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Human migration, railways and the geographic distribution of leprosy in Rio Grande do Norte State – Brazil

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Summary

Introduction—Leprosy is a public health problem in Brazil where 31,044 new cases were detected in 2013. Rio Grande do Norte is a small Brazilian state with a rate of leprosy lower than other areas in the same region, for unknown reasons.

Objectives—We present here a review based on the analysis of a database of registered leprosy cases in Rio Grande do Norte state, comparing leprosy's geographic distribution among municipalities with local socio-economic and public health indicators and with historical documents about human migration in this Brazilian region.

Results—The current distribution of leprosy in Rio Grande do Norte did not show correlation with socio-economic or public health indicators at the municipal level, but it appears related to economically emerging municipalities 100 years ago, with spread facilitated by railroads and train stations. Drought-related migratory movements which occurred from this state to leprosy endemic areas within the same period may be involved in the introduction of leprosy and with its present distribution within Rio Grande do Norte.

Conclusions—Leprosy may disseminate slowly, over many decades in certain circumstances, such as in small cities with few cases. This is a very unusual situation currently and a unique opportunity for epidemiologic studies of leprosy as an emerging disease.

Introduction

Leprosy is still an important public health problem with 215,656 new cases detected worldwide in 2013. India had 126,913 new cases or 58.8% of the total, followed by Brazil with 31,044 new patients or 14.4% of the world's cases.¹ Within Brazil there are considerable differences in the new case detection rate (NCDR) among states, which in 2013 ranged from 1.4 new cases per 100,000 inhabitants in Rio Grande do Sul to 91.6 in Mato Grosso.²

Leprosy was endemic in Europe until the nineteenth century when, before the introduction of antibiotic therapy, it nearly disappeared, possibly as a result of improvement in socio-economic conditions.³ Genotyping studies of *Mycobacterium leprae* show that its dissemination around the world occurred with human migratory movements,⁴ which is in agreement with historical data that leprosy was introduced in the Americas with European settlement. In Brazil, the first cases were reported in 1600 in the city of Rio de Janeiro, followed by other important ports of entry for Europeans and for African slaves. For example, in the cities of Recife and Salvador, where the number of cases of leprosy was already considered to be very high, leprosaria were opened in 1714 and 1787, respectively.⁵ There is some evidence that the disease has spread within Brazil with domestic migratory movements.⁶

Rio Grande do Norte is a northeastern state which has always had one of the lowest leprosy NCDR in Brazil, with 8.21 new cases per 100,000 in 2013, a much lower rate than the neighbouring states of Ceará (25.34/100,000) and Paraíba (17.39/100,000). In 2013, the state's NCDR was the lowest among all 16 states from the North and Northeast Regions and the 8th lowest among all 27 Brazilian states.² Despite this, there are municipalities within the state where leprosy NCDR is 'very high' or even hyper-endemic according to the national leprosy control programme criteria.^{7,8}

The objective of this study was to analyse possible factors in the maintenance of a low-endemic level of leprosy in the state and the significant differences in NCDR between municipalities. The spatial distribution of leprosy across the state will be considered, comparing its occurrence with local indicators for the quality of health services, population socio-economic status, and migratory movements of the last century.

Materials and Methods

Study Area

Rio Grande do Norte state, located in the northeast of Brazil, has an area of 52,810.7 km² with 167 municipalities and 3,168,027 residents (1.6% of the Brazilian population) in 2010.⁹ It is bordered by Ceará state to the west and Paraíba state to the south, whereas the north and east are bordered by the Atlantic Ocean. According to the last national census,¹⁰ 60% of the

state's municipalities have less than 10,000 inhabitants and 33% of the state's population lives in the two largest cities: Natal (803,739 residents) and Mossoró (259,815 residents). Economically, the state has developed very slowly¹¹ and has the seventh lowest gross domestic product (GDP) *per capita* among the 27 Brazilian states.¹²

Sources of Data

The Brazilian Ministry of Health has maintained a national notification programme for diseases called SINAN (Information System for Notifiable diseases). DATASUS is an open-access database containing information on the number of leprosy cases reported to SINAN since 2001, by municipality of residence. This system also has demographic and socioeconomic data for every municipality based on the national censuses of 1990, 2000 and 2010 (<http://www.datasus.gov.br>).

Risk Factors for Leprosy

Local NCDRs of leprosy by municipality (2001 to 2013) were compared with municipal socio-economic and public health indicators which were available in the DATASUS database.¹³ These indicators were: illiteracy rate (2000 and 2010), *per capita* household income (2000 and 2010), percentage of people living with less than 70 US dollars/month *per capita* (2000 and 2010), unemployment rate (2000 and 2010), percentage of houses without sanitary facilities (2000), percentage of houses without trash collection (2000), infant mortality (2001 to 2013), vaccination coverage (2001 to 2013) and malnutrition of children younger than 1 year of age (2001 to 2013). The arithmetic mean for each variable was calculated from yearly measurements or from the years of the national census (2000 and 2010).

Railways and Train Stations

As preliminary analysis suggested that endemic municipalities were linked by old state railways, we included the existence of a train station in each municipality as an indicator of municipal development in the early 20th century, when the railways played an important role in the state.^{14,15}

Analysis of Data

Leprosy new case detection rate (NCDR) is the rate of new cases of leprosy diagnosed in one area in one year divided by the population of that area in that year. To account for discontinuous case finding activities in different years, we calculated the average NCDR for the interval (2001 to 2013) dividing the total number of new cases detected in the whole period by the sum of the yearly population size registered during the same interval. NCDRs are expressed as number of people per 100,000 residents per year. Logistic multivariate analysis of NCDR risk factors was performed using STATA software (v11.2, StataCorp, USA).

Results

Annual NCDR for Rio Grande do Norte from 2001 to 2013 are shown in Figure 1 and exhibit a relatively stable rate of approximately nine new cases per 100,000 inhabitants with one detection peak observed in 2005.

The average NCDR by municipality for the same period is shown in Figure 2.

During these 13 years, 148 municipalities of Rio Grande do Norte state (89%) reported at least one new case of leprosy (total of 3,927) in their resident population. Forty municipalities (24%) had a NCDR greater than 10 cases/100,000 people per year which is considered to be high-level endemic, and one municipality (Mossoró) presented an average NCDR considered hyper-endemic according to Brazilian Ministry of Health criteria.⁸ Approximately half of the state's cases occurred in people residing in the municipalities of Mossoró (1,421 cases and average NCDR of 45.4 cases/100,000 people/year) and Natal (620 cases and average NCDR of 6.1 cases/100,000 people/year).

It is interesting to observe that municipalities with high-endemic rates of leprosy seem to be linked by the state's old railways (Figure 2). In univariate analysis, the presence of a train station in the municipality during the first half of the 20th century was associated with average municipal rate of leprosy (2001-2013) greater than 10 cases/100,000 people per year (OR = 6.0; 95%IC = 2.5–13.9). This remained associated with high NCDR in a multivariate logistic model (adjusted OR = 7.9; 95%IC = 2.9–21.4), which included nine other possible risk factors specified in the methodology section and shown in Table 1.

Discussion

The state of Rio Grande do Norte has always had a low leprosy NCDR, which has been documented since the first reports on leprosy in Brazil written in 1889 and 1933.⁵ The first known case in the state was documented in 1862, with only five additional cases reported between 1862 and 1900. The number of leprosy cases was much lower than in other states during the same period, such as Rio de Janeiro (1,734 cases registered before 1887), Bahia (1,411 cases before 1890) or Pernambuco (1,440 cases before 1879).¹⁶ Notwithstanding the small number of cases, in 1926 a leprosarium was opened in Rio Grande do Norte to comply with national guidelines for leprosy control.¹⁷ According to records of the leprosarium's primary doctor, among 140 people isolated in the institution between 1926 and 1930, only one patient had signs of leprosy which began in the 19th century, while all of the others developed signs after 1915.¹⁶

Historically Rio Grande do Norte's economic growth was poor and did not attract migratory movements.¹¹ In the 18th and 19th centuries, the state was not an important area for sugarcane plantations, thus the number of African slaves was very low in Rio Grande do Norte.¹⁸ Natal, the capital of the state, was founded in 1599 and grew very slowly. In 1900, only 16,056 people were living in the city, much fewer than in other cities in the same northeast region such as Recife, Pernambuco where there were 113,106 people and Fortaleza, Ceará with 48,639 residents.¹⁹ Thus, it is possible that leprosy was introduced much later in this state than in other areas of Brazil.

Another consideration is that most Rio Grande do Norte cities are still relatively small without the significant population crowding that increases the number of potential exposures to *Mycobacterium leprae*.²⁰ This may influence the state's low endemicity with NCDR of less than 10 cases per 100,000 inhabitants (Figure 1). The peak NCDR in 2005 can be attributed to active case finding campaigns developed in the state during that year.^{7,21}

The lower NCDR in most municipalities of Rio Grande do Norte could reflect a worse public health structure, lack of leprosy services, or absence of case finding activities to effectively diagnose leprosy.³ Alternatively, the greater frequency of the disease in the 40 municipalities with high NCDR could be associated with crowding in a larger population or worse economic or hygiene conditions in those municipalities. Figure 2 shows that areas with larger population in the state are not the same as those with higher NCDR. Logistic multivariate analysis did not show significant association between high NCDRs and municipal markers for economics, sanitation and measures of public health assistance (Table 1). In 2005, the Rio Grande do Norte leprosy control programme promoted a workshop for representatives from 80% of the state's municipalities which led to the development of campaigns to detect leprosy cases in 125 municipalities.²¹ This extensive campaign caused a 42% increase in the state's annual NCDR, but 68% of those cases were detected in the same 40 highly endemic municipalities. In that year no case was detected in 78 municipalities, out of which 41 developed leprosy campaigns.^{21,22} These data suggest that there is an actual irregular distribution of leprosy cases across the state, with higher incidence of cases in some municipalities.

In 2004 Kerr-Pontes *et al.*²⁰ observed that the presence of a railroad in a municipality was a predictor of leprosy incidence rate in Ceará, Rio Grande do Norte's neighbour state. The similarity with our results stimulated our further investigation into the history and the importance of railways in this part of the Northeast Region, especially because most railroads have been out of service in both states since the 1950's when they were replaced by paved roads.¹⁴ Interestingly we found a historic link between the building of railroads and important migratory movements that occurred in these states a hundred years ago.

In this region of Brazil the most important cause for emigration is prolonged drought. At the end of the 19th and beginning of the 20th century, these episodes had vast consequences and became known as 'the big droughts' ('as grandes secas'). The big droughts of 1877-1879 and 1888-1889 were a true hecatomb in the Brazilian Northeast region, when around 3 million people emigrated from drought-affected areas to main cities, and 600,000 people died in the states of Ceará, Rio Grande do Norte and Paraíba.²³ The cities who received migrants faced chaos with no infrastructure to absorb them and an alternative put forth by the Brazilian Government was to force the exodus of this migrant population to work in Pará State and Amazon Region.²⁴ Opportunities to work in rubber extraction stimulated a continuous migratory flow of Northeast workers to the Amazon region from 1877 to 1920, during which time there were seven severe droughts.^{24,25}

Unfortunately, living and work conditions for migrants to the North region were very difficult and many of them returned to their states of origin, even many years after relocation.²⁴ These bidirectional migratory movements should be considered as a factor in

the introduction and dissemination of leprosy in the Northeast region, since the disease was considered a public health problem in Pará state from 1804, 60 years before the first cases were reported in Rio Grande do Norte and Ceará state.¹⁶ In fact, an important epidemiologic report about leprosy in Brazil, written in 1933, indicated that people from Rio Grande do Norte who used to work in the Amazon region brought leprosy when they returned.⁵ A similar type of introduction is suggested for leishmaniasis in Ceará.²⁶

Another action taken by the Brazilian government to address economic hardship during these severe droughts was the employment of thousands of people on railway construction across the Northeast. The railways were designed to facilitate aid to the populace during future calamities, including transport of essential items to municipalities or carrying people from critical drought-stricken zones to main cities when necessary.²⁷ Additionally, the railways would promote economic growth overall by moving agricultural and animal goods from farms to central markets. Cities developed along those railways.^{14,27}

Mossoró, the second largest city in the state, showed an average NCDR of 45.4 cases per 100,000 inhabitants per year from 2001 to 2013, a coefficient 7.5 fold larger than the NCDR in Natal, the capital and largest city in the state. Again, migratory patterns from a century ago may be involved in this difference. From the late 1800s to 1927, the population of Mossoró increased from 7,748 to 20,300, with a particularly rapid expansion of residential neighbourhoods with poor public infrastructure and families with lower incomes.²⁸ Currently, these neighbourhoods form a cluster of high leprosy case detection rates in Mossoró^{7,29,30} and remain associated with measures of poverty.³⁰

Natal, located on the Atlantic coast, was geographically more distant from the zones affected by the droughts than Mossoró.³¹ In the beginning of the 20th century, the expansion of Natal occurred concomitantly with planned urban development which included construction of large avenues and squares as reflecting the European *Belle Époque* architectural movement.³² Thus, the large number of migrants displaced by droughts was unwelcome in Natal and most were compulsorily relocated to other areas.^{23,32} Contrasting with Mossoró, there were no rapid growing poor neighbourhoods in Natal during that period. Significant migration to Natal from rural areas occurred much later, from the 1950s to 1970s, which has since contributed to the city's growth.³³ During these more recent decades there was also emigration from Rio Grande do Norte to other states, but it was not as massive as in the beginning of the 20th century and happened towards the Southeast Region as destination,³³ an area where leprosy is not highly endemic as in Pará state.

Final Considerations

Historical and epidemiological data point to a late introduction and to a slow spread of leprosy in Rio Grande do Norte during the last century. This is a very unusual situation currently and a unique opportunity for epidemiologic studies of leprosy as an emerging disease. Considering that after infection with *M. leprae* few people will develop the disease, that leprosy is only transmitted by multibacillary patients and that in this type of disease the incubation period is unknown but very long,³ it is reasonable to hypothesise that if some individuals returned infected from endemic areas to their original municipalities, it probably

took some years before few of them became a source of infection. Interestingly, in 2010 a case of leprosy in a chimpanzee was reported with a possible 30-year incubation period,³⁴ which may indicate a potential for similar decades-long incubation periods in humans. As most of the state's municipalities are small cities, it is also reasonable to consider that those first cases did not transmit the disease to a large number of individuals within their communities, leading to a very slow process of dissemination of leprosy. These observations could explain why migration that occurred a century ago may be involved in the current epidemiologic situation for leprosy in this Brazilian state. Despite the state being an area of low endemicity in comparison with other areas in Brazil, this analysis demonstrates municipalities with very high new case detection rates which merit special attention from the state leprosy control programme.

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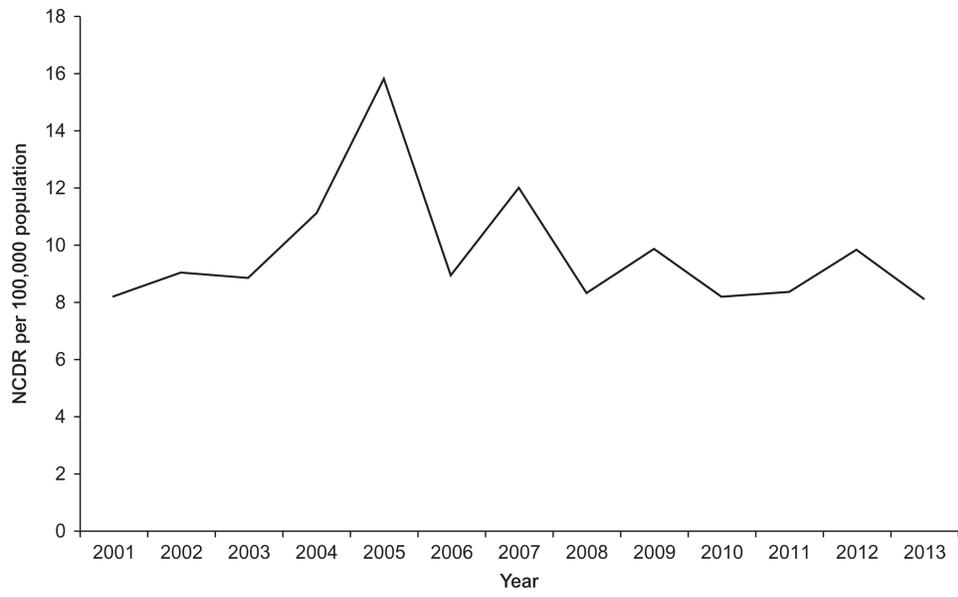


Figure 1. Annual leprosy NCDR per 100,000 residents – Rio Grande do Norte State / Brazil – 2001 to 2013.

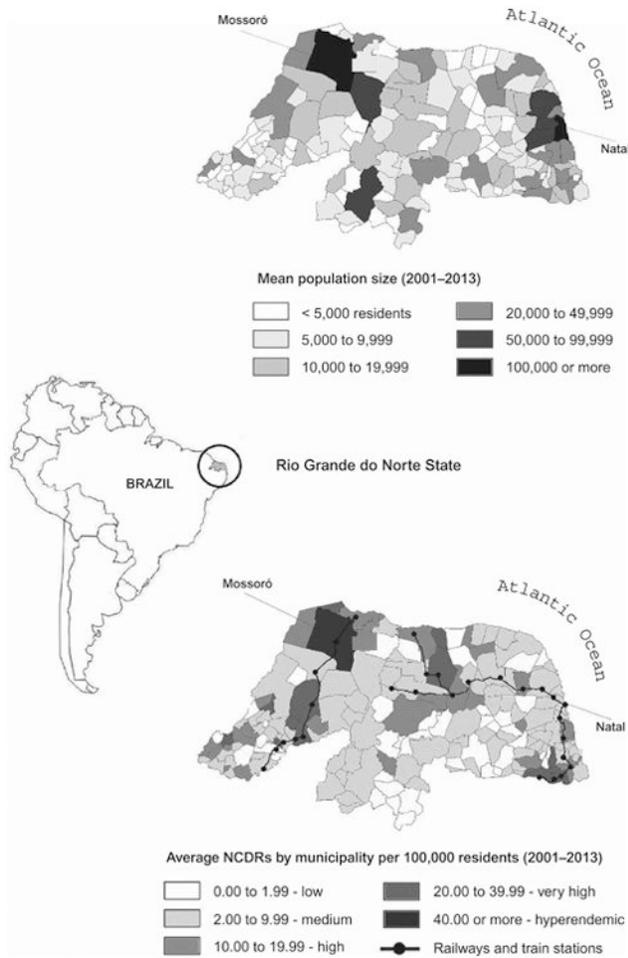


Figure 2. Mean Population Size and Average NCDR by municipality of residence in Rio Grande do Norte State (Brazil) from 2001 to 2013. Illustrations on railways route and train stations were adapted with permission from Gabriel Leopoldino Paulo de Medeiros.¹⁴

Table 1

Crude and adjusted measures of association between high average leprosy NCDR from 2001-2013 and municipal markers for economics, sanitation and measures of public health assistance in 167 state municipalities.

Covariates	Odds ratio (95% C.I.)	
	Unadjusted	Adjusted (aOR)
Presence of train station	6.0 (2.55 – 13.98)	7.92 (2.93 – 21.41)
Illiteracy rate	1.04 (0.97 – 1.11)	1.10 (0.98 – 1.24)
Per capita household Income	0.99 (0.99 – 1.00)	0.99 (0.98 – 1.01)
People with income <= US\$ 70/month (%)	0.99 (0.99 – 1.00)	0.94 (0.86 – 1.03)
Unemployment tax	1.05 (0.95 – 1.15)	1.03 (0.93 – 1.14)
Houses without sanitary facilities (%)	0.99 (0.94 – 1.02)	0.99 (0.95 – 1.02)
Houses without trash collection (%)	0.97 (0.94 – 1.02)	0.97 (0.92 – 1.02)
Infant Mortality per 1,000	1.04 (0.96 – 1.13)	1.04 (0.96 – 1.13)
Vaccination coverage (%)	1.02 (0.97 – 1.09)	1.02 (0.95 – 1.09)
Malnutrition in children < 1year of age (%)	0.98 (0.67 – 1.43)	0.95 (0.62 – 1.48)