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Original Article

Effect of social development in reducing tuberculosis mortality In northeastern Brazil areas

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Abstract
Introduction: Tuberculosis (TB) is the primary cause of death among infectious diseases affecting groups in extreme poverty. Social improvements could reverse this situation in Brazil. This study aims to demonstrate the spatial relationship between social development (SD) and TB mortality in Natal, a city in northeastern Brazil.
Methodology: Ecological study. The study population comprised TB deaths recorded in the Mortality Information System between 2008 and 2014. The units of analysis were 59 human development units (HDUs). Raw and smoothed mortality rates were calculated using the global empirical Bayes method. Primary components analysis was used to develop the SD indicators. An association between TB mortality and SD was verified using multiple linear regression analysis. Spatial autocorrelation was verified using models with global spatial effects. Analyses were performed using Statistica version 12.0, ArcGIS version 10.2, Statistical Package for the Social Sciences version 20.0, and OpenGeoDa 1.0.1. The significance level was established at 5% ($p < 0.05$).
Results: The TB mortality rate with non-random spatial distribution ranged between 0.52 and 8.90 per 100,000 inhabitants. The spatial lag model was chosen because it presented the highest log-likelihood value, lowest AIC, and highest R2. A negative association was found between TB mortality and SD ($R^2 = 0.207$; $p = 0.03$).
Conclusions: The results show a negative association between TB mortality and the high SD indicator. This study can support decision-making in terms of collective projects within public health in order to link the health field to other sectors, aiming for social well-being and human development.

Key words: tuberculosis; mortality; social development; spatial analysis.

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Introduction

Tuberculosis (TB) is one of the primary causes of death from infectious disease in the world [1], mainly due to HIV co-infection, unequal social development (SD), and limited access to health services. SD involves the progression of society in terms of its quality of life and social capital, as well as the methods or resources that would be used to create conditions for all people to develop their own capacities and resources [2].

The elimination strategy (End TB Strategy) proposal by the World Health Organization (WHO) in 2015 began a new phase, mainly in the 30 high-burden countries (TB-HBC), which concentrate 87% of all TB cases in the world. Of the 9 million people who became sick in these countries in 2015, only 6 million were properly diagnosed, so that 3 million individuals have not yet been diagnosed and are at risk of dying [3]. There is therefore a greater circulation of TB-causing bacillus in contexts of low SD where TB patients live, a fact that increases the exposure and risk of the population in general [4].

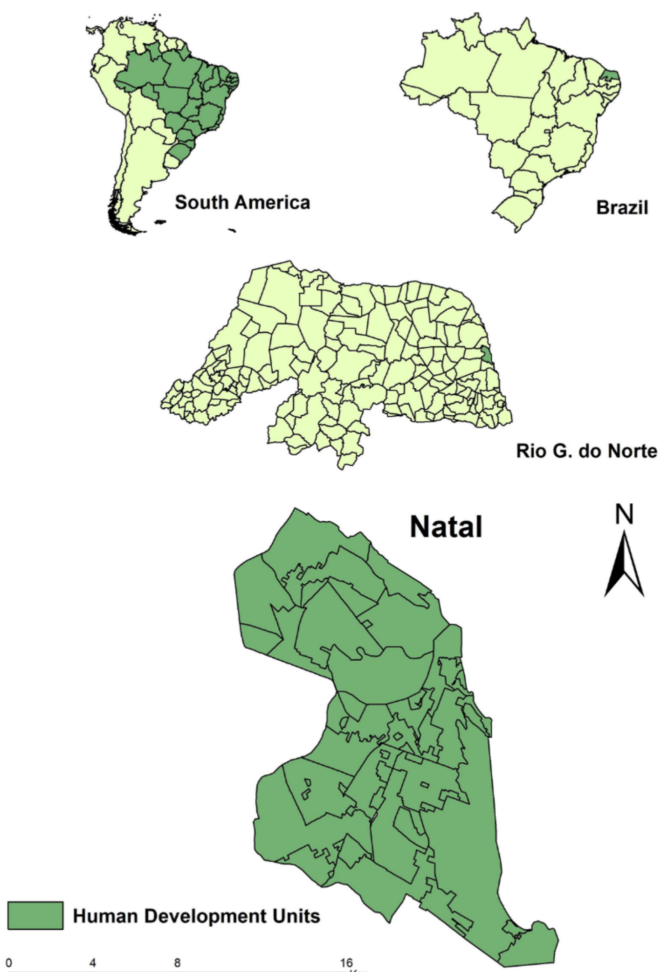
More than 95% of TB-related deaths occurred in the TB-HBC, which are countries with low SD [5,6]. Studies [7,8] stress that populations living under these conditions face difficult access to quality health services, which results in delayed diagnosis, non-adherence to treatment, and, in the worst scenario, death. Public policies that encourage improved SD therefore effectively influence the occurrence and dynamics of TB in a given area or social context. The

End TB Strategy thus embodies not only new diagnostic technologies (more sensitive and less demanding tests, applicable in contexts where resources and equipment are extremely scarce), but also the adoption of universal health systems and bold policies intended to improve SD [9].

Studies have been conducted in Brazil since the publication of the End TB Strategy to verify the effect of social protection programs launched in the country to control or break the TB spread circle [10]; however, few sought to understand the impact or changes caused by these programs specifically in vulnerable territories through geospatial intelligence [11]. Among the studies that used geospatial intelligence methodology [12], none used indexes that included SD in its scope and complexity.

The United Nations Development Program proposed a new division of Brazilian metropolises according to the criterion of containing more homogeneous areas and, consequently, making their indexes for more reliable and consistent evaluations, called human development units (HDUs) [13]. These regions have made it possible to understand key SD issues, such as inequality, gender disparity, and poverty, that can impact TB morbidity and mortality, but few studies use this new division.

Figure 1. Localization of the study setting, Natal, Rio Grande do Norte, Brazil and Latin America**.**



With regard to geospatial intelligence, the specificity in each scenario requires geostatistical application and analysis that allow studies aimed at specific territories or groups, and, in this perspective, the investigation can become a reference and be replicable in other areas or territories where TB is still a major challenge. Therefore, this study aimed to demonstrate the spatial relationship between SD and mortality from TB in HDUs in a city in north-eastern Brazil.

Methodology

Study design and setting

This is an ecological study, in which the exposure and outcome were measured at the population or community level. In other words, data were aggregated by area [14]. The study was carried out in Natal, the capital of Rio Grande do Norte, Brazil, with an area of 169.9 km², 810,870 inhabitants in 2010, and a demographic density of 4,805,24 inha./km².

Geographically, Natal is divided into 36 neighbourhoods, five health administrative regions, 911 census sectors, and 59 HDUs [15,16]. The HDUs were designed to generate more homogeneous areas regarding socioeconomic conditions, with the objective of portraying intra-municipal inequalities more proficiently [16]. In 2019, there were 51 cases of TB per 100,000 inhabitants, and mortality was 3.6 cases per 100,000 inhabitants [17] (Figure 1).

Population, source of information, and selection criteria

The study involved TB cases that progressed to death (as primary cause, according to the International Classification of Diseases, version 10 (ICD10), with codes from A15.0 to A19.0) and were reported to the Mortality Information System (MIS) from 2008 to 2014, for people who lived in the urban area of the city.

Data analysis

The first stage consisted of geocoding addresses by standardizing and matching addresses to TB-related deaths with the information contained in the digital map of the StreetBase® road segment in UTM/WGS84, using TerraView version 4.2.2. The data were analyzed for the spatial analysis according to the area, using the

HDUs. TB mortality was calculated for the period under study (TxTBM), dividing the total number of standardized deaths $\sum 0$ (by the standard population in the middle of the period $\sum Pop$ the urban population of each HDU in 2010 (year corresponding to the middle of the study period, as well as the year of the last population census in Brazil carried out by the Brazilian Institute of Geography and Statistics) [15] — multiplied by 100,000 and then multiplied by 1/7, which refers to the study period (2008 to 2014), as shown in the formula below [14]:

$$TxTBM = (\frac{\sum 0}{\sum Pop}) \times \frac{1}{7} \times 100.000$$

In order to minimize the instability of raw rates and eliminate random fluctuation due to the existence of HDUs with small populations, mortality rates were smoothed using the empirical Bayes method. This method calculates a weighted average between the gross rate of each HDU and the global rate of the municipality, generating a second rate [18].

The Global Moran's I was used to measure the spatial autocorrelation of TB mortality rates [18,19], using the Statistical Package for the Social Sciences (SPSS) version 20.0 and OpenGeoDa 1.0.1. The choropleth maps were built using ArcGis 10.2. For the construction of the SD indicator, we used the information base of the HDUs of the *Atlas of Human Development of the Brazilian Metropolitan Regions* [15]. The variables used are listed in Table 1.

The principal components analysis (PCA) technique was used to construct the SD indicators [20,21]. Kaiser's criterion was used for the selection of indicators [22]. These techniques were processed in Statistica 12.0. Bivariate correlation analysis was performed between SD and TB mortality. The correlation plot of SD and TB mortality in the 59 HDUs was built using Statistica 12.0.

Multiple linear regression analysis was applied to analyze the impact of SD in reducing TB mortality in the areas included in this study [23]. The dependent variable was mortality rate per TB, and the independent variables or covariates were indicators generated from the PCA after each of the covariates (SD indicators) was standardized. An exploratory analysis was performed with the standardized covariates to evaluate the presence of outliers using dot plot charts. The collinearity between the covariates was analyzed using variance inflation factors (VIFs) calculation [24]. The homogeneity of the residuals was evaluated using the spread-level plot. The spatial autocorrelation of the final model residuals was evaluated with Moran's I test, using a neighborhood matrix by contiguity [25].

When spatial autocorrelation was verified, we resorted to models with global spatial effects, which were designed to capture the structure or spatial correlation in only one parameter and add it to the linear regression model [26,27]. The spatial lag model was used, which attributes the ignored spatial correlation to the dependent variable, as well as the spatial error model, which considers the spatial effects as an element to be removed [27].

Table 1. Dimensions and eigenvectors of the original variables for the construction of social development indicator (SD-) (SD+), Brazil (2008-2014).

Dimension	Variables	Code	SD-	SD+
Education	Illiteracy rates in the 18 years old or older population	V1	0.236072	-0.162877
	Percentage of 18 years old or older population with complete middle school	V2	**-0.301001**	0.076610
	Percentage of 25 years old or older population with complete middle school	V3	**-0.300480**	0.059820
	Percentage of 25 years old or older population with a bachelor's degree	V4	-0.266357	-0.218910
Income	Proportion of the poor (proportion of individuals with a per capita household income equal to or lower than BRL140.00 per month, from August 2010).	V5	**0.293603**	-0.213293
	Percentage of total income earned by 20% of the population with the lowest per capita household income	V6	0.213651	**0.592325**
	Percentage of total income earned by the 20% of the population with the highest per capita household income	V7	-0.254491	**-0.377776**
	Proportion of people vulnerable to poverty	V8	**0.299792**	-0.142353
	Percentage of total income earned by the 10% of the population with the highest per capita household income	V9	-0.242032	**-0.342462**
	Unemployment rate in the 18 year old or older population	V10	**0.290971**	0.105002
Living conditions	Percentage of the population living in households with a bathroom and running water	V11	-0.246533	**0.278188**
	Percentage of the population living in urban households with garbage collection service	V12	-0.239177	**0.303390**
	Percentage of the population living in households with electricity	V13	-0.239396	0.240100
	Percentage of the population living in a household with density of more than 2 people per bedroom	V14	**0.295643**	-0.037304

We chose the model with the highest log-likelihood value, which can be interpreted as the test of a hypothesis that compares goodness of fit between two models [28]. The Akaike information criterion (AIC) compares the quality of a set of statistical models [29]. Finally, the residuals of the selected model were analyzed using Moran's I to verify whether spatial autocorrelation was eliminated after the spatial model was utilized.

Ethical aspects

The Institutional Review Board at the University of São Paulo at Ribeirão Preto, College of Nursing, approved the study (certificate of ethical assessment no. 41398915.6.0000.5393).

Results

A total of 154 TB-related deaths were identified, eight (5.2%) of which were excluded due to a lack of information concerning addresses. Of the 146 remaining cases, 141 (91.55%) were geocoded by address. Sixty-eight (48.2%) were processed using

Figure 2. TB mortality in a city in the northeast of Brazil (2008-2014).

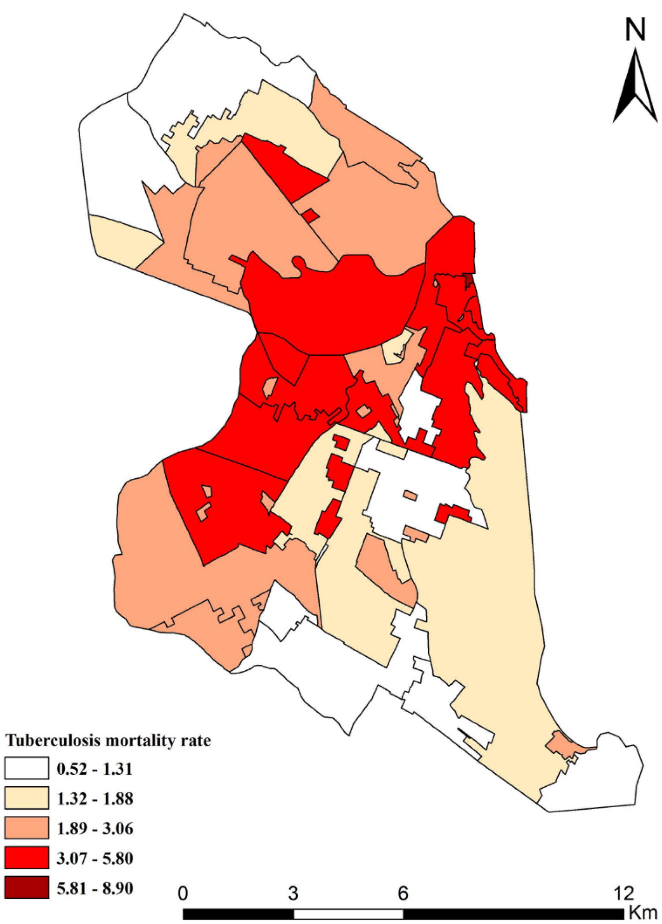
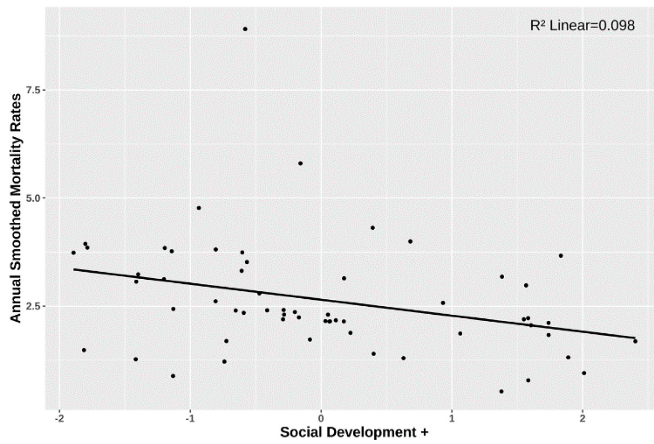


Figure 3. Correlation plot of social development indicator (SD-) (SD+) and TB mortality in n a city in the northeast of Brazil (2008-2014).



Terraview, and 73 (51.8%) were processed using Google Earth. Regarding the number of deaths for each year of the study, we found 30 cases in 2008, 21 cases in 2009, 22 cases in 2010, 20 cases in 2011, 14 cases in 2012, 18 cases in 2013, and 16 cases in 2014 (Supplementary Table 1).

Figure 2 presents the smoothed TB mortality rate. Higher rates in the distribution of mortality were identified in the east and west districts. The HDUs located in the north and south of the city presented the lowest rates. The Supplementary Figure 1 shows the plots of outliers of the Gross rates and Global empirical bayesian rates. The result of Moran's I ($I = 0.324$, $p = 0.002$) revealed a spatial autocorrelation for TB mortality.

Regarding the choice of variables used to build SD indicators, they were grouped into the dimensions of education, income, and housing conditions and were based on the concept of SD adopted in the study, as well as determining factors of TB and its mode of transmission.

When PCA was applied, two indicators of SD were constructed: the first retained 76.12% of the variance of the set of data, and the second accumulated 9.18%, totaling 85.30% of the variance and presenting eigenvalues above one, according to the criteria of the study. The results obtained from PCA (Table 1) considered the covariance matrix.

It is possible to observe that the first indicator presented more characteristics of low SD (SD-), represented mainly by the variables -V2, -V3, V5, V8, V10, and V14 (values above 3 are highlighted); thus, the higher and more positive the score, the worse the SD of the HDU. For indicator 2, the variables demonstrated high SD (SD+), comprised mainly of the variables V6, V7, V11, and V12; thus, the more positive the score, the greater the SD.

The distribution of the variables for each dimension of SD is displayed in Table 1, with its respective contribution of variance.

Figure 3 shows correlation graphs between the SD indicators (SD + and SD-) and TB mortality rates.

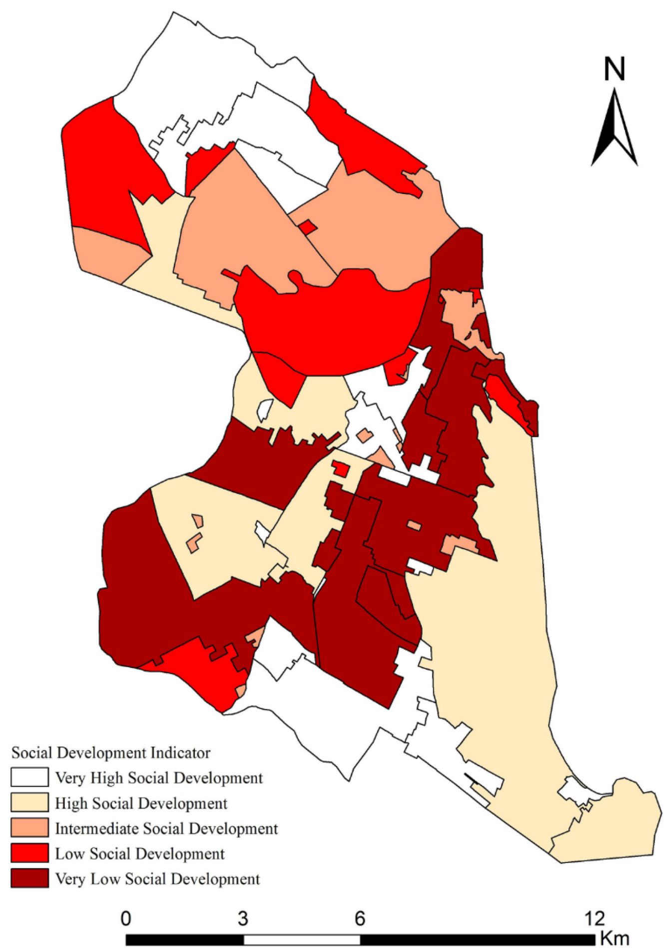
The multiple linear regression model revealed a statistically significant relationship between the SD indicator (SD+) and TB mortality rates ($R^2 = 0.098$; $p = 0.0156$). Analysis of the model's residuals using Moran's I ($I = 0.238$, $p = 0.008$) revealed spatial autocorrelation. The linear regression model was therefore not appropriate, considering the need to introduce spatial effects. For this reason, spatial lag and spatial error models were adopted.

As only the model with the SD indicator (SD+) was statistically significant in the previous stage, it was introduced into the spatial regression model. The spatial error model showed no significant relationship between SD+ and TB mortality. For results obtained with spatial lag, R^2 was 0.207, the log-likelihood value was -94.217, and AIC was 194,436. Table 2 presents the main results of both models. The spatial lag model was chosen because it presented the highest log-likelihood value, lowest AIC, and highest R^2.

Table 2 also shows a negative association between TB mortality and the SD indicator (SD+) in the final model, meaning that an increase of one unit (one standard deviation) in this indicator decreased the mortality rate by approximately 0.3 deaths per 100,000 inhabitants.

The classification map of HDUs (Figure 4) presents the most and least critical areas based on the SD indicator. The SD was classified in quintile according to values of very low SD, low SD, intermediate SD, high SD, and very high SD. In comparison to the map of TB mortality rates distribution (Figure 2), most of the areas with the highest mortality rates coincide with the HDUs classified as having a low or very low level of SD. When Figure 2 is compared to Figure 4, the critical areas in terms of SD and the highest mortality rates are located in the east and west regions.

Figure 4. Map of social development in a city in the northeast of Brazil (2008-2014).



Discussion

The results showed a pattern of non-random distribution of TB mortality, which was confirmed by geospatial intelligence techniques, such as the Moran Index. The results confirmed, therefore, that TB mortality is an event that has spatial dependence, which means that its occurrence depends on where the

Table 2. Regression models of impact of social development on TB mortality. Natal, Brazil (2008 - 2014).

	Linear regression model		Final model (spatial lag)		
	Estimate	P-value	Estimate	P-value	Confidence intervals
Intercept	2.647	0.000	1.766	0.000	
Social development (SD-)	0.067	0.194	-	-	-0.25 – 0.156
Social development (SD+)	-0.369	0.015	-0.296	0.030	-0.426 – -0.171
Rho (ρ)	-	-	0.334	0.021	
R^2	0.093	-	0.207	-	
Log likelihood	-96.414	-	-94.217	-	
AIC	198.828	-	194.436	-	

individual lives. From a geostatistical perspective, the mortality rate in a region is more similar to the rates in its neighboring locations than the other areas in the region under study [30].

Important social changes have taken place in the last two decades in Brazil [31], but there is still an unequal distribution of risks and diseases in the different population groups. Disparities in the development of TB mortality led to variation in the indexes of the city's regions. The results of this study are therefore in agreement with those reported by both Brazilian [28,32] and international studies [5,33,34], showing the influence of socioeconomic factors on the occurrence of TB and deaths, indicating an unequal distribution of TB mortality and forming clusters among population groups with low SD.

A study [6] conducted in Latin American countries and the Caribbean reported the following determinants of mortality: women's literacy, basic sanitation, running water and sanitary sewer, and nutritional status. These results corroborate this study's findings. Another investigation [32] reported a relationship between TB mortality and social inequality expressed by the number of illiterate persons, heads of household with up to three years of schooling, and an income of up to twice the minimum wage.

A global study [35] reported that expenditure on social protection programs, which are intended to promote SD, was inversely related to the prevalence, incidence, and mortality of TB. A study [36] conducted in European countries concluded that association with TB mortality was actually stronger in areas where less than 11% of the gross domestic product (GDP) was devoted to social protection, showing the need for greater financial investment in TB control.

Studies in Brazil in general have focused on the *Bolsa Família* Program (family benefits) [10] as a social protection measure; however, this is a focused and selective policy, the objective of which has an emergency nature in the sense of removing people from extreme poverty, which is important in the short term (i.e., temporary and static) but does not translate into a change in SD. It was thus important in this study to consider variables that expressed not only eradication of poverty, but also the generation of jobs and income, as well as urban and social harmony. This was a positive point of this study and can be used in future studies to measure the impact of SD on how TB progresses, in order to support the implementation of universal social policies.

As the first to show the impact of SD on reducing TB mortality, this study is interesting in terms of advancing knowledge and reaffirming the End TB Strategy with regard to promoting bold policies and universal systems of social policies. It reports the progress of Brazilian social policies; however, with current fiscal and economic crises and austerity policies faced by the country, many advancements reported here may no longer be true in the future, which will certainly reverberate on TB mortality rates, as has happened in Europe [37].

In terms of the relevance of the methodology applied and its validity, the use of geographic information systems (GIS) and geospatial intelligence techniques allowed to analyze the spatial distribution of TB mortality and its association with SD, observing a huge inequality between the territories of the same city, with the presence of worse living conditions in some areas when compared to others. This indicates disparity and inequality in health. In these areas, identified as more problematic, TB control actions should be intensified and added to comprehensive care and intersectoral actions [38].

The study presented relevant evidence for the intensification of TB management in the territories identified and for improving the detection of people with TB and their contacts by overcoming cultural, economic, organizational, and geographical barriers to equity and the early search for care. In addition, highlighting more problematic areas can contribute to community development and civic organizational activities in these areas, contributing to health and community services to identify TB among risk groups and mobilize them to seek health services, as suggested in the literature [39].

An issue of the study was transforming a subjective construct, SD, into a metric variable in order to introduce it into a regression model, since it is an abstract concept and subjective. However, when the broader and comprehensive indexes from HDUs were used, this ensured more reliable and consistent results [40]. The use of PCA was also pertinent because the variables were highly correlated, and when the method was implemented, original variables were transformed into principal components, which brought variance relevant for the composition of new explanatory variables of SD. This procedure allowed to study these abstract variable with more consistency and improve the stability of regression indexes [21].

We verified that a borderline R^2 (0, 09) was found when the multiple linear model was applied. Nevertheless, the spatial dependency of residuals in this model led to the conclusion that it was not sufficient to explain TB mortality. When spatial factors were included through models with global spatial effects, a significant improvement was therefore verified in the explanatory potential of the independent variable, an improvement of 20% ($R^2 = 0.207$), which confirmed the hypothesis that one not only has to test SD globally, but must also consider geographical localization.

Some authors [26] note that the introduction of spatial factors into the analysis of a given disease may reveal new meanings when compared to traditional models employed in epidemiology, as events such as TB mortality are not random or independent, but rather depend on the characteristics of the affected areas. TB mortality is thus not only a social issue, but depends on the way communities or areas respond to the problem, in addition to the available social and health resources [41]. However, even if the insertion of spatial effects has significantly improved the explanatory potential of TB mortality, it should be considered in future studies that other unmeasured factors are related to TB mortality in the municipality.

This study's limitations include the fact that secondary data were used, so the way data were recorded may have led to bias. Another limitation involves the information system restrictions, which did not reveal whether TB deaths occurred before or after a diagnosis was established. It would be interesting to verify this information in future studies. Another limitation of the study is the size of the studied population, since deaths from TB tend to be a rare phenomenon when compared to other health conditions like diabetes and hypertension. However, this situation did not influence the study's findings, since the authors used adequate methods to analyze the amount of observations.

Conclusions

The results of this study show a non-random pattern of TB distribution with significant spatial autocorrelation. An association was found between SD and TB mortality, showing that the better the SD, the lower the number of deaths caused by TB. This study also reveals the importance of taking into account the spatial component to understand the occurrence and distribution of TB mortality, since the hypothesis of a spatial association between TB mortality and SD has been confirmed.

This study improves the understanding of the impact of social determinants on TB mortality, which supports decision-making concerning collective projects in the public health sphere, linking the health sector to infrastructure, housing, social welfare, and civil society itself, in order to implement effective actions intended to boost SD and end TB.

Acknowledgements

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Authors' contributions

AARQ and RAA participated in the conception of the study, as well as the analysis and interpretation of the data and the wording of the article. FCN participated in the analysis and interpretation of the data and a critical review of the intellectual content. TZB, ATIB, and MCCG were involved in revising the manuscript critically for important intellectual content. DTS, MAMA, LSA, MY, TCS, and PFP participated in drafting the manuscript, reviewing the literature, and the relevant critical review of the intellectual content. All the authors have read and approved the final manuscript.

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Annex – Supplementary Items

Supplementary Table 1. Population and number of annual cases of death from tuberculosis in Natal-RN, Brazil.

Code UDH	Population	Cases 2008	Cases 2009	Cases 2010	Cases 2011	Cases 2012	Cases 2013	Cases 2014
1240810200001	18,999	1	1	1	0	1	0	1
1240810200018	2,794	0	0	0	0	0	0	0
1240810200019	27,471	0	0	0	0	0	0	1
1240810200002	14,371	1	0	2	1	1	1	0
1240810200020	29,883	0	0	1	0	1	0	0
1240810200021	11,971	0	1	0	0	0	0	1
1240810200022	14,875	0	0	0	0	0	0	1
1240810200023	3,658	0	0	0	0	0	0	0
1240810200024	906	0	0	0	0	0	0	0
1240810200025	2,522	0	0	0	0	0	0	0
1240810200026	464	0	0	0	0	0	0	0
1240810200010	7,561	0	2	0	0	0	0	0
1240810200027	328	0	0	0	0	0	0	0
1240810200028	965	1	0	1	1	1	0	0
1240810200029	345	0	0	0	0	0	0	0
1240810200003	4,799	1	0	1	0	0	0	0
1240810200030	17,857	0	1	0	2	1	3	2
1240810200031	20,983	1	1	0	1	0	3	0
1240810200032	13,935	0	0	0	0	0	0	0
1240810200033	5,039	1	0	0	1	0	0	0
1240810200034	675	0	0	0	0	0	0	0
1240810200035	8,389	1	1	0	0	0	0	1
1240810200011	7,083	0	0	0	0	0	0	0
1240810200036	1,062	0	0	0	0	0	0	0
1240810200037	3,079	0	0	1	0	0	0	0
1240810200038	1,333	1	0	0	0	0	0	0
1240810200039	1,079	0	0	0	0	0	0	0
1240810200004	28.567	0	0	0	0	0	0	0
1240810200041	48.542	0	0	0	1	1	2	2
1240810200042	16.105	1	0	1	0	0	1	0
1240810200043	1.077	0	0	0	0	0	0	0
1240810200044	1.282	0	0	0	0	0	0	0
1240810200045	25.783	2	1	1	3	0	2	0
1240810200012	1,415	0	0	0	0	0	0	0
1240810200046	29.206	3	1	0	1	1	1	0
1240810200047	1,156	0	0	0	0	0	0	1
1240810200048	31,245	3	0	0	1	2	1	0
1240810200049	53,158	5	3	4	2	2	0	1
1240810200050	1,263	0	0	0	0	0	0	0
1240810200005	43,331	1	0	1	1	0	0	0
1240810200051	2,457	0	1	0	0	0	0	0
1240810200052	665	0	0	2	0	0	0	0
1240810200053	60,939	3	1	0	1	0	1	1
1240810200054	1,877	1	0	0	0	0	0	0
1240810200013	36,697	0	1	1	1	0	0	0
1240810200055	11,711	0	0	0	1	0	0	0
1240810200056	49,745	1	3	1	0	1	0	3
1240810200057	1,317	0	0	0	0	1	0	0
1240810200058	14,594	0	0	0	0	0	1	1
1240810200059	54,545	0	2	3	0	0	1	0
1240810200060	975	0	0	0	0	0	0	0
1240810200006	9,446	0	1	0	0	1	0	0
1240810200007	6,618	0	0	0	1	0	0	0
1240810200008	20,853	2	0	1	1	0	1	0

1240810200009	1,173	0	0	0	0	0	0	0
1240810200014	302	0	0	0	0	0	0	0
1240810200015	1,663	0	0	0	0	0	0	0
1240810200016	16,712	0	0	0	0	0	0	0
1240810200017	6,894	0	0	0	0	0	0	0

Supplementary Figure 1. Tuberculosis mortality in Natal, Brazil (2008-2014). Gross rates (**A**) and Global empirical Bayesian rates (**B**).