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Time trend and identification of risk areas for physical disability due to leprosy in Brazil: An ecological study, 2001-2022

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Abstract

Background Leprosy is a chronic infectious disease that affects the peripheral nerves, leading to neurological damage and physical disability. This study analyzed the temporal trend in the rate of new leprosy cases with grade 2 physical disability in Brazil and identified spatial clusters of risk for physical disability.

Methods This is an ecological study of all new cases of leprosy with grade 2 physical disability (G2D) at diagnosis between 2001 and 2022 in Brazil, macro-regions, states and municipalities. Data were extracted from the National System of Notifiable Diseases and the Brazilian Institute of Geography and Statistics. Sociodemographic and clinical variables such as age, sex, race/colour, education and clinical form of the disease were analyzed, as well as the rate of new cases of leprosy with grade 2 physical disability at the time of diagnosis per million inhabitants. Data analysis was divided into three stages: 1- Descriptive analysis of the socio-demographic and clinical profile; 2- Time series analysis: In this stage, the joint-point regression model was used; 3- Spatial analysis, using global and local Moran statistics.

Results There were 50,466 new cases of leprosy with G2D during the period studied, 97.4% aged > 14 years, 70.2% male, 45.7% brown, 87.6% with low education, 90.2% multibacillary and 47.5% dimorphic clinical form. There was a downward trend in the detection of leprosy with physical disability grade 2, with an average annual reduction of 2.8% (13.6/1 million in 2001 and 9.1/1 million in 2022). The southeast, south and north regions showed a downward trend. A total of 14 states and 4 capitals showed a decrease in the rate, the most significant being Roraima (-11.0%/year). Tocantins was the only state with an upward trend (3.2%/year). 635 (14.1%) municipalities were in the high-high quadrant. These municipalities belong to 12 Brazilian states and accounted for 30% ($n = 15,139$) of all cases recorded in the country over the 22 years analyzed.

Conclusions These results suggest an overall decrease in the detection of leprosy with physical disability in Brazil and highlight geographical disparities in the occurrence of leprosy disability. Interventions to promote early diagnosis should be targeted at areas with the highest rate of new cases with grade 2 disability.

Keywords Leprosy, Grade 2 physical disability, Clusters of risk areas, Study ecological, Time trend analysis

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Background

Leprosy is a chronic infectious dermato-neurological disease primarily caused by Mycobacterium leprae and, more rarely, by Mycobacterium lepromatosis. Both species are acid-fast bacilli with a preference for peripheral nerves. The pathophysiology and immune response to neural invasion by *M. leprae* can result in partial or total damage to nerve trunks, affecting autonomic, sensory and motor fibers innervating structures in the dermis, epidermis and muscles, leading to functional changes and physical disability [1–6].

In 2022, 174,000 new cases of leprosy were reported worldwide. Brazil remains the world's second most affected country, with 19,000 new cases in 2022, accounting for 92% of the new cases diagnosed in the Americas, making it a World Health Organization priority country for leprosy [7]. Worldwide, 9,554 new cases with grade 2 physical disability (G2D) were detected, which corresponds to a rate of 1.2 cases per million population. In Brazil, the proportion of new cases with G2D among those assessed at diagnosis increased from 7.1% in 2011 to 11.5% in 2022, an increase of 62.0% [8].

Despite the significant reduction in the global prevalence of leprosy in recent decades, mainly due to the introduction of multidrug therapy in the early 1980s and advances in scientific research, leprosy remains an important public health problem, especially in places exposed to a context of social vulnerability [9–11]. In addition, leprosy belongs to the group of neglected tropical diseases [12–14].

In 2021, WHO launched the Global Leprosy Strategy 2021–2030 - "Towards Zero Leprosy". The new strategy focuses on interrupting transmission and achieving zero autochthonous cases of leprosy. One of the pillars of the strategy is the need to treat leprosy and its complications and to prevent new disabilities. To achieve this goal, research is needed, particularly on the time trends of physical disability indicators and the identification of risk areas [15].

Nerve impairment is a critical aspect of leprosy, as it is closely related to the disabling potential of the disease. Currently, physical disability (PD) is graded on a scale of 0 to 2, with 0 indicating no PD, grade 1 indicating sensory loss, and grade 2 indicating the presence of permanent PD in the eyes, hands and feet, such as lagophthalmos, trichiasis, clawing of hands and feet, plantar perforation, bone resorption, and others [16, 17].

It is estimated that between 3 and 4 million people may be living with visible physical disabilities due to leprosy [15]. These disabilities contribute to social stigma, reduced social participation, increased vulnerability, greater risk of mental disorders, and social and economic losses for the individual and their family. In addition, the indicator rate of new cases of Grade 2 physical disability per million population has been recommended by WHO for regional monitoring of the risk of physical disability in the population [18–23].

Based on the above, this study analyzed the temporal trend in the rate of new cases of leprosy with grade 2 physical disability in Brazil and identified spatial clusters of risk for physical disability.

Methods

Study design, population and period

This is an ecological study [24] involving all new cases of leprosy with grade 2 physical disability at the time of diagnosis between 2001 and 2022.

Study area

The study area is Brazil, its macro-regions, states and municipalities. Brazil currently consists of five macro-regions (North, Northeast, South, Southeast and Midwest), 27 federal entities (including the Federal District) and 5,568 municipalities. The size of Brazil presents a challenge to any scientific study because of the regional differences in economic, demographic, political and environmental characteristics. Brazil has a land area of approximately 8.5 million square kilometers, making it the fifth largest country in the world in terms of area, and a resident population of approximately 203 million people, with a population density of 23.86 inhabitants per square kilometer [25].

Data source

The data were extracted from the National System of Notifiable Diseases (SINAN), available in the database of the Department of Informatics of the Unified Health System (DATASUS) (http://datasus.saude.gov.br/). SINAN collects records of leprosy and other notifiable diseases throughout the country. The population data needed to calculate the indicators are obtained from the Brazilian Institute of Geography and Statistics (IBGE).

The following criteria were used to extract the data Year of diagnosis (2001 to 2022); discharge (unfulfilled, cure, transfer to the same municipality, transfer to another municipality, transfer to another state, transfer to another country, death, abandonment), type of entry (new case), assessment of physical disability at the time of notification (grade 2). The data collection and analysis period took place from December 2023 to April 2024.

Study variables

Two sets of variables were included. The first group consisted of socio-demographic and clinical variables: age, sex, race/colour, education, operational classification and clinical form of the disease. The second group consisted of an epidemiological indicator - the rate of new leprosy cases with grade 2 physical disability at the time of

diagnosis per 1 million inhabitants. This indicator allows the disability caused by leprosy to be assessed in the general population.

For the calculation, the numerator is the number of new cases with grade 2 physical disability at diagnosis, living in a particular place and diagnosed in the year of assessment, and the denominator is the population living in the same place and during the same period. In addition, there is no established assessment parameter. However, for the purposes of analysis, we have arbitrarily adopted the following classification < 2 per 1 million inhabitants, 2 to 4.99 per 1 million inhabitants, 5 to 9.99 per 1 million inhabitants and > 10 per 1 million inhabitants.

Study steps

Step 1 - Descriptive analysis of socio-demographic and clinical profile: In this stage, the socio-demographic and clinical variables were described in absolute value and relative frequency (%).

Step 2 - Time series analysis: In this stage, the inflection point regression model was used to determine the time trend in the rate of new leprosy cases with grade 2 physical disability at the time of diagnosis per million population. The inflection point regression model was used. This model examines whether a line with multiple segments is statistically better at describing the time trend of a data set than a straight line or a line with fewer segments [26].

The joinpoint regression model for the observations: ($x1$, $y1$),..., (xn, yn), where $x1 \leq \ldots \leq xn$ represents the time variable, and yi, i = 1, 2,..., n is the response variable, being given by:

$$\sum y_i|x_i] = \beta_0 + \beta_1 x_1 + \gamma_1 (x_i - \tau_1) + \ldots + \gamma_n (x_i - \tau_n)$$

Where β0, β1, γ1,..., γn are regression coefficients and yk, K = 1, 2,..., n, n < N, is the k-th unknown joinpoints where:

$$(x_i - \tau_k) = (x_i - \tau_k)\, if\, (x_i - \tau_k) > 0$$

$$= 0, \text{otherwise.}$$

In this way, the model makes it possible to check the trend of the indicator (whether it is stationary, increasing or decreasing) and the points at which this trend changes (joins), which makes it possible to identify the annual percentage change (APC) and that of the whole period (average annual percentage change - AAPC). The following parameters were used in the analyses: minimum of 0 joins and maximum of 4; model selection: test with 4,499 permutations; 5% significance; 95% confidence interval and autocorrelation of errors based on the data. Analyzes were performed in the Joinpoint regression program, version 4.6.0.1 (National Cancer Institute, Bethesda, MD, USA). The analyzis was performed in four spatial units: Brazil, five regions, 27 states and their respective capitals.

Step 3 - Spatial analysis: Global and local Moran's statistics (Moran's Index and p-value) were used to analyze the spatial dynamics. The global Moran's index (MI) measures the degree of autocorrelation in a given set, based on the product of the deviations from the global mean.

The MI values can oscillate within a spectrum between − 1 and + 1, with values close to -1 indicating negative spatial autocorrelation, values close to + 1 indicating positive spatial autocorrelation and values close to zero indicating no autocorrelation. The pseudo significance test is used to determine whether or not the null hypothesis is rejected (H0: spatial homogeneity; H1: spatial heterogeneity) [27, 28].

Global Moran's Index (Global I) is given by the equation:

$$I = \frac{\sum_{i=1}^{n} \sum_{j=1}^{n} w_{ij} \left(z_i - \bar{z}\right) \left(z_j - \bar{z}\right)}{\sum_{i=1}^{n} \left(z_i - \bar{z}\right) 2}$$

where n is the number of areas, zi is the value of the attribute considered in area i, z is the average value of the attribute in the study region and wij, the elements of the normalised spatial proximity matrix.

Once global autocorrelation (spatial heterogeneity) has been confirmed, we move to the second stage, which is characterized by the use of the Local Indicator of Spatial Association (LISA). LISA aims to quantify the degree of spatial association to which each location in the sample set is subject as a function of a neighbourhood model. The result is the local pattern of the spatial distribution of the variable under analysis [27].

In this case, the following equation is used:

$$I_i = \frac{z_i \sum_{j=1}^{n} w_{ij} z_j}{\sum_{j=1}^{n} z_j^2}$$

where n is the number of areas, zi is the value of the attribute considered in area i, z is the average value of the attribute in the study region and wij are the elements of the normalised spatial proximity matrix.

While Q1 (positive values, positive averages) and Q2 (negative values, negative averages) indicate points of positive spatial association, in the sense that a location has neighbors with similar values; Q3 (positive values, negative averages) and Q4 (negative values, positive averages) indicate points of negative spatial association, in the sense that a location has neighbors with different values [27]. Municipalities located in Q1 are considered priorities for intervention.

Table 1 Epidemiologic characterization of leprosy cases with grade 2 physical disability. Brazil, 2001–2022

Variable	Population ($n=50,466$)
Age*	% (*n*)
≤ 14 years	2.6 (1,316)
> 14 years	97.4 (49,139)
Sex**	
Male	70.2 (35,428)
Female	29.8 (15,030)
Race/color	
Ignored/Blank	10.3 (5,218)
White	29.6 (14,957)
Black	12.9 (6,505)
Yellow	1.1 (528)
Brown	45.7 (23,039)
Indigenous	0.4 (219)
Education	
≤ 8 year	87.6 (44,197)
< 8 years	12.1 (6,107)
Not applicable	0.3 (162)
Operational classification	
Paucibacillary	9.7 (4,912)
Multibacillary	90.2 (45,515)
Unclassified/Ignored/Blank	0.1 (39)
Clinical form	
Undetermined	2.9 (1,450)
Tuberculoid	8.3 (4,179)
Dimorphic	47.5 (23,982)
Virchowian	33.3 (16,794)
Unclassified/Ignored/Blank	8.0 (4,061)

Legend: * 0.02% ($n=11$) records with unknown age. **0.02% ($n=8$) records with unknown sex

Ethical aspects

By using secondary data in the public domain, the study does not need to be evaluated by the Research Ethics Committee, in accordance with Resolution 510/2016 CEP/CONEP, from the National Health Council of the Ministry of Health.

Results

Between 2001 and 2022, 50,466 new cases of leprosy with G2D were reported in Brazil, an average of 2,293.9 cases/year. In terms of demographics, 97.4% ($n=49,139$) of the cases analyzed were individuals older than 14 years, 70.2% ($n=35,428$) of the population studied was male. Blacks (brown and black) represented 45.7% ($n=23,039$) and 12.9% ($n=6,505$), respectively. In addition, 87.6% ($n=44,197$) had little schooling (≤ eight years of schooling). The clinical profile of the population was characterized by the multibacillary operational classification (90.2%; $n=45,515$), with the dimorphic clinical form accounting for 47.5% ($n=23,982$) (Table 1).

In Brazil, the rate of new cases with G2D decreased from 13.6/1 million in 2001 to 9.1/ 1 million in 2022, with a downward trend (AAPC: -2.8%; CI: -3.6 to -2.1; $p<0.001$). Three regions show a downward trend: (i) Southeast, where the rate decreases from 10.4/1 million in 2001 to 5.0/1 million in 2022 (AAPC: -4.9%; CI: -5.6 to -4.1; $p<0.001$); (ii) Southern region, rate from 6.3/1 million in 2001 to 2.7/1 million in 2022 (AAPC: -4.8%; CI: -7.1 to -2.6; $p<0.001$); and (iii) Northern region, rate from 32.5/1 million in 2001 to 19.4/1 million in 2022 (AAPC: -3.0%; CI: -3.9 to -2.0; $p<0.001$). The stationary trend was observed in the Northeast and Midwest regions (Fig. 1).

During the period analyzed, 14 states showed a downward trend, five in the north, three in the northeast, two in the Midwest, three in the southeast and one in the south. The state with the highest rate of decline

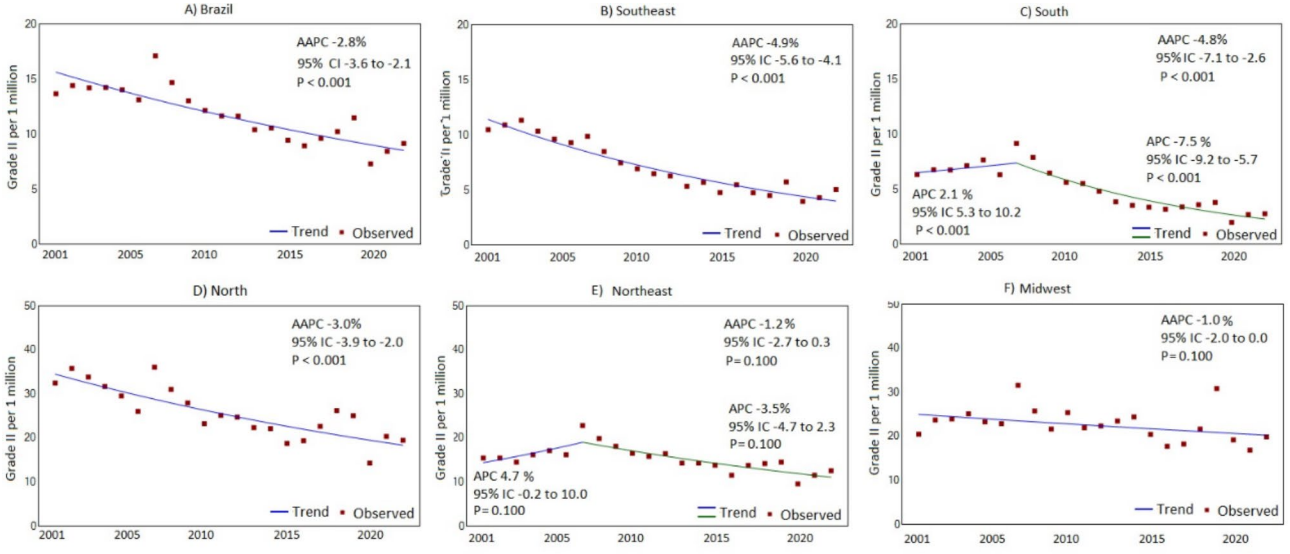

Fig. 1 Time trend analysis of the rate of new leprosy cases with grade 2 physical disability at diagnosis, in Brazil and regions, 2001–2022

Table 2 Average annual percentage change (AAPC) and rate of grade 2 physical disability in Brazilian regions and States, 2001–2022

Spatial unit	Rate[1]		AAPC (CI 95%) p-value
	2001	2022	
North	**32.5**	**19.4**	**-3.0* (-3.9 to -2.0);*p* < 0.001**
RO	29.3	19.6	-4.6* (-6.5 to -2.7); *p* < 0.001
AC	46.6	21.6	-3.7 (-10.3 to 3.4); *p* = 0.301
AM	33.6	7.8	-5.6* (-6.8 to -4.4); *p* < 0.001
RR	54.9	9.4	-11.0* (-14.2 to -7.7); *p* < 0.001
PA	32.9	18.3	-3.1* (-4.1 to -2.1); *p* < 0.001
AP	11.6	8.1	-3.8* (-6.1 to -1.5); *p* < 0.001
TO	26.3	64.1	3.2* (1.3 to 5.2); ***p*** < 0.001
Northeast	**15.4**	**12.5**	**-1.2 (-2.7 to 0.3);*p* = 0.103**
MA	42.3	27.1	-2.0 (-4.0 to 0.0); *p* = 0.112
PI	28.3	17.7	-2.7* (-4.1 to -1.3); *p* < 0.001
CE	20.1	11.3	-2.7* (-3.8 to -1.7); *p* < 0.001
RN	4.1	4.5	0.3 (-3.9 to 4.8); *p* = 0.916
PB	14.5	6.5	-2.4* (-3.9 to -1.0); *p* < 0.001
PE	12.1	15.8	0.5 (-3.1 to 4.1); *p* = 0.808
AL	4.4	11.1	1.2 (-1.3 to 3.8); *p* = 0.326
SE	6.9	6.3	-0.7 (-3.9 to 2.7); *p* = 0.709
BA	6.4	7.9	1.0 (-1.0 to 3.2); ***p*** = 0.301
Midwest	**20.5**	**19.8**	**-1.0 (-2.0 to 0.0);*p* = 0.179**
MS	14.7	9.0	-1.9 (-5.4 to 1.6); *p* = 0.364
MT	36.9	52.4	1.4 (-0.1 to 2.9); *p* = 0.121
GO	17.7	13.3	-2.6* (-4.9 to -0.1); *p* < 0.001
DF	13.0	4.6	-4.3* (-6.8 to -1.7); ***p*** < 0.001
Southeast	**10.4**	**5.0**	**-4.9* (-5.6 to -4.1);*p* < 0.001**
MG	16.0	8.4	-4.5* (-6.9 to -2.1); *p* < 0.001
ES	25.1	12.7	-3.7 (-8.5 to 1.3); *p* = 0.173
RJ	13.8	3.6	-5.6* (-7.4 to -3.8); *p* < 0.001
SP	5.2	3.3	-3.1* (-4.1 to -2.1); ***p*** < 0.001
South	**6.3**	**2.7**	**-4.8* (-7.1 to -2.6);*p* < 0.001**
PR	14.1	3.7	-6.4* (-9.1 to -3.7); *p* < 0.001
SC	1.4	2.8	-1.8 (-4.2 to 0.6); *p* = 0.152
RS	1.5	1.6	-1.6 (-3.6 to 0.5); *p* = 0.181
Brazil	**13.6**	**9.1**	**-2.8* (-3.6 to -2.1);*p* < 0.001**

Legend: * Statistical significance ($p < 0.05$); [1–] Rate of grade 2/ 1 million inhabitants; AAPC: *Average Annual Percent Change*; RO: Rondônia; AC: Acre; AM: Amazonas; RR: Roraima; PA: Pará; AP: Amapá; TO: Tocantins; MA: Maranhão; PI: Piauí; CE: Ceará; RN: Rio Grande do Norte; PB: Paraíba; PE: Pernambuco; AL: Alagoas; SE: Sergipe; BA: Bahia; MG: Minas Gerais; ES: Espírito Santo; RJ: Rio de Janeiro; SP: São Paulo; PR: Paraná; SC: Santa Catarina; RS: Rio Grande do Sul; MS: Mato Grosso do Sul; MT: Mato Grosso; GO: Goiás; e DF: Distrito Federal

was Roraima, which fell from 54.9/1 million in 2001 to 9.4/1 million in 2022 (AAPC: -11.0%; $p < 0.001$). The only state with an upward trend was Tocantins, from 26.3/1 million in 2001 to 64.1/1 million in 2022 (AAPC: 3.2%; $p < 0.001$) (Table 2).

Regarding the state capitals, a downward trend was observed in four capitals: Manaus/AM (AAPC: -14.5%; $p < 0.001$) and Macapá /AP (AAPC: -5.8%; $p < 0.001$) in the North, Brasília/DF (AAPC: -11.9%; $p < 0.001$) in the Midwest and São Paulo/SP (AAPC: -7.0%; $p < 0.001$) in the Southeast. No capital city showed an upward trend in G2D during the period analyzed (Table 3).

Table 3 Average annual percentage change (AAPC) in the rate of New Leprosy cases with Grade 2 physical disability at diagnosis, in the Capital cities of Brazil. 2001–2022

Spatial unit	Rate[1]		AAPC (CI 95%) p value
	2001	2022	
North			
Porto Velho	19.7	17.3	-5.0 (-11.4 to 1.8); *p* = 0.102
Rio Branco	51.7	8.2	-13.7 (-50.1 to 49.2); *p* = 0.616
Manaus	27.0	7.2	-14.5* (-4.0 to -26.0); *p* < 0.001
Boa Vista	46.6	4.8	0.3 (-15.8 to 19.4); *p* = 1.005
Belém	19.5	15.3	5.5 (-2.2 to 13.7); *p* = 0.235
Macapá	16.3	4.5	-5.8* (-1.4 to -10.4); *p* < 0,001
Palmas	13.2	102.4	-0.3 (-5.5 to 5.1); *p* = 0.967
Northeast			
São Luís	26.7	29.8	-3.6 (-9.3 to 2.4); *p* = 0.246
Teresina	61.9	17.3	-4.4 (-8.7 to 0.0); *p* = 0.193
Fortaleza	23.2	7.4	1.1 (-3.8 to 6.2); *p* = 0.775
Natal	2.6	3.9	0.7 (-4.1 to 5.6); *p* = 0.828
João Pessoa	9.5	3.5	6.5 (-2.1 to 15.9); *p* = 0.134
Recife	14.2	20.1	-1.3 (-5.2 to 2.7); *p* = 0.516
Maceió	2.2	13.5	-1.3 (-6.8 to 4.4); *p* = 0.673
Aracaju	6.1	1.6	-2.0 (-8.0 to 4.4); *p* = 0.581
Salvador	4.3	5.7	-3.7 (-10.3 to 3.5); *p* = 0.394
Midwest			
Campo Grande	8.6	10.0	-3.2 (-10.3 to 4.4); *p* = 0.442
Cuiabá	33.7	24.5	-4.1 (-9.4 to 1.5); *p* = 0.159
Goiânia	25.3	4.1	4.0 (-0.4 to 8.6); *p* = 0.131
Brasília	13.0	4.2	-11.9* (-0.5 to -24.7); *p* < 0.001
Southeast			
Belo Horizonte	6.9	1.7	-6.3 (-13.8 to 1.9); *p* = 0.113
Vitória	13.5	18.5	-16.4 (-39.9 to 16.5); *p* = 0.387
Rio de Janeiro	13.7	2.2	2.9 (-3.1 to 9.4); *p* = 0.394
São Paulo	2.7	1.0	-7.0* (-11.5 to -2.4); *p* < 0.001
South			
Curitiba	8.2	3.9	-3.8 (-8.3 to 0.9); *p* = 0.164
Florianópolis	0.0	0.0	-5.1 (-56.0 to 104.5); *p* = 0.993
Porto Alegre	0.0	0.7	27.8 (-6.0 to 73.7); *p* = 0.172

Legend: * Statistical significance ($p < 0.05$); [1–] Rate of grade 2/ 1 million inhabitants; AAPC: *Average Annual Percent Change*

Municipalities with rates of new leprosy cases with G2D > 10/million were mainly concentrated in the northern and Midwest regions of Brazil. It should be noted that in the years of the Covid-19 pandemic, the number of municipalities in this stratum of endemicity was lower than in previous years. For example, in 2019, 14.5% ($n = 807$) of the municipalities had a G2D rate > 10/1 million. In 2020, this percentage was 10.0% ($n = 559$) (Fig. 2).

Moran's local statistics showed spatial dependence in all the years analyzed ($p < 0.05$) (Table supplementary 1). The local statistics indicated the existence of spatial clusters, concentrated in the North and Midwest regions. The

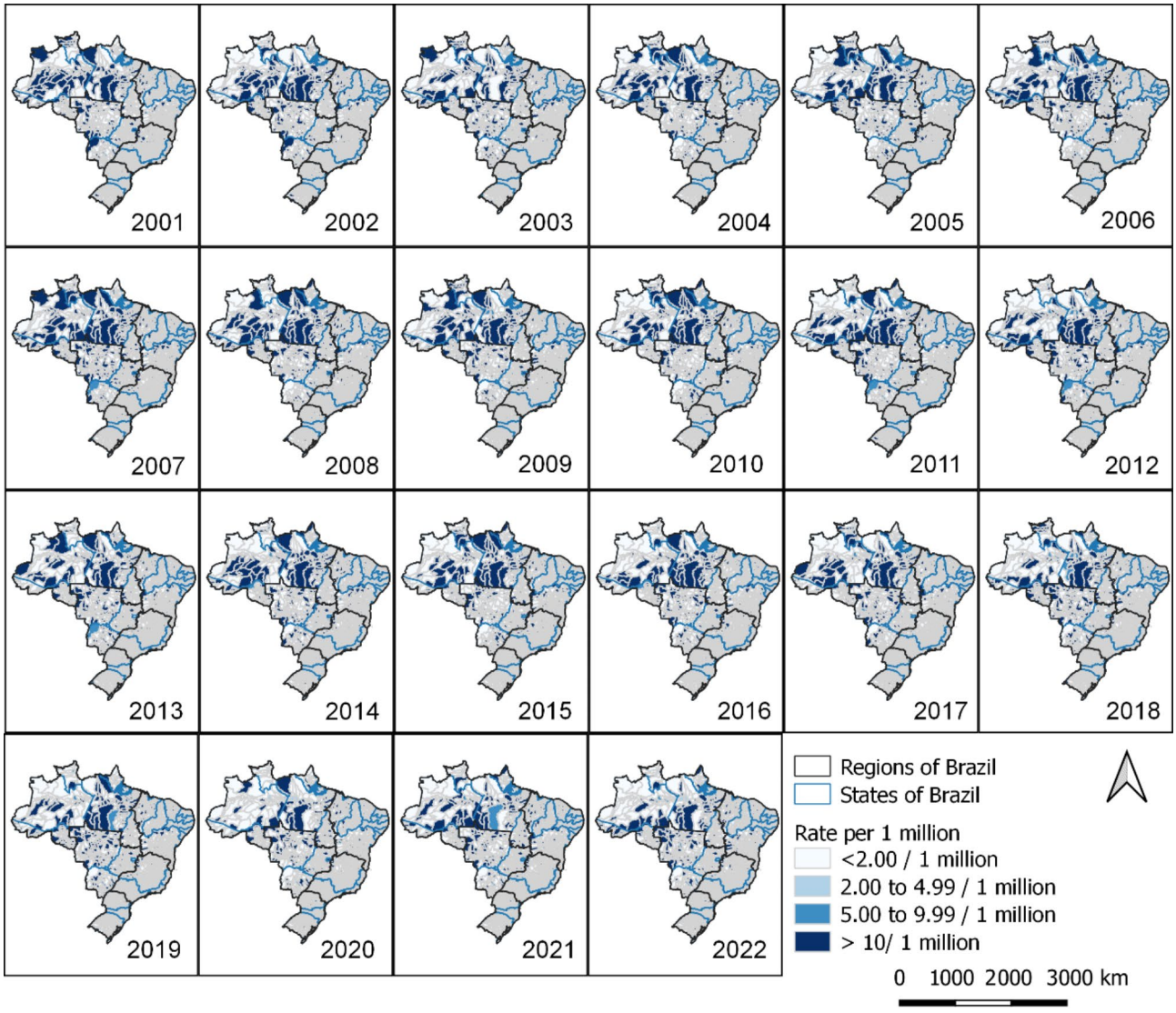

Fig. 2 Rate of new leprosy cases with grade 2 physical disability at diagnosis, by municipality of residence and year of diagnosis. Brazil, 2001–2022

number of municipalities in quadrant Q1 (High-high) varied between the years, ranging from 170 (3.1%) in 2001 to 118 (2.1%) in 2019. It should be noted that in the years of the Covid-19 pandemic, the number of municipalities in the High-High quadrant was lower than in the pre-pandemic years: 91 (1.6%) in 2020, 88 (1.6%) in 2021 and 59 (1.1%) in 2022. In addition, there was a change in the spatial pattern over the time series, with a reduction in municipalities in the North and an increase in municipalities in the Midwest in the Q1 quadrant (Fig. 3).

Considering the rate for the period 2001–2022, 40.1% ($n = 2234$) of Brazilian municipalities had a G2D rate > 10/1 million. Although there was a concentration in the North and Midwest regions of Brazil, clusters were found in the other regions. In the Moran map, 635 (14.1%) municipalities were in the high-high quadrant. These municipalities belong to 12 Brazilian states, one in the Northeast (Maranhão), one in the South (Paraná), two in the Southeast (Minas Gerais and Espírito Santo), all three in the Midwest (Goiás, Mato Grosso and Mato Grosso do Sul) and five in the North (Acre, Rondônia, Amazonas, Amapá and Tocantins). In addition, these municipalities together accounted for 30% ($n = 15,139$) of all cases recorded in the country during the 22 years analyzed (Fig. 4).

In addition, three spatial clusters were observed: the first consisting of five states in the north, three in the Midwest and one in the northeast; the second observed in the southeast, between Minas Gerais and Espírito Santo and a third located in the state of Paraná (Fig. 4).

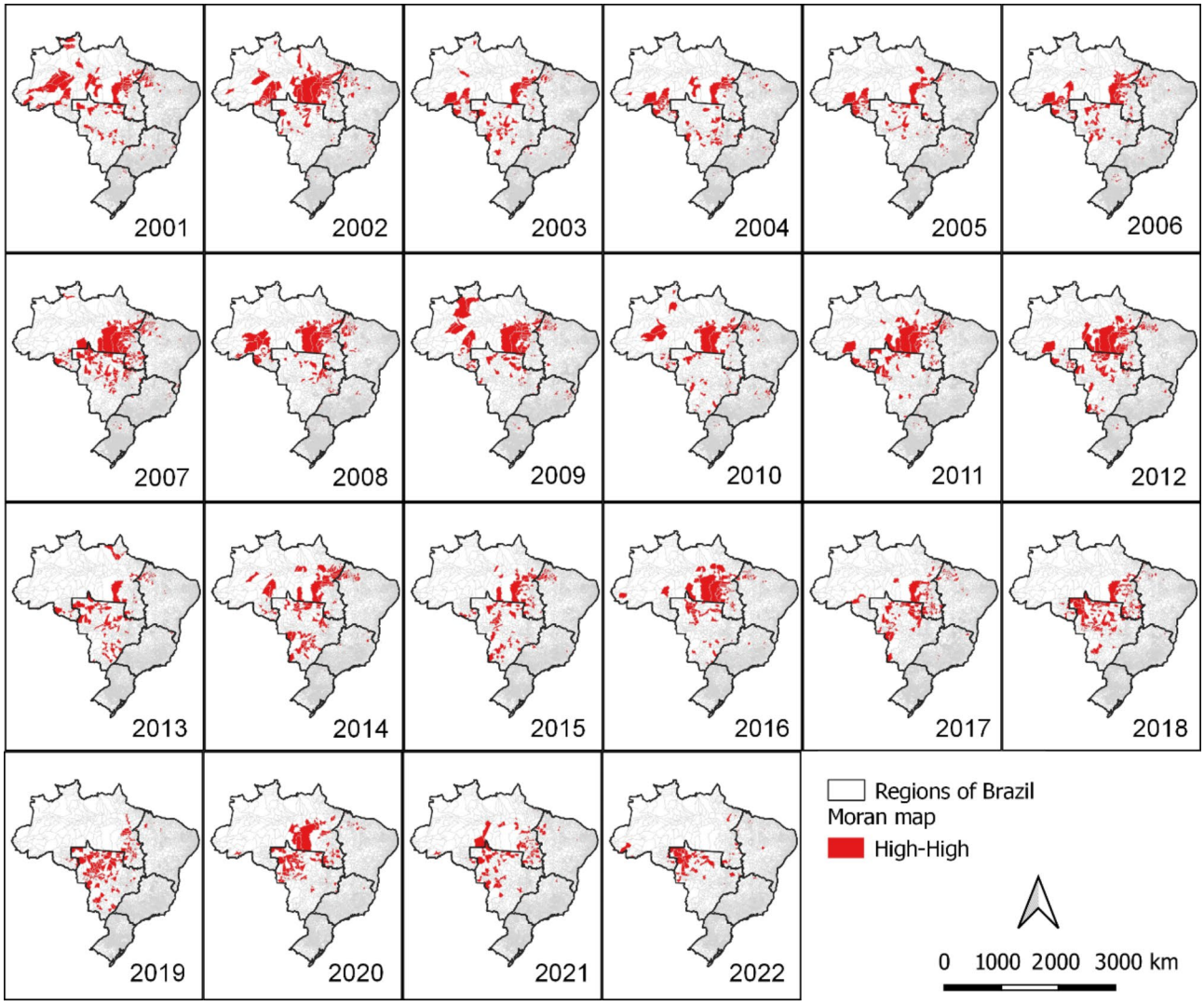

Fig. 3 Moran's map of the rate of new leprosy cases with grade 2 physical disability at diagnosis, by municipality of residence and year of diagnosis. Brazil, 2001–2022

Discussion

This study described the temporal trend and identified the areas at risk of developing physical disability due to leprosy in Brazil over a twenty-one year time series. A variation in the trend was observed over the period, with three regions showing a decreasing trend and two showing a stationary trend in the coefficient of Grade 2 physical disability, suggesting the persistence of late-diagnosed cases. Despite global reductions in the detection rates of new leprosy cases [29–31], Brazil still reported more than fifty thousand new cases with grade 2 physical disability between 2001 and 2022.

The highest rates of new cases of leprosy with G2D were concentrated among adult males with black skin, low levels of education, and living in the northern and midwest regions of Brazil. National and international studies show a higher prevalence of the disease among men with lower levels of education, which may reflect social and economic inequalities, especially in neglected populations [32–39]. In general, men are more vulnerable to the disease and its more severe forms, often due to behaviours that make it difficult for them to seek appropriate health care, combined with a lack of specialized services to meet their specific needs [32, 40].

Patients with the multibacillary clinical form are more likely to develop physical disabilities. In our study, they accounted for 80.8% of the reported cases. The presence of leprosy disabilities is an indicator of late diagnosis and treatment [41–43]. This underscores the need to define and strengthen public health interventions aimed at early diagnosis and comprehensive care of people affected by *M. leprae*, especially those with severe forms of the disease, in order to reduce disability, mitigate associated stigma, and reduce disease transmission [42, 44–46].

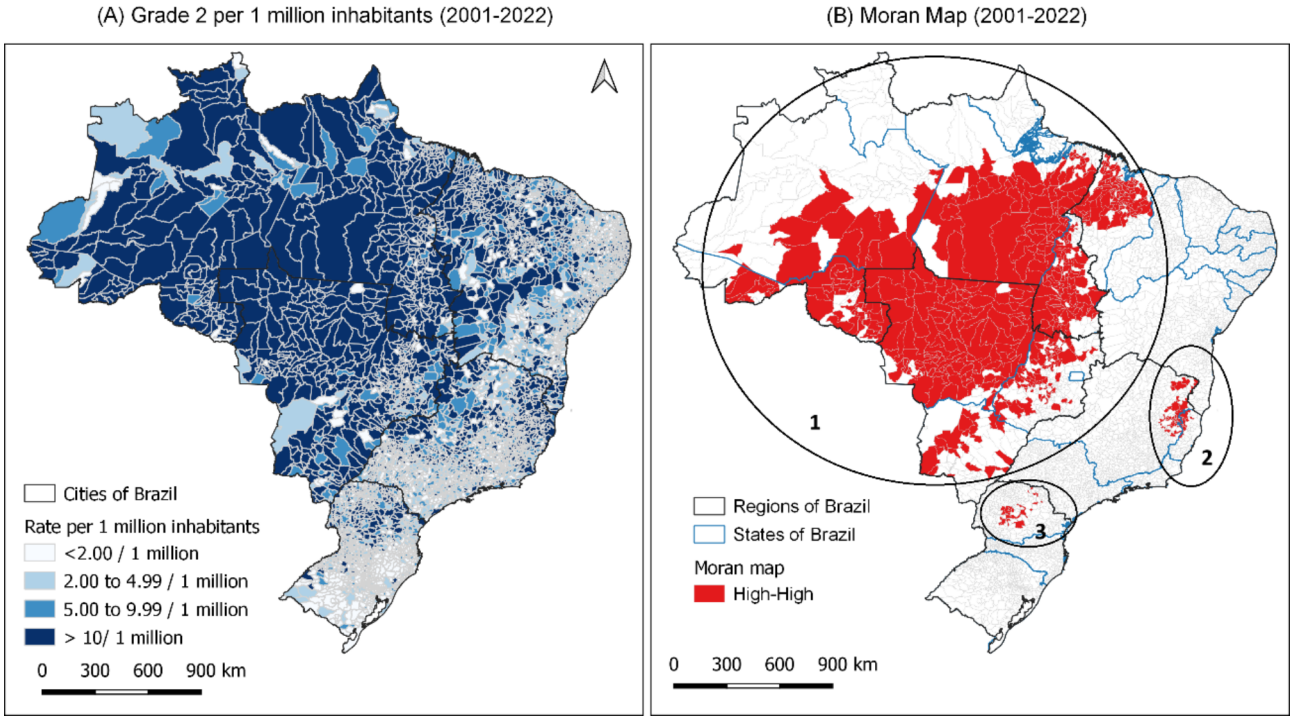

Fig. 4 Moran's map of the rate of new leprosy cases with grade 2 physical disability at diagnosis, by municipality of residence and year of diagnosis. Brazil, 2001–2022

The results show that there has been a decrease in the rate of new cases with G2D in Brazil. The Southeast, South and North regions showed a decreasing trend, while the Northeast and Midwest regions showed a stable trend. These results are consistent with other studies of leprosy conducted in Brazil, which have generally shown a reduction in the burden of leprosy in Brazil [45–47].

Roraima was the state with the highest rate of decline, from 54.9/1 million in 2001 to 9.4/1 million in 2022. A study conducted in this state between 2001 and 2017 showed a decrease in prevalence and case detection rates, demonstrating a trend toward elimination of the disease [48]. In an analysis measuring the severity of the disease in Brazil, Roraima, Paraíba, Rio Grande do Sul and Espírito Santo have better results in the fight against leprosy [49]. This decrease can be attributed to the implementation of the National Leprosy Control Programme in Brazil, which promoted and facilitated the decentralization of leprosy control to primary health care [46].

None of Brazil's state capitals showed an upward trend. Manaus/AM, Macapá/AP, Brasília/DF and the capital São Paulo/SP showed a downward trend. This finding may be related to two factors: (i) the ability of large centers to have better infrastructure and health care, which may facilitate early diagnosis [15], (ii) the higher hidden prevalence of the disease [50–52]. This second factor seems to be the most appropriate to explain the stationary trend in the vast majority of capital cities. In São Paulo, for example, a study showed the hidden prevalence of the disease, whose real prevalence was six times higher than the observed prevalence [50]. The other Brazilian capitals show stationary behavior and some remain hyperendemic for leprosy, requiring additional efforts in the process of eliminating the disease [53, 54].

When analyzing the municipalities, endemicity fluctuated over the period analyzed, especially during the Covid-19 pandemic, where there was a decrease in the rates of new leprosy cases with G2D compared to previous years in the series. For example, in 2019, 14.5% ($n = 807$) of the municipalities had a rate > 10/million. In 2020, this percentage was 10.0% ($n = 559$). The Covid-19 pandemic has had an impact on diagnoses, increasing the hidden prevalence of the disease, as health systems in Brazil and around the world have turned their attention to controlling the pandemic, affecting the ability to maintain service provision and ensure adequate care for the population, especially for chronic and neglected diseases [15, 55–57].

The Covid-19 pandemic has created challenges in the follow-up and treatment of leprosy patients in primary health care centers throughout Brazil. This has led to delays in appointments, the need to reschedule appointments, treatment extensions due to drug shortages, and barriers to contact assessment and active case finding. These factors have had a negative impact on the leprosy program in all regions of the country [15, 55, 56, 58, 59].

The impact of the pandemic has been observed worldwide: the World Health Organization published a report showing a decrease in the number of countries and territories sharing leprosy statistics, from 166 (out of 221) in 2019 to 127 in 2020 and 143 in 2021, as well as a 37% global decrease in the detection of new cases of the disease [60]. Our study also noted the impact of the pandemic on high-risk areas: the number of municipalities in the high-high quadrant was lower than in the pre-pandemic years: 91 (1.6%) in 2020, 88 (1.6%) in 2021, and 59 (1.1%) in 2022.

Despite all the methodological care taken, this study has important limitations. First, it used secondary data from SINAN, which is directly influenced by the capacity of municipalities to detect and report new leprosy cases. In this way, the capacity of local surveillance services directly influences the records and thus the results of this study. Second, assessing the degree of physical disability is still a challenge for many municipalities, especially smaller ones with few human resources. Thus, the quality of the neurological examination and the degree of disability may influence the results.

Analysis and interpretation of these results are important for the development and evaluation of leprosy surveillance activities in Brazil. It suggests the need to strengthen active case finding and continuous monitoring of leprosy patients. These measures are essential to ensure an effective approach to control and to prevent the spread of the disease and its disabilities. Another flaw inherent in the study is the ecological fallacy, a common error in research and studies, especially those dealing with aggregated data.

Our results show spatial inequalities in the incidence of leprosy disability, which may be related to differences in services between health regions and in the implementation of disease control interventions, particularly with regard to timely diagnosis and treatment. In addition, these findings highlight the importance of discussing the control of neglected diseases such as leprosy and the development of new technologies for their diagnosis and treatment, including here the implementation of rapid tests for diagnosis and the use of pharmacological alternatives as preventive therapies, including the single-dose rifampicin regimen. These initiatives are essential to improve the effectiveness of public health strategies to control this disease.

Supplementary Information

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Supplementary Material 1

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TSM and CDF: Data collection, interpretation of findings, analysis, interpretation, drafting of the manuscript and study supervision. TRMOF, MBS, RJVCB, DUSM, RFC, and TFAS: Data collection, interpretation of findings, analysis and drafting of the manuscript.

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Data availability
Availability of data and materials The data were extracted from the National System of Notifiable Diseases (SINAN), available in the database of the Department of Informatics of the Unified Health System (DATASUS) (http://datasus.saude.gov.br/).

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
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Competing interests
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