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Clinical and epidemiological indicators and spatial analysis of leprosy cases in patients under 15 years old in an endemic area of Northeast Brazil: an ecological and time series study

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ABSTRACT

Objective This study aimed to analyse the clinical and epidemiological indicators, temporal trends and the spatial distribution of leprosy in patients under 15 years old in an endemic area of Northeast Brazil.

Design Regional surveillance study of all reported cases.

Setting State of Sergipe, endemic area of Northeast Brazil.

Methods An ecological and time series study was conducted, based on secondary data reported by the Brazilian Information System on Notifiable Diseases for leprosy cases diagnosed in Sergipe state (2002–2015). The analysis of temporal trends was performed using the Joinpoint Regression Programme through Poisson regression. We performed spatial analysis by Kernel estimator and Moran index.

Results The incidence rate was reduced from 6.29 to 3.78 cases per 100 000 inhabitants in 2002 and 2015, respectively. However, Sergipe was still classified as highly endemicity in 2015. The mean number of household contacts (HHC) examined was significantly lower than those registered. Clinical data indicated that 21.4% of the patients developed leprosy reactions, and 31.3% presented with some physical disability in the multibacillary groups. Patients diagnosed by examination within the HHC presented better indicators, such as lower percentage of leprosy reaction and physical disability. Spatial analysis showed the most risk areas distributed on the northeast and cities around the capital, Aracaju.

Conclusion The data indicate that there is a persistence of active *Myobacterium leprae* transmission and a delay in disease detection, following a pattern of high endemicity in many municipalities. The early detection by HHC examination is important to stop transmission and also to detect the cases in a less severe state.

Strengths and limitations of this study

- ► This is a surveillance study that includes all notified cases of leprosy, in a state of Brazil with moderate prevalence of the disease.
- ► This is the first summary of leprosy cases in patients under 15 years old in Sergipe state, Northeast Brazil.
- ► This study was conducted using secondary data reported by Brazilian Information System on Notifiable Diseases and this source of data may have data sets missing.
- ► We also mapped the leprosy cases and physical disability in children under 15 years in areas of higher prevalence of leprosy in the general population, using geoprocessing tools.
- ► We compared the leprosy patient detection mode and how it affects the disease severity at diagnosis and the occurrence of leprosy reactions and physical disabilities.

INTRODUCTION

Leprosy is a chronic infectious disease caused by infection with *Mycobacterium leprae*.[1] This pathogen exhibits tissue tropism for phagocytes in the skin and Schwann cells within peripheral nerves and it presents a long incubation time (from 2 to 7 years).[2 3] The disease can manifest across a broad spectrum of symptoms and the diagnosis is made based on the clinical signs (cutaneous lesions with altered sensitivity and neurological lesions). Patients are then classified as multibacillary (MB) and paucibacillary (PB) for treatment purposes, according to criteria accepted by Brazilian Ministry of Health (BMH) and International Leprosy Association (ILA).[1 2 4–7]

Despite control efforts including the widespread use of multidrug therapy (MDT), and the stabilisation of the reported new

case detection rate in the last few years, leprosy remains endemic in many developing countries.[3–6 8–11] In 2014, the WHO reported 213 899 new leprosy cases in 121 countries or territories.[4] Brazil ranks as the second most burdened country in the world concerning number of new cases (31 064 in 2014) and has by far the highest number of cases reported in Americas.[4 12 13] Within Brazil, the highest prevalence has been reported in the North, Northeast and Midwest regions.[8 9] The incidence of leprosy (referred as the new case detection rate) in Sergipe in 2010 was 18.4 per 100 000.[8] In 2013, 2439 new cases were diagnosed in children under 15 years old in Brazil, yielding a detection rate of 5.03 per 100 000 inhabitants.[4]

Studies have demonstrated that leprosy presents higher incidence in population with low educational degree, precarious health services and domiciliary infrastructure settlements and reduced investment in prevention and control.[14–16] Moreover, the high incidence rate in children under 15 years is important to indicate that there is early exposure of the population to the bacillus, that is associated with elevated prevalence in general population, being a good indicator of a high transmission and bad quality of the control programmes.[10 12 17–20] There is no study reporting the incidence of leprosy in children under 15 years in Sergipe state.

Recently, studies mapping the occurrence of infectious diseases according to their spatial distribution using 'Geographic Information Systems (GIS)' have provided important information for public health programmes, revealing areas of priority for intervention programmes to more efficiently plan and implement control measures.[2 9 16 21–23] The use of GIS in leprosy may allow the identification of spatial–temporal distributions and profile of incidence in defined geographical areas, this potentially contributing to the effectiveness of interventions.

Despite breakthroughs in the epidemiological of leprosy, further improvements in understanding of the disease dynamics in different regions are important for the support of health services as a means for leprosy control. Spatial analysis studies can provide important understanding of the transmission patterns of *M. leprae* and allow the identification of risk factors.[21 23] The aim of this study was to describe the (1) various clinical and epidemiological indicators of leprosy to analyse (2) temporal trends and (3) the spatial distribution of leprosy cases in patients under 15 years old in an endemic area of Northeast Brazil.

METHODS

Study design

The source of all data from this study was the leprosy cases and the information of each individual case notified by the health centres of the municipalities to the SINAN (Information System on Notifiable Diseases) from the state of Sergipe, Brazil. This is an important database of the Secretariat of Health of all States of Brazil, to report information about sociodemographic, clinical features and the address of notifiable diseases. Leprosy is a notifiable disease in Brazil, and as a legislative requirement, all leprosy cases have to be notified to the SINAN, including information about social and demographic features, clinical forms and follow-up of each patient. Sergipe is located on the coast of Northeast Brazil. The State has 75 municipalities and the capital is Aracaju. It has a population of 2 068 017 inhabitants and an area of 21 910 354 km², equivalent to 0.26% of the national territory. The median population per county was 27 573.56 in 2015.[16] Population data were obtained from the IBGE (Brazilian Institute of Geography and Statistics), based on population estimates for the intercensus years (2002–2015). An ecological and time series epidemiological study was conducted, based on the leprosy cases reported by SINAN. The historical (from 2002 to 2015) reporting of leprosy cases in children under 15 years old was analysed. We also compared those data with data in all ages and with the occurrence of physical disability. The incidence of leprosy (referred as the new case detection rate) in Sergipe in 2010 was 18.4 per 100 000.[8]

The clinical and epidemiologic indicators collected by Investigation and Notification Form from SINAN were gender, age, ethnicity, address, operational classification (PB and MB), clinical form (according to the more refined Ridley-Jopling classification,[24 25] based on histopathological analyses: indeterminate leprosy, true tuberculoid, borderline leprosy and lepromatous leprosy), leprosy reaction (LR), number of affected nerves, degree of physical disabilities, number of household contacts (HHC) registered and examined and the patient detection mode.

The parameters adopted by BMH and ILA were followed for interpreting the incidence rate of leprosy in patients under 15 years old. As such, this is classified as low (<0.50 cases per 100 000 inhabitants), medium (0.50–2.49), high (2.50–4.99), very high (5.00–9.99) and hyperendemic (≥10.00).[4]

Spatial analysis

Thematic maps were constructed in each municipality for the period examined according to the leprosy incidence rate in patients under 15 years old and in general population, and for patients presenting with physical disability (incapacity degree 1 or 2). The kernel technique was applied to identify the intensity of the distribution of leprosy cases in the state of Sergipe. This technique shows the statistically generated surface density for the visual detection of hot spots that indicates agglomeration of cases in a spatial distribution. This is an appropriate data interpolation for application in point location data. The point distribution was transformed into a smoothed surface and presented as a continuous map, representing different levels of case intensity. The amount of smoothing, that is, the width of the radius of influence was defined as 3000 m, since this value generated an adequate representation of the distribution of the leprosy cases in

the municipalities, minimising the overlapping bias or the occurrence of subdistribution patterns smoothed.[16 21]

We performed either spatial autocorrelation analysis between disease detection rates for each group. The Moran Global Index (MGI)[26] was calculated to identify clusters with risks for disease occurrence. We construct a spatial proximity matrix obtained by the contiguity of spatial correlation. The MGI was calculated as follows:

(MGI Mathematical Equation 1)

$$I = \frac{[(n\sum_i^n \sum_j^n \omega_{ij}(\gamma_i - \breve{y})\ (\gamma_j - \breve{y}))]}{[\sum_i^n (\gamma_i - \breve{y})^2 \sum_j^n \omega_{ij}]}$$

ω_{ij} is a contiguity matrix element (ω); γ_i is the incidence rate of municipality i; γ_j is the incidence rate of municipality j; $\breve{y}$ is the mean of sample and the symbol n represents the total number of municipalities.[26]

The MGI provides a general grouping measure and it is possible to know if there are significant differences between the analysed areas. However, it does not indicate the clusters localisation. To do that, we performed the Moran Local Index diagram[26] to build maps and identify the areas with spatial dependence (Local Index of Spatial Association—LISA) of the annual detection means, as follows:

(LISA Mathematical Equation 2)

$$I = \frac{n[(Z_i \sum_j^n {}_{ij} Z_j)]}{(\sum_j^n Z_j^2)}$$

$Z_i = yi - \bar{y}$; $Zj = yj - \bar{y}$; ω_{ij} is a contiguous matrix element ω; yi is the incidence rate of municipality i; yj is the incidence rate of municipality j; $\bar{y}$ is the sample mean and the symbol n represents the total number of cities.[26] The Moran Map was used to indicate the clusters and their relationship with the neighbours. This analysis verifies the existence of spatial dependence and risk patterns: Q1 (high/high) and Q2 (low/low), which indicate municipalities with similar values between their neighbours and Q3 (high/low) and Q4 (low/high) for municipalities with different values between their neighbours and no spatial association. A spatial proximity matrix obtained by the contiguity criterion was adopted. The level of significance was 5% and the MGI (I) varying between −1 and +1, representing the spatial autocorrelation of leprosy detection rate in the geographic space analysed to identify spatial clusters and risk areas. Values between 0 and +1 indicate positive spatial autocorrelation (Q1 and Q2) and between −1 and 0 negative spatial autocorrelation (Q3 and Q4).[26 27] Both Moran Index and Kernel maps were constructed using TerraView software V.4.2.2.

Statistical analysis

The crude annual incidence rates were calculated for the general population, according to the population data from IBGE. For patients younger than 15 years, the annual rates were age-standardised, and the standard population used was the population under 15 years from IBGE. Demographic and clinical data were compared across the different subgroups and according to operational classification and the patient detection mode. Percentage, mean and SD of the groups were calculated. For groups' comparison, we first analyse if the data followed normal distribution by the D'Agostino and Pearson normality test, and statistical differences between the groups were determined by Mann-Whitney and Kruskall-Wallis tests. All analyses were performed using SPSS Statistics V.24.0. Results were considered statistically different when P-values<0.05 were obtained.

In order to enable trend analysis, annual incidence rate of leprosy was calculated as dependent variables (y), and the years of the study period as the independent variables (x). Initially, trend analysis was performed with the Joinpoint programme, V.4.0.4. This programme estimates the Annual Percentage Change (APC) of a segmented linear regression (Jointpoint regression) and identifies inflection points. Each inflection point reflects changes in the increase or decline of leprosy rates.[27] The joinpoint regression provided the adjustment of a series of lines as well as their inflection points on a logarithmic scale by means of the annual trend test. All the models were run under the same specifications. The minimum number of observations from a joinpoint to either end of the data was three and the minimum number of observations between two joinpoints was four. The maximum number of joinpoints allowed was two. To obtain the adjustment based on the best line of each analysed segment, the Monte Carlo permutation method was used as a test of significance. From the definition of the follow-ups, the APC and the average AAPC, with their respective 95% CIs, were estimated and tested. If the occurrence of an inflection point with inverted direction was verified, the study periods were analysed separately. The number of inflections used in the analysis was the result of models defined by the programme itself, in order to allow the best representation of the trend, with the lowest number of inflection points. The result showed growth (positive APC values), reduction (APC negative values) or maintenance (APC value equal to zero) of the trend throughout the historical series analysed (2006–2014). Poisson regression is used to determine the number of segments required to properly explain the relationship between two variables.[27] We considered the points of trend change that presented P-value<0.05.

Patient and public involvement statement

There was no patient and public involvement in this study. The study was based on secondary data.

RESULT

Trends in reported Leprosy incidence among children

The incidence of leprosy in children under 15 years has declined from 6.29 cases per 100 000 inhabitants in 2002, to 3.78 in 2015, confirmed by Joinpoint regression analyses (APC=−5.3 and P-value<0.05; figure 1A and B). Similarly, the leprosy incidence rate in the general

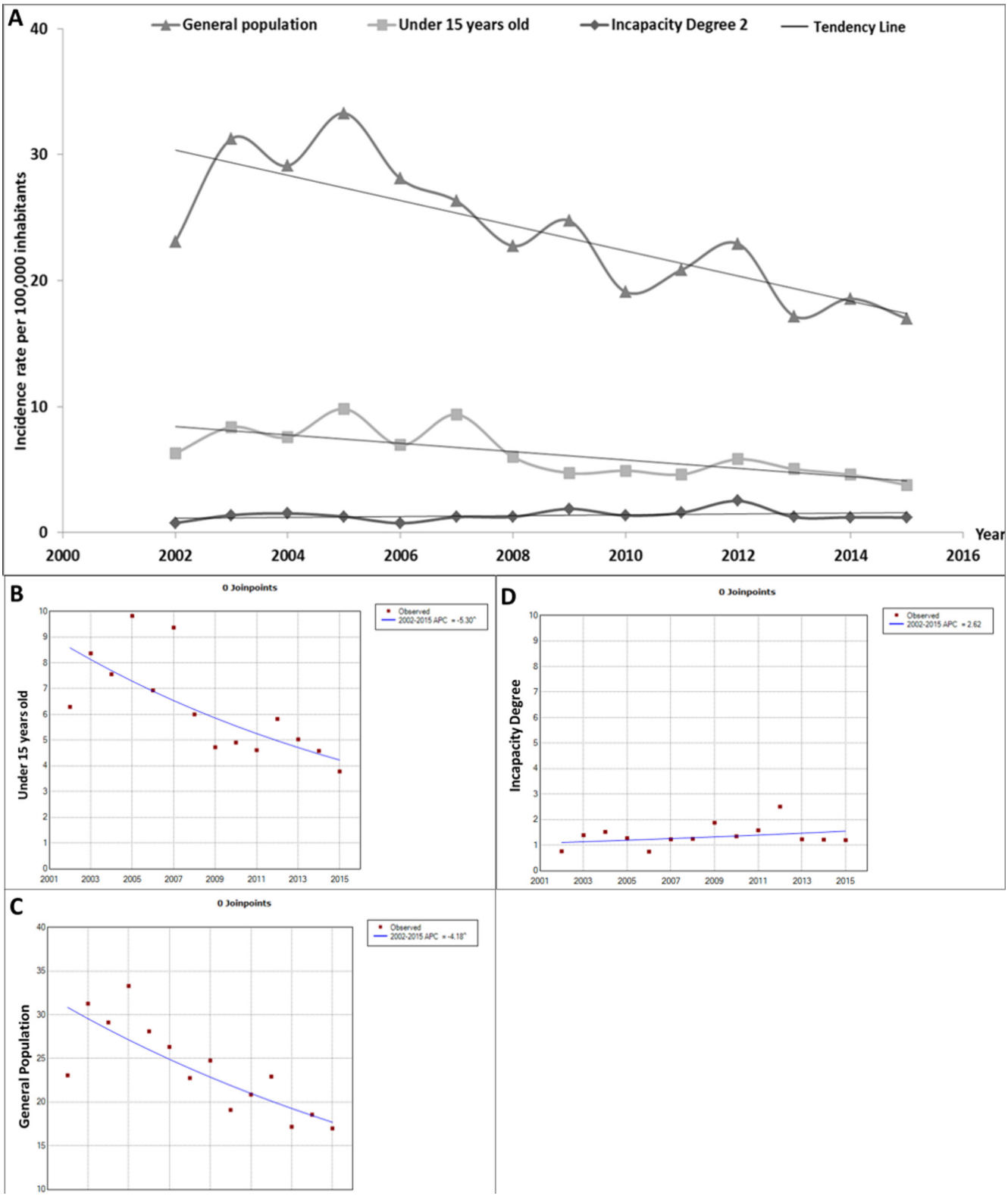

Figure 1 Leprosy incidence rates and temporal trend in state of Sergipe, Northeast Brazil, 2002–2015. (A) Leprosy incidence rate (per 100 000 inhabitants) in general population (▲), in patients under 15 years old (■), degree 2 of physical disability (♦) and the tendency line. Temporal trend of standardised incidence rates by Joinpoint Regression for (B) patients under 15 years old, (C) general population and (D) incapacity degree. Data were considered statistically different when P-value<0.05.

population of Sergipe decreased from 23.08 cases to 16.99 per 100 000 inhabitants between 2002 and 2015 (figure 1A and C). The occurrence of degree 2 physical disability, however, increased in this period (0.76 in 2002 to 1.2 in 2015, respectively); however, it is a non-significant increasing trend (APC=2.6 and P-value=0.20; figure 1A

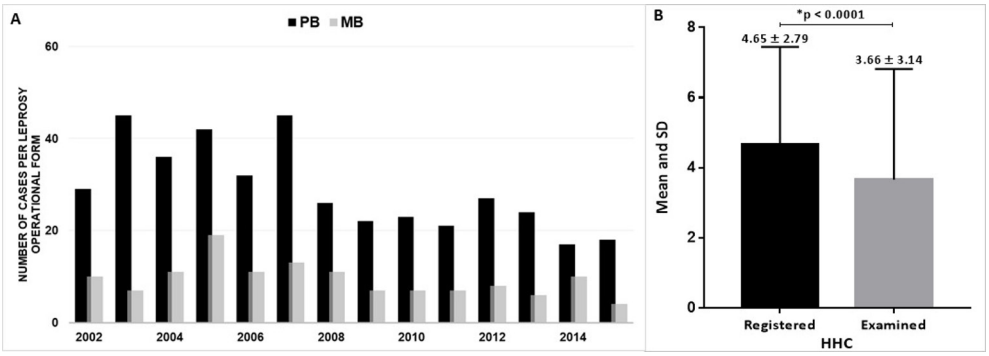

Figure 2 Epidemiological, clinical and operational indicators in leprosy patients, state of Sergipe, Brazil, 2002–2015. (A) Number of leprosy cases according to the clinical operational classification (paucibacillary, PB (■) and multibacillary, MB (■) forms). (B) Mean and SD (mean ±SD) of the number of household contacts (HHC) that were registered and examined for leprosy diagnosis. Data were considered statistically different when P-value<0.05. *Mann-Whitney test.

and D). The composition of leprosy cases according to the operational classification (PB and MB) was relatively stable across this period, with majority of cases presenting as PB (figure 2A). We also observed the mean number of HHC registered (4.65±2.79) was slightly, but significantly, higher than the number examined (3.66±3.14; P-value<0.0001; figure 2B).

Demographics of childhood Leprosy cases

Next, we evaluated the association among clinical and epidemiological variables according to the leprosy operational classification (patients presenting as PB and MB). Patients presenting as MB or PB were in similar age to (10.5±2.81 and 10.07±3.38, respectively). Despite the extended incubation period of *M. leprae*/leprosy, six cases (1.11%) were reported in children less than 1 year of age. Of the 538 leprosy cases identified among children under 15 years old, the majority were PB (407 (75.7%) PB and 131 (24.3%) MB; table 1). When stratified on gender, however, the proportion of boys presenting with MB (63.4%) was significantly higher than presenting with PB (48.4%; P-value=0.003). An interesting difference was observed when we calculated the ratio (PB/MB) according the ethnic groups. Among those identified as black, the ratio (43/24) was 1.79. Conversely, the ratio of white was higher 4.88 (88/18; P-value=0.02).

As expected, the occurrence of LRs was significantly higher in MB (21.4%) than PB (4.9%; P-value<0.0001) patients. The occurrence of degree 2 of physical disability was also higher in MB (4.6%), than in PB patients (0.74%; P-value=0.0001). Consistent with this, we observed that the mean of number of affected nerves was higher in MB (0.5±1.03), than PB (0.19±0.54; P-value=0.04).

Impact of case detection methods on Leprosy presentation

We also performed analysis of association among clinical and epidemiological variables according to the leprosy patient detection mode. The patients were grouped in: spontaneous demand (SDem: patients that looked for medical assistance by themselves); forwarded (FW: patients that were forwarded from a primary clinic to a leprosy reference centre); examined HHC and other. We observed that patients detected by the examined

Table 1 Association of demographic and clinical data according to the operational classification of leprosy (PB and MB) in children under 15 years in Sergipe state, Brazil (2002–2015)

Variables	Operational classification		
	PB (n=407)	MB (n=131)	P value
Age mean±SD	10.07±3.38	10.5±2.81	*0.46
Gender, n (%)			
Male	197 (48.4)	83 (63.4)	+0.003
Ethnicity, n (%)			
White	88 (21.6)	18 (13.7)	#0.02
Black	43 (10.5)	24 (18.3)	
Brown	251 (61.7)	78 (59.5)	
Indian	4 (0.9)	3 (2.3)	
Leprosy reaction, n (%)	20 (4.9)	28 (21.4)	+<0.0001
Physical disability degree, n (%)			
0	337 (82.8)	90 (68.7)	#0.0001
1	26 (6.4)	18 (13.7)	
2	3 (0.74)	6 (4.6)	
Number of affected nerves (mean±SD)	0.19±0.54	0.5±1.03	*0.04
Number of lesions (mean±SD)	1.61±1.14	9.92±12.03	*<0.0001
HHC registered (mean±SD)	4.6±2.71	4.85±3.04	*0.14
HHC examined (mean±SD)	3.54±3.04	4.05±3.44	

*Mann-Whitney test.
+Fisher's exact test.
#X^2 test.
We missed data in some variables.
HHC, household contacts; MB, multibacillary; PB, paucibacillary.

Table 2 Demographic and clinical aspects accordingly to the detection mode of leprosy cases in children under 15 years in Sergipe state, Brazil (2002–2015)

Variables	Patient detection mode				
	Spontaneous demand (n=234)	Forwarding (n=210)	Examined HHC (n=69)	Other (n=25)	P value
Age mean±SD	10.54±3.28	10.02±3.15	9.6±3.38	9.6±3.22	*0.04
Gender, n (%)					
Male	123 (52.6)	110 (52.4)	38 (55.1)	09 (36)	#0.41
Leprosy reaction, n (%)	17 (7.3)	28 (13.3)	2 (2.9)	1 (4.0)	#0.02
Physical disability degree, n (%)					
0	199 (85.1)	150 (71.4)	55 (79.7)	18 (72)	#0.04
1	17 (7.3)	21 (10)	5 (7.2)	1 (4.0)	
2	1 (0.43)	08 (3.8)	0 (0.0)	0 (0.0)	
Number of affected nerves (mean±SD)	0.24±0.67	0.34±0.81	0.06±0.25	0.25±0.5	*0.48
Number of lesion (mean±SD)	3.64±6.25	4.09±8.68	2.04±2.96	4±5.2	*0.04
HHC registered (mean±SD)	4.57±2.53	4.59±2.74	5.57±3.81	3.45±1.96	*0.04
HHC examined (mean±SD)	3.71±3.02	3.02±2.98	4.64±4.06	2.04±1.77	*0.01

*Kruskal-Wallis test.
#X^2 test.
We missed data in some variables.
HHC, household contacts.

HHC method presented lower mean age (9.6±3.38) than those detected by either the SDem (10.54±3.28) or FW methods (10.02±3.15; P-value=0.04; table 2). Interestingly, the percentage of LR among the examined HHC group (2.9%; P-value=0.02) was lower than that observed among SDem (7.3%) and FW (13.3%). In addition, degree 2 of physical disability was not observed among patients detected in examined HHC group, while SDem and FW presented 0.43% and 3.8%, respectively (P-value=0.04). Furthermore, patients identified among examined HHC presented with lower numbers of lesions (2.04±2.96; P-value=0.04) than SDem (3.64±6.25) and FW (4.09±8.68). Taken together, these data reinforce the importance of HHC examination for the detection of leprosy patients before advancement to more severe symptoms.

Spatial analyse data

Next, we performed the spatial analysis of leprosy cases in the general population, in patients under 15 years old, and in patients presenting with physical disability (both degrees 1 and 2). Moran maps have showed higher risk clusters (Q1—in red; figure 3A-C) in similar areas when comparing the maps regarding leprosy cases in children under 15 years old, in general population, and patients presenting some physical disability (degrees 1 and 2). The higher risk clusters (Q1) were localised in Sergipe state centre and in the metropolitan area around the capital of State. The municipalities with no spatial association (Q3—in blue) were localised in the Semiarid region, in the northwest area and in the south region.

Similarly, the Kernel estimator, through data interpolation, showed densities (hot spots) of the highest incidence rates located at the northeast and east centre regions and in the counties around the state capital (Aracaju city; figure 3D-F). Lower intensity was observed on the western region. Municipalities with intermediate to high incidence values are seen in yellow and red tones of each subfigure. Low incidence areas were reported on west coast municipalities, mostly in smaller counties with small populations.

DISCUSSION

Previous studies have demonstrated that the high leprosy cases detection in patients under 15 years old is a bad parameter for leprosy control programme, because it indicates early bacillus transmission from undiagnosed cases.[18] Some authors have speculated either about the risk of vertical/transplacental transmission or through breastfeeding.[12]

In Brazil, the highest leprosy incidence rate in children was reported in the North area (11.91 cases per 100 000 inhabitants), followed by Northeast (8.12).[12] We observed the leprosy incidence rate was reduced in children under 15 years old from 2002 to 2015 in Sergipe state, however considering the parameters adopted by BMH, the state was classified as very high endemicity in 2002, and still as high endemicity in 2015. It remains also with elevated incidence rate and stationary tendency of degree 2 of physical disability. Those data reinforce either that the

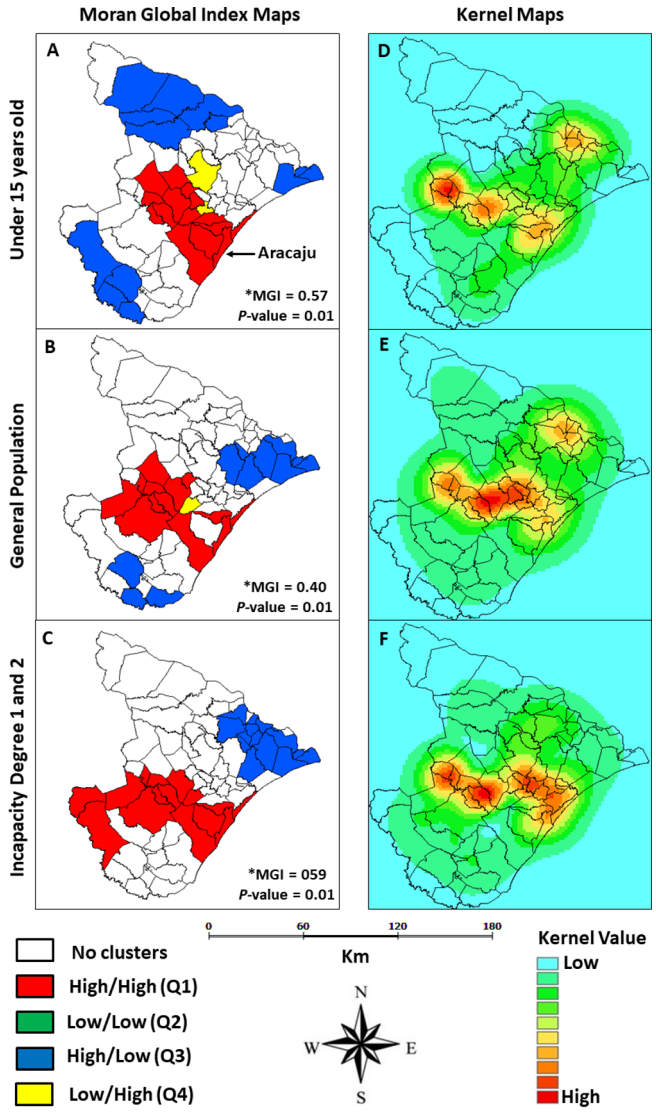

Figure 3 Spatial analysis maps. Moran Global Index (MGI) maps and Kernel maps were constructed by TerraView Software V.4.2.2. The *MGI was calculated to identify the occurrence of clusters. Moran (A) and Kernel (B) maps of leprosy cases in patients under 15 years old. Moran (C) and Kernel (D) maps of leprosy cases in the general population. Moran (E) and Kernel (F) maps of occurrence of incapacity degrees 1 and 2. Sergipe state, Northeast Brazil (2002—2015).

transmission is intense at early age, there is lack of an effective public health and the disease control is focused in the MDT.[12 18] A similar study performed at Fortaleza city (Brazil), reported also that although a decreasing has been observed on overall detection rate, the number of new cases in those under 15 years old remains stable.[13]

LRs and physical disability are the most severe leprosy clinical complications.[8 28 29] In addition, the increase or stability of the prevalence of degree 2 of physical disability indicates persisting late diagnosis.[13 29] The early diagnosis of leprosy is essential to the prevention of deformities, whose repercussions are still more catastrophic in children and adolescents.[28] Our data reported 21.4% children with LR and 31.3% with some physical disability in the MB groups. Furthermore, MB patients presented higher mean of affected nerves. Generally, patients under 15 years old do not use to present LR, but studies have reported a low frequency of LR, varying between 1.36% and 8.33%.[28] Those data reinforce that, although there is a decreasing incidence in leprosy, patients have been exposed to bacillus early in life and diagnosed belatedly and hence they have been also developing into some clinical complications.

We have observed either that the mean of HHC examined was significantly lower than those registered by SINAN. Moreover, leprosy patients detected by examination in HHC presented lower mean of age, affected nerves, number of lesions, occurrence of LR and no physical disability, when compared with those identified by spontaneous demand or forwarded by others. On the other hand, mostly of patients presenting as degree 2 of physical disability were identified into those forwarded to a leprosy reference centre, probably because they started presenting some physical disability. HHC and neighbours are the most important *M. leprae* active sources. The risk of a person developing leprosy is nine times greater among HHC and up to four times greater among contacts with neighbours.[12] Therefore, our data reinforce the importance of leprosy early diagnosis by exam in patients and their HHC. Besides that the treatment and the home visits by public health programmes, and an efficient health programme in schools could represent important actions for the early diagnosis and the reduction of leprosy clinical complications, especially in children.

Spatial analysis of health events aim to identify geographical patterns by maps of risk and to point out areas of higher severity and to facilitate the planning of public health interventions.[9] The Kernel maps showed the spatial dynamic of leprosy, with a heterogeneous geographical pattern and the highest risk areas for leprosy infection. The highest incidence on counties around the Capital can be due there was a leprosarium at the Nossa Senhora do Socorro (a city of the metropolitan area of Aracaju) that has presented elevated detection rate in mostly evaluated years. Moreover, that area presents reference centre to leprosy diagnosis and treatment and hence they have several patients forwarded to these leprosy clinics. It can be also associated with weather featuring such as humidity, considering either that counties near to São Francisco River presented also elevated incidence. In the Malawian Karonga district, a positive relationship between the proximity of water and leprosy incidence was previously reported.[5] Some authors have hypothesised that *M. leprae* survives longer outside of human body in humid compared with dry atmospheres.[9 13]

Interestingly, higher risk clusters were identified in similar areas when we analysed the occurrence of leprosy cases in children, in general population and patients presenting physical disability. It corroborates the hypothesis that the early transmission of *M. leprae* and the occurrence of leprosy in children under 15 years old is directly related to the late

diagnosis, which explains the occurrence of patients with degree 2 of physical disability in the same geographic distribution.[28] The maps present certain disagreements regarding the occurrence of leprosy cases in the state of Sergipe because they use distinct techniques of spatial analysis. The Kernel estimator produces a continuous surface, with densities calculated at all locations, based on total number of cases and not considering the geographical boundaries of the municipalities.[27 30 31] The Kernel technique presents greater advantages to the quick visualisation of areas that deserve attention, besides not being affected by political-administrative division, while the Moran technique, constructs maps considering the political-administrative divisions of the state and the clusters are based on the number of cases divided by the municipalities.[27 30]

Our study had some limitations, particularly because it was conducted using secondary data reported by SINAN. This source of date can present numbers under notification and data sets missing. However, in Brazil, we have a specific normative that is an obligation to notify several diseases to SINAN, and leprosy is one of them. SINAN is an important database of the Secretariat of Health of all States of Brazil, to report information about sociodemographic, clinical features and the address of each diagnosed case. This source of data can present under notification because Leprosy is an asymptomatic disease and the active search would be important to detect more cases, but all diagnosed cases are reported to SINAN. The limitation mentioned about missing data is not very important in the case of the disease prevalence, but the complete information about the cases follow-up, such as degree of neurological disability at the end of treatment, LRs and treatment details, because it is a secondary database that depends on other doctors or nurses from the healthcare centres to fulfil the information. Despite this, those data reported high endemicity of leprosy cases in patients under 15 years old, and this study do not focus on patient follow-up.

In summary, our study demonstrated that the leprosy incidence rate has decreased in Sergipe state. However, it is still classified as high endemicity considering the WHO proposed ratios for children under 15 years. Patients detected by examination in collectivity or HHC presented better indicators. Altogether, the epidemiological data and spatial analysis indicate that there is persistence of active transmission of *M. leprae* and later case detection in Sergipe state, increasing the risk of transmission in children. In addition, the spatial analysis brings new advantages to comprehend the leprosy dynamic, and reinforce the superimposed regions of high occurrence areas of patients presenting degree 2 of physical disability and cases in children lower than 15 years, and highlights the need to strengthen effective disease control measures, mainly in primary healthcare.

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