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Socio-economic and environmental effects influencing the development of leprosy in Bahia, north-eastern Brazil

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Abstract

OBJECTIVES To investigate spatial clusters and possible associations between relative risks of leprosy with socio-economic and environmental factors, taking into account diagnosed cases in children under 15 years old.

METHODS An ecological study was conceived using data aggregated by municipality to identify possible spatial clusters of leprosy from 2005 to 2011. Relative risks were calculated accounting for the respective covariate gender. The second stage of the analysis consisted of verifying possible associations between the relative risks of leprosy as a dependent variable, and socio-economic and environmental variables as independent. This was performed using a multivariate regression analysis according to a previously defined conceptual framework.

RESULTS Overall rates have decreased from 0.88/10 000 in 2005 to 0.52 in 2011. Spatial scan statistics identified 4 high-risk and 6 low-risk clusters. In the regression model, after allowing for spatial dependence, relative risks were associated with higher percentage of water bodies, higher Gini index, higher percentage of urban population, larger average number of dwellers by permanent residence and smaller percentage of residents born in Bahia.

CONCLUSIONS Although relative risks of leprosy in Bahia have been decreasing, they remain very high. The association between relative risks of leprosy and water bodies in the proposed geographic scale indicates that hypothesis linking *M. leprae* and humid environments cannot be discarded. Socio-economic conditions such as inequality, a greater number of dwellers by residence and migration are derived from the urbanisation process carried out in this State. Precarious settlements and poor living conditions in the cities would favour the continuity of leprosy transmission.

keywords leprosy, spatial scan statistic, environmental factors, socio-economic factors, spatial regression, Brazil

Introduction

Leprosy is an infectious disease caused by *Mycobacterium leprae*, whose progenitor strain may have originated from East Africa and spread to Asia and South America (Monot *et al.* 2009). Leprosy transmission has not been completely understood, although the main infection route is likely to be from person-to-person via nasal and oral droplet dispersion (Hatta *et al.* 1995; Rodrigues & Lockwood 2011).

Leprosy dynamic transmission and causation are complex. Apart from individual factors, such as immunity and proximity to infecting contacts, they also involve composition of the local population (e.g. gender, age, education, employment, ethnicity, housing and social level), which may be associated with its geographical distribution.

Some geographical evidence, such as differences in spatial pattern in the disease distribution (Montenegro *et al.* 2004; Kerr-Pontes *et al.* 2004, 2006; Magalhães & Rojas 2007; Alencar *et al.* 2012) and spatial clusters (Rodrigues *et al.* 2008; Queiroz *et al.* 2010; Alencar *et al.* 2012) have contributed to the hypothesis that socio-economic conditions and environment are important in the continuation of leprosy transmission, regardless of a causal relationship. Although leprosy has been considered related to poverty (Kerr-Pontes *et al.* 2004; Lockwood 2004; Rodrigues & Lockwood 2011; Salgado & Barreto 2012) this link has been difficult demonstrate at a national, community, or even individual level (Lockwood 2004).

Another indirect route of infection has been suggested. To date, the role of the environment in the disease transmission is not clear. Some evidence suggests that *M. leprae* may be found in the environment (Sterne *et al.*

1995; Matsuoka *et al.* 1999; Lavania *et al.* 2008; Turankar *et al.* 2012) and may be a zoonosis in some regions including the southern United States (Truman & Fine 2010; Truman *et al.* 2011). This hypothesis has been raised due to *M. leprae's* viability outside of the human body, as it has been found in soil samples in highly prevalent areas of India (Lavania *et al.* 2008; Turankar *et al.* 2012), water samples collected in Brazil (Salem & Fonseca 1982) and in Indonesia (Matsuoka *et al.* 1999). It has also been harboured in animal species, such as the nine-banded armadillo (*Dasypus novemcinctus*) and primates (Truman & Fine 2010).

In spite of WHO's campaigns to reduce prevalence worldwide, new cases in children continue to occur, demonstrating that the interruption of leprosy transmission has not yet been possible. According to WHO (2010), 244 796 new cases were detected worldwide in 2009. Brazil is the second leading country in new cases (37 610 cases in 2009) and has the highest prevalence rate in the world (2.19/10 000 inhabitants), which demonstrates that the disease is still endemic. In Brazil, leprosy is believed to have been introduced from Europe and Africa, and spread after the Discovery of America (Truman *et al.* 2011). High endemicity in some areas has been explained by the fact that indigenous populations had a lack of exposure to infection when leprosy was first introduced, which would have caused an epidemic (Talhari *et al.* 1981; Penna *et al.* 2009). Currently, leprosy is concentrated in a small portion of the population, predominantly located in the Amazon region (Penna *et al.* 2009). Other intriguing spatial clusters occur in the north-eastern region of Brazil, which has the driest biomes of the country. An important question arises from this background: are compositional effects and/or environmental conditions associated to leprosy? The State of Bahia, in the north-eastern region, has the most interesting geographic characteristics in Brazil to test this hypothesis because it is covered by three compartmentalised biomes: savannah like, Atlantic rainforest and *caatinga*, which vary greatly in climate, vegetation and soils. Besides this, development, socio-economic characteristics and economic activity at municipality level also vary spatially in the state.

Thus, the main purpose of this study was to investigate possible spatial clusters and associations between the relative risks of leprosy and socio-economic and environmental factors, taking into account the new diagnosed cases in children under 15 years old.

Methodology

An ecological study was conceived using 417 municipalities that make up the whole State of Bahia. The first stage consisted of an exploratory spatial analysis to identify possible clusters of leprosy in the State. The rationale of spatial pattern analysis is that as age and gender are taken into account, resulting high or low clusters indicate that the spatial pattern is not due to these aspects of population composition. In this case, other compositional effects are expected to be associated to the pattern.

This study was designed to comprehend only young individuals. So far, the length of latency after infections of *M. leprae* has not been possible to determine (Suzuki *et al.* 2010), but has been reported to range from 5 to 15 years (Lockwood 2004). Due to the length of latency, data of new cases in children help twofold: reducing the effect of people's mobility – as young people had less time in which to move – and allowing to identify places with the most recent transmission. Epidemiological data corresponded to all new diagnosed cases of leprosy in children under 15 years old that occurred from 2005 to 2011. The study period was defined to be close to the Brazilian Demographic Census database from 2010.

Relative risks were calculated to account for gender as a covariate, using the software SaTScan (Kulldorff 1997). A spatial scan statistical test was also performed using SaTScan to identify possibly significant high or low clusters of leprosy. Due to the area effect on spatial scan test (Gregorio *et al.* 2006), we performed two spatial configurations, the first for the State of Bahia, the second for Bahia and surrounding states (Espírito Santo, Minas Gerais, Goiás, Tocantins, Maranhão, Ceará, Rio Grande do Norte, Pernambuco, Alagoas, Paraíba, Sergipe e Piauí). The focus of this study is on Bahia, but the surrounding states may affect the resulting relative risks calculation. The tested hypothesis was of no departure from the expected values in a bicaudal test using Poisson distribution. Spatial scan statistics arranged a circular window of variable size on the map surface, allowing its centre to move in such a way that for a given position and size the window included a different set of near neighbours. Iteration was set to allow the inclusion of up to 10% of population at risk. If the window included a neighbouring centroid, the whole municipality area was also included. Statistical significance of a given cluster was ascertained by a likelihood ratio test using Monte Carlo procedures, by repeating the same analytic exercise on a large number of random replications of the data set generated under the null hypothesis and comparing the rank of the maximum likelihood from the real data set with the maximum likelihoods from the random data sets (Kulldorff 2014). The null hypothesis was rejected when $P < 0.05$ for the most likely cluster and $P < 0.02$ for the secondary clusters.

The second stage of the analysis consisted of verifying possible associations between the relative risks of leprosy for people under 15 years old as a dependent variable, and socio-economic and environmental variables as independent, through a multivariate regression analysis, according to a previously defined conceptual framework proposed by Victora *et al.* (1997). This framework comprised three levels, each containing several variables (Table 1). Initially, distal variables were tested and the meaningful were kept in the model. The same procedure was taken with the variables in the medial level and finally with the proximal level. Ordinary least squares (OLS) models and spatial regression models were developed in R (R Development Core Team 2014). OLS are linear regression models ($Y = \alpha + \beta_1 X_1 + \ldots + \beta_n X_n + \varepsilon$; where, Y is the dependent variable, $X_1, \ldots, X_n$ are the explanatory variables and ε corresponds to the residuals), where the values of the intercept (α) and the slopes ($\beta_1, \ldots, \beta_n$) are estimated using the OLS method.

Study area

The State of Bahia (Figure 1) in the north-eastern Brazil, with a population of ~14 million inhabitants, has 72.1% of its inhabitants living in urban areas. Poverty, defined as 60% of the median national income (about US $128.00 per capita in 2010), affects 49.9% of the population, basic sanitation extends to 47.7% of dwellings, and 16.6% of people over the age of 15 years are illiterate (Instituto Brasileiro de Geografia e Estatística 2011). Population density across the state varies between 847.4 inhabitants/km^2 in the metropolitan region of Salvador and 24.5 inhabitants/km^2 on average.

Data

Incidence data of leprosy cases under 15 years old by municipality were collected from the Brazilian Disease Notification System (*Sistema Nacional de Informação de Agravos de Notificação* – SINAN) for the studied period. Leprosy is considered a notifiable disease in Brazil and all cases must be recorded in this National System. Resident population data corresponded to the Brazilian Demographic Census from 2010 (Instituto Brasileiro de Geografia e Estatística 2011).

We selected several socio-economic variables believed to be associated to leprosy according to literature. They encompassed literacy in people >5 years old; mean monthly income by householder; average number of dwellers by permanent residence; gross domestic product by municipality; percentage of permanent residence with inadequate sanitation; percentage of illiterate people >15 years old; male resident population; per cent of urban residents; geometric grow rate; demographic density; per cent of residents born in Bahia; Gini Index and municipal development index. The municipal development index is calculated by the Federation of Industries of the State of Rio de Janeiro, which closely follows the annual social and economic development of Brazilian municipalities reporting on employment and income, education and health issues. This index varies from 0 to 1 (minimum to maximum development) and uses 15 indicators. The data sources included the *Instituto Brasileiro de Geografia e Estatística* (2011), Department of Data and Information Technology (*Informações Demográficas e Socioeconômicas do Departamento de Informática do SUS* – DATASUS, 2010) and the Federation of Industries of the State of Rio de Janeiro – FIRJAN (2010).

Environmental variables included climate types, biomes, presence of significant water bodies and pre-eminent lithology, calculated as a percentage area over each municipality. Calculations were performed in ArcGIS 10.1 (ESRI; Redlands, CA).

Cartographic base of municipalities in Bahia corresponded to the shape files from the Brazilian Demographic Census, in Polyconic Projection and the

Table 1 Conceptual framework for regressions

Hierarchical levels	
Distal level	Regional Climates: Central Tropical, Eastern Tropical, Equatorial Zone Tropical. Biomes: Caatinga, Savannah like, Atlantic Rainforest. Geology: Archean, Cenozoic, Mesoproterozoic, Mesozoic, Neoproterozoic, Paleoproterozoic, Paleozoic Water bodies
Medial level	Geometric grow rate, Gross National Product, Demographic density, Gini Index, FIRJAN index.
Proximal level	Average number of dwellers by permanent residence, per cent of literate people above 5 years old, average monthly income by permanent dweller (in Brazilian currency), per cent of illiterate people above 15 years old, per cent of dwellers by inadequate sanitation, per cent of males, resident population in urban areas, per cent population born in Bahia, per cent population born in the State of Pernambuco

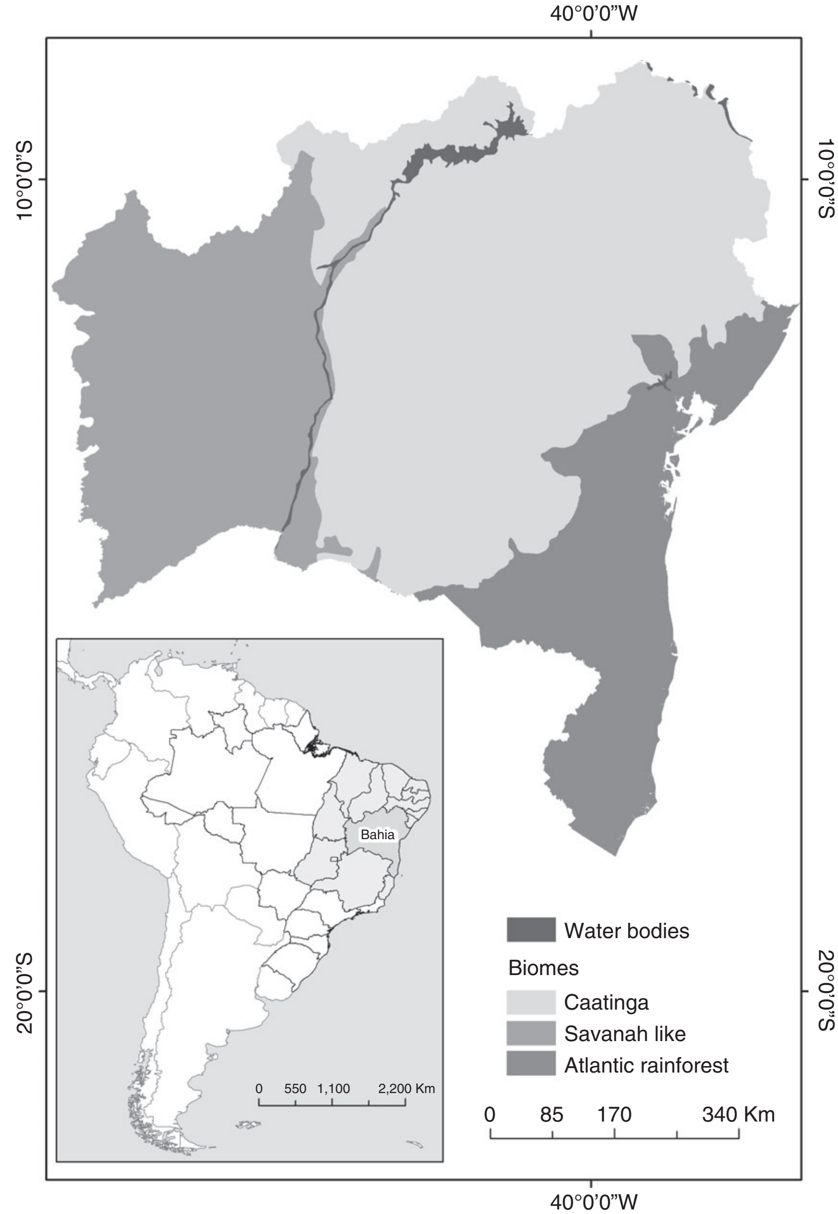

Figure 1 Biomes in the State of Bahia, Brazil. Source: IBGE (2004).

Geocentric Reference System for the Americas 2000 (SIRGAS 2000 – *Sistema de Referência Geocêntrico para as Américas*) as Datum. Environmental digital cartographic databases corresponded to shape files from Instituto Brasileiro de Geografia e Estatística (2004) available online.

Thematic maps for cluster and explanatory variables were elaborated in ArcGIS 10.1 through chorochromatic and choroplethic techniques.

Results

During the study period, 1674 new cases of leprosy in children under 15 years old were reported in Bahia, who comprised 7.87% of overall cases (21 278). Overall rates have fallen from 0.88/10 000 in 2005 to 0.52 in 2011 (Table 2).

Relative risks and spatial clusters are depicted in Figure 2. Spatial scan statistics for the State identified 4 high-risk and 6 low-risk clusters (Table 3 and Figure 2b).

Table 2 Overall rates of leprosy from 2005 to 2011, in Bahia, Brazil

Year	Number of municipalities with notified cases	Number of cases	Overall rate
2005	95	315	0.88
2006	84	264	0.74
2007	75	243	0.68
2008	69	227	0.63
2009	80	240	0.67
2010	67	199	0.55
2011	62	186	0.52

In the second test, considering the surrounding states, 8 clusters were identified as high risk and 9 as low (Table 4 and Figure 2d). Geographical representation of the two analyses shows that at a regional scale, leprosy in children under 15 years old is highly influenced by the surrounding states, mainly in the north-western and southern regions of Bahia.

The best non-spatial model showed significant positive associations with the presence of water bodies, Gini Index, average number of dwellers by permanent residence and percentage of the urban population. Percentage of residents born in Bahia is negatively associated in the model (Table 5). Testing for spatial dependence, regression residuals were significant for Global Moran's I. Moran's I measures spatial autocorrelation (effect of distance on the distribution of a variable), ranging from −1 to +1, and equals 0 when there is no spatial autocorrelation. Non-independent residuals in a regression cause the underestimation of the calculation of the sum of squares, potentially giving rise to the incorrect rejection of a null hypothesis (a Type I error) (Harris & Jarvis 2011). Lagrange multiplier diagnostics for spatial dependence show that the lag model is the most appropriate to explain spatial variance in the State (Table 5).

In the spatial model, percentage of area occupied by water bodies, Gini Index and percentage of urban population were significant. Additional explanation was given by the spatial components of the average number of dwellers by permanent residence and percentage of residents born in Bahia (Figure 3).

Discussion

Our analysis of spatial patterns of leprosy among under 15-year-olds in the State of Bahia from 2005 to 2011 revealed that rates remain very high although they are continuously decreasing. According to the Brazilian Health Ministry, for children under 15 years of age,a detection rate equal or above 1/10 000 is considered hyperendemic, and between 0.5 and 1/10 000 very high.

High relative risks tend to form spatial clusters. When analysing Bahia and the surrounding states, clusters we found are included in the 10 most likely geographic clusters identified by the Brazilian National Hansen's Disease Control Program (*Programa Nacional de Controle da Hanseníase* – PNCH) (Penna *et al.* 2009). From a public health perspective, taking into account results for the State of Bahia is more conservative, as the surrounding states affect the rates for Bahia, decreasing the importance of some high clusters non-contiguous to the 10 most likely at the national scale.

In the regression model, after allowing for spatial dependence, relative risks of leprosy in Bahia were associated with a higher percentage of water bodies, greater Gini index, higher percentages of urban population, greater average number of dwellers by permanent residence and a lesser percentage of residents born in Bahia.

Some important considerations may be inferred from the results. Relative risks of leprosy in the state are not associated with specific climate or biome. Only percentage of water bodies by municipality was associated with relative risks in both models. *Caatinga*, savannah like and tropical rainforest are quite different in species composition and occupy very delimited areas in the State (Figure 1). Even in the drier *caatinga*, relative risks are higher than expected. It is worth noting that in the *caatinga*, where the climate is semi-arid, high clusters occur around Sobradinho, which is the main reservoir in the State. São Francisco River basin drains most areas of the State (58.46%), in the western region, which contains ~21% of the State population, 43.8% of which are in rural areas. Some important reservoirs, such as Sobradinho and the Hydroelectric Complex of Paulo Afonso cover 4701 km^2 of the north/north-western part of the State, and the reservoir of Pedra do Cavalo covers 198.9 km^2 in the central/eastern regions. Some evidence has suggested an association between leprosy incidences and prevalence with humid environments and proximity to water bodies and rivers. In a cohort study in the rural areas of Malawi, Sterne *et al.* (1995) found that incidence rates declined with increasing distance from a river or from the shore of Lake Malawi. Greater rates were also found where drainage density and precipitation were higher. Desikan and Sreevatsa (1995) showed more direct evidence in the laboratory, where *M. leprae* has a better chance of survival in moist and humid conditions. In Brazil, the five main clusters occur in the Amazon region (Penna *et al.* 2009), where the environment is predominately hot and humid. High relative risks in *caatinga* could weaken the hypothesis regarding to the association

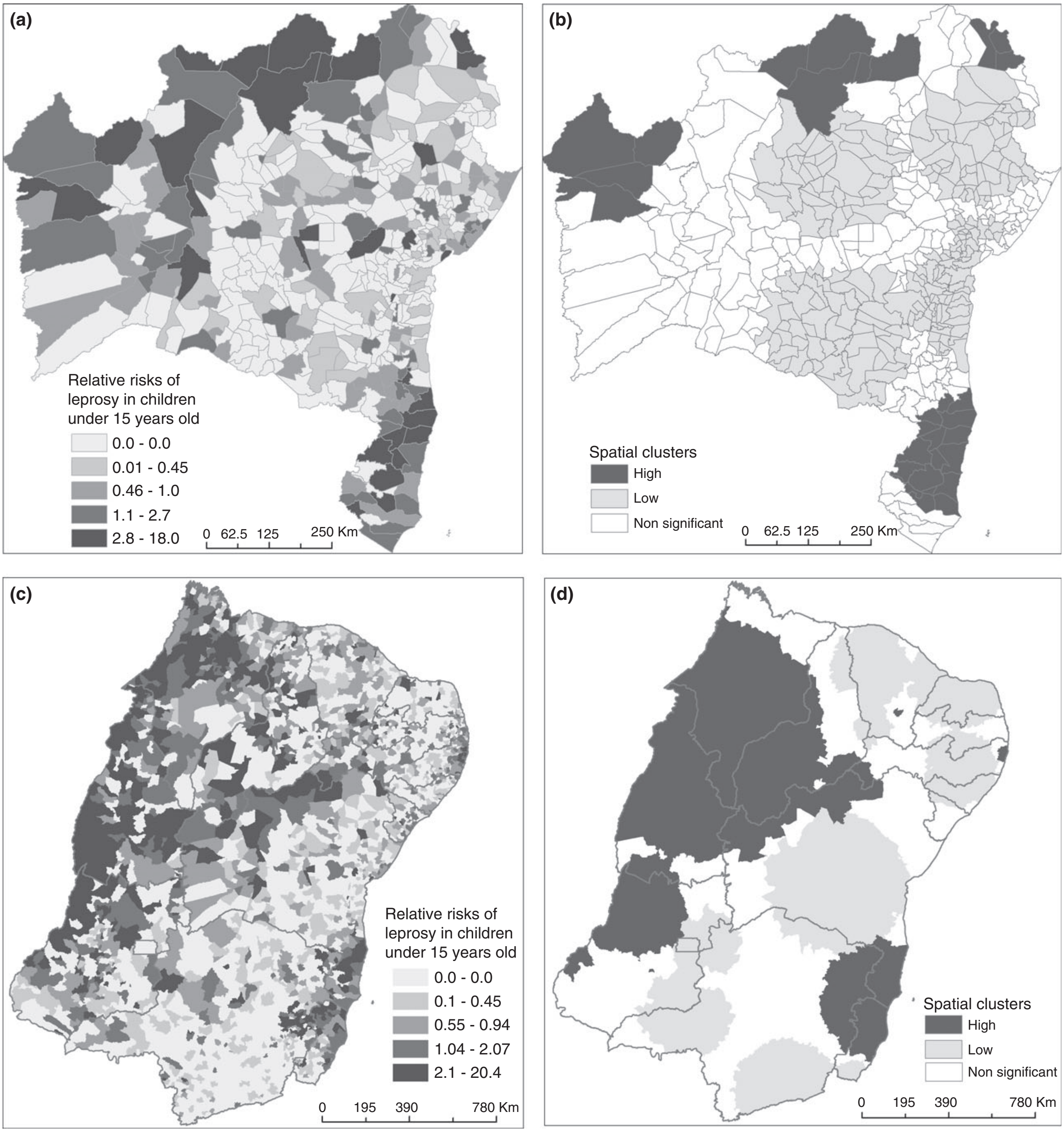

Figure 2 Leprosy in children under 15 years old for the studied period 2005–2011: (a) relative risks in the State of Bahia, (b) spatial clusters in the State of Bahia, (c) relative risks in Bahia and surrounding states and (d) spatial clusters in Bahia and surrounding states.

between *M. leprae* and humid environments. Nevertheless, high-risk clusters in *caatinga* occur around large water bodies where the water table is supposed to be higher, and able to provide sufficient humidity in soil.

Leprosy is known mostly to affect poor populations, but the relationship between poverty and the disease is still ambiguous and requires further research to establish their links (Nsagha *et al.* 2011). The main argument for

Table 3 Spatial clusters of leprosy under 15 years old in the State of Bahia, from 2005 to 2011.

Clusters	Number of municipalities	Observed cases	Expected cases	Relative risk	*P*-value
1	16	337	86.30	4.64	0.00
2	5	179	47.13	4.13	0.00
3	52	28	161.89	0.16	0.00
4	52	37	154.77	0.22	0.00
5	4	103	27.13	3.98	0.00
6	43	33	110.65	0.28	0.00
7	53	71	167.11	0.40	0.00
8	15	8	51.34	0.15	0.00
9	3	52	15.63	3.40	0.00
10	4	3	20.01	0.15	0.01

Table 4 Spatial clusters of leprosy under 15 years old in the State of Bahia and surrounding States, from 2005 to 2011

Clusters	Number of municipalities	Observed cases	Expected cases	Relative risk	*P*-value
1	357	3700	1255.57	3.71	0.00
2	326	82	1313.84	0.06	0.00
3	14	1656	512.87	3.55	0.00
4	261	344	1143.54	0.28	0.00
5	284	284	960.85	0.28	0.00
6	227	206	671.25	0.30	0.00
7	160	1316	743.25	1.86	0.00
8	79	68	314.65	0.21	0.00
9	79	339	127.62	2.70	0.00
10	103	210	501.71	0.41	0.00
11	17	322	130.43	2.51	0.00
12	1	92	14.14	6.54	0.00
13	26	56	192.08	0.29	0.00
14	20	5	76.77	0.07	0.00
15	1	162	70.25	2.32	0.00
16	5	29	7.03	4.13	0.00
17	29	33	80.81	0.41	0.00

Table 5 Regression results

	Estimate	SE	*z* value	Pr(>|z|)
OLS regression				
(Intercept)	−1.81	1.35	−1.34	0.18
'Caatinga'	−0.00	0.00	−0.82	0.41
Water bodies	0.04	0.02	2.27	0.02
Gini index	3.84	0.90	4.25	0.00
Average number of dwellers by permanent residence	0.43	0.20	2.10	0.04
Per cent of urban population	0.02	0.00	6.32	<0.00
Per cent of residents born in Bahia	−0.04	0.01	−3.83	0.00
Spatial regression				
(Intercept)	−2.46e+00	2.08e+00	−1.18	0.24
Caatinga	−1.11e−03	1.12e−03	−0.99	0.32
Water bodies	3.85e−02	1.93e−02	1.99	0.05
Gini index	3.36e+00	1.02e+00	3.29	0.00
Average number of dwellers by permanent residence	1.22e−01	2.53e−01	0.48	0.63
Per cent of urban population	1.71e−02	2.66e−03	6.45	0.00
Per cent of residents born in Bahia	−2.28e−05	1.51e−02	−0.00	0.99
Lag of Caatinga	1.29e−03	1.58e−03	0.82	0.41
Lag of water bodies	−2.24e−02	3.46e−02	−0.65	0.52
Lag of Gini index	1.47e+00	1.74e+00	0.84	0.40
Lag of average number of dwellers by permanent residence	8.63e−01	4.25e−01	2.03	0.04
Lag of per cent of urban population	3.13e−03	4.70e−03	0.67	0.51
Lag of per cent of residents born in Bahia	−5.94e−02	1.99e−02	−2.99	0.00

this unclear correlation is that some countries that rank low on the human development index have low rates of new cases. According to World Bank statistics in 1995, Brazil was 9th among the ten largest countries by gross domestic product (GDP at purchasing power parity), and in 2011, it was in 8th place (World Bank 2013). However, wealth is unequally distributed, which can be measured by some indexes. According to The World Bank, Development Research Group (2014), the Gini index measures the extent to which the distribution of income or consumption expenditure among individuals or households within an economy deviates from a perfectly equal distribution. A Lorenz curve plots the cumulative percentages of total income received against the cumulative number of recipients. The Gini index measures the area between the Lorenz curve and a hypothetical line of absolute equality, expressed as a percentage of the maximum area under the line. The range of the Gini index is between 0 and 1 (0 and 100%), where 0 indicates perfect equality (when all values are the same, i.e. a large population where everyone has the same income) and 1 (100%) indicates maximum inequality, that is a large population where only one person has all the income. In 1991, the Gini index in Brazil was 63.7%, and in the State of Bahia it was above average (65.3%) (Instituto Brasileiro de Geografia e Estatística 1994). In 2010, the index fell in Brazil (53.6%), and Bahia continued to present an above average value (55.0%) (Figure 3d) (Instituto Brasileiro de Geografia e Estatística 2011). Although the

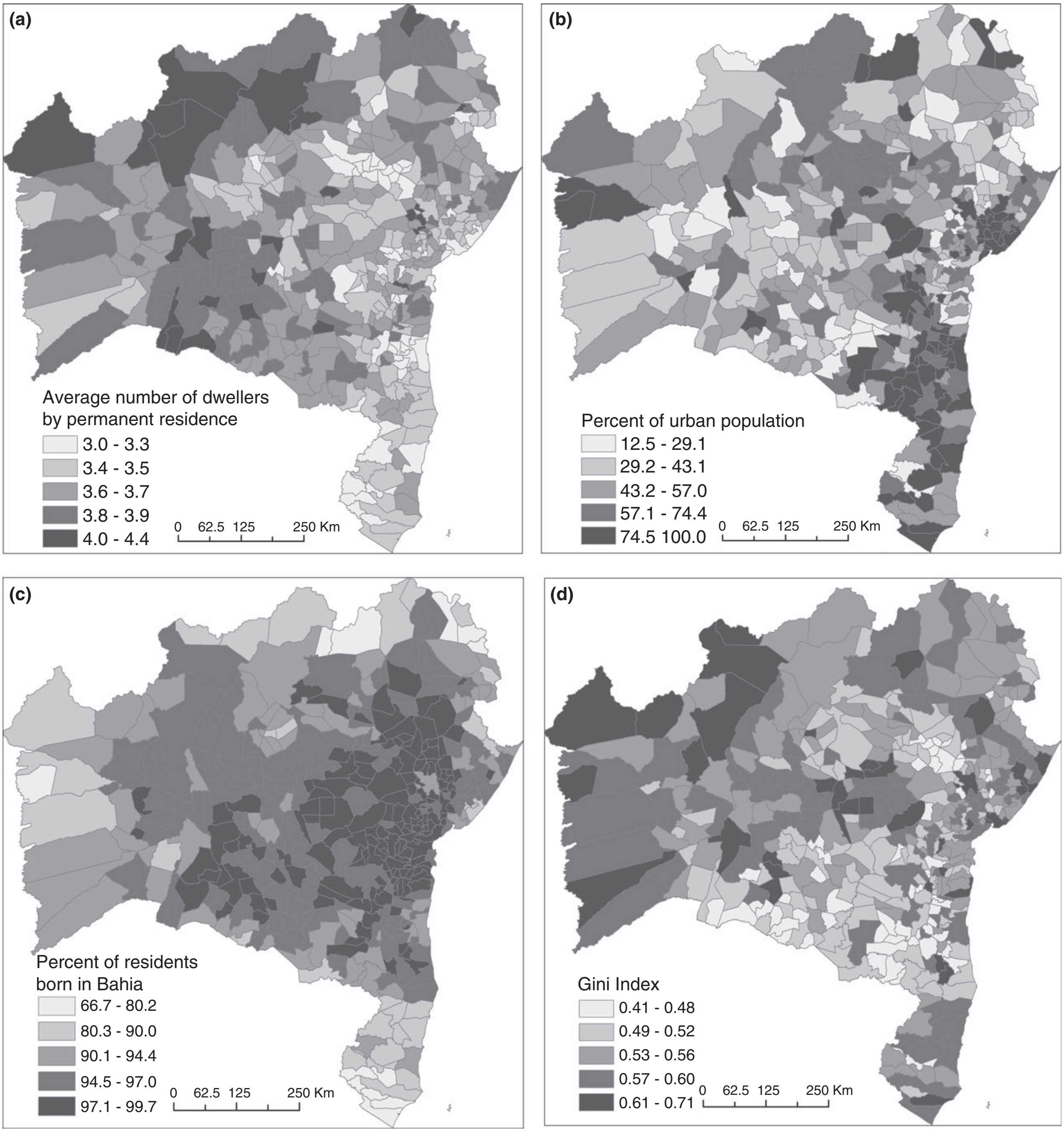

Figure 3 Variables associated to leprosy in Bahia: (a) average number of dwellers by permanent residence, (b) Per cent of urban population, (c) Per cent of residents born in Bahia and (d) Gini Index. Sources: IBGE (2011), DATASUS (2010).

Gini index has been improving in the last 19 years, the country still remains one of the most unequal in the world.

Income inequality is inversely associated to health status (Wilkinson & Pickett 2006). In Brazil, inequality is engrained in the differences across regions and educational levels (Salardi 2005), labour market segmentation, and discrimination against women and non-White people (Lustig & Lopez-Calva 2013). Its causes are complex and include various historical, political, economic and cultural factors (Skidmore 2004). Leprosy has been associated with inequality in other States in Brazil (Kerr-Pontes *et al.* 2004) as well as food shortages in Brazil (Kerr-Pontes *et al.* 2006) and Bangladesh (Feenstra *et al.* 2011).

Urbanity, inequality, great number of dwellers by residence and migration are all closely interrelated. In Bahia, inequality is higher in urban areas, which could help to explain the positive association of leprosy and the percentage of urban population. However, it seems that there is no consensus in the literature about the association between leprosy and urbanity. In some countries, higher leprosy rates are found in rural areas, such as in Greece (Kyriakis 2010), while in others, urban settlements are clearly associated with the disease such as in Brazil (Martelli *et al.* 1995; Kerr-Pontes *et al.* 2004; Imbiriba *et al.* 2009; Paschoal *et al.* 2013) and the Philippines (Scheelbeek *et al.* 2013). In Brazil, leprosy in urban areas has been explained as being due to fast urbanisation and intense population migration from rural areas (Martelli *et al.* 1995; Silva *et al.* 2010; Magalhães *et al.* 2011; Murto *et al.* 2013). In the State of Maranhão, north-east of Brazil, a recent matched case–control design study with cases diagnosed between 2009 and 2010 found that the past 5 years of migration were associated with increases in cases of leprosy (Murto *et al.* 2013). In our study, been born in other states than Bahia was associated to higher relative risks. Better job opportunities continue to attract rural populations to urban areas, which leads to more dwellers per residence in poor urban settlements. At the area level, the average number of dwellers per residence is positively associated with leprosy. Precarious settlements and poor living conditions on the outskirts of cities would favour the continuity of leprosy transmission.

Some constraints of this study are inherent to the adopted approach. Modelling risks at the aggregate level is prone to the ecological fallacy, where the associations observed at the group level might not apply to individual level (Robinson 1950). On the other hand, the ecological study design allows one to understand how compositional effects affect health, which could not be achieved by individual attributes (Susser 1994).

Conclusions

The present study shows that leprosy is still active in north-eastern Brazil, mainly in urban environments. Migration from rural to urban settlements, more people per residence and inequality are the result of a historical process in north-eastern Brazil that fosters infectious disease transmission. Our findings may be useful to raise awareness of the high levels of risk, which may lead to early diagnosis by leprologists, general clinicians and paediatricians in the high cluster areas. Increasing income equality, educational levels and access to a high-quality health services are challenges to be faced in the control endemic diseases such as leprosy.

The association with water bodies in the proposed geographic area indicates that the hypothesis linking *M. leprae* and humid environments cannot be discarded. This issue can only be fully addressed through direct observation.

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