JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Vulnerable territories to tuberculosis-diabetes mellitus comorbidity in a northeastern Brazilian scenario

Giana Gislanne da Silva de Sousa[1], Mellina Yamamura[2], Márcio Flávio Moura de Araújo[3], Antônio Carlos Vieira Ramos[4], Ricardo Alexandre Arcêncio[4], Ana Cristina Pereira de Jesus Costa[5], Livia Maia Pascoal[1,5], Floriacy Stabnow Santos[5], Maria Aparecida Alves de Oliveira Serra[5], Iolanda Graepp Fontoura[6], Hamilton Leandro Pinto de Andrade[6], Livia Fernanda Siqueira Santos[5], Jaisane Santos Melo Lobato[6], Cláudia Regina de Andrade Arrais Rosa[6], Marcelino Santos Neto[1,5]

[1] *Nursing Graduate Program, Federal University of Maranhão, São Luís, Maranhão, Brazil*
[2] *Department of Nursing, Federal University of São Carlos, São Paulo, Brazil*
[3] *Oswaldo Cruz Foundation, Eusébio, Ceará, Brazil*
[4] *University of São Paulo at Ribeirão Preto College of Nursing, Ribeirão Preto, São Paulo, Brazil*
[5] *Health and Technology Graduate Program, Federal University of Maranhão, Imperatriz, Maranhão, Brazil*
[6] *Center of Social Sciences, Health and Technology, Federal University of Maranhão, Imperatriz, Maranhão, Brazil*

Abstract

Introduction: Epidemiological investigations on tuberculosis-diabetes comorbidity using spatial analysis should be encouraged towards a more comprehensive view of the health of individuals affected by such comorbidity in different contexts. This study analyzes the territories vulnerable to tuberculosis-diabetes comorbidity in a municipality in northeastern Brazil using spatial analysis techniques.

Methods: An ecological study was carried out in Imperatriz, Maranhão, Brazil. Tuberculosis-diabetes cases reported in the Brazilian Notifiable Diseases Information System between 2009 and 2018 were analyzed. Kernel density estimation and spatial scanning techniques were used to identify the areas with the greatest occurrence of spatial clusters.

Results: A heterogeneous spatial distribution was found, ranging from 0.00 to 4.12 cases/km^2. The spatial scanning analysis revealed three high-risk spatial clusters with statistical significance ($p < 0.05$), involving eleven strictly urban sectors with a relative risk of 4.00 (95% CI: 2.60–6.80), 5.10 (95% CI: 2.75–7.30), and 6.10 (95% CI: 3.21–8.92), indicating that the population living in these areas had a high risk of tuberculosis-diabetes comorbidity.

Conclusions: The highest concentration of cases/km^2, as well as risk clusters, were found in areas with high circulation of people and socio-economic and environmental vulnerabilities. Such findings reinforce the need for public health interventions to reduce social inequalities.

Key words: tuberculosis, diabetes, comorbidity, georeferencing.

J Infect Dev Ctries 2022; 16(5):813-820. doi:10.3855/jidc.15797

(Received 17 September 2021 – Accepted 29 December 2021)

Introduction

Tuberculosis (TB) and diabetes mellitus (DM) are correlated global health problems. Data obtained through a systematic review and meta-analysis demonstrated that people with DM are 1.5 to 3.5 times more likely to develop active TB. This risk varies according to the geographical characteristics, type of diagnostic approach, and population's income, denoting that the DM epidemic may impact the incidence of TB worldwide [1].

In 2019, about 10 million people suffered from TB worldwide; of these, 0.35 million cases were attributed to DM [2], and it is assumed that the number of patients with TB-DM comorbidity is greater than the number of patients with TB and Human Immunodeficiency Virus (HIV) [3]. The International Diabetes Federation (IDF) has estimated that the number of people living with DM worldwide will increase from 463 million in 2019 to 700 million in 2045 [4], impacting TB morbidity and mortality [1]. Therefore, the extent of the DM epidemic jeopardizes the overall goal of ending TB by 2050 [4].

The TB-DM association became known in the first half of the 20th century and had fatal consequences until the discovery of insulin and its ability to control glucose and the implementation of antibiotics to treat TB [5]. However, in recent years, this association has re-emerged with the rapid growth of the DM epidemic, especially in low- and middle-income countries with a slow decline in TB cases, causing important repercussions on health systems [5,6].

Given the above, the importance of carrying out studies to investigate the association between TB-DM comorbidity and social and environmental risk factors in a given territory is reinforced. Traditional epidemiological approaches have limited capacity to fill the gaps related to this theme [7,8], requiring new approaches such as geoprocessing to understand the epidemiological risk factors that involve the coexistence of these diseases in certain territories [9].

Among the tools used to control comorbidities are geographic information systems (GIS), considered useful for mapping diseases because they identify social and environmental risk factors and susceptible populations [10]. Furthermore, these tools use spatial analysis techniques and statistical calculations that make it possible to detect significant differences between spatial patterns and verify whether the cases are geographically grouped [11].

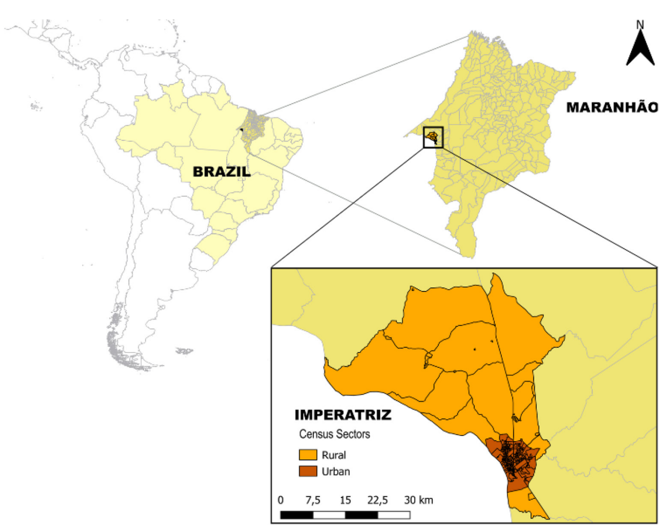
Over the past decade, there has been significant development of techniques to identify spatial clusters of diseases. TB [12] and DM [13] have stood out among the diseases that have been extensively investigated through spatial analysis allowing the identification of high-risk areas or clusters. Previous studies have identified spatial variations and high-risk areas for TB and DM [8,9], but the literature is still scarce concerning their comorbidity.

A review of the sociodemographic characteristics and clinical and epidemiological indicators of TB-DM cases found an incipient approach regarding the spatial analysis of cases, showing that such comorbidity has a heterogeneous distribution, molecular grouping, and spatial aggregation of cases [14]. Besides, GIS allowed identifying high-risk areas for TB-DM occurrence in Los Angeles, California, United States [15].

None of the previous studies addressed scenarios in Brazilian territories, such as the city of Imperatriz, Maranhão (MA), located in northeastern Brazil. This region is considered endemic for TB, with a high incidence rate (24.5/100,000 inhabitants) and mortality (1.6 deaths/100,000 inhabitants) [16]. DM is one of the main comorbidities associated with TB [17]. Thus, epidemiological studies aimed at clarifying the relationship between such diseases should be encouraged toward a comprehensive view of the health of individuals in different contexts. Such investigations are important health surveillance tools that provide subsidies for the planning and implementation of health and social care interventions [5,6].

This study analyzes the territories vulnerable to tuberculosis-diabetes comorbidity in a municipality in northeastern Brazil using spatial analysis techniques.

Figure 1. Map of Brazil emphasizing the state of Maranhão and the census sectors of Imperatriz, MA.



Methods

Study design

An ecological study was conducted using the census sectors of Imperatriz (MA) as units of analysis.

Study area

Imperatriz is a municipality located in the southwest region of Maranhão State, at a distance of 626 km from the capital city, São Luís, in northeastern Brazil (Figure 1). The city has an area of 1,368.988 km^2 and an estimated population of 259,337 inhabitants, 94% of whom live in the urban areas [18]. The city comprises of 246 census sectors (218 urban and 28 rural) distributed in 160 neighborhoods [19]. It also has a high human development index (HDI: 0.731). However, this city is inserted in a scenario characterized by poor socioeconomic status and a high incidence of operational indicators for TB [20].

Data sources

The study included all TB-DM cases registered in the Brazilian Notifiable Diseases Information System (SINAN in Portuguese) from January 2009 to December 2018. Data were obtained through the Health Surveillance Service (HSS) of the Regional Health Management Unit of Imperatriz (RHMUI) in November 2019, in which all the compulsory TB notifications were collected.

Sociodemographic data (age, gender, race/skin color, and education) and clinical data (clinical form of TB, associated diseases/conditions, sputum smear microscopy, chest x-ray, and culture) registered in the system were collected and analyzed. Essential address information such as street name, house number, neighborhood, zip code, and zone was used for the spatial analysis.

Data analysis

The cases were geocoded using standardized and matched addresses with the municipality's cartographic database available in the ESRI geodatabase. The Batch Geocode [21] tool was used for cases not located in the ESRI database, allowing Google Earth to search for coordinates.

The TerraView 4.2.2 software was used to map TB-DM cases using tabular information that does not have a spatial reference. These data were transported to a map and incorporated into a Geographic Information System (GIS). Then, the shapefiles of the TB-DM cases were joined with the shapefile of the census sector area, making it possible to identify the distribution of cases.

A descriptive analysis of the spatial behavior of the events was carried out to verify the intensity of occurrence of the TB-DM cases using the Kernel estimate, which consists of a non-parametric interpolation technique that transforms the spatial distribution into a density surface, allowing the visualization of spatial patterns and areas of disease concentration [22].

The basic parameters used in Kernel estimation are the radius of influence and the Kernel estimation function. A very small radius can generate a very discontinuous surface, while a large radius can generate a very smooth surface. In this perspective and to avoid problems using very small or large rays, the Incremental Spatial Autocorrelation (ISA) was used, which measures the spatial correlation of distances and defines the best conformation of the spatial grouping, thus indicating the best radius of influence. Such analysis is available in ArcGIS software 10.5 [23,24].

Spatial scanning statistics were used to identify spatial clusters of the TB-DM comorbidity. Three Excel spreadsheets were created. The case file (spreadsheet #1) contained information on the number of the census tract where the event occurred, date of occurrence, gender, and age of the subjects with TB-DM comorbidity. The second file (spreadsheet #2) contained the geographic coordinates of the centroids generated using TerraView 4.2.2. Finally, the third file (spreadsheet #3) contained population information from the census tracts, considering the gender and age of subjects, in line with the general universe results[17].

The median age of the individuals with TB-DM was used as a standardization factor.

The spatial scanning technique was processed using SatScan 9.3 [26], controlling the occurrence of TB-DM cases by the size of the population from the census sectors by age and gender distribution, in addition to attempts to detect high and low relative risk clusters [27]. Besides, a non-geographic overlapping of the

Table 1. Sociodemographic and clinical characteristics of TB-DM cases and TB cases. Imperatriz-MA (2009 to 2018).

Variables	TB-DM comorbidity (%)	TB (%)
Gender		
Female	31 (38.27)	236 (37.76)
Male	50 (61.73)	389 (62.24)
Age (years)		
0-9	1 (1.23)	59 (9.44)
20-39	13 (16.05)	271 (43.36)
40-59	30 (37.04)	180 (28.80)
≥ 60	37 (45.68)	115 (18.40)
Race/skin color		
Yellow	2 (2.47)	12 (1.92)
Black	12 (14.81)	79 (12.64)
White	20 (24.70)	142 (22.72)
Brown	47 (58.02)	383 (61,28)
Indigenous	0 (0.00)	4 (0.64)
Not informed	0 (0.00)	5 (0.80)
Education (years)		
> 8	11 (13.58)	197 (31.52)
≤ 8	53 (65.43)	313 (50.08)
Not informed	16 (19.76)	99 (15.84)
Not applicable	1 (1.23)	16 (2.56)
Place of residence		
Rural	0 (0.00)	9 (1.44)
Urban	80 (98.77)	606 (96.96)
Not informed	1 (1.23)	10 (1.60)
Clinical forms of TB		
Pulmonary + extrapulmonary	1 (1.23)	11 (1.76)
Extrapulmonary	1 (1.23)	68 (10.88)
Pulmonary	79 (97.54)	546 (87.36)
X-ray		
Normal	1 (1.23)	20 (3.20)
Abnormal	72 (88.90)	505 (80.80)
Indicative of other diseases	1 (1.23)	10 (1.60)
Not performed	7 (8.64)	86 (13.76)
Not informed	0 (0.00)	4 (0.64)
Sputum smear microscopy		
Negative	24 (29.63)	189 (30.24)
Positive	46 (56.80)	271 (43.36)
Not performed	10 (12.34)	155 (24.80)
Not applicable	1 (1.23)	10 (1.60)
Sputum culture		
Positive	2 (2.47)	18 (2.88)
Negative	7 (8.64)	50 (8.00)
In progress	0 (0.00)	2 (0.32)
Not performed	72 (88.89)	555 (88.80)
Total	**81.00**	**625.00**

DM: Diabetes mellitus; TB: Tuberculosis.

clusters, a maximum cluster size of 50% of the exposed population, and 999 replications were adopted. Clusters with a p-value < 0.05 were considered statistically significant. The thematic maps were created using ArcGIS 10.5 [28] software.

Ethical approval

The Research Ethics Committee of the Federal University of Maranhão (UFMA) granted ethical approval for the study under opinion no. 3.694.535/2019.

Results

From 2009 to 2018, 721 TB cases were reported in Imperatriz, and 81 were associated with DM. In 15 TB cases, the TB-DM comorbidity issue was registered as "ignored/blank" in the notification system.

Table 1 shows the sociodemographic and clinical characteristics of the TB-DM cases. TB-DM and TB only cases were predominantly male (61.7% and 62.24%), of brown race/skin color (58.02% and 61.28%), and with less than eight years of education (65.43% and 50.08%). A total of 45.68% of the subjects with TB-DM were over 60 years of age, while 43.36% of TB-only cases were between 20 and 39 years. Considering the place of residence, 98.75% of the TB-DM cases and 96.96% of the TB cases were residents of urban areas. As for the clinical variables, 97.53% of the TB-DM cases had pulmonary TB, of which 88.89% had an abnormal x-ray, 56.8% had a positive sputum smear microscopy, and 88.9% did not have a sputum culture collected. Among the TB cases, most patients had pulmonary TB (87.36%) and an abnormal x-ray (80.8%), in addition to a predominance of positive sputum smear microscopy (43.36%), and 88.80% of these cases did not have a sputum culture collected.

Seventy-six cases were geocoded, corresponding to approximately 94% of the notifications. Of these, 70 (92.1%) were analyzed using TerraView and 6 (7.9%) using Batch Geocode. It was not possible to geocode 6 cases (6%) that presented inconsistencies in the addresses provided, such as blank (2%) or incomplete

Figure 2. Areas with the highest density of TB-DM cases from 2009 to 2018, Imperatriz (MA), Brazil.

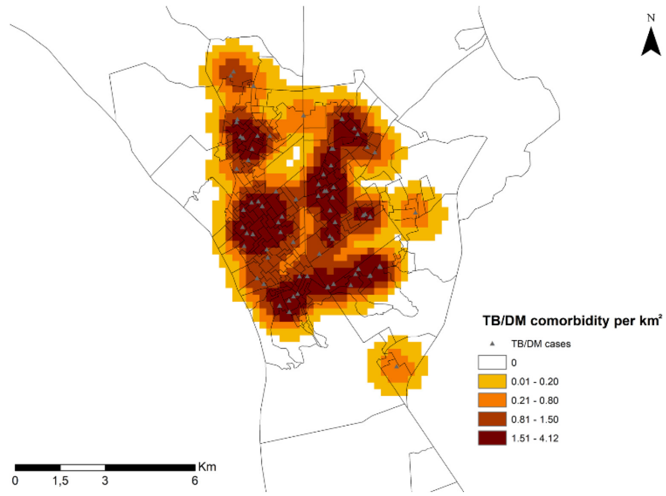
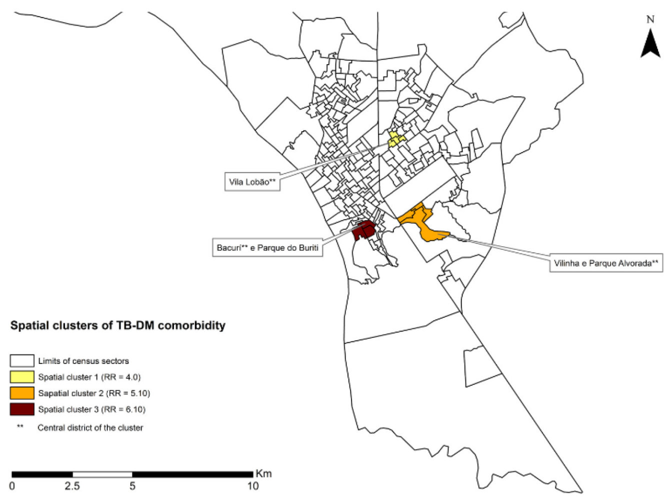


Figure 3. Spatial clusters of TB-DM comorbidity controlled by census sector population, gender, and age, Imperatriz (MA), Brazil, 2009-2018.



RR: relative risk.

Table 2. Characterization of spatial clusters of TB-DM cases controlled by census sectors population, gender, and age. Imperatriz-MA (2009 to 2018).

Spatial agglomerates	Number of census sectors	Number of cases	Population (hab)	RR (95% CI)	*p* value	Neighborhoods
1	4	5	4844	4.00 (2.60 - 6.80)	< 0.001	Vila Lobão
2	4	7	5011	5.10 (2.75 - 7.30)	< 0.001	Vilinha; Parque Alvorada
3	3	5	2952	6.10 (3.21 - 8.92)	< 0.002	Bacuri; Parque Buriti

RR: relative risk; CI: Confidence Interval.

addresses (4%). All geocoded cases occurred in urban areas.

The Kernel estimate found that the spatial distribution of TB-DM cases was heterogeneous, ranging from 0.00 to 4.12 cases/km^2. Such distribution occurred from the central parts of the urban areas with dispersion to the northeast, northwest, southwest, and southeast in areas circumscribed to the neighborhoods Centro, Nova Imperatriz, Santa Rita, São José, Bacuri, Parque do Buriti, Vilinha, Parque Alvorada, Vila Lobão, and Vila Cafeteira, which had higher density of cases (Figure 2).

The spatial scan analysis revealed three high-risk spatial clusters. The relative risk (RR) varied from 4.00 to 6.10, and the maximum value was found in cluster #3. According to this result, the population residing in the census sectors belonging to the Bacuri and Parque do Buriti neighborhoods presented the highest risk for TB-DM (Figure 3).

Spatial cluster #1 (RR: 4, 95% CI: 2.60–6.80, $p <$ 0.001) encompassed four census sectors of the Vila Lobão neighborhood. Spatial cluster #2 (RR: 5.10, 95% CI: 2.75–7.30, $p <$ 0.001) also involved four census sectors, located in Vilinha and Parque Alvorada, while spatial cluster #3 had the highest risk (RR: 6.10, 95% CI: 3.21–8.92, $p <$ 0.002) and included three census sectors belonging to the Bacuri and Parque do Buriti neighborhoods. The main characteristics of the spatial clusters are summarized in Table 2.

Discussion

This study aimed to analyze the territories vulnerable to TB-DM comorbidity in a city in northeastern Brazil using spatial analysis techniques. The information found regarding the geospatial factors associated with TB-DM comorbidity is important for better elucidation of the spatial dynamics of this comorbidity and its relationship with local characteristics [10].

Concerning the clinical-epidemiological profile of the cases, this study corroborates the findings of previous studies concerning the predominance of males, of mixed race/skin color, with low education level, aged over 60 years, with pulmonary TB, altered chest radiography, and positive sputum smear results [29,30]. The sociodemographic profile of TB-DM cases and the characteristics associated with this comorbidity are important. They may expand the knowledge regarding the extent to which these diseases impact the population, supporting decision-making and public policies [30].

The spatial analysis highlighted the location data obtained from the addresses registered in the SINAN database. The percentage of geocoded cases (approximately 94%) proved to be satisfactory [31], and studies using secondary data were similar, with percentages of georeferencing ranging from 69% [32] to 92% [31].

The data collection process used to obtain the addresses is not perfect, and inconsistencies in the information reported by subjects or filled out in the system may have occurred. Inadequate notification is a recognized problem that compromises data quality stored in databases [32].

Given the above, there is a need for periodic training of professionals responsible for notifying and monitoring diseases. Another important issue concerns the investments in digital mapping, especially in areas of recent and disordered growth, which can improve data quality, thus minimizing inconsistencies and loss of information [32].

All geocoded cases occurred in urban areas, corroborating previous studies [7,33]. The socio-environmental conditions combined with the accelerated urbanization process explain the high incidence of TB in urban areas. In addition, poorly ventilated spaces and high density of people in the house, which are common in urban areas, increase the risk of TB [34].

Factors related to the urbanization process such as sedentary lifestyle and diet also favor DM. The association of these factors contributes to TB-DM in urban areas. On the other hand, residents of rural areas have less access to TB and DM diagnoses, leading to underreporting [6].

The Kernel estimate showed that the “hot areas” were concentrated in the census sectors of central neighborhoods. However, there is a dispersion to some of the peripheral neighborhoods that, despite being far from the center, are also regions with a large circulation of people, configuring a heterogeneous distribution of the comorbidity.

Imperatriz stands out in the state of Maranhão for its urban area, population size, demographic density, and gross domestic product (GDP), and it is considered an educational, commercial, and healthcare hub [35]. Such characteristics explain the intense circulation of people in Imperatriz, especially in the central region. The high density of people in houses, workplaces, health facilities, and public vehicles increases the possibility of acquiring TB [33].

As a result of accelerated urbanism, the city of Imperatriz grew in a disorganized manner, resulting in the existence of subnormal areas that lack public services. Such physical and environmental problems compromise the living conditions and negatively affect its inhabitants [36,37]. Hence the regional characteristics related to the urbanization process favor the occurrence of TB and DM.

Through the spatial scanning analysis, three high-risk clusters for TB-DM were identified. People residing in the census sectors belonging to Bacuri and Parque do Buriti, located in the southwest region, are the most vulnerable.

These regions have poor environmental quality, unplanned growth, and other issues, including floods in the rainy season and deficient basic sanitation [37]. Such conditions favor the spread of diseases and highlight the absence of public policies to improve environmental conditions. These areas are densely populated and have low income [36,37], high DM load [35], and conditions that favor the occurrence of TB [38], increasing the risk of TB-DM comorbidity.

The census sectors linked to Vila Lobão, Vilinha, and Parque Alvorada are also areas of significantly high-risk that share the characteristics mentioned above in addition to other vulnerabilities, such as a high number of inhabitants per house, poor-ventilated and poor-lighted houses, and high incidence of risk factors for TB [21,39].

A combination of the risk factors mentioned above has also been reported in a previous study that identified three clusters in Imperatriz with a heterogeneous distribution of TB cases (Bacuri, Vila Lobão, and Parque Alvorada), similar to the results obtained in our study [40].

Previous studies have shown that low socioeconomic status, low education, insufficient medical resources [36], and behavioral factors linked to the urbanization process (poor eating habits, sedentary lifestyle, smoking, and alcoholism) are risk factors for DM [9]. The combination of these factors may have contributed to the occurrence of the high-risk clusters of TB-DM that were identified.

The spatial clusters detected highlight the disparities found in the urban perimeter of Imperatriz, pointing to the need for public administration improvements since the city's urban areas are segmented and characterized by extreme socio-spatial inequalities [35,36].

It is noteworthy that the census sectors that presented the highest risk are located in unplanned urban areas that differ in basic public services provided [37]. In this case, territorial inequalities hamper access to healthcare services [31]. It was observed that the Family Health Strategy teams (health workers responsible for monitoring groups of families in defined geographical areas) covered only 60.9% of the territory of Imperatriz [41]. This fact may have contributed to the underreporting of cases and raises questions about how the areas investigated are being assisted and how access to healthcare services affects the control and surveillance of TB-DM.

This study was the first to identify spatial clusters of TB-DM in the Brazilian scenario. However, areas at risk for TB-DM comorbidity have been investigated in other world regions through different statistical techniques [8,10,15].

Studies conducted in the United States [15] and Mexico [10] identified spatial aggregations of TB-DM cases in endemic regions, especially those inhabited by immigrants [15]. A study conducted in India also used the Poisson-based model and spatial scanning to detect places where the high endemicity of TB overlaps with that of DM. The geographical overlap in the study mentioned above was inconsistent, with only a partial overlap of cases in the southern states [9].

The overlap between TB and DM has been found in areas with a prevalence of DM above 7% [42], as in Brazil, which has a prevalence above 9% [4]. In a previous study conducted in Imperatriz, DM was the most frequent disease among the diseases associated with TB [17]. Therefore, there is evidence that the relationship between these diseases exists at an ecological level.

It is known that TB has a strong relationship with poverty and barriers to accessing healthcare services, and this is particularly worrying when TB is associated with DM [10]. There is a need for additional studies to assess the characteristics related to the territorial distribution of the TB-DM comorbidity, including socio-economic aspects, access barriers, and healthcare services coverage in the ecological units of analysis.

It is worth mentioning that studies with a geoecological approach subsidize healthcare managers and professionals in the planning, monitoring, and evaluation of actions, constituting useful tools in the evaluation of health systems. Maps can raise managers' and workers' awareness, provide a situational diagnosis, raise hypotheses, and enable the understanding of epidemiological factors that play a key role in disease spread. [11].

This study's limitations include possible failures in the notification system, such as incomplete notification and underreporting. This investigation and previous studies have detected inadequate notification of TB cases and comorbidities [29,30]. The patient address can be left blank in the SINAN system, and for this reason, omissions and gaps in the registers were expected. Furthermore, the ecological fallacy inherent to ecological studies (the observation of a phenomenon's existence at an aggregate level to explain phenomena at an individual level) may have occurred [39].

Conclusions

The highest concentration of TB-DM cases/km² and spatial clusters occurred in areas with a high circulation of people and socio-economic and environmental vulnerabilities. Such findings may contribute to the implementation of interventions aimed at high-risk areas and the integrated management of health problems, subsidizing public health interventions to social reduce inequalities.

Acknowledgements

The authors thank the financial support provided by the Foundation for Research and Scientific and Technological Development of Maranhão and by the Coordination for the Improvement of Higher Education Personnel (CAPES Brazil, process code 001).

Authors' contributions

GGSS and MSN conceived the study. MSN provided supervision for the study. All the authors were involved in the implementation of the study. FSS, LFSS, JSML, and CRAAR extracted data from the information system. GGSS, MY, RAA, IGF, and HLPA performed the statistical analysis. LMP, ACPJC, MFMA, MAAOS, and ACVR analyzed the data. GGSS and MSN wrote the initial draft manuscript. All authors reviewed and edited the draft manuscript. All authors reviewed and approved the final version of the manuscript to be published.

References

1. Al-Rifai RH, Pearson F, Critchley JA, Abu-Raddad LJ (2017) Association between diabetes mellitus and active tuberculosis: a systematic review and meta-analysis. PLoS One 12: e0187967.
2. World Health Organization (2020) Global tuberculosis report 2020. Available: https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf?ua=1. Accessed: 22 October 2020.
3. Zheng C, Hu M, Gao F (2017) Diabetes and pulmonary tuberculosis: a global overview with special focus on the situation in Asian countries with high TB-DM burden. Glob Health Action 10: 1-11.
4. International Diabetes Federation (2019) IDF Diabetes Atlas Ninth edition 2019. Brussels, Belgium: International Diabetes Federation. Available: https://www.diabetesatlas.org/upload/resources/material/20200302_133351_IDFATLAS9e-final-web.pdf. Accessed 28 October 2020.
5. Cadena J, Rathinavelu S, Lopez-Alvarenga JC, Restrepo BI (2019) The re-emerging association between tuberculosis and diabetes: lessons from past centuries. Tuberculosis (Edinb) 16: 89-97.
6. Workneh MH, Bjune GA, Yimer SA (2017) Prevalence and associated factors of tuberculosis and diabetes mellitus comorbidity: a systematic review. PloS One 12: e0175925.
7. Ekeke KN, Ukwaja K, Chukwu JN, Charles CN, Anthony OM, Eruke EE, Festus OS, Isaac A, Ifeanyi A, Samuel A, Osagie I, Job BO, Nelson OM, Chukwuka A, Moses CA, Obinna KM, Oshi DC (2017) Screening for diabetes mellitus among tuberculosis patients in Southern Nigeria: a multi-centre implementation study under programme settings. Sci Rep 7: 44205.
8. Blanco-Guillot F, Delgado-Sánchez G, Mongua-Rodríguez N, Cruz-Hervert P, Ferreyra-Reyes L, Ferreira-Guerrero E, Yanes-Lane M, Montero-Campos R, Bobadilla-Del-Valle M, Torres-González P, Ponce-de-León A, Sifuentes-Osornio J, Garcia-Garcia L (2017) Molecular clustering of patients with diabetes and pulmonary tuberculosis: a systematic review and meta-analysis. PLoS One 12: e0184675.
9. Hernandez AM, Jia P, Kim H, Cuadros DF (2020) Geographic variation and associated covariates of diabetes prevalence in India. JAMA Netw Open 3: e203865.
10. Blanco-Guillot F, Castañeda-Cediel ML, Cruz-Hervert P, Ferreyra-Reyes L, Delgado-Sánchez G, Ferreira-Guerrero E, Montero-Campos R, Bobadilla-Del-Valle M, Martínez-Gamboa RA, Torres-González P, Téllez-Vazquez N, Canizales-Quintero S, Yanes-Lane M, Mongua-Rodríguez N, Ponce-de-León A, Sifuentes-Osornio J, García-García L (2018) Genotyping and spatial analysis of pulmonary tuberculosis and diabetes cases in the state of Veracruz, Mexico. PloS One 13: e0193911.
11. Ibiapina É, Bernardes A (2019) Health maps and the contemporary visibility regime. Saúde e Sociedade 28: 322-36. [Article in Portuguese].
12. Shaweno D, Karmakar M, Alene KA, Ragonnet R, Clements AC, Trauer JM, Denholm JT, McBryde ES (2018) Methods used in the spatial analysis of tuberculosis epidemiology: a systematic review. BMC Med 16: 193.
13. Zhang X, Chen X, Gong W (2019) Type 2 diabetes mellitus and neighborhood deprivation index: a spatial analysis in Zhejiang, China. J Diabetes Res 10: 272-282.
14. Sousa GGS, Pascoal LM, Ferreira AGN, Rolim ILTP, Santos LFS, Neto MS (2020) Clinical-epidemiological characterization of tuberculosis/diabetes comorbidity: integrative review. Revista Enfermagem UERJ 28: 50225.
15. Rosales M, Lan E, Guevara RE, Yumul JL, Morales DM, Higashi JM, Chang AH (2019) Spatial patterns of tuberculosis and diabetes mellitus in Los Angeles county, California. Researchsquare: https://doi.org/10.21203/rs.2.13623/v1.
16. Silva JC, Brito OS, Souza DS (2019) Morbidity indicators and epidemiological characterization of tuberculosis in Imperatriz-MA, Brazil. Evidentia 16: 1-10. [Article in Portuguese].
17. Silva IP, Pontes AN, Silva BC, Silva, I, Bichara, C (2016) Clinical and epidemiological aspects of tuberculosis in the municipality of Imperatriz, Maranhão. Centro Científico Conhecer–Goiânia 13: 1386. [Article in Portuguese].
18. Brazilian Institute of Geography and Statistics (2020) Brasil/Maranhão/Imperatriz. Available:

https://cidades.ibge.gov.br/brasil/ma/imperatriz/panorama. Accessed: 22 October 2020. [Site in Portuguese].
19. Brazilian Institute of Geography and Statistics (2020) Maps. Cartographic bases. Available: http://mapas.ibge.gov.br/bases-e-referenciais/bases-cartograficas/cartas. Accessed: 17 October 2020.
20. Ministry of Health (2018) Overview of tuberculosis in Brazil: situational diagnosis based on epidemiological and operational indicators. Available: http://bvsms.saude.gov.br/bvs/publicacoes/tuberculose_brasil_indicadores_epidemiologicos_operacionais.pdf. Accessed: 5 January 2021. [Available in Portuguese].
21. Batchgeo (2020) Geocoding with Batchgeo. Available: http://batchgeo.com/br/. Accessed 20 May 2020.
22. Câmara G, Carvalho MS (2004) Analysis of punctual events. In: Druck S, Carvalho MS, Câmara G, Monteiro AVM editors. Spatial analysis of geographic data. Brasília. Embrapa. Available: http://www.dpi.inpe.br/gilberto/livro/analise/cap2-eventos.pdf. Accessed 20 May 2020. [Article in Portuguese].
23. Zhang Y, Wang X, Feng T, Fanget CZ (2019) Analysis of spatial-temporal distribution and influencing factors of pulmonary tuberculosis in China, during 2008–2015. Epidemiol. Infect. 147: e25.
24. Qi Z, Yang W, Wang YF (2017) Epidemiological analysis of pulmonary tuberculosis in Heilongjiang province China from 2008 to 2015. Int J Mycobacteriol 6: 264-267.
25. National Institute for Space Research (2022) TerraView version 4.2.2. Available: http://www.dpi.inpe.br/terralib5/wiki/doku.php?id=start Accessed 07 May 2022.
26. SaTScan (2022) Software for spatial, temporal, or space-time scan statistics version 9.3. Available: https://www.satscan.org/. Accessed 07 May 2022.
27. Kulldorff M, Nagarwalla N (1995) Spatial disease clusters: detection and inference. Stat Med 14: 799-810.
28. ESRI (2022) ArcGIS version 10.5 Available: https://qgis.org/en/site/. Accessed 07 May 2022.
29. Abreu RGD, Sousa AIAD, Oliveira MRF, Sanchez MN (2017) Tuberculosis and diabetes: probabilistic linkage of databases to study the association between both diseases. Epidemiologia e Serviços de Saúde 26: 359-368.
30. Abreu RGD, Rolim LS, Sousa AIA, Oliveira MRF (2020) Tuberculosis and diabetes: association with sociodemographic characteristics and diagnosis and treatment of tuberculosis. Brazil, 2007-2011. Rev Bras Epidemiol 23: e200009.
31. Arroyo LH, Yamamura M, Protti-Zanatta ST, Fusco APB, Palha PF, Ramos ACV, Uchoa SA, Arcêncio RA (2017) Identification of risk areas for the transmission of tuberculosis in the municipality of São Carlos, São Paulo State, Brazil, 2008 to 2013. Epidemiol Serv Saúde 26: 525-534.
32. Magalhães MAFM, Matos VP, Medronho RA (2014) Evaluation of data of address in SINAN using locally georeferencing of tuberculosis cases by two methods in Rio de Janeiro. Cad Saúde Colet 22: 192-199.
33. Delgado-Sánchez G, García-García L, Castellanos-Joya, Cruz-Hervert P, Ferreyra-Reyes L, Ferreira-Guerrero E, Hernández A, Ortega-Baeza VM, Montero-Campos R, Sulca JA, Martínez-Olivares M, Mongua-Rodríguez N, Baez-Saldaña R, González-Roldán JF, López-Gatell H, Ponce-de-León A, Sifuentes-Osornio J, Jiménez-Corona ME (2015) Association of pulmonary tuberculosis and diabetes in Mexico: analysis of the National Tuberculosis Registry 2000-2012. PLoS One 10: e0129312.
34. Cavalin RF, Pellini ACG, Lemos RRGD, Sato APS (2020) TB-HIV co-infection: spatial and temporal distribution in the largest Brazilian metropolis. Rev Saúde Pública 54: e112.
35. Maranhense Institute of Socioeconomic and Cartographic Studies (2020) Development regions of the Maranhão State: an advanced proposal. São Luís: IMESC, Available: http://imesc.ma.gov.br/src/upload/publicacoes/382564664c4eb6e9b71374f5eda9fa1816222222.pdf. Accessed: 22 November 2020. [Available in Portuguese].
36. Sousa JM (2015) Plot of urban-regional dynamics in Southern Maranhão: reflections from the economic centrality of Açailândia, Balsas and Imperatriz. Federal University of Uberlândia. 558 p.
37. Santos RL, Nunes FG, Santos AM (2020) Environmental quality of Imperatriz municipality in Maranhão State/Brazil: a multicriterial analysis of intra-urban indicators. Caminhos de Geografia 21: 1-20.
38. Vladimir Munayco C, Mújica ÓJ, Del Granado M, Barceló A. (2017) Burden of tuberculosis attributable to diabetes in the adult population of the Americas. Rev Panam Salud Publica 19:e125.
39. Mao Q, Zeng C, Zheng D, Yang Y (2019) Analysis on spatial-temporal distribution characteristics of smear positive pulmonary tuberculosis in China, 2004-2015. Int J Infect Dis 80: 36-44.
40. Silva JCD, Santos LFS, Santos FS, Pascoal LM, Dias ICCM, Costa ACPDJ, Santos Neto M (2021) Space and space-temporary clusters of tuberculosis in a northeast Brazilian municipality. Saud Pesq 14: e8493.
41. Ministry of Health (2020) Primary care coverage. Available: https://egestorab.saude.gov.br/paginas/acessoPublico/relatorios/relHistoricoCoberturaAB.xhtml. Accessed: 23 November 2020. [Available in Portuguese].
42. Rouquayrol MZ, Silva MG (2018) Rouquayrol epidemiology & health, 8th edition. Rio de Janeiro: MedBook 744 p. [Book in Portuguese].

Corresponding author
Gislanne da Silva de Sousa, M.Sc
Nursing Graduate Program, Federal University of Maranhão, São Luís, Maranhão, Brazil
Tel: +55 98 999073147
Fax: +55 61 3686 2756
Email: giana.sousa@discente.ufma.br

Conflict of interests: No conflict of interests is declared.