for early detection, establishing treatment, obtaining a cure and interrupting the chain of infection^{14,32}. Furthermore, the marked social inequality in Brazil, observed in access to health, education, income distribution, and basic sanitation resources, are closely related to the risk of becoming infected with tuberculosis in different social strata, as observed in different scenarios^{14,33,34}.

It is worth mentioning that the underreporting of cases in SINAN makes it impossible to know the epidemiological situation of this disease, hindering the planning of actions aimed at its control³⁵. As weaknesses, the gaps in filling in the records stand out, which are of paramount importance for health management and planning. In this perspective, improving the quality of the records offered is fundamental, in relation to filling in the fields and updating the data from the Health Information Systems (SIS)³⁶.

Inherent in ecological studies, the ecological fallacy stands out as a limitation of this study, which consists of observing the existence of a phenomenon at an aggregate level, does not necessarily imply that this same existing relationship remains at the individual level³⁷. Furthermore, the need for further studies emerges, mainly because no evaluation of any socioeconomic measure or access and coverage of the assistance provided in the ecological units of analysis of the investigated scenario has been carried out.

Despite the limitations mentioned above, this investigation stands out for its originality, in

view of the lack of studies that have investigated the identification of spatial and spatiotemporal clusters in Imperatriz-MA, and the characterization of the census sectors that present a high risk for the occurrence of tuberculosis. It is also noteworthy that such ecological units of analysis were considered risk territories for the development of the disease, as they are regions with greater population densities where the flow of people is intense or with precarious living conditions²⁹⁻³¹, where socio-spatial inequality it is a reality.

CONCLUSION

The investigation revealed areas in space and space-time referring to the census sectors belonging to the neighborhoods Downtown, Mercadinho, Bacuri, Parque Anhanguera, Nova Imperatriz, Vila Lobão, Vila Redenção, Santa Rita, Vila Cafeteira, among others, which are priorities for control and disease surveillance, highlighting important aspects to be considered in terms of service management and organization. Such findings constitute a subsidy for the management of health systems and services in the search for improving living conditions and reduce social inequities, through the planning, monitoring and evaluation of health actions.

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