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ORIGINAL ARTICLE



Spatial epidemiological approach to tuberculosis in Pernambuco

Abordagem epidemiológica espacial da tuberculose em Pernambuco Abordaje epidemiológico espacial de la tuberculosis en Pernambuco

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ABSTRACT

Background and Objectives: Pernambuco is among the states with the highest detection and mortality rates for tuberculosis, a disease directly related to social and health inequalities. We proposed to analyze the epidemiological characteristics of tuberculosis from 2011 to 2020 in the health macroregions of Pernambuco. **Methods:** this was an ecological study of notified cases of tuberculosis confirmed in the macroregions of the state of Pernambuco between 2011 and 2020. The behavior of tuberculosis in Pernambuco over time and space was analyzed. **Results:** there were 56,700 confirmed cases of tuberculosis per municipality of residence in Pernambuco during the study period. The overall average detection rate for the period was 35.6/100,000 inhabitants, with the highest rate recorded in macroregion 1, with 58.45 cases/100,000 inhabitants, and the lowest in macroregion 3, with 19.74 cases/100,000 inhabitants. The results show an increase in the concentration of cases in the state's Metropolitan Region. **Conclusion:** tuberculosis control requires contextual actions to improve people's general living conditions. Social support is aimed at socially vulnerable people in general, and there is no specific support for this public.

Keywords: Tuberculosis. Epidemiology. Social Determinants of Health. Space-Time Analysis.

RESUMO

Justificativa e Objetivos: Pernambuco está entre os estados com maiores coeficientes de detecção e mortalidade por tuberculose, doença diretamente relacionada às iniquidades social e de saúde. Propõe-se analisar as características epidemiológicas da tuberculose no período de 2011 a 2020 nas macrorregiões de saúde de Pernambuco. **Métodos:** estudo ecológico que considerou os casos notificados confirmados para tuberculose nas macrorregiões do estado de Pernambuco entre 2011 e 2020. Analisou-se o comportamento da tuberculose em Pernambuco no tempo e no espaço. **Resultados:** houve um registro de 56,7 mil casos confirmados de tuberculose por município de residência em Pernambuco no período do estudo. A média geral da taxa de detecção no período foi de 35,6/100

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mil habitantes, sendo a maior taxa registrada na macrorregião 1, com 58,45 casos/100 mil habitantes, e a menor, na macrorregião 3, com 19,74 casos/100 mil habitantes. Os resultados mostram aumento na concentração de casos na Região Metropolitana do estado. **Conclusão:** o controle da tuberculose necessita de ações contextuais, no sentido de melhorar a condição geral de vida das pessoas. O suporte social é destinado às pessoas em vulnerabilidade social no geral, não havendo suporte específico a esse público.

Descritores: Tuberculose. Epidemiologia. Determinantes Sociais da Saúde. Análise Espaço-Temporal.

RESUMEN

Justificación y Objetivos: Pernambuco se encuentra entre los estados con mayores tasas de detección y mortalidad por tuberculosis, enfermedad directamente relacionada con las desigualdades sociales y sanitarias. El objetivo es analizar las características epidemiológicas de la tuberculosis entre 2011 y 2020 en las macrorregiones sanitarias de Pernambuco. **Métodos:** estudio ecológico que analizó los casos notificados confirmados de tuberculosis en las macrorregiones del estado de Pernambuco entre 2011 y 2020. Se analizó el comportamiento de la tuberculosis en Pernambuco en tiempo y en espacio. **Resultados:** hubo 56.700 casos confirmados de tuberculosis por municipio de residencia en Pernambuco durante el período de estudio. La tasa media global de detección en el período fue de 35,6/100.000 habitantes, registrándose la tasa más alta en la macrorregión 1, con 58,45 casos/100.000 habitantes, y la más baja en la macrorregión 3, con 19,74 casos/100.000 habitantes. Los resultados muestran un aumento de la concentración de casos en la región metropolitana del estado. **Conclusión:** el control de la tuberculosis requiere acciones contextuales para mejorar las condiciones generales de vida de las personas. El apoyo social está dirigido a las personas socialmente vulnerables en general, y no hay apoyo específico para este público.

Palabras Clave: Tuberculosis. Epidemiología. Los Determinantes Sociales de la Salud. AnálisisEspacio-Temporal.

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease that persists with high prevalence in Brazil and worldwide, and is the leading cause of death from a single infectious agent. In 2020, 10.6 million people were infected with TB and more than one million people died from the disease worldwide.

Brazil is the only country in the Americas present on two lists of priority countries for the World Health Organization (WHO) (TB and TB-Human Immunodeficiency Virus (HIV)).¹ The Ministry of Health epidemiological bulletin reveals that Brazil remains among the 30 countries with the most cases of TB and TB-HIV co-infection, becoming a priority for disease control according to theWHO. In 2020, 66,819 new cases were reported, generating an incidence coefficient of 31.6 cases per 100,000 inhabitants and approximately 4,500 deaths from the disease were recorded, reaching 2.2 deaths per 100,000 inhabitants, considering the country's capitals.²

Pernambuco is among the states with the highest incidence and mortality rates for TB. The capital, Recife, has the second highest incidence rate among Brazilian capitals, at 106 per 100,000 inhabitants, behind only Manaus, which has a rate of 114/100,000 inhabitants. This pattern in the distribution of TB in Brazil, centered on Metropolitan Regions, is related to the persistence of peripheral urban areas, whose characteristics include the presence of low-income populations and less access to basic services and infrastructure. Moreover, the periphery is often marked by a lack of public investment and the presence of social problems, such as violence and lack of job opportunities, which favor the spread of the disease.³

TB is therefore a socially determined disease, directly related to poverty, inequality and social exclusion, which in turn will influence people's health status. Social vulnerability exposes individuals to greater contact with the etiological agent and subsequent illness due to nutritional deficiency, lack of basic health services and precarious working and housing conditions. As it is a disease of great proportions, it is observed that it has a strong influence in poorer countries and in the outskirts of metropolitan areas, which justifies the high incidence in countries with a low Human Development Index (HDI).⁴

The lack of access to information, resulting from low levels of education and failure to promote health, increases the number of cases of the disease. Low levels of education can negatively influence the understanding of the importance of correct treatment and the risks of abandoning the therapeutic process, creating obstacles to controlling this disease and thus contributing to the emergence of new strains resistant to anti-TB drugs.⁵

Considering TB characteristics, it is important to understand it from the perspective of One Health. This approach considers the interconnections between human, animal and environmental health, bringing an interdisciplinary view and their interactions over time. The One Health approach is becoming an essential concept for public policy makers seeking strategies for more efficient administration and better governance. However, few of them cover all the pillars of the approach to prevent diseases, protect and promote health, due to the low importance given to the institutional, political and social factors associated with a One Health approach.⁶

The COVID-19 pandemic has had a significant impact on TB numbers. Due to difficulties in accessing services, the number of people affected by TB worldwide fell from a peak of 7.1 million in 2019 to 5.8 million in

2020 (-18%), returning to the 2012 level. This scenario shows that the number of people with undiagnosed and untreated TB has increased, resulting in higher TB deaths and increased community transmission of the infection.⁷

The term "syndemic" is suggested to explain the harmful interaction between TB and COVID-19, given that the aforementioned social, economic and environmental contexts, which determine populations'living conditions, enhance the interaction between coexisting diseases and the excessive burden of the resulting consequences.⁸

The aim is to understand the epidemiological aspects of this disease in Pernambuco in the pre-pandemic period, focusing on spatial and temporal approaches, aiming to identify characteristics present in certain areas that may influence the expression of the TB incidence coefficient before the influence of the pandemic.

METHODS

This is an ecological study that considered all confirmed cases of TB reported in the state of Pernambuco from 2011 to 2020.

Pernambuco is one of the most unequal states in Brazil in terms of income concentration. It has a Gini Index (per capita household income) of 0.62, with the smallest municipality showing 0.47, and the largest, 0.63, with the lowest values detected in the municipalities of the countryside (rural area). With the HDI, the opposite happens: the municipalities of the Metropolitan Region of Recife (MRR) have the highest values, with the index varying from 0.48 to 0.78. The state has an HDI of 0.72. The inequality map of Brazilian capitals published in 2019 points to Recife as the most unequal among the capitals. Moreover, the state is in third place in income concentration.⁹

In compliance with the principle of decentralization of health actions proposed by the Brazilian Health System (In Portuguese, *Sistema Único de Saúde* - SUS), Pernambuco is subdivided into four Interstate Health Macroregions (IHM): Metropolitan Region; *Agreste*; *Sertão*; and *Vale do São Francisco* and *Araripina* (Figure 1). These territorial arrangements bring together more than one health region, with the aim of agreeing on interregional actions, services and interests, constituting an example of coordination at various levels beyond borders.¹⁰

The data was extracted from the SUS Information Technology Department (In Portuguese, *Departamento de Informática do SUS*- DATASUS) (datasus.saude.gov. br).¹¹ All confirmed TB cases residing in the state of Pernambuco between 2011 and 2020 were included in the study. The selections used were "confirmed TB cases", "year of notification", "municipality of residence" and "Macrorreg.Saúde/Munic.de resid" in the period 2011-2020. Cases outside the investigation period, with incomplete or missing data and cases of drug-resistant



Figure 1. Map of the state of Pernambuco, Brazil, highlighting its four health macroregions.

TB were excluded from the study.

In order to differentiate the macroregions (MR) in relation to socioeconomic characteristics, a table was created with data on population density, Gini index, urbanization rate and number of commercial buildings.

The absolute number of TB cases per municipality and state was addressed as well as the TB detection rate according to its spatial distribution. For comparative purposes, the information was considered for five-year periods (2011-2015 and 2016-2020). Instead of the traditional nomenclature "incidence coefficient", this article chose to use the "detection rate", considering that the chronicity of TB cases does not allow for a true incidence, since it is not known when a patient became infected. However, there is no difference between the calculation methods.

The detection rate calculation was obtained using the formula:

Number of TB cases reported in Pernambuco between 2011-2020 Mid-period adjusted population x 10n

For the temporal approach, descriptive statistics of detection rates by MR and for the state were presented in tables, considering the total study period and each five-year period.

In order to verify the behavior of the response variable in space, the incidence rate was initially distributed by municipality, classifying them according to quartiles, in which the higher the incidence, the darker the color. The state of Pernambuco was visually divided into four MR: Metropolitan Region;*Agreste;Sertão*; and *Vale do São Francisco* and *Araripina*.

The spatial autocorrelation measure used was the global Moran's Index, which tests whether the connected areas present greater similarity regarding the indicator studied than expected in a random pattern, ranging from -1 to +1. The degree of existing autocorrelation can be quantified, being positive for direct correlation, negative for inverse correlation.¹²

In addition to the global Moran's Index, the local index was used, which resulted in a "Moran's map" of the average TB incidence rate, since it allows finding the "pockets" of spatial dependence not observed in the global indices, such as possible clusters and outliers. The relationships between the value of the measured attribute and its neighbors can be observed in the local indexgraphical analysis, called the Moran scatter diagram, or in the two-dimensional thematic map, called the Box Map. $^{\rm 12}$

The graph is divided into quadrants: Q1, Q2, Q3 and Q4. The points located in Q1 and Q2 indicate areas in which the measured value of the attribute resembles the average of its neighbors. The first indicates a positive value and a positive average, and the second, a negative value and a negative average. The points located in Q3 and Q4 indicate that the value of the measured attribute does not resemble the average of its neighbors. In this case, Q3 indicates a negative value and a positive average, and Q4 indicates a positive value and a negative average. The areas located in Q3 and Q4 can be seen as extremes, or as transition areas, since they do not follow the pattern observed for their neighbors.¹³

Since this was a study that used official secondary data from the public domain, without identifying subjects, there was no need for assessment by a Research Ethics Committee (REC). The study followed the Brazilian National Health Council (In Portuguese, *Conselho Nacional de Saúde* - CNS) recommendations in its CNS Resolution 466 of December 12, 2012.

RESULTS

There were 56,711 confirmed cases of TB recorded per municipality of residence in Pernambuco during the study period. The overall average detection rate during the period was 35.6/100,000 inhabitants, with large disparities between the MR: the highest rate was recorded in MR 1, with 58.45 cases/100,000 inhabitants, and the lowest in MR 3, with 19.74 cases/100,000 inhabitants.

From 2011 to 2015, the detection rate for TB in Pernambuco was 34.1/100,000 inhabitants, with the highest rate being recorded in MR 1, with 55.99/100,000 inhabitants, and the lowest in MR 4, with 20.47/100,000 inhabitants. In the following period, Pernambuco recorded 37.32 cases/100,000 inhabitants, with MR 1 continuing to present the highest value (61.27 cases/100,000 inhabitants) compared to 18.89 cases/100,000 inhabitants in MR 3.

Below are indicators that may influence the persistence of TB as a public health concern. It can be seen that, although there is a mathematical similarity between the Gini Index, the urbanization rate and the HDI-income among the MR, the population density and the number of establishments in MR 1 are higher when compared to the other MRs (Table 1).

Table 1. Distribution of population density, Gini Index, urbanization rate, HDI-R* and commercial facilities rate for each health macroregion. Pernambuco, 2022.

Variables	Macro 1	Macro 2	Macro 3	Macro 2
Population density	516.8	120.46	40.9	27.25
GiniIndex	0.517	0.514	0.529	0.522
Urbanization rate	62.18	62.95	61.86	59.62
HDI-I	0.569	0.579	0.579	0.57
Trade	908.5	295.5	365.8	264.8

*HDI-I: Human Development Index - income

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TB detection rates for MR1 were higher in all periods compared to the other MR (Table 2).

The highest ranges in TB detection rates are found in MR 1 (10.44–615.96 per 100,000 inhabitants), and the lowest in MR 3 (1.70–60.00 per 100,000 inhabitants). In the first five-year period, 50% of municipalities in MR 1 had up to 38.3 cases/100,000 inhabitants, rising to 44.95 in the second. This increase between periods was accompanied by all other MR. It is also observed that the median in MR 1 is higher than that of the others, showing that the problem is more present in this than in the other MR (Figure 2). The comparison of the spatial distribution of the gross coefficient of the TB incidence rate in Pernambuco between the periods 2011-2015 (3A), 2016-2020 (3B) and 2011-2020 (3C). For all periods, the highest incidence rates were observed in MR 1 (above 37/100 thousand inhabitants) (Figure 3).

The letters D, E and F represent the Moran map of the TB incidence rate. One can see the existence of high-high clusters in the MRR and surrounding areas. Low-low clusters tend to be concentrated in the *Sertão* region of Pernambuco, which is home to MR 3 and 4 (Figure 3).

Period	Values	MR1	MR2	MR3	MR4
2011-2015	Minimum	10.44	4.63	2.91	2.87
	Average	55.99	20.41	20.73	20.47
	Maximum	615.96	103.22	60.57	42.06
2016-2020	Minimum	5.22	0.00	1.70	5.56
	Average	61.27	25.64	18.89	20.80
	Maximum	613.1	104.69	60.94	45.87
2011-2020	Minimum	9.55	4.24	8.77	4.22
	Average	58.45	22.99	19.74	20.52
	Maximum	608.63	104.03	56.12	43.86

Table 2. Tuberculosis detection rates by macroregion per 100,000 inhabitants. Pernambuco, 2011-2015 and 2016-2020.



Legend: A. Comparison of detection rate by macroregion in the period; B. Comparison of detection rate by macroregion considering the five-year periods.

Figure 2. Violin plots of median tuberculosis detection rates. Pernambuco, Brazil, 2022.



Figure 3. Spatial and temporal evolution of the gross incidence rate of tuberculosis (3A,B,C), and Moran map of the detection rate (3D, E, F).

DISCUSSION

There was an increase in the TB detection rate in Pernambuco between the five-year periods, with large disparities in values between the regions located in the countryside of the state (*Sertão, São Francisco* and *Araripe*) and the Metropolitan Region, with the highest values observed in the latter for the entire period, in addition to having the highest population density and the highest concentration of commercial establishments. The average detection rate for Pernambuco during the study period was higher than that for Brazil for the same period. Spatial analysis showed the existence of highhigh clusters, with municipalities with high detection rates surrounded by others also with high rates in the MRR and surrounding areas.

This geographic disparity points to the relationship between clusters of TB cases and areas of high population density, which, in the case of Brazil, is compounded by specific issues. Metropolitan Regions, although notably responsible for part of the country's economic growth, due to the disorderly process of urbanization, have a chronic lack of urban infrastructure that has historically led people to seek housing in illegal subdivisions, a phenomenon known as peripheralization. These areas are characterized by great distance between social strata, high poverty, low levels of education, and difficulty in accessing essential services, among others.^{13,14} The Social Vulnerability Atlas shows that the Gini coefficient is 0.616, in all Brazilian metropolises, and 0.593, in the rest of the country.¹⁵

The implementation and dissemination of specific control measures, such as improving patient search strategies, access to diagnosis and treatment within the care network structure adopted in Brazil, resulted, in the last ten years, in a 20.2% reduction in the incidence rates of the disease in Brazilian territory, which caused the rate to fall from 38.7 cases/100,000 inhabitants, in 2006, to 30.9 cases/100,000 inhabitants, in 2015, and from there to 35.28 cases per 100,000 inhabitants, in 2021.¹⁶

Continuing global efforts to control TB, the Sustainable Development Goals (SDGs) agenda succeeds that of the Millennium Development Goals (MDGs) and is more comprehensive and less individualistic, placing care for TB and other diseases within the objective of ensuring universal health coverage by strengthening the Primary Health Care network. Brazil's achievement in the MDGs served as a basis for adherence to the global target of reducing deaths by 95% and the incidence rate of the disease by 90% by 2035.¹⁷

Even with the reduction in TB cases in Brazil, Pernambuco is still the only northeastern state with a TB detection rate above 34 cases/100,000 inhabitants, exceeding the national average. Along with other Brazilian states located mainly in the North region, it continues to negatively contribute to the failure to achieve global TB control goals.¹⁶

It can be seen that Pernambuco is moving in the opposite direction to other states in the northeast. Although far from achieving the SDGs, in Ceará, for a similar period, a decrease in incidence rates was observed, even though the problematic issue of the concentration of the highest rates in the MR remains.¹⁸In Paraíba, spatially similar findings were observed for the same period in the population under 15 years of age.¹⁹ For the North region, a study carried out in Belém (PA) showed an incidence of 97.5/100 thousand inhabitants, well above the national average.²⁰

Within this scenario, the significant increase in the TB detection rate between the two five-year periods may be related, in part, to the economic crisis of 2015, which occurred in Brazil, in which the Gross Domestic Product (GDP) fell by 3.62%, suffering the worst result in 25 years. This drop in GDP directly impacts Brazilian families, with a drop in purchasing power and other social factors, generating an increase in health needs and demand for public services, while the expansion of countries' health policies follows economic growth and declines in times of crisis and recession.²¹ This vicious cycle may have impacted TB numbers in Pernambuco.

Bringing health data to this situation, a study is cited that found that the implementation of regionalized health surveillance in Pernambuco was incomplete for the first MR.²² This fact implies the harm to the planning and promotion of strategies appropriate to the different realities of the municipalities, as would be the case of TB in Pernambuco.

The fact that TB is a multifactorial disease, with a biological cause, but whose expression in populations goes beyond individual determinants (smoking, alcoholism, etc.), clinical and socioeconomic factors (HIV co-infection, poverty, malnutrition, etc.), also partly explains the situation of the disease in Pernambuco. In this case, it is worth noting that the state is one of the most unequal in the country, and that the capital, Recife, was recently classified as the one where the poor are the poorest, which is reflected in neighboring municipalities.^{18,19} Additionally, there is the fact that the Metropolitan Regions where the highest income ratios were recorded between the poorest and the richest, in ascending order, were Recife (21.0), Salvador (21.3), João Pessoa (21.6), Natal (23.9) and Aracaju (24.4).²³

Hence, addressing the characteristics of Brazilian metropolitan regions, especially in the northeast, is imperative. Since its inception, the MRR has remained marked by social inequities. The process of economic dynamism with road improvements and industrialization that began in the 1980s and 1990s was not accompanied by positive social changes. Thus, Recife and its surrounding areas, despite economic improvements, have stabilized within the condition of an incomplete, peripheral and unequal regional metropolis.²⁴

This issue deserves to be addressed globally. According to a 2019 United Nations report, around 1% of the richest Brazilians hold a third of the country's income, resulting in the second highest concentration of income in the world. Brazil's historical trajectory is biased towards protecting people at the top of the economic pyramid and making the lower-income population extremely vulnerable. In short, this situation acts as a filter, preventing any economic growth from being converted into social benefits. Applying these facts to TB, since it is a disease with a social background, it can be concluded that, if government action is not targeted at the most global determinants, TB control will always be far from happening.²⁵

Spatial analysis reinforces what has already been explained, showing that TB tends to persist in areas where population growth is not accompanied by urban development, as occurs in most metropolitan regions in northeastern Brazil that suffer chronically from social vulnerability. The municipalities in Pernambuco that presented the lowest TB detection rates were Santa Filomena (Macro 4), Ibirajuba (Macro 2) and Terezinha (Macro 3).These last two did not show any cases of TB in the second five-year period (2016-2020). All three municipalities with the lowest rates are located in the countryside of the state, which may demonstrate a relationship of locomotion, employment opportunities and study in the capital, thus resulting in lower transmissibility compared to MR 1, which encompasses the highest rates of detection of the disease.

The fact that TB is a multifactorial disease, with a biological cause, but whose expression in populations goes beyond individual determinants (smoking, alcoholism, etc.), clinical and socioeconomic factors (HIV co-infection, poverty, malnutrition, etc.), also partly explains the situation of the disease in Pernambuco. In this case, it is worth noting that the state is one of the most unequal in the country, and that the capital, Recife, was recently classified as the one where the poor are the poorest, which is reflected in neighboring municipalities.^{18,19}

As a limitation of this study, the use of secondary data, although useful, provides information of a general nature that, due to underreporting, may result in incompleteness of publicly available data. To mitigate the limitations, cross-validation strategies were adopted, comparing information from different sources to correct discrepancies. In addition, the application of statistical methods allowed us to correct gaps in the data, reinforcing the validity and reliability of results.

It is considered that this study was carried out before the pandemic period, when it would have been necessary to address other determining factors in the TB situation. In this case, the term "syndemic" should be cited as a process of synergistic interaction between two or more diseases, in which the effects are mutually potentiated. In the case of TB, during the pandemic period, globally and nationally, it was observed that the number of people with undiagnosed and untreated TB increased, resulting first in a greater number of deaths from TB and more community transmission of the infection and then, with some delay, a greater number of people developing TB.⁸ The importance of this study is highlighted in the sense that it was carried out without the bias of the pandemic, in which there was a great reduction in both the general

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economic gain and the supply of health services, which could be compromising.

Considering the concept of One Health, TB control requires contextual actions to improve people's general living conditions. In an unequal state like Pernambuco, this goal is difficult to achieve. Social support, which is so necessary in this situation, exists in Brazil, but it is intended for people in social vulnerability in general, with no specific support for people living with TB.

It is concluded that TB remains a serious public health problem in Pernambuco, especially in the MRR. The findings of this study help to perpetuate an image of TB as being linked to neglected and stigmatized segments that lack effective actions to eliminate the disease. Space-related information can support targeted and evidence-based decisions, such as monitoring data quality to improve the information system or establishing integrative social protection policies for key populations. Macroeconomic policies, mainly considering better income distribution, should be the government's target.

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AUTHORS' CONTRIBUTIONS

Gisele Matias de Freitas contributed to bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review and statistics. **Louisiana Regadas de Macedo Quinino** contributed to project management, bibliographic research, introduction, methodology, discussion, interpretation and description of results, and review. **Helena Manhães de Vasconcellos**contributed to methodology, interpretation of results, preparation of tables, review and statistics. **Isabel Soares Diniz Oliveira** contributed to methodology, interpretation of results, preparation of tables, review and statistics.

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