Epidemiological and spatial characterization of leprosy in Aracaju, Sergipe, Brazil

Caracterização epidemiológica e espacial da hanseníase em Aracaju, Sergipe, Brasil

Caracterización espacial de la endemicidad de lepra en los barrios de Aracaju, Sergipe, Brasil

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Abstract

Leprosy is a chronic infection, being considered a serious public health problem due to its magnitude and high disabling potential. In this perspective, this study aimed to analyze the epidemiological profile of leprosy patients and spatial characteristics of the disease in Aracaju, Sergipe, Brazil. This was an ecological, descriptive and analytical study of 559 leprosy patients from Aracaju, from 2011 to 2015. All information was obtained from Information System for Notifiable Injuries, Ministry of Health of Brazil. Descriptive and analytical statistical analyzes and spatial characterization methods were used. A decreasing tendency in the detection of leprosy cases during the study period was observed, with the relative frequency going from 23% (n = 129) in 2011 to 14.5% (n = 81) in 2015. The tuberculoid form was the most common (28.2%, n = 158), followed by dimorphic (24.5%, n = 137), undetermined (21.5%, n = 120) and lepromatous (20.6%; n = 115). The multibacillary operational classification also corresponded to the majority of notifications (52.4%, n = 293), with the associated factors age $\geq$ 16 years (OR = 2.42, 95% CI = 1.12-5.25) and male gender (OR = 2.74, 95% CI = 1.94-3.86) (p $<$0.05). A high risk cluster for the illness and the higher density of the mean detection incidence by the Kernel estimate was more concentrated in the central-northern portion of Aracaju. Statistical analysis allowed a better understanding of the epidemiological profile of leprosy patients and the identification of critical areas for illness and spread of the disease.

Keywords: Leprosy; Epidemiology; Spatial analysis; Geoprocessing.

Resumo

A hanseníase é uma infecção crônica, considerada um grave problema de saúde pública devido à sua magnitude e alto potencial incapacitante. Este estudo teve como objetivo analisar o perfil epidemiológico dos pacientes com hanseníase e as características espaciais da doença em Aracaju, Sergipe, Brasil. Estudo ecológico, descritivo e analítico com 559 pacientes com hanseníase de Aracaju, de 2011 a 2015. Todas as informações foram obtidas no Sistema de Informação de Agravos de Notificação do Ministério da Saúde do Brasil. Foram utilizadas análises estatísticas descritivas e analíticas e métodos de caracterização espacial. Observou-se uma tendência decrescente na detecção de casos de hanseníase durante o período do estudo, com a frequência relativa passando de 23% (n = 129) em 2011 para 14,5% (n = 81) em 2015. A forma tuberculóide foi a mais comum (28,2%, n = 158), seguido por dimórfico (24,5%, n =

137), indeterminado (21,5%, n = 120) e virchowiano (20,6%; n = 115). A classificação operacional multibacilar também correspondeu à maioria das notificações (52,4%, n = 293), com os fatores associados idade ≥ 16 anos (OR = 2,42; IC 95% = 1,12-5,25) e sexo masculino (OR = 2,74,995 % CI = 1,94-3,86) (p <0,05). O cluster de alto risco para a doença e a maior densidade da incidência média de detecção pela estimativa de Kernel concentrou-se mais na porção centro norte de Aracaju. A análise estatística permitiu um melhor entendimento do perfil epidemiológico dos pacientes com hanseníase e a identificação de áreas críticas para adoecimento e disseminação da doença.

Palavras-chave: Hanseníase; Epidemiologia; Análise espacial; Geoprocessamento.

Resumen

La lepra es considerada un grave problema de salud pública por su magnitud y alto potencial invalidante. Este estudio analizó el perfil epidemiológico de los pacientes con lepra y las características espaciales de la enfermedad en Aracaju, Sergipe, Brasil. Estudio ecológico, descriptivo y analítico con 559 leprosos de Aracaju, de 2011 a 2015. Toda la información fue obtenida del Sistema de Información de Enfermedades Notificables del Ministerio de Salud de Brasil. Se utilizaron análisis estadísticos descriptivos y analíticos y métodos de caracterización espacial. Hubo una tendencia decreciente en la detección de casos de lepra durante el período de estudio, con una frecuencia relativa que pasó del 23% (n = 129) en 2011 al 14,5% (n = 81) en 2015. La forma tuberculoide fue los más frecuentes (28,2%, n = 158), seguidos de dimórficos (24,5%, n = 137), indeterminados (21,5%, n = 120) y Virchowian (20,6%; n = 115). La clasificación operativa multibacilar también correspondió a la mayoría de notificaciones (52,4%, n = 293), con factores asociados a edad ≥ 16 años (OR = 2,42; IC 95% = 1,12-5,25) y sexo hombres (OR = 2,74,995% IC = 1,94-3,86) (p <0,05). El grupo de alto riesgo para la enfermedad y la mayor densidad de la incidencia promedio de detección según la estimación de Kernel se concentraron más en la parte norte-central de Aracaju. El análisis estadístico permitió comprender mejor el perfil epidemiológico de los pacientes con lepra y la identificación de áreas críticas para la enfermedad y la propagación de la enfermedad.

Palabras clave: Lepra; Epidemiología; Análisis espacial; Geoprocesamiento.

1. Introduction

Leprosy is a chronic granulomatous infection caused by *Mycobacterium leprae* (Rodrigues & Lockwood, 2011). Due to its magnitude and high disabling potential, it has still been considered a serious public health problem worldwide (Rocha, Lima, Stevens, Gutierrez, & Garcia, 2015; Rodrigues & Lockwood, 2011; Saúde, 2009).

The World Health Organization (2014) showed that, despite the fact that leprosy prevalence coefficients had a gradual reduction over the last years, Brazil remains the second country with the largest number of leprosy cases (WHO, 2014), especially in the North, Midwest and Northeast regions (Saúde, 2009). Associated with this, for Sales et al (2020), the North and Northeast regions also showed a high amount of Multibacillary operational classification, which would indicate a delay in diagnosis, risk for development of physical limitations, increasing the transmission and the prevalence of the pathology in these locations (Sales, Sousa, Machado, de Moura Rocha, & de Oliveira, 2020).

In most Brazilian states, the late leprosy diagnosis usually occurs around one year and a half to two years after the onset of signs and symptoms. Among the factors contributing to this situation are the late search for health services, lack of information on the disease signs and symptoms, and the deficit in health attendance and/or trained professionals in the health care network (Arantes, Garcia, Filipe, Nardi, & Paschoal, 2010).

The main form of the disease contagion occurs through direct contact with bacilliferous patients, from whom the bacilli emerge mainly from nasal secretions (Huang, 1980). Thus, it can be understood that the early recognition of leprosy and timely treatment are key elements for the interruption of its propagation (Lastória & Abreu, 2012). Therefore it is essential and necessary: the active detection of cases, which means a systematic search of patients through an epidemiological investigation of contacts; collective and group-specific examinations; examinations of people who spontaneously demand health services; and community mobilization, performing, in all these situations, a dermatoneurological exam for an early and adequate leprosy diagnosis (Saúde, 2009).

Considering the importance of studies that evaluate the influence of sociodemographic factors associated with diseases, which have contributed to better targeting of health prevention and promotion actions, this study aimed to analyze the epidemiological profile of leprosy patients and the spatial characteristics of the disease in Aracaju, Sergipe, Brazil, from 2011 to 2015.

2.   Methods

This is an cross-sectional study, with analytical approaches, based on secondary data from Information System for Notifiable Injuries (ISNAIN) - Ministry of Health, referring to leprosy patients living in any of the 38 districts of Aracaju, Sergipe, Brazil.

Individuals who started treatment from 2011 to 2015 were included, of all ages and whose records complete the variables necessary for the study. Thus, of the 683 leprosy cases available in the database, only 559 had adequate information, being this sample number used to performed the present study.

In addition to sociodemographic data of leprosy patients, other variables were analyzed, such as initial treatment for leprosy; clinical form of the disease; and operational classification received. Variables related to the epidemiological profile were analyzed according to the operational classification of leprosy (Paucibacillary or Multibacillary).

For statistical analysis, univariate and bivariate techniques were used to obtain the distribution of absolute and relative frequency values. Associations were investigated using the Chi-square test of Pearson's independence, being Odds Ratio (OR) estimated as a measure of association, with their respective 95% confidence intervals (95% CI) using the Mantel-Haenzel method. In all cases, significance was set at 5% ($p < 0.05$). The software *IBM® SPSS - Statistical Package for the Social Sciences (20.0 Version)* was used.

The TerraView 4.2 Program was also used to produce thematic maps on leprosy indicators. The Kernel estimation was used to describe how much the density of a point is capable of influencing the districts (Bailey & Gatrell, 1995) and also to identify risk clusters in the spatial distribution of the mean incidence of cases (Carvalho, Pina, & Santos, 2000). The Moran Local Index was calculated, in order to express areas with the greatest similarities, represented by clusters.

This study was approved by the Research Ethics Committee from Federal University of Sergipe (Parecer Nº 1.439,812 - CAAE: 52822915.0.0000.5546). All researchers followed the guidelines and regulatory standards recommended in Resolution No. 466/12 of the National Health Council on research involving human beings.

3. Results

In the city of Aracaju, from 2011 to 2015, 559 cases of leprosy were identified and well delineated. In this period, a decreasing tendency can be observed in cases detection, with

a decrease in the relative frequency from 23.1% (n = 129) in 2011 to 14.5% (n = 81) in 2015 (Table 1).

The mean age of leprosy patients, for each year of this period, was 43.9 ± 18.3 years in 2011; 45 ± 8.4 years in 2012; 45.6 ± 15.5 years in 2013; 48.2 ± 19.2 years in 2014; and 46.3 ± 21.9 years in 2015. The overall mean was 45.8 ± 16.6 years. Brown color skin/race was predominant [58.9% (2011), 60% (2012), 68.7% (2013), 62.5% (2014) and 56.7% (2015)], with an overall mean of 61.5% (n = 344). White and black color skin/race corresponded to a general average of 19.9% (n = 111) and 16.5% (n = 92), respectively. As for schooling, the majority had complete or incomplete elementary education (Table 2).

Although males represented most notifications in the last two years of the study period, there was no significant difference in total notification between genders: 49% (n = 274) for males and 51% (n = 281) for females (Table 1).

As for leprosy clinical form, the tuberculoid was the most common (28.2%, n = 158), followed by dimorphic (24.5%, n = 137), undetermined (21.5%, n = 120) and lepromatous (20.6%, n = 115). The multibacillary operational classification corresponded to the majority of notifications (52.4%, n = 293), especially in 2014, when a significant increase in this frequency was observed (Table 1).

Table 1 - Distribution of absolute and relative frequencies, of leprosy notification characteristics in the second year of the disease in Aracaju, Sergipe, Brazil, from 2011 to 2015.

Variables	Year of reference											
	2011 (n= 129) (23.1%)		2012 (n= 130) (23.2%)		2013 (n= 115) (20.6%)		2014 (n= 104) (18.6%)		2015 (n= 81) (14.5%)		Total (n= 559) (100%)	
	N	%	N	%	N	%	N	%	N	%	N	%
Gender												
Male	60	47	62	48	51	44	54	52	47	58	274	49
Female	69	53	68	52	64	56	50	48	34	42	285	51
Clinical form												
Undetermined	35	27	31	24	19	17	18	17	17	21	120	21,5
Tuberculoid	23	18	31	24	44	38	35	34	25	31	158	28,2
Dimorphic	33	26	42	32	24	21	24	23	14	17	137	24,5
Lepromatous	31	24	21	16	23	20	21	20	19	23	115	20,6
Unidentified	7	5	5	4	5	4	6	6	6	7	29	5,2
Operational classification												
Paucibacillary	60	47	63	48	57	50	45	43	41	51	266	47,6
Multibacillary	69	53	67	52	58	50	59	57	40	49	293	52,4

N (absolute frequency); % (relative frequency). Source: ISNAIN /DATASUS/MS.

In the association between operational classification and sociodemographic profile of leprosy patients, patients aged ≥ 16 years and male were mostly multibacillary, while in paucibacillary the variables statistically associated were age ≤ 15 years and female (p <0.05). A higher percentage of multibacillary was found among individuals with brown skin color/race and of paucibacillary between white/yellow skin color/race, without statistical evidence of association (p> 0.05) (Table 2).

Paucibacillary classification were 2.42 more likely to occur in younger group or multibacillary classification were more likely to occur in older group (OR = 2.42; 95% CI = 1.12-5.25). Regarding gender, paucibacillary classification were 2.74 more likely to occur in males or multibacillary classification were more likely to occur in females (OR = 2.74, 95% CI = 1.94-3.86) (Table 2).

Leprosy patients with high schooling were 1.58 more likely to be classified as paucibacillary or those with low school education were more likely to be classified as multibacillary (OR = 1.58, 95% CI = 1.11-2.26) (Table 2).

Table 2 - Associations between epidemiological profile of leprosy patients and operational classification of the disease in Aracaju, Sergipe, Brazil (n = 559), from 2011 to 2015.

Epidemiological profile	Operational classification		p	OR	95% CI
	Paucibacillary N (%)	**Multibacillary** N (%)			
Age group					
≤ 15 years	21 (67.7)	10 (32.3)	**0.021**	**2.42**	**1.12-5.25**
≥ 16 years	245 (46.4)	283 (53.6)			
Gender					
Male	96 (35)	178 (65)	**< 0.001**	**2.74**	**1.94-3.86**
Female	170 (59.6)	115 (40.4)			
Race					
Brown and black	203 (46.6)	233 (53.4)	0.408	1.18	0.79-1.78
White and Yellow	60 (50.8)	58 (49.2)			
Schooling					
High school/higher education	109 (54.8)	90 (45.2)	**0.011**	**1.58**	**(1.11-2.26)**
Illiterate/Elementary	143 (43.3)	187 (56.7)			

p = Chi-square test result; OR = Odds Ratio, 95% CI = 95% Confidence Interval. Statistically significant values in bold. Source: ISNAIN /DATASUS/MS.

Regarding spatial analysis, three clusters were observed, based on the mean incidence rate of the disease in the years studied, characterized as high, medium and low risk for leprosy illness in Aracaju, Sergipe and represented in red, yellow and blue, respectively

(Figure 1). The clustered districts in the high-risk cluster for leprosy corresponded to 15.3% (n = 6) of the total territory, including Bugio, Cidade Centenário, José Conrado de Araújo, Santos Dumont and Soledade. The Atalaia district is linked to the medium risk cluster, equivalent to 2.6% (n = 1) of the territory, while the districts of Centro, Grageru, Luzia, Pereira Lobo, Salgado Filho, São José and Suiça represent 17.9% (n = 7) of the districts and appear in the cluster characterized as low risk for leprosy (Figure 1A)

Figure 1A showed that the highest risk of disease in the population is located in the northernmost part of Aracaju, the median risk in the easternmost region and low risk in the most central area. The map estimating the Kernel intensity showed that the mean detection coefficient of leprosy had a more intense density concentration center-north portion of the territory studied (Figure 1B).

It is worth mentioning that, in several districts, there was more than one level of Kernel density estimation. Among the medium, high and very high densities, the first occurred in the largest number of districts [a total of 16 (41%)], followed respectively by 13 (33.3%) and 6 (15.4%) for the other districts (Figure 1B). Those with higher risk of illness (Figure 1A) had the highest levels of Kernel density estimation (Figure 1B).

Figure 1 - Spatial analysis with risk cluster for leprosy (**A**) and Kernel density estimation (**B**), based on the average incidence rate of cases in Aracaju, Sergipe, Brazil from 2011 to 2015.
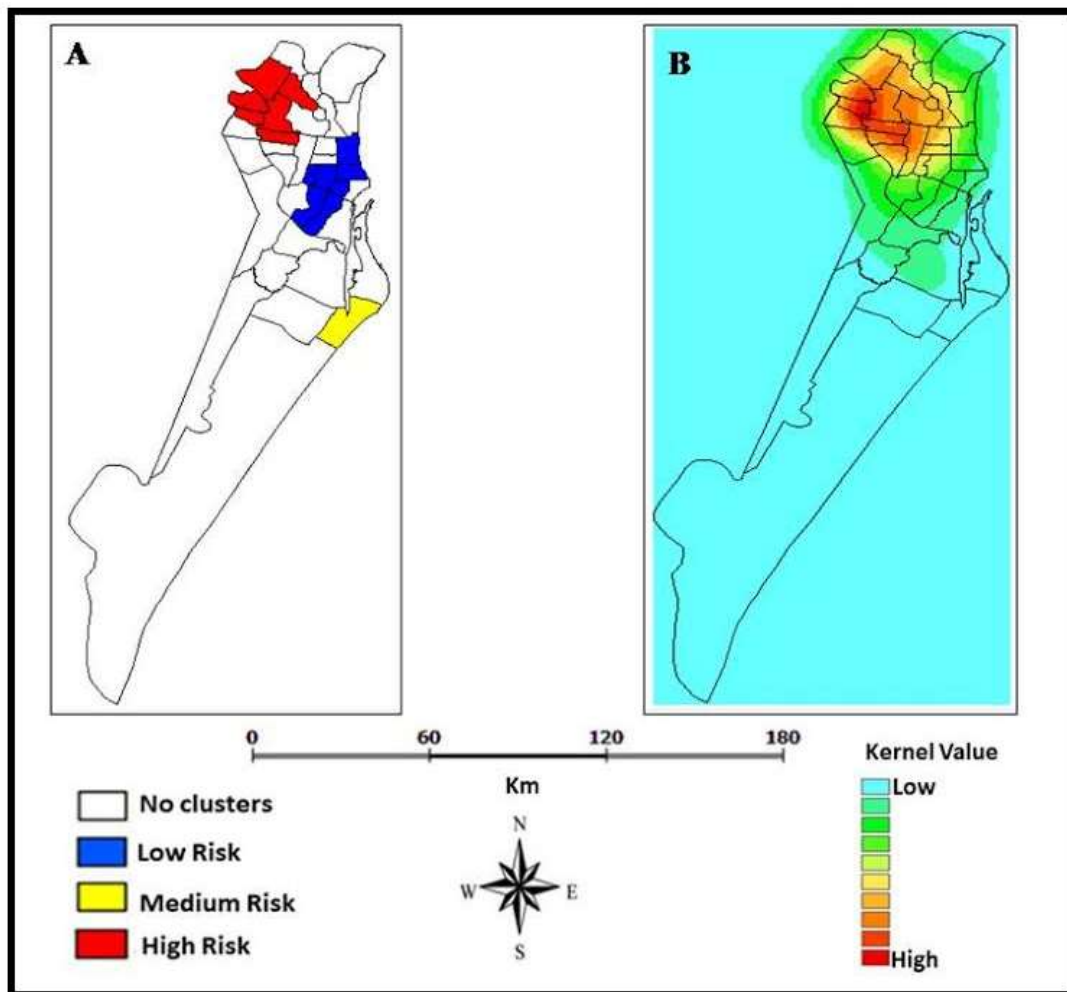
Source: ISNAIN /DATASUS/MS.

Figure 2 represents, according to the results described in Table 1, the spatial distribution of leprosy clinical forms. The tuberculoid form reached the largest number of districts (n=17), followed by the dimorphic (n=13), lepromatous (n=9), indeterminate (n=7) and unidentified (n=1) forms.

Figure 2 - Spatial distribution of leprosy in Aracaju, Sergipe, regarding the clinical forms in the Districts from 2011 to 2015. (A) undetermined, (B) tuberculoid, (C) dimorphic, (D) lepromatous, (E) unidentified. (F) Figures' subtitles: Case intervals (from 5 to 5).
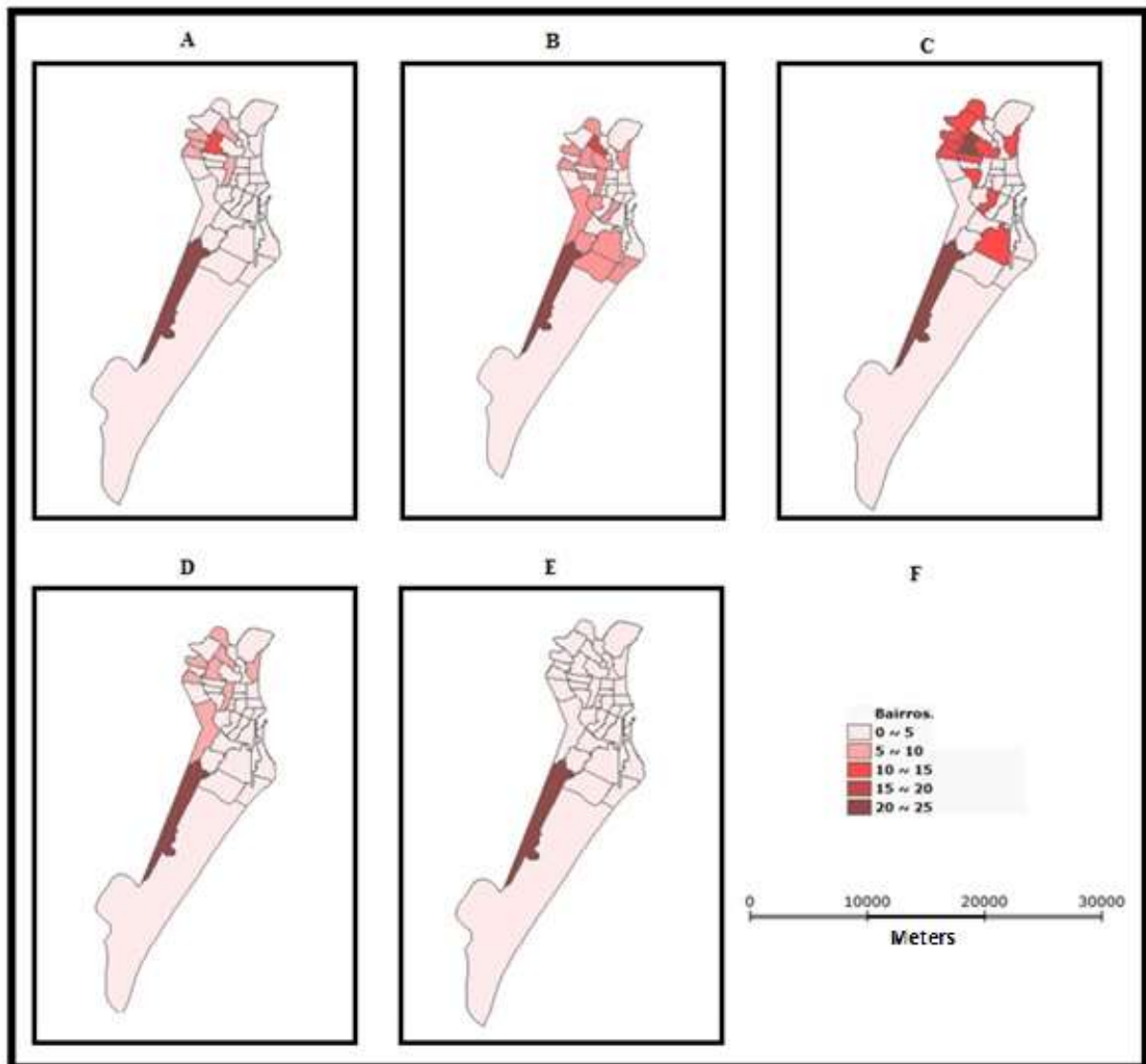
Source: ISNAIN /DATASUS/MS.

4. Discussion

In the present study, a detection behavior of leprosy cases with decreasing tendency was identified in the period studied, but still far from the goals established by Ministry of Health of Brazil (Brasil, 2016). This reduction should be considered with reservations, since it may be an effect resulting from the substitution of the active cases detection by the passive; the lack of awareness from professionals and/or the community; or even the disease wrong diagnosis(Paula Araujo Opromolla, Dalben, & Cardim, 2005).

In the epidemiological profile of leprosy patients, brown skin color/race and low schooling predominated, with a mean age of 45.8 ± 16.6 years and a nearly egalitarian distribution between sexes in leprosy patients. Other similar studies also reported evident predominance of brown skin color/race and low schooling in the characterization of this public (dos Santos, de Castro, & Falqueto, 2008; Miranzi, Pereira, & Nunes, 2010; Rocha et al., 2015). Low educational study was similar to Oliveira et al (2020) in the state of Piuaí that showed more cases with incomplete basic teaching those of the 1st to 4th grade, primary bearer from 5th to 8th series and illiterate (E. H. de Oliveira et al., 2020). The mean age of 45.8 ± 16.6 years was similar to that found in other studies (Miranzi et al., 2010; Paula A Opromolla, Dalben, & Cardim, 2006; Paula Araujo Opromolla et al., 2005).

As for gender, the total relative frequency of 49% for males and 51% for females differs from the values found in the literature, with the majority of reports among males (Miranzi et al., 2010; Paula Araujo Opromolla et al., 2005; Rocha et al., 2015). It should be emphasized that, in the present study, most of these reports among male patients only occurred in the last two years of the study period. This result differs from the analysis described by Façanha et al (2020) in the city of Caxias in the state of Maranhão, despite the slight difference; the occurrence was higher in males (Façanha et al., 2020).

The descriptive and spatial results showed that, among the clinical forms of leprosy, tuberculoid was considered the most common (28.2%), followed by dimorphic (24.5%), undetermined (21.5%) and lepromatous (20.6%). These results do not agree with some national studies, which reported the dimorphic clinical form as the most common (Ferreira, Ignotti, & Gamba, 2012; Vieira, Aragoso, Carvalho, & Sousa, 2014). Similar to national studies and divergent from those found in the present study, Oliveira et al (2020), reported in Paraíba, that among the clinical forms the one with the highest notification was dimorphic, followed by tuberculoid, virchowian and indeterminate (A. E. V. M. de Oliveira, Araújo, de Queiroga, Bezerra, & Chaves, 2020).

In the tuberculoid form the disease is limited by an efficient immunocellular response from the host. Cutaneous lesions, isolated and asymmetrical, are well-defined erythematous-hypochromic or erythematous lesions, usually with elevated external borders and normal center, presenting significant sensitivity alteration (Lastória & Abreu, 2012). In the dimorphic, identified in this study as the second most common among leprosy patients, there is considerable immunological instability, which favors a great variation in its clinical manifestations, either in the skin, nerves or in systemic compromise. Skin lesions are numerous, including erythematous plaques, hypochromic spots with ferruginous borders,

erythematous or brownish spots and erythematous-ferruginous or violaceous plaques. Neural lesions are early, asymmetrical, often leading to physical disabilities (Araújo, 2003).

In one of the less frequent clinical forms in this study, the undetermined, the occurrence of hypo or anesthesia areas, paraesthesia, hypochromic and/or erythemohypochromic spots, with or without decreased sweating and rarefaction of hairs, can be verified. In the lepromatous form, also uncommon in the studied population, there was diffuse erythema and infiltration, erythematous skin plaques, infiltrates and poorly defined borders, tubercles and nodules, madarosis, mucosal lesions and relevant sensitivity alterations (Saúde, 2009).

Regarding the disease operational classification, the multibacillary, defined by Ministério da Saúde as "the cases with more than five skin lesions" (Brasil, 2016), was the majority of notifications (52.4%) in this study, similarly to a research conducted in Brazilian Northeast State (Brito et al., 2014). However, it should be pointed out that individuals with age ≥ 16 years, male, brown/black skin color/race and low schooling represented the majority of multibacillary classifications, while in paucibacillary the associated variables were age $\leq$ 15 years, female, white/yellow race/skin color and average or higher schooling. Male gender, associated with the multibacillary type, and female gender with the paucibacillary, was also evidenced in a study with a similar design (Teixeira, Silveira, & França, 2010), as well as the results of leprosy patients aged ≤ 15 years and female, corresponding to the majority of paucibacillary patients according to a national study (Moura, Fernandes, Bastos, Luna, & Machado, 2012).

The occurrence of cases in children under 15 years old reinforces the precocity of exposure and the persistence of disease transmission in childhood. Such situations are important for assessing the magnitude of this problem (Moura et al., 2012). Despite being considered a more common disease among adults, leprosy should be considered as a possible occurrence in the child's age group, highlighting the necessity to perform differential diagnoses of common dermatitis at early age (Lana et al., 2007).

The findings of this study highlight the importance of carrying out educational interventions with clear, simple and objective approaches and with adaptation to the public sociodemographic level. It may also highlight the importance of expanding health care services for the disease early detection and of professional training for those working in the basic care network, providing an early diagnosis, treatment and adequate follow-up of leprosy patients in the studied territory.

5. Conclusion

It was understood that the socioeconomic, clinical and demographic profile of leprosy patients in the municipality between the years studied had a greater representation in those over 60 years of age, female, brown, with incomplete elementary education, diagnosed in the tuberculoid clinical form and in multibacillary operational classification, with the highest risk for those above 16 years of age and males belonging to this classification.

As it is a disease considered neglected and has a close relationship with places that are under or below the poverty line, in Aracaju, it presented high numbers, case concentrations and endemicity rates in neighborhoods with the worst social indicators in the municipality, according to the analysis spatial distribution. Despite this, neighborhoods with good and regular socioeconomic conditions were surrounding areas at risk for illness, and it is also important to monitor these places so that the disease does not spread.

Even though the spatial distribution of leprosy is heterogeneous in the territory, there were strong concentrations of number density and average incidence of cases in the central and northern portions of Aracaju. This highlights the relationship between leprosy and precarious socioeconomic conditions, because these regions exhibit a profile of social vulnerability associated with low income and less years of schooling for their population.

Thus, it is concluded that the use of geostatistics was fundamental for understanding the panorama of geographic distribution and the profile of leprosy patients in Aracaju, being relevant for allowing a greater and better knowledge of the situation of leprosy in the municipality.

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