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Spatiotemporal pattern and factors related to childhood tuberculosis

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Padrão espaço-temporal e fatores relacionados à tuberculose na infância

Patrón espacio-temporal y factores relacionados con la tuberculosis en la infancia

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ABSTRACT

Aim: To identify the spatiotemporal pattern of childhood tuberculosis and the sociodemographic factors related to it.
Method: This is an ecological study, which used the municipalities of the state of Ceará as units of analysis. The Notifiable Diseases Information System was used as a data source from January 2001 to December 2017. It was conducted a descriptive analysis of the characteristics of the cases, the temporal and spatial pattern of the incidence of the disease and regression with sociodemographic indicators.
Results: An average incidence of 3.48 cases/100 thousand inhabitants was identified, with a reduction of 5.7% during the period 2003-2017 ($p<0.001$). The following were related to childhood tuberculosis: proportion of the population in households with piped water ($\beta=0.05$), proportion of the population in households with density >2 ($\beta=0.09$) and number of female heads of household with children under 15 years of age ($\beta=0.0003$).
Conclusion: Indicators of housing conditions and vulnerability were related to childhood tuberculosis.
Keywords: Tuberculosis. Child. Adolescent. Epidemiology. Spatial analysis.

RESUMO

Objetivo: Identificar o padrão espaço-temporal da tuberculose na infância e os fatores sociodemográficos a ela relacionados.
Método: Estudo ecológico, que utilizou como unidades de análise os municípios do estado do Ceará. Utilizou-se como fonte de dados o Sistema de Informação de Agravos de Notificação durante janeiro de 2001 a dezembro de 2017. Realizou-se análise descritiva das características dos casos, do padrão temporal e espacial da incidência da doença e regressão com indicadores sociodemográficos.
Resultados: Identificou-se incidência média de 3,48 casos/100 mil hab., com redução de 5,7% de durante o período de 2003-2017 ($p<0,001$). Foram relacionados à tuberculose na infância: proporção da população em domicílios com água encanada ($\beta=0,05$), proporção da população em domicílios com densidade >2 ($\beta=0,09$) e número de mulheres chefes de família e com filhos menores de 15 anos ($\beta=0,0003$).
Conclusão: Indicadores de condições de moradia e vulnerabilidade foram relacionados a tuberculose na infância.
Palavras-chave: Tuberculose. Criança. Adolescente. Epidemiologia. Análise espacial.

RESUMEN

Objetivo: Identificar el patrón espacio-temporal de la tuberculosis en la infancia y factores sociodemográficos relacionados con ella.
Método: Estudio ecológico, que utilizó municipios del estado de Ceará como unidades de análisis. Se utilizó el Sistema de Información de Enfermedades de Declaración Obligatoria de enero 2001 a diciembre de 2017. Se realizó análisis descriptivo de las características de los casos, patrón temporal y espacial de la incidencia de enfermedad y regresión con indicadores sociodemográficos.
Resultados: Se identificó una incidencia promedio de 3,48 casos/100 mil hab., con una reducción de 5,7% durante el período 2003-2017 ($p<0,001$). Se relacionaron con la tuberculosis en la infancia: proporción de población en viviendas con agua corriente ($\beta=0,05$), proporción de población en viviendas con densidad >2 ($\beta=0,09$) y número de mujeres jefas de hogar con hijos menores de 15 años ($\beta=0.0003$).
Conclusión: Los indicadores de las condiciones de vivienda y vulnerabilidad se relacionaron con la tuberculosis infantil.
Palabras clave: Tuberculosis. Niño. Adolescente. Epidemiología. Análisis espacial.

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INTRODUCTION

Tuberculosis (TB) is still a global public health problem. Globally, the World Health Organization (WHO) points out that, in 2020, about 5.8 million people became ill and 1.3 million died. This data places the disease as one of the main causes of death by infectious agent on a global scale[1]. In Brazil, this problem must also be highlighted, since it is among the 20 countries that carry 84% of the global burden of the disease. According to data from the 2021 TB Epidemiological Bulletin, in 2020,66,819 new cases were diagnosed in Brazil, resulting in an incidence coefficient of 31.6 cases/100,000 inhabitants[2]. There is a marked decrease in the notification of TB cases from 2020 onwards due to the COVID-19 pandemic, which express considerable underreporting of the real burden of the disease in Brazil and worldwide[1–2].

This disease mainly affects adults living in developing nations. However, children can also be infected and become ill with TB, and this public is often neglected. It is known that, in 2020, childhood TB (defined by the WHO as TB in individuals aged <15 years) occurred in 11% of all cases of the disease[1]. Globally, India has the highest number of cases in this age group, with an estimated 306,000 cases for 2020. It is followed by Indonesia (n=99,000), Nigeria (n=77,000), Pakistan (n=74,000) and the Philippines (n=73,000). Brazil occupies the 30th position with an estimated 4,400 cases[1].

Several factors can contribute to the contagion of the TB bacillus in childhood. It is noteworthy that contact with adults in areas with a high prevalence of active TB can lead to the appearance of a state called Latent TB Infection (LTBI), especially when it occurs in small households, with poor ventilation, high household density and low lighting[3]. Even though 90% of people do not get ill after contact with the bacillus, the progression from the latent to the active phase of the disease is due to factors such as age, nutritional status, BCG vaccination and immune status[3].

It is noteworthy that, in children, TB manifests more commonly in extrapulmonary forms, especially in children under five years of age. In 2016, 10% of all new TB cases in the world were reported in children and the particularities of diagnosis, treatment and prevention of the disease have only recently gained prominence in the scientific community[3].

Thus, although childhood TB is frequent, it may be underreported due to difficulties in diagnosis, as the clinical picture and radiological tests cannot be specific for the presence of the bacillus in this group. In addition, children up to 10 years of age have difficulties in expectorating their sputum, compromising the results of sputum smear microscopy and making early screening for the disease difficult[4].

Given the above, it is noticed that in Brazil there is a growing increase in morbidity among children, which leads to the need to develop studies that address TB in this specific group[5]. Furthermore, as the disease is associated with the population's living conditions and the social determinants of health, knowing how it is distributed in time and space can be fundamental for the adoption of more effective health strategies for this public.

In view of this, health geoprocessing tools can be used in this situation to better visualize the situational context of childhood TB. Spatial analysis in health also enables to describe the behavior of the disease in each geographic unit represented on a map, providing a better understanding about the regions that need more attention, in addition to facilitating the planning of actions and determining the impact of programs derived from actual public policies[6]. Thus, this study aims to identify the spatiotemporal pattern of childhood tuberculosis and the sociodemographic factors related to it.

METHOD

This is an epidemiological study of ecological type, which used municipalities in the state of Ceará as units of analysis. The state has the eighth largest population in the country (estimated at around 9.13 million inhabitants), 184 municipalities, a population density of 56.76 inhabitants per km^2 (11th in the national ranking) and a nominal monthly per capita income of around 850 BRL (https://www.ibge.gov.br). Few data are found at the regional and local level about TB in the age group studied; however, data from 2020 indicate that Ceará represented 4.3% of all TB cases in the 0-10 age group in Brazil. In the Northeast, about 19% of the cases were from Ceará, which places the state in the third position in the region in relation to the total number of cases, behind only of Pernambuco and Bahia[5].

The data source used was the TB cases registered in the Notifiable Diseases Information System (*Sistema de Informação de Agravos de Notificação* - SINAN) that occurred among residents of the state of Ceará under 15 years of age in the period from January 2001 to December 2017. SINAN is filled by information contained in the notification and monitoring form of the disease, records that must be completed by health professionals and typed by professionals from the municipal health department who, later, send them to the state department. The notifications encompassed cases of pulmonary, extrapulmonary and mixed TB. LTBI cases and in special treatments are not inserted in SINAN. The socioeconomic variables included in the notification form used in this study were: age, gender, race/color and area of residence.

The database used for this study was made available by the Ceará Health Department (SESA), and it comprised all cases reported as "new TB cases" under the age of 15 years[1]. Thus, the study included a population of 2,611 new childhood TB cases during the period. The incidence was calculated for each municipality in the indicated period using the average number of TB cases in the group and in naming the reference population <15 years of age obtained through the last Demographic Census carried out in 2010, multiplied by 100,000 inhabitants.

Initially, it was conducted a descriptive analysis of the sociodemographic characteristics of the analyzed cases. Subsequently, a trend analysis was conducted to indicate the temporal pattern of childhood TB incidence in the state. Therefore, regression by inflection points was performed. These regressions indicate whether one or more segments should be added in a linear regression to indicate any change in temporal trend, which refutes the null hypothesis that no points should be added. Its results are possible to estimate the Annual Percentage Change (APC) of the studied trend. Thus, the model was adjusted assuming that the number of inflection points could range from zero to two, which means a straight line or a line with two or three segments. A confidence interval of 95% (95%CI) and a significance level of 5% were established in all temporal trend analyses[7].

For the spatial analysis, the thematic map of the average gross incidence of childhood TB in the municipalities of Ceará was initially created and then these rates were smoothed using the local empirical Bayesian method to reduce the instabilities caused by the gross rates. The application of this method is necessary, since it generates rates closer to reality, as it considers not only the rate value of a given municipality, but weights it in relation to those that border it through a spatial proximity matrix. For the construction of the aforementioned matrix, it was considered the criterion of contiguity, assigning the value 1 to municipalities that have common borders and 0 to municipalities that do not share borders[7].

For the identification of spatial clusters, two different methods were used, with the same goal. The first concerns the spatial autocorrelation function, through the Global and Local Moran Index. The Moran Global Index was used to test the spatial dependence hypothesis and provide a general measure of association for the entire study area. Once the presence of global spatial autocorrelation was verified, the Local Moran Index (Local Index Spatial Analysis - LISA) was applied to verify the presence of spatial aggregates and quantify the degree of spatial association in each municipality of the sample set, considering $p<0.05$[7].

The results of Local Moran Index are presented through the Moran Map and Lisa Map. The Moran Map allows you to graphically visualize the degree of similarity between neighbors, represented by four quadrants: in red are the municipalities with high rates and that are close to municipalities with equally high rates (High/High spatial pattern); in green are the municipalities that have low rates and that are surrounded by municipalities that also have low rates (Low/Low spatial pattern); The municipalities in yellow (High/Low spatial pattern) and blue (Low/High spatial pattern) represent areas of epidemiological transition and that have high and low rates, but are very close to municipalities that have low and high rates, respectively[7].

The second method used to detect spatial clusters of childhood TB was the analysis of purely spatial scanning using the Scan statistical technique. In addition to identifying spatial clusters, the scan is also able to locate areas of risk for TB among children. With the purpose of identifying purely spatial clusters, the Poisson distribution model was used, and the following requirements: no geographical superposition of clusters, maximum cluster size equal to 50.0% of the exposed population, clusters in a circular shape and 999 replications. The calculation of the relative risk (RR) was performed for each municipality in Ceará, and those with values >1 have a relative risk for childhood TB that is higher than the risk for Ceará as a whole.

Furthermore, the analysis of the relationship between socioeconomic and demographic indicators with the incidence of childhood TB (outcome) was performed using the regression method. The following indicators (predictor variables) were used: Theil index - L, Gini index, proportion of the population in households with piped water, proportion of the population in households with toilet and piped water, proportion of the population in households with garbage collection, proportion of population in households with electricity, proportion of population in households with density >2, proportion of children aged 0 to 5 years out of school, proportion of children aged 6 to 14 years out of school, life expectancy at birth, proportion of people in households without electricity, proportion of people in households with inadequate walls, proportion of people in households with inadequate water supply and sanitation, total fertility rate, female heads of household with children under 15 years of age, proportion of children aged 0 to 5 years in school, proportion of children aged 5 to 6 years in school and proportion of children aged 6 to 14 years of age in school. All these indicators were taken from the Atlas of Human Development in Brazil (https://atlasbrasil.org.br/acervo/biblioteca).

The indicators mentioned were inserted into a multiple linear regression model (Ordinary Least Squares – OLS). The variables that remained related to childhood TB incidence in the OLS model ($p<0.05$) were also analyzed by a geographically weighted regression model (GWR), since the spatial dependence of the regression residuals was observed. The GWR regression allows analyzing phenomena with different distributions in space. Thus, the GWR model generated a regression coefficient for each of the 184 municipalities of the state, as a social indicator can act as a risk factor in a given territory and a protective factor in another. However, the values presented in the tables correspond to a mean of these values[8]. Two thematic maps for each indicator were created: one for the regression coefficient and another for the statistical significance, considering $p<0.05$.

Several software were used in this study. The local empirical Bayesian rate and the spatial autocorrelation function were calculated by TerraView 4.2.2. Purely spatial scan analysis was performed by SaTScan 9.6. The OLS regression was performed in Stata 12 and the GWR spatial regression was performed in GWR4.0.9. All thematic maps were produced in QGIS 2.4.17 software.

This research was sent for ethical consideration by the *Universidade Estadual do Ceará*, being approved under protocol nº 2,687,046. It is reiterated that at the time of data collection, the researcher, together with the Surveillance Center of the Health Department of the State of Ceará, removed any attributes that identified the study population such as name, mother's name and address.

RESULTS

From 2001 to 2017,2,611 cases of childhood TB were reported in Ceará. It was observed that the studied population had a median age of eight years (IQR: 3 – 12), with a slight predominance of males (50.3%; n=1,313). There was an expressive number of cases reported as browns (75.4%; n=1,468) and residents in the urban area (84.7%, n=2,139) (Table 1).

Table 1 – Descriptive analysis of the sociodemographic characteristics of childhood tuberculosis cases in Ceará from 2001 to 2017. Fortaleza, Ceará, Brazil, 2021

Sociodemographic characteristics	N	%
Age (median)	8	3 – 12
Gender		
Male	1313	50.3
Female	1297	49.7
Race/color*		
White	326	16.8
Black	116	6.0
Yellow	20	1.0
Brown	1468	75.4
Indigenous	16	0.8
Area of residence**		
Urban	2139	84.7
Rural	373	14.7
Peri-urban	16	0.6

*309 cases were excluded that were ignored.
**5 cases were excluded that had the variable Area of residence as "ignored" or "not informed".
Source: Research data, 2018

The average incidence of childhood TB was 3.48 cases/100,000 inhabitants. In the period 2001-2003, there was a 39.5% increase in the incidence of childhood TB (95%CI: -5.0 – 104.0), however, without statistical significance. On the other hand, in the period 2003-2017 there was a change in the temporal pattern of the disease, with the insertion of an inflection point to demonstrate a significant decrease of 5.7% per year (95%CI: -5.7 – -4.0) in the incidence of TB. However, when considering the entire period studied, a non-significant decrease of 1% per year (95%CI: -5.4 – 3.6) in the incidence of the disease in the childhood population is detected (Table 2).

Figure 1A shows that a significant part of municipalities of Ceará had at least one reported case of TB among people aged <15 years in the analyzed period. Important cities for the state had a high incidence, especially Fortaleza (15.3 cases/100,000 inhabitants) and Sobral (16.2 cases/100,000 inhabitants) and, therefore, they are highlighted in a darker color on the map. With the application of the local empirical Bayesian method (Figure 1B), the instabilities caused by municipalities with zero incidences were reduced and only the city of Campos Sales continued with zero incidence. In addition, it was possible to observe more apparent spatial patterns, especially in Fortaleza (and the metropolitan region) and Sobral, whose Bayesian rates were 13.6 and 10.1 cases/100,000 inhabitants, respectively.

For the detection of clusters, the spatial autocorrelation test was performed using the Global and Local Moran Indexes. The Global Moran Index was equal to 0.31 (p=0.01), indicating a positive spatial autocorrelation across the state. The Moran map, a map generated from the calculation of the Local Moran Index, shows that the high-high pattern of distribution is found in the metropolitan region of the capital Fortaleza, as well as in Sobral, an important municipality in the interior of the state, and in neighboring cities (Figure 1C). From the LISA map (Figure 1D), the statistical significance of each of these clusters was classified.

The Scan technique allowed to identify two statistically significant clusters (p<0.05) purely spatial of childhood TB in the state. The primary cluster, that is, the one with the lowest probability of having occurred by chance, was composed by Fortaleza and seven cities in its metropolitan region (Maracanaú, Pacatuba, Itaitinga, Horizonte, Pindoretama, Aquiraz and Eusébio), whose RR=3.7 (p<0.001). The secondary cluster was formed by Sobral and Forquilha, whose RR=2.3 (p<0.001) (Figure 1E).

The Scan technique also allowed identifying the risk of becoming ill with childhood TB in the cities of Ceará. Thus, it was found that in most municipalities in Ceará, the risk of children becoming ill with TB is lower than the risk of the state as a whole (Figure 1F). On the other hand, the greatest risks of new infections in childhood were evidenced in the cities of Fortaleza (RR=3.6), Sobral (RR=2.4) and Eusébio (RR=1.9).

After identifying the clusters, the indicators that could be related to the incidence of childhood TB were analyzed. The statistically significant indicators were inserted in the multivariate models and the results of the OLS and GWR regressions can be seen in Table 3. The OLS model explained 19% of the variation in the incidence of the disease, furthermore, positive spatial autocorrelation was identified in the regression residuals (I=0.14; p<0.001), indicating spatial dependence and suggesting the need to apply a geographic model.

Thus, after finding significant variables in the OLS model and its subsequent insertion in the GWR spatial model, it was found that the socioeconomic factors that influence childhood TB in Ceará were: proportion of the population in households with piped water (β=0.05), proportion of the population in households with density >2 (β=0.09) and number of female heads of household with children under 15 years of age (β=0.0003) (Table 3). By applying the GWR regression, it was obtained a 37% explanation of the model.

Table 2 – Temporal pattern of childhood tuberculosis in the state of Ceará, 2001-2017. Fortaleza, Ceará, Brazil, 2021

Period	APC	95%CI	p-value
2001-2003	39.5	-5.0 – 104.9	0.08
2003-2017	-5.7	-7.4 – -4.0	<0.001
2001-2017	-1.0	-5.4 – 3.6	0.66

APC: Annual Percent Change; 95%CI: 95% Confidence Interval
Source: Research data, 2018

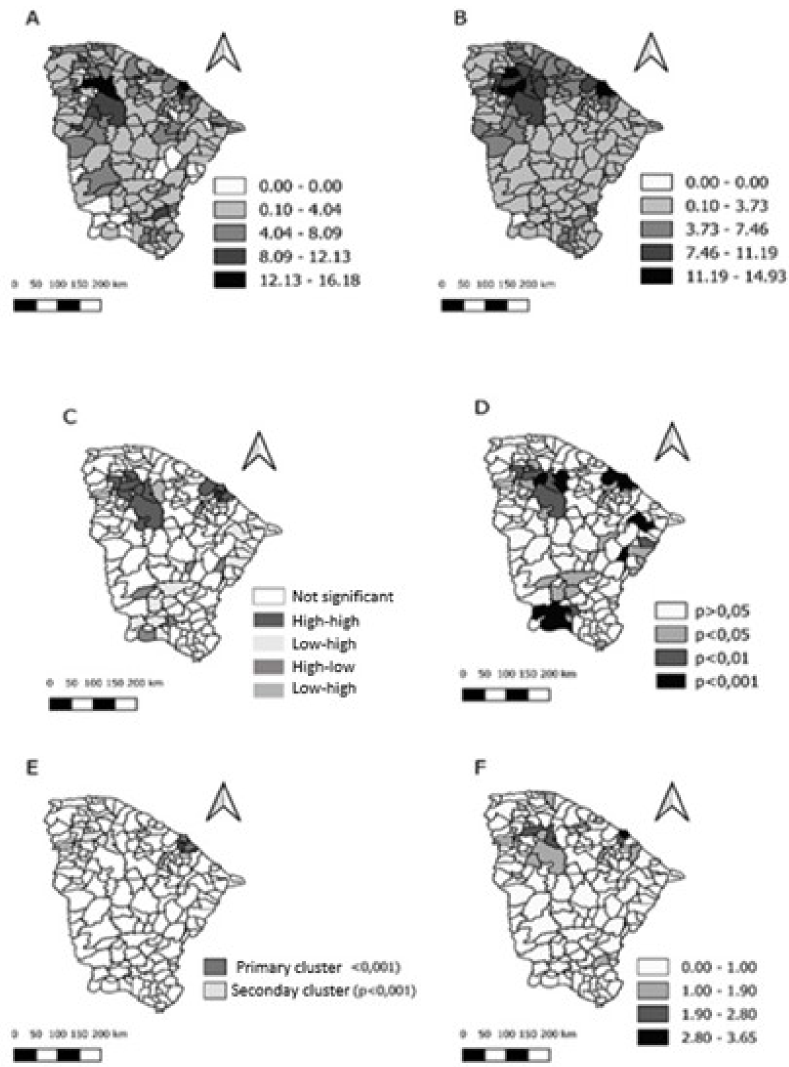

Figure 1 – Spatial pattern of childhood tuberculosis incidence in Ceará from 2001 to 2017. Fortaleza, Ceará, Brazil, 2021
Note: Figure 1A: childhood TB incidence gross rate; Figure 1B: incidence smoothed by the local empirical Bayesian method; Figure 1C: Moran map of spatial clusters; Figure 1D: LISA map with statistical significance of clusters; Figure 1E: Clusters at higher risk for childhood TB; Figure 1F: Municipal risks of childhood TB.
Source: Research data, 2018

Table 3 – Indicators related to childhood tuberculosis incidence in Ceará from 2001 to 2017. Fortaleza, Ceará, Brazil, 2021

	OLS Model			GWR Model	
	Coefficients	Standard Error	P	Coefficients	Standard Deviation
Population in households with piped water (%)	0.07	0.02	<0.001	0.05	0.03
Population in households with density >2 (%)	0.11	0.04	0.002	0.09	0.07
Female heads of household with children under 15 years of age	0.0001	0.00002	<0.001	0.0003	0.00004

Source: Research data, 2018

Figure 2 shows the thematic maps from the GWR regression results. It was found that in practically the entire macro-region of Fortaleza there was a positive relationship between the proportion of the population in households with piped water and the incidence of childhood TB (Figures 2A and 2B). Furthermore, in the macro-region of Sobral, on the border with Piauí, a positive relationship was observed between the proportion of the population in households with density >2 and childhood TB (Figures 2C and 2D). Finally, there was a relationship between the number of female heads of household with children under 15 years of age and the incidence of childhood TB in northern Ceará (Figures 2E and 2F).

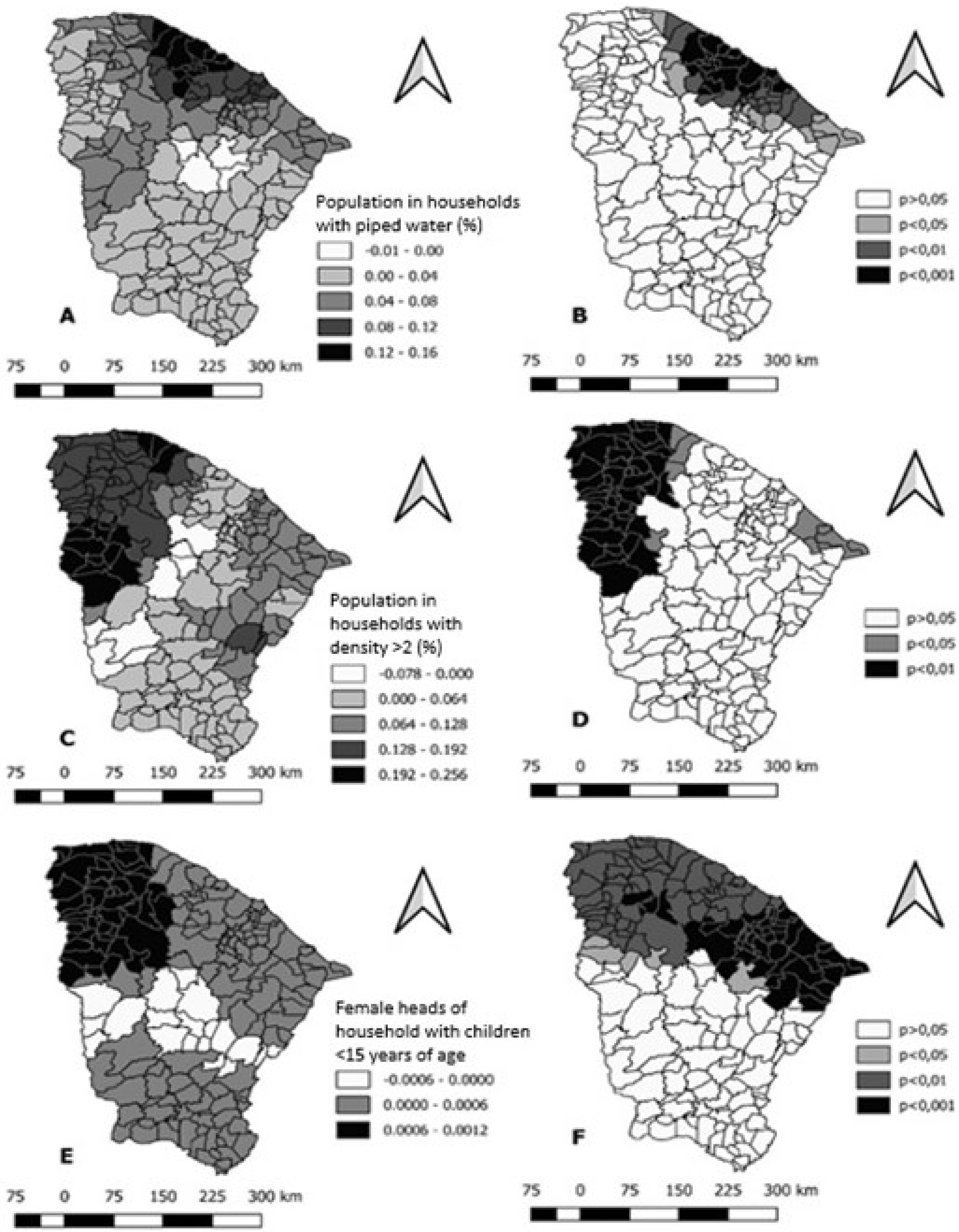

Figure 2 – Spatial distribution of indicators related to childhood tuberculosis incidence in Ceará from 2001 to 2017. Fortaleza, Ceará, Brazil, 2021

Note: Figure 2A: regression coefficients for population in households with piped water. Figure 2B: statistical significance of the relationship between household population with piped water and childhood TB; Figure 2C: regression coefficients for population in households with density >2; Figure 2D: statistical significance of the relationship between population in households with density >2 and childhood TB; Figure 2E: regression coefficients for female heads of household with children <15 years of age; Figure 2F: Statistical significance of the relationship between female heads of household with children <15 years and childhood TB.

Source: Research data, 2018

DISCUSSION

The findings of the present study point out to the need for greater attention to childhood TB in Ceará, as there was an extremely young ill child population with a median age of eight years. This age pattern differs from studies conducted in other regions of the country, such as in Rondônia, which had a mean age of 14.8 years, and in the state of Sergipe, which showed that the incidence of the disease was directly proportional to advancing age[9–10]. Therefore, the population in the studied region is even younger than in other regions of Brazil and, therefore, it is opportune to outline strategies considering this identified peculiarity.

It should be noticed that children are particularly vulnerable to TB, as they represent the weakest link between the complex mechanisms currently involved in the control of this infection, such as case tracking, contact search, LTBI, early diagnosis and instant treatment[3]. The World Health Organization (WHO) pioneered the initiative to publicize information about TB in this age group. After that, several countries started to disclose data from their childhood TB programs, however, there is still little information available globally and many issues have not yet been addressed, such as identification in extrapulmonary forms, latent infections and special treatments. Faced with this problem, there is a need for a set of adequate notifications to be possible of planning measures to combat infection in the child population.

TB has a diffuse distribution throughout the national territory. This is an expected characteristic, since illness is associated with urbanization processes and more than 80% of the Brazilian population live in urban areas[11]. These data draw attention to directing the focus to these areas, making it imperative for Brazilian states and municipalities to act in the fight against TB, especially among children from zero to four years of age, who are more vulnerable because they are more dependent on contact with adults[10].

The literature points out that one of the main obstacles in the management of the disease is the large proportion of undetected childhood TB cases, which has led many children to die without diagnosis or treatment. There are also institutional reasons why childhood TB has been neglected, as the child survival movement has not embraced TB as a major problem due to the historical absence of accurate estimates that demonstrate the true impact of the disease on child morbidity and mortality[12].

Moreover, this study identified a small decrease in the incidence of childhood TB over the 2003-2017 time series, however, there was no significant change when considering the entire period analyzed (2001-2017). The results from Ceará are similar to those from Brazil, since the rate in children remains around 4.0/100 thousand inhabitants during 2010 to 2017, from 2018 onwards there is an increase in the national standard, culminating in 5.7/100 thousand inhabitants[5]. Unfortunately, these numbers may be underreported due to the COVID-19 pandemic, which may erroneously appear that there is a decrease in the incidence of the disease[1–2]. Thus, it is noteworthy that both the rates recorded and projections for 2022 are still far from being considered ideal by the WHO[1].

It is noteworthy that, currently, one of the main actions for disease prevention is the treatment of latent tuberculosis infection (LTBI), focusing on children under five years of age and radiological clinical findings[10]. These health interventions are on the rise, especially among children. Furthermore, the hypothesis is that the increase in the incidence at a first moment (2001-2003) may suggest better screening of cases, thus strengthening the active search and qualifying the surveillance of health indicators, avoiding, underreporting cases.

Regarding the spatial analysis, the occurrence of spatial dependence of childhood TB rates in the territory of Ceará was identified. Emphasis is given to the metropolitan regions of the capital Fortaleza and Sobral, which presented both the highest patterns of infection incidence, as well as the highest relative risks for new infections. This pattern of illness corroborates a study conducted in another state in the Brazilian Northeast[13], which also showed high incidence rates of tuberculosis in large cities and their metropolitan regions.

These findings are probably justified by the fact that cities such as Fortaleza and Sobral present secondary urban agglomerations to the insertion of commercial centers that attract the population to the labor market. However, due to unrestrained migration, there is an increase in the number of unplanned housing and low social conditions that result in the precariousness of the sanitation and sewage network[14]. Thus, urban agglomerations in poor sanitary conditions can favor the emergence of infectious diseases, including TB.

Added to this, the characteristics of regions with high risk for TB transmission, for the most part, are economically vulnerable places that reflect social inequality. Research conducted with groups with low income points out that this population tends to present more health problems than those with better living conditions[15]. From this perspective, it is essential to direct actions based on national guidelines, adopting surveillance and strategic planning with greater attention in areas considered priorities.

The increased incidence of childhood TB in large cities may also be related to conducting disease screening more effectively. On the other hand, the investigation pointed out the insufficiency of professionals to carry out home visits or to follow up the patient during the directly observed treatment (DOT)[16]. In view of this, it appears that the need to provide both an adequate work structure for health teams, as well as a staff of professionals sufficient to provide qualified care. When there is an adequate number of health workers with satisfactory working conditions, it is possible to have more efficiency in the knowledge of the epidemiological situation of the population, as well as the diagnosis, management and control of tuberculosis cases[1].

The results of this study showed that as increases the proportion of people living in households with density >2, the incidence of childhood TB also increases. This problem is due to the low economic conditions, since individuals with low income have houses with limited rooms. Thus, the coexistence of many people in the same room increases the risk of disease transmission among family members, especially TB, whose transmission occurs through the air. Therefore, houses with few rooms and many residents result in less ventilation, which favors an environment of higher infectivity[3].

Furthermore, it was also possible to identify in municipalities closer to Fortaleza the positive relationship between the proportion of the population in households with piped water and the incidence rate of childhood TB. Although paradoxical, this result is related to the previous indicator of household density, as both have population clusters as characteristics, concentrated primarily in the underdeveloped urban area. Thus, although these populated areas have water treatment, they face other social problems, such as poverty. In this context, areas that have a higher population density, and have a greater deficiency in health investments, are more susceptible in developing diseases[17].

It was also possible to observe an increase in the incidence of childhood TB as the percentage of households in which women are heads of household also increases. This situation brings to light the phenomenon of the feminization of poverty, characterized by the progressive impoverishment of women and social exclusion. This reflects the underemployment conditions experienced by women, mainly due to the demand for domestic and child care, lack of time for professional training and the need to enter the labor market[18]. In view of this, the residents of these households are also more conducive to illness from infectious and parasitic diseases[11].

In view of the above, since socioeconomic vulnerability is directly related to childhood TB, there is a need for different problem management strategies aimed at children to ensure adequate control of the problem[19]. Among these strategies, the implementation of income transfer programs, such as the *Bolsa Família* program, stands out. The literature shows that the benefit had a positive effect on the health of populations, ensuring greater access to better nutrition, health services and improved environmental conditions in the homes of low-income people. These phenomena resulted in a better quality of life for children and a reduction in the overall coefficient of infant mortality[20].

Another program that has a positive impact on the control of childhood tuberculosis is the Health at School Program (*Programa Saúde na Escola - PSE*)[9], especially for being an excellent device in the dissemination of information and in the active search of cases in children. In addition, other income transfer program, housing, school dropout and even transportation programs can indirectly contribute to the protection against TB, but they need studies as for their real effects. Thus, it is noticed that intersectoral actions are fundamental in the fight against this disease, since the chain of transmission does not occur only through biological factors, but also through social and environmental factors.

This study presents some limitations. Among them, it is highlighted the use of secondary databases that may be subject to incompleteness and non-compliance with filling. In addition, the use of municipalities as units of analysis may present greater heterogeneity of socioeconomic characteristics instead of neighborhoods, however, these are not available for the analyzed data. Furthermore, the coefficients of the indicators included in the final regression model are very close to zero and must be interpreted with caution.

CONCLUSION

Through this study, it was observed that there was no change in the temporal pattern of childhood TB between the period from 2001 to 2017. As for the spatial pattern, it was possible to identify the formation of clusters of the disease in the metropolitan regions of Fortaleza and Sobral. The factors related to the incidence of the disease were: proportion of the population in households with piped water, proportion of the population in households with density >2 and number of female heads of household with children under 15 years of age.

Thus, there is a need for more effective public health strategies aimed at TB illness in children and adolescents, especially in areas with a higher risk of new infections. The strengthening of primary health care, screening strategies and differential diagnosis are key points in the management of the disease in this group. Finally, the promotion of housing with adequate sanitary supply and the increase in the coverage of income transfer programs, especially in regions with high incidence, can be important strategies in breaking the chain of transmission of the disease.

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