

Persisting leprosy transmission despite increased control measures in an endemic cluster in Brazil: the unfinished agenda

CARLOS H. ALENCAR*, ALBERTO N. RAMOS JR*,
JAQUELINE C. BARBOSA*, LIGIA R.F.S. KERR*,
MARIA L.W. DE OLIVEIRA** &
JORG HEUKELBACH***

**Department of Community Health, School of Medicine, Federal University of Ceará, Fortaleza, Brazil*

***School of Medicine, Federal University of Rio de Janeiro – Rio de Janeiro (RJ), Brazil*

****Anton Breinl Centre for Public Health and Tropical Medicine, School of Public Health, Tropical Medicine and Rehabilitation Sciences, James Cook University, Townsville, Australia*

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Summary

Objective: To provide an evidence base for improvement of leprosy control in Brazil's high transmission areas.

Design: We obtained data from municipalities in a major disease cluster from databases for notifiable diseases of four states (Maranhão, Pará, Tocantins, Piauí), including notifications from 2001 to 2009. Indicators for monitoring and evaluation of leprosy according to the World Health Organization were evaluated with emphasis on the rates of new cases presenting grade-2 disabilities and among children <15 years of age, indicating late diagnosis and active transmission, respectively.

Results: A total of 82,463 leprosy cases were detected in the area (mean annual case detection rate: 95.9/100,000; RR = 4.56 as compared to the rest of Brazil; 95% CI: 4.45–4.66, $P < 0.0001$). There was a steady decrease of detection rates in the study period, from 100.8 to 75.6/100,000 inhabitants. In children <15 years of age, 9,009 cases of leprosy were detected (28.40/100,000), significantly more than in the rest of Brazil (RR = 5.80; 95% CI: 5.39–6.25, $P < 0.0001$). New cases with grade-2 disabilities/100,000 population maintained a stable trend at a high level (4.43 cluster vs. 1.28 rest of country; RR = 3.46; 95% CI: 3.11–3.84, $P < 0.0001$), whereas the proportion of new cases with grade-2 was slightly lower than the country's average (5.51% vs. 6.75%; RR = 0.84; 95% CI: 0.81–0.86, $P < 0.0001$).

Conclusions: Despite recently improved leprosy control measures, there is still major active transmission and late diagnosis in the cluster. Further specific actions are needed to improve early case detection and prompt treatment with the aim to reduce disease burden in the population, considering social inequities.

Introduction

Leprosy is still endemic in Brazil: in 2009, more than 38,000 cases were notified in the country (93% of cases in the Americas), presenting the highest detection rate worldwide, with 19.64 cases/100,000 inhabitants.¹⁻² There are tremendous regional differences of case detection rates in Brazil, evidenced by areas with virtually no transmission, mainly in the southern regions, and other regions with extremely high detection rates.³⁻⁵ These areas are also the richest and poorest regions in the country, respectively.

As a consequence, the National Hansen's Disease Control Program focussed activities more and more on highly endemic disease clusters. These well-defined clusters are based on data from compulsory case notification, provided by the nation-wide unique disease surveillance system, and were identified by spatial analysis.⁶ Due to the nature of analysis, municipalities with low detection rates geographically close to those with high detection rates were included in the clusters. By intensifying case finding in these municipalities with low detection rates, a further reduction of transmission and disease burden caused by hidden prevalence cases, and improved early case detection, can be expected.⁴⁻⁵

The disease cluster with greatest geographical extension includes parts of the four states Maranhão, Pará, Tocantins and Piauí in the north and northeast regions of the country (Figure 1).^{4,6} The area has a total population of about 10 million. This represents only 1/20 of Brazil's population, but with its 7,524 new cases detected in 2009 included about 1/5 of all notified cases. The case detection rate in the cluster was 75.6/100,000 inhabitants in that same year.⁷

Recently, the Brazilian Research Council (*Conselho Nacional de Desenvolvimento Científico e Tecnológico*, CNPq) and the Department of Science and Technology of the Brazilian Ministry of Health (DECIT) provided substantial funding for research projects in the 10 major and most significant endemic leprosy clusters in collaboration with the National Hansen's Disease Control Program. Thus we were able to perform multidisciplinary epidemiological research in the most significant of these clusters (denominated INTEGRAHANS – MAPATOPI – an acronym derived from the four involved federal states Maranhão, Pará, Tocantins, and Piauí), to provide an evidence base for improvement of leprosy control in Brazil's high transmission areas.⁸⁻⁹

In the present investigation, we analysed epidemiological data from this cluster in detail, focussing on time trends and indicators for early case detection and active transmission.

Methods

All 373 municipalities located in a major leprosy endemic cluster, defined by the National Hansen's Disease Control Program were included (Figure 1).⁶ This area is composed of four states in north and central Brazil with a population distribution as detailed in Table 1.

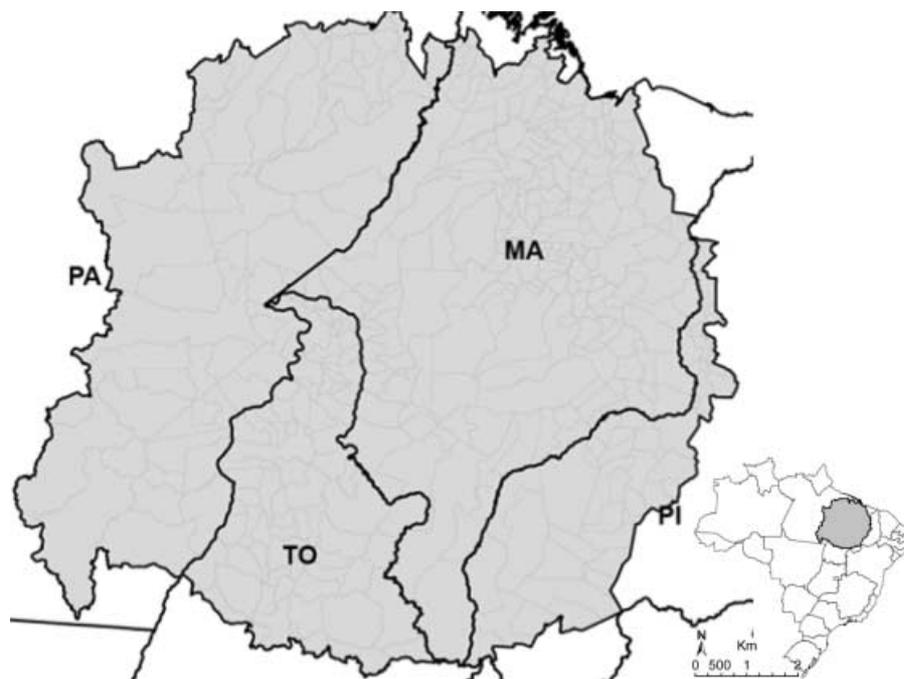


Fig. 1. Cluster of high transmission risk situated in the states Maranhão, Pará, Tocantins and Piauí.

We obtained secondary epidemiological data from the state databases of notifiable diseases (*Sistema de Informação de Agravos de Notificação – SINAN*) and then merged datasets. Notifications from 1st January 2001 to 31st December 2009 were included in analysis. For calculation of leprosy case detection rates, population estimates of the respective years were obtained from the database of the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística – IBGE*).¹⁰

Table 1. Population data of a high risk leprosy cluster in north Brazil.

	Number of Municipalities	Population in 2009	Proportion of Population (%)
Maranhão State			
Cluster	168	5,734,305	
State	217	6,367,111	90.1
Pará State			
Cluster	60	2,326,116	
State	144	7,431,041	31.3
Tocantins State			
Cluster	79	641,056	
State	139	1,292,063	49.6
Piauí State			
Cluster			
State	223	3,145,164	39.7
Total			
Cluster	373	8,877,378	
All four States	723	18,235,379	48.7

We calculated the indicators for monitoring and evaluation according to the “Enhanced Global Strategy for Further Reducing the Disease Burden due to Leprosy” by WHO¹¹: rate of new cases/100,000 population, rate of new cases with grade-2 disabilities/100,000 population, cure rate (for monitoring progress); proportion of cases presenting with grade-2 disabilities, proportion of child cases, proportion of female patients, and proportion of multibacillary cases among new cases (for evaluating case detection); and proportion of new cases verified as correctly diagnosed, proportion of treatment defaulters, and proportion of relapses (for assessing the quality of services). Indicators were also observed over time. The proportion of patients who developed new or additional disabilities during multidrug therapy is not presented, as this information was available in < 50% of cases.

Stata 11 software was used for statistical analysis. Significance of the difference of relative frequencies was assessed using the Pearson chi squared test. We calculated rate ratios (RR) and respective exact confidence intervals.

Results

In the period from 2001 to 2009, a total of 82,463 leprosy cases were detected in the cluster. Table 2 details the indicators for monitoring and evaluation according to the World Health Organization’s Enhanced Global Strategy. The mean general case detection rate in the study period was 95.9/100,000 per year, whereas in the rest of Brazil 21.0 cases/100,000 inhabitants were notified (RR = 4.56; 95% CI: 4.45–4.66, *p* < 0.0001). In Pará, case detection was highest (134.8/100,000).

Table 2. Indicators for monitoring and evaluation according to the Enhanced Global Strategy for Further Reducing the Disease Burden due to Leprosy (WHO), in a leprosy endemic cluster in North Brazil, 2001 to 2009.

	Maranhão*	Pará*	Tocantins*	Piauí*	Total cluster	Rest of Brazil
Indicators for monitoring progress						
New cases detected/100.000 pop.	84.45	134.87	91.02	81.40	95.93	21.03
New cases detected < 15 years/100.000 pop.	24.30	44.57	24.11	25.31	28.40	4.89
New cases with grade-2 disabilities/100.000 pop.	4.39	5.25	3.65	3.60	4.43	1.28
Treatment completion/cure rate	84.9	80.0	87.3	83.1	83.3	86.1
Indicators for evaluating case detection						
% assessment of disabilities at diagnosis	77.7	91.1	80.9	93.9	83.9	90.2
% new cases grade-2	6.69	4.27	4.96	4.71	5.51	6.75
% new cases female patients	43.3	40.0	43.5	50.1	43.0	46.1
% multibacillary	56.1	52.4	40.8	40.9	52.3	53.5
% clinical form						
Indeterminate	21.8	27.9	34.9	33.6	26.0	21.2
Tuberculoid	24.8	20.6	25.4	28.8	23.9	26.6
Borderline	38.0	41.3	27.9	22.3	36.7	33.9
Lepromatous	15.4	10.2	11.8	15.3	13.4	18.3
Indicators for evaluating quality of services						
% new cases correctly diagnosed	99.0	99.1	97.4	98.8	99.0	98.7
% treatment defaulters	6.1	9.6	3.9	5.2	7.0	4.8
% relapses	3.0	3.2	3.0	2.2	2.4	3.1

*Only municipalities in endemic cluster

During the period of study, the detection rate declined from 100.8 to 75.6/100,000 inhabitants per year in the cluster, with a more pronounced decrease since 2006 (Figure 2). The largest decrease (63%) was observed in Pará, but this area still had the highest detection rate in 2009, as compared to the other states. Tocantins' municipalities showed a detection rate of 77.8 to 88.4/100,000 and a tendency of stabilization in the last four years. The municipalities in Maranhão showed a downward trend since 2005, and Piauí did not reveal any clear trend. In the rest of Brazil, this indicator was around 16/100,000 inhabitants/year during the observation period (Figure 2).

The trend in < 15 year-olds showed similar patterns to the general case detection rate, with elevated rates in all four states (Figure 2). Similar to the general population, the highest detection rate in children was found in Pará (Table 2). In children < 15 years of age, a total of 9,009 cases of leprosy (28.6% of all Brazilian child cases) were detected in the cluster (detection rate: 28.40/100,000), which was significantly higher as compared to the rest of Brazil (RR = 5.80; 95% CI: 5.39–6.25, *P* < 0.0001; Table 2).

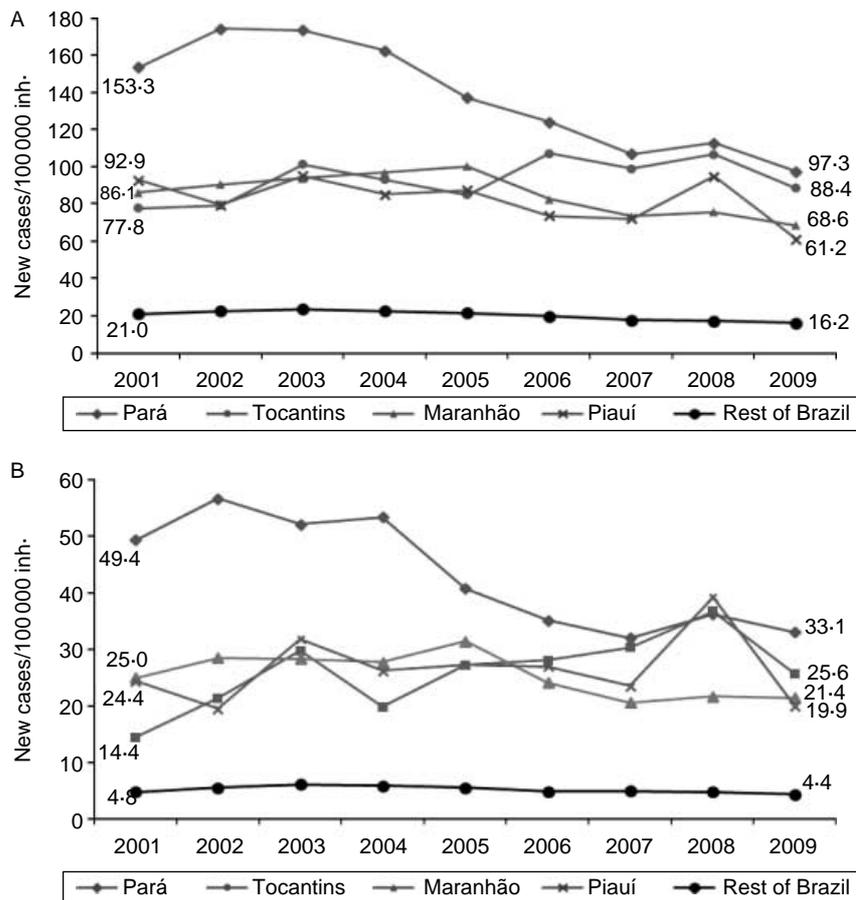


Fig. 2. New cases of leprosy detected/100,000 population per year in a high-risk area in Brazil, 2001 to 2009: (A) general detection rate; (B) < 15 year-olds.

The rate of new cases with grade-2 disabilities/100,000 population was significantly higher in the cluster than in the rest of Brazil (RR = 3.46; 95% CI: 3.11–3.84, $P < 0.0001$). On the other hand, the proportion (%) of new cases with grade-2 was lower than the country's average (RR = 0.84; 95% CI: 0.81–0.86, $P < 0.0001$) (Table 2). The rate of new cases with grade-2 disabilities/100,000 population showed a similar trend as the general detection rate (Figure 3). The detection rate showed an inverted trend.

With the exception of Tocantins, defaulter rates were higher than in the rest of Brazil, but the number of relapses was lower. The proportion of multibacillary cases at the time of diagnosis was 52.3% in the cluster (RR = 0.98; 95% CI: 0.97–0.98, $P < 0.001$). The largest proportion was detected in the State of Maranhão (56%). Borderline or lepromatous clinical forms represented 50% of cases in the cluster and 52% in the rest of Brazil (RR = 0.96; 95% CI: 0.95–0.97, $P < 0.001$); the lowest proportion was in the states of Tocantins (39.7%), and Piauí (37.6%) (Table 2).

In total, in the cluster there were 84.9% (69,220) leprosy cases with their degree of disability assessed at diagnosis, less than in the rest of Brazil. Maranhão had the lowest proportion of cases evaluated (79.0%), whereas in Piauí and Pará more than 90% of cases in the cluster were evaluated (Table 2). Among available cases, 18.1% (13,112) had a disability of grade-1 and 5.5% (3,811) of grade-2 (Table 2).

Discussion

In the past years, the Hansen's Disease Control Program of Brazil's Ministry of Health has focussed its actions to a greater extent on defined geographical areas (clusters). The present study shows that in one of these major clusters which encompasses about 5% of Brazil's population, the overall detection rate was more than four times higher than in the rest of the country, and in <15 year-olds even about six times. This shows that active leprosy transmission is continuing at high levels in the region. In addition, the indicators suggest late diagnosis in many cases. Despite the successes made in the last years, there is thus still a long

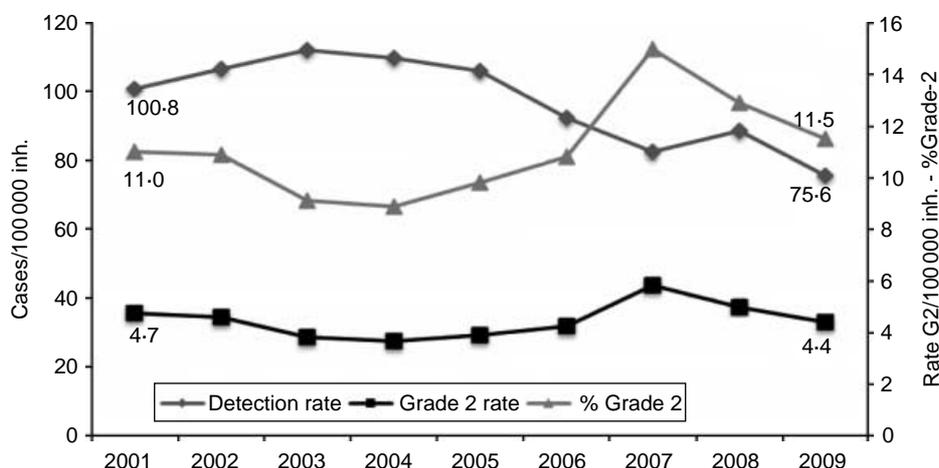


Fig. 3. Trend of new cases detected/100,000 population, rate of new cases with grade-2/100,000 population and proportion of new cases with grade-2 disabilities in a leprosy endemic cluster in North Brazil, 2001 to 2009.

way to go to reach low detection rates. The study also reinforces that prioritizing and intensifying control measures in these clusters should be maintained.⁶

The ascending trend of leprosy detection rates since the 1980s in Brazil seems to have reached its peak and is expected to show a tendency of stabilisation/reduction in the next few years.^{5-6,12} The time series from 2001 to 2009 presented in our study shows stable detection rates of the cluster municipalities in three states. Pará detection rates declined considerably, but remained at very high levels. This was paralleled by the trend of the detection rate in children. These trend observations are likely caused by operational factors and not by epidemiological behaviour of the disease.¹²⁻¹³ Increased actions performed by the State Control Programs have been established in the observation period, and in fact it can be expected that in future years detection rates and indicators for late diagnosis will decrease, if the current control programme's policy continues. For example, in Pará the reduction of detection rates was paralleled by an increase of population coverage with the Family Health Program from 13% in 2001 to almost 40% in 2009.¹⁴ On the other hand, in Piauí where coverage of the Family Health Program is almost 100% for several years, lowest values were observed for grade-2 disability/population. In addition, there was the highest proportion of newly diagnosed cases assessed for disabilities, and more than a third of cases were diagnosed early, in indeterminate clinical form. The decentralised actions of this primary health care approach may have influenced positively leprosy control measures.¹⁵⁻¹⁶

In 2009, WHO launched a new global target based on grade-2 disabilities/100,000 population, and a reduction goal of at least 35% by the end of 2015 as compared to 2010 was set.¹¹ From 1995 to 2009, Brazil has reduced grade-2 disabilities in newly diagnosed patients/population by only about 13% every 5 years, which is far away from this target.^{11,17} In the same period, India and Thailand showed reduction rates of this indicator of 54% and 36% every 5 years, whereas China reduced this indicator by 8%, after a more pronounced reduction in the previous years.¹⁷ On the other hand, these reductions may also be caused by different operational approaches, and data should be interpreted with care.¹⁸

Whereas this new indicator and the target may reflect better the progress of control measures,¹⁹ this is still based on entire countries. Clearly, this may be appropriate for small countries, but care should be taken in the case of nations with continental dimensions such as Brazil and India, which show tremendous regional differences of leprosy detection rates, with areas where the disease is virtually nonexistent, and other regions with ongoing transmission.⁵ As mentioned above, Brazil's Ministry of Health has approached this problem by targeting high risk areas for transmission, identified by spatial analysis.⁶

In the endemic cluster, the rate of new cases with grade-2/100,000 population remained stable over the study period, with the exception of a peak in 2007. In 2007 a change in the grade coding was undertaken and not all municipalities used this new code; as a result this peak should not be considered with the same confidence as data of the other years.²⁰ In the same period, the general detection rate showed a decrease after an initial increase, whereas the proportion of new cases with grade-2 disabilities showed an inverse trend. This may reflect established control actions in the area: increased actions to detect leprosy cases revealed lower proportions of grade-2 disabilities at diagnosis, and early diagnosis improved over time. On the other hand, there may be other operational problems present, such as the quality of assessment of disabilities, and possibly over-diagnosis of grade-2.²⁰ The rate of new cases with grade-2 disabilities per 100,000 population has been considered to be less influenced by operational factors – it focuses attention on prevention of disabilities and stimulates early detection and is probably a robust marker of the level of the occurrence of the

disease in the community.^{19–20} In addition, the proportion of grade-2 cases in a population will give a proxy of the general burden of disease on the population level, independent from case detection rates and prevalence.^{17,19}

Our analysis also suggests late diagnosis of leprosy to an important extent in the cluster. The proportion of new cases with grade-2 disabilities was highest in Maranhão, indicating late diagnosis mainly in this state. In addition, in Maranhão, indeterminate leprosy was less common and frequency of multibacillary cases highest. Maranhão is one of the poorest states in Brazil, and decentralisation including population coverage of the Family Health Program is yet far below the target.

On the other hand, the proportion of female patients and multibacillary cases among new cases showed higher levels outside the cluster than inside. This may reflect a recent success of strategies of leprosy control directed to the highly endemic areas of Brazil.⁵ However, leprosy control should not only focus on areas with a high number of cases, but also on most vulnerable areas and populations, considering economic and social differences present in low and middle income countries.^{21–22}

Similar to many other infectious diseases, leprosy has been considered a poverty-related disease.^{23–24} In Brazilian municipalities with more heterogeneous income distribution, the chance of leprosy as a public health problem was higher.²⁵ In fact, the index of subjective poverty in the study area is close to 90%, while in the South Region of Brazil, where there is no active transmission of leprosy,⁵ this index is about 15%.²⁶ There is also evidence about association of leprosy incidence and social conditions in the Amazon region, which comprises some states of the cluster studied here.²⁷ In this context, the ongoing social governmental policies for reducing extreme poverty will certainly minimise vulnerability of the population to a variety of diseases, including leprosy.²⁸

An evidence-based approach has been successfully implemented by the National Hansen's Disease Control Program, through the application of Operational Research in collaboration with several stakeholders such as non-governmental organizations, which helped to define and address areas for improvement of the control programmes at local and state levels.²⁹

Conclusions

The endemic cluster under study presented high levels of leprosy detection rates both in the general population and in children < 15 years, and of grade-2 disabilities, indicating ongoing transmission and late diagnosis. Despite established leprosy control in Brazil, in highly endemic areas, focussed integrated actions are needed to further improve early case detection and prompt treatment with the aim to reduce disease burden in the population. As leprosy and its complications are associated with poverty, interventions should also consider social inequities in the region.

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