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RESEARCH ARTICLE

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## EPIDEMIOLOGICAL AND OPERATIONAL PATTERNS OF LEPROSY IN THE STATE OF TOCANTINS, 2001-2020: REGRESSION BY INFLECTION POINTS

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### ABSTRACT

**Objective:** To analyze the trend of epidemiological and operational indicators of leprosy in the state of Tocantins, Brazil, from 2001 to 2020. **Methodology:** This is a population-based ecological study, with temporal analysis of new leprosy cases based on Poisson regression by inflection points (Joinpoints), using secondary data reported between 2001 and 2020. **Results:** A total of 24.413 cases were reported. The overall detection coefficient showed four temporal trends. The Médio Norte Araguaia, Cerrado Tocantins Araguaia and Ilha do Bananal regions showed a significant downward trend in the AAPC (3.1%, 4.6% and 5.3%, respectively). Only the Amor Perfeito region showed a significant growth trend of 2.7%. In the evaluation of the Annual Percent Change (APC), the Bico do Papagaio region had a significant increase of 12.1% between 2001 and 2008 and a significant decrease of 10.3% between 2008 and 2020. In the Capim Dourado region, the APC had a significant decrease of 6.3% between 2001 and 2013 and a significant increase of 34.5% between 2013 and 2018. **Conclusion:** Leprosy remains in high magnitude in Tocantins, indicating active transmission, late diagnosis, heterogeneous trend in case detection in the eight health regions and persistence of hyperendemicity, requiring strengthening of surveillance measures.

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## INTRODUCTION

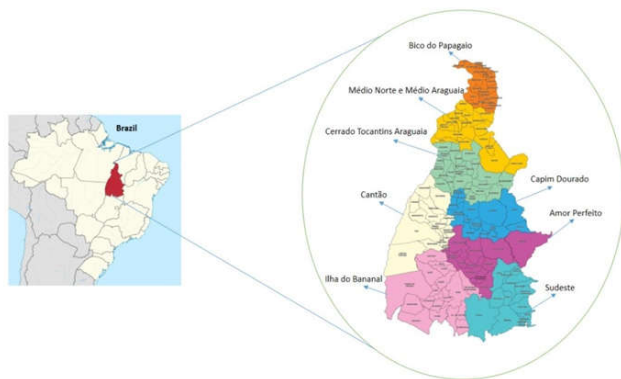
Leprosy is a chronic, neglected, potentially disabling and infectious disease caused by *Mycobacterium leprae* that preferentially affects peripheral nerves and skin (Monteiro, 2015a; BRAZIL, 2016; World Health Organization, 2021). Despite the significant decrease in the global burden of leprosy since the introduction of multidrug therapy (MDT), the disease remains a public health problem, especially in underdeveloped countries (World Health Organization, 2021; World Health Organization, 2020a; World Health Organization, 2020). The characteristic of a neglected tropical disease is due to its greater occurrence in places where low-income populations predominate, under precarious living conditions, which contributes to the perpetuation of inequalities, thus representing an obstacle to the evolution of the sustainable development goals in different regions (World Health Organization, 2021; Pescarini, 2020).

In addition, people affected by leprosy experience stigma, discriminationsocial (Monteiro, 2014; BRAZIL, 2019). The burden of disease and its disabilities can be mitigated through timely detection and treatment in health services (World Health Organization, 2021; BRAZIL, 2019; Monteiro, 2002). In the world, Brazil remains the second country with the highest number of cases, after India. In 2019, 202,185 new cases were reported to the World Health Organization (WHO) worldwide, of which 29,936 occurred in the Americas; and, within these, 27,864 cases (93%) were reported in Brazil (World Health Organization, 2021).Tocantins is the second most hyperendemic state in the country. In 2019, it registered 96.44 new cases per 100,000 inhabitants, and its capital, Palmas, had the highest detection coefficient among the capitals – 226.99 per 100,000 inhabitants.<sup>9,10</sup> Specifically, the *Capim Dourado* health region, located in the center of the state, was characterized as the most hyperendemic area, with an explosion of cases in recent years (BRAZIL, 2021). The heterogeneous occurrence of leprosy in different territories is related to social vulnerability and underdiagnosis of new cases (BRAZIL, 2021; Monteiro, 2017; Monteiro, 2021), which affects the ability of

health services to plan control activities (Monteiro, 2018; Santana, 2018). In addition, Primary Health Care (PHC) faces difficulties in monitoring patients and their disabilities during and after the end of treatment (BRAZIL, 2016; Monteiro, 2015b). Faced with the problem of underdiagnosis, intervention projects that promote active search and early diagnosis must be carried out, and examples show that these have been able to show promising results in the actual detection of cases and in reducing hidden prevalence (Monteiro, 2018; Santana, 2018). In this context, analyzing the trend of epidemiological and operational indicators of leprosy in the state of Tocantins and its health regions can support control programs in the intervention of the disease transmission chain. Furthermore, the explanation for fluctuations in the trend of cases over the last 20 years was based on the analysis of interventions and actions carried out in this territory.

## METHODS

**Study location:** Located in the North region of Brazil, the state of Tocantins is part of the Amazon region and has predominant *Cerrado* vegetation (a type of forest that resembles Savannah). It is the newest state in the country and has a territorial extension of 277,622 km<sup>2</sup> and an estimated population of 1,590,248 people in 2020. It comprises 139 municipalities (Figure 1) and is divided into 8 health regions created by the Bipartite Inter-Management Commission (BIC) in 2012, namely: *Capim Dourado*, *Ilha do Bananal*, *Sudeste*, *Cerrado Tocantins Araguaia*, *Meio Norte Araguaia*, *Amor Perfeito*, *Cantão* and *Bico do Papagaio*. This division considered the municipalities with their populations and demographic densities, aiming at offering minimum actions and services in each region. The Hospital for Tropical Diseases (HTD), located in the town of Araguaína, in the far north of the state, is the only reference service for tertiary care for people affected by leprosy (Tocantins, 2012). In Tocantins, the population coverage of PHC by Family Health Strategy Teams (FHEt) has been above 70% since 2008; and, in 2020, it was 93%, while coverage by community health workers (CHW) remained at 94% for this population (Brazil, 2021a).



**Figure 1. Map of the state of Tocantins according to municipalities and health regions**

**Study design and population:** A time-trend ecological study was conducted using secondary data on leprosy from the last 20 years (2001 to 2020), totaling 24,413 new cases of the disease.

**Data source:** Data were obtained from the Department of Informatics of the Brazilian Unified Health System (DATASUS, as per its Portuguese acronym) (BRAZIL, 2021b). These data come from compulsory notification forms, which consist of a standardized form with sociodemographic, clinical and treatment information filled out by health professionals. A leprosy case is defined by the WHO as a person who manifests clinical signs of the disease and requires specific treatment (World Health Organization, 2020). Records of cases residing in municipalities in other states were excluded. Population data were obtained from the Brazilian Institute of Geography and Statistics (IBGE, as per its Portuguese acronym), based on data from the state population censuses (2010) and

population estimates for the inter-census years (2001-2009 and 2011-2020).

**Selected Indicators:** The indicators selected for the study were those recommended by the National Program for the Evaluation and Monitoring of Leprosy: detection coefficient in the overall population (indicates the magnitude, morbidity and trend of the disease); detection coefficient in children under 15 years of age (indicates active transmission); proportion of contacts examined among those registered (measures the capacity of services to carry out contact surveillance of new leprosy cases and timely detection); proportion of multibacillary cases (MB) (indicates late diagnosis); proportion of paucibacillary (PB) cases (indicates early diagnosis); detection coefficient according to sex (indicates the ability to access health services considering gender differences), proportion of cases in the indeterminate clinical form and in the tuberculoid clinical form (indicate early diagnosis); proportion of cases in the borderline clinical form and in the virchowiane clinical form (indicating late diagnosis); proportion of new cases with grade 0, grade 1 and grade 2 physical disability (evaluates delay in diagnosis as a quality indicator for case detection activities); and proportion of cases not evaluated in the diagnosis regarding the degree of incapacity (indicates failure in case follow-up).

**Data analysis:** The sociodemographic, clinical and epidemiological characteristics of new cases diagnosed between 2001 and 2020 were described, according to the following variables: sex, years of study, race, age group, operational classification, clinical form, degree of physical disability at diagnosis and at cure, and evaluation of contacts. In order to perform the analysis of the leprosy trend by modeling using regression by inflection points, the detection coefficients were calculated from the IBGE population estimates for the years of the study. The state of Tocantins was used as a geographic unit of analysis. The investigation of temporal trends for the period of 20 years of observation was carried out using the Joinpoint regression model. The purpose of this analysis was to identify a significant change in the linear trend (on a log scale) over the study period (Kim, 2000). The year of occurrence was considered as an independent variable; and, as dependent variables, the selected leprosy indicators.

The analysis started with the minimum number of joinpoints (for example, 0 joinpoints, which is a straight line) and then one or more joinpoints were tested to see if they were significant and would therefore be included in the model. In this test, up to 4 joinpoints were reached. Each significant joinpoint, which indicated a change in slope, was retained in the final model. In order to describe the linear trends by period, the Annual Percent Change (APC) was calculated for each of these trends with a regression line adjusted for the natural logarithm of the indicators. In cases where more than one slope was identified, the Average Annual Percent Change (AAPC) over the entire period (when available) was also calculated, based on an underlying joinpoint model. The AAPC was estimated as the weighted geometric average of the AAPC, with weights equal to the length of each segment in the time interval (Kim, 2000; Clegg, 2009). An increase in the indicators was considered when the trend was increasing and the minimum value of the confidence interval was greater than 0. Conversely, a decrease was considered when there was a decline in the trend and the maximum value of the confidence interval was below 0. A stability was defined when the confidence interval included 0. Joinpoint regression analyses were performed using the Joinpoint Regression Program, version 4.1.0 (US National Cancer Institute, Bethesda, MD, USA). The calculations of the indicators, as well as the design of tables and figures, were made using Microsoft Excel® software.

**Ethical aspects:** The study was based on secondary data from leprosy records in the public domain, available for access on the DATASUS website, whose anonymous data do not allow the identification of people. Accordingly, it was not necessary to submit the study project to a Research Ethics Committee.

## RESULTS

Between 2001 and 2020, 24.413 new leprosy cases were reported in the state of Tocantins, with an average of 1,220.65 cases/year. Of these, 2,031 were under 15 years of age (8.32%). Grade 2 physical disability was present in 5.70% (n= 1,391) of these cases. The MB operational classification prevailed, with 57.85% (n=14,123), and the borderline clinical, form with 41.97% (n= 10,244). The proportion of contacts examined reached 76.14% in the 20-year period. Almost 45.00% of the cases were not evaluated regarding the degree of physical disability at the time of cure (n= 10,963) (Table 1).

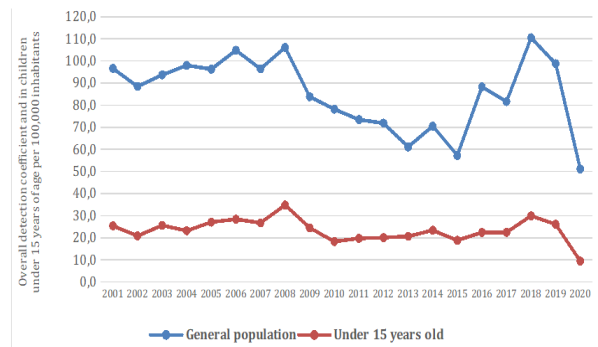
**Table 1. Sociodemographic and clinical characterization of new leprosy cases reported in the state of Tocantins, Brazil, 2001-2020**

Variables	Number (24,413)	%
<b>Sex</b>		
Male	13,618	55.78
Female	10,795	44.22
<b>Years of Study</b>		
Unanswered	2,616	10.72
Illiterate	2,416	9.90
1-4 years	6,386	26.16
5-8 years	6,338	25.96
9-11 years	5,209	21.34
12 or more	1,448	5.93
<b>Race</b>		
Unanswered	388	1.59
Yellow	624	2.56
Brown	15,260	62.50
White	4,467	18.30
Black	3,503	14.35
Indigenous	171	0.70
<b>Age Group</b>		
0-14 years	2,031	8.32
15 years and more	22,382	91.68
<b>Operational Classification of Disease</b>		
Paucibacillary	10,290	42.15
Multibacillary	14,123	57.85
<b>Clinical Form</b>		
Indeterminate	6,258	25.63
Tuberculoid	4,127	16.90
Borderline	10,244	41.97
Virchowian	2,679	10.97
Not classified	1,105	4.53
<b>Degree of physical disability at diagnosis</b>		
Grade 0	14,324	58.67
Grade 1	5,512	22.58
Grade 2	1,391	5.70
Not evaluated	3,186	13.05
<b>Degree of physical disability at cure</b>		
Unanswered	6,072	24.87
Grade 0	10,346	42.38
Grade 1	2,509	10.28
Grade 2	595	2.44
Not evaluated	4,891	20.03
<b>Evaluation of Contacts</b>		
Contacts Registered	84,628*	100.00
Contacts Examined	64,441**	76.14

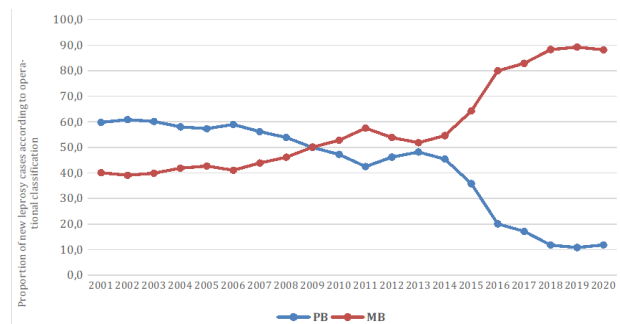
\*Total of contacts registered and

\*\*Total of contacts examined

The detection coefficients in general and in children under 15 years of age remained hyperendemic throughout the evaluation of the historical series and showed an average of 85.32 and 23.36 cases per 100,000 inhabitants, respectively (Figure 2). The percentage of cases diagnosed in the MB operational classification showed an increasing trend from 2009; and, in 2020, it reached 88.1% of the cases (Figure 3). All health regions in the state of Tocantins showed an average of the overall detection coefficient above 40 cases per 100,000 inhabitants, being, therefore, considered hyperendemic according to the classification of the Brazilian Ministry of Health. The *Ilha do Bananal* and *Capim Dourado* regions had an average annual detection coefficient above 110 cases per 100,000 inhabitants and are the most hyperendemic, while the *Sudeste* and *Bico do Papagaio* regions were

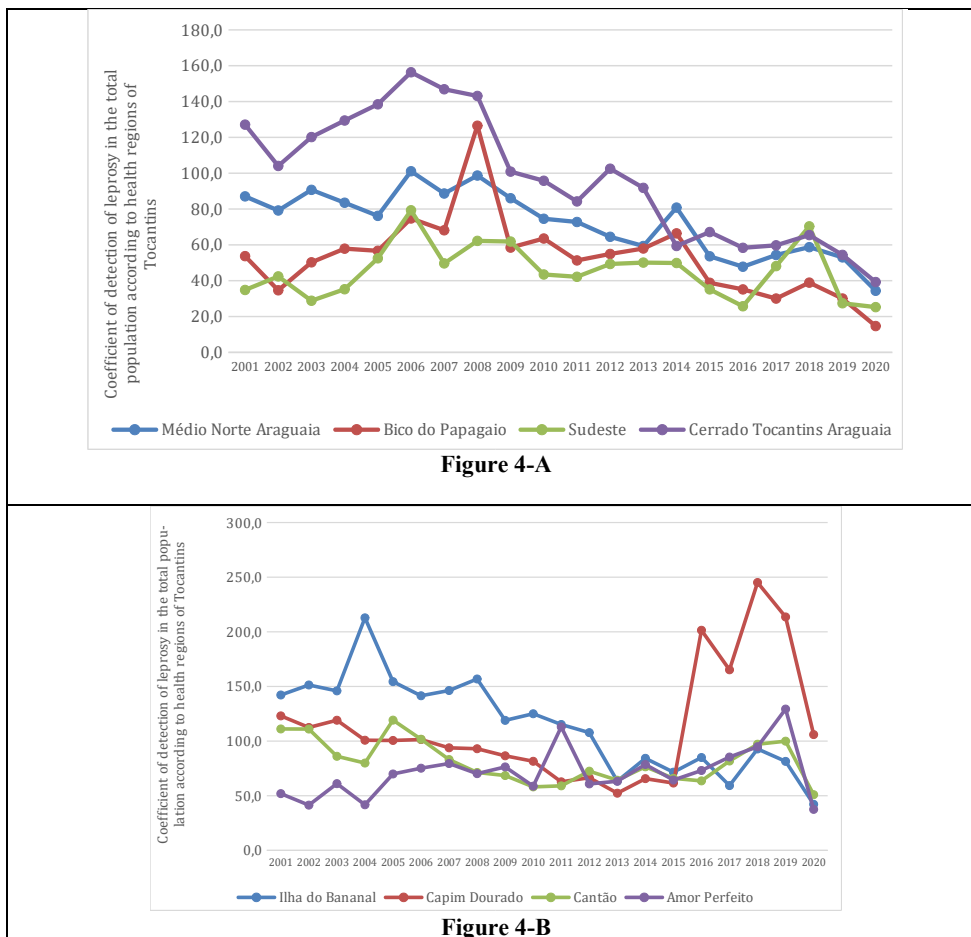


**Figure 2. Historical series of the detection coefficient in the overall population and in those under 15 years of age per 100,000 inhabitants in the state of Tocantins, Brazil, 2001-2020**



**Figure 3. Historical series of the percentage of cases diagnosed in the MB and PB operational classification in the state of Tocantins, Brazil, 2001-2020**

less hyperendemic, with average annual coefficients of 45.67 and 53.13 cases per 100,000 inhabitants, respectively (Figure 4). The overall detection coefficient of new leprosy cases in the population of the state of Tocantins showed four temporal trends, with stability in the period from 2001 to 2007 (*Trend 1*), a significant decrease of 6.2% between 2007 and 2015 (*Trend 2*), stability between 2015 and 2018 (*Trend 3*) and a significant drop of 28.2% between 2018 and 2020 (*Trend 4*). The leprosy detection coefficient in children under 15 years of age showed a trend towards stability in the period 2001-2020 (AAPC: -1.0; 95% CI -2.8 to 0.8). The temporal trend of the coefficient of detection of new cases in women followed the pace of case detection in the overall population, with a significant drop of 6.4% between 2006 and 2015 (*Trend 2*) and 30.5% between 2018 and 2020 (*Trend 4*). The proportion of cases diagnosed in the PB operational classification showed a significant decrease trend of 2.7% between 2001 and 2014 (*Trend 1*) and 25.3% between 2014 and 2020 (*Trend 2*). This decrease was 10.5% considering the total period (2001-2020). The proportion of MB cases increased significantly by 3.3% in the period from 2001 to 2014 (*Trend 1*) and by 14.4% between 2014 and 2017 (*Trend 2*), with an increase of 1.1% between 2017 and 2020, but it was not significant (*Trend 3*). In the total period, the proportion of MB cases increased significantly by 4.7%. The percentage of cases diagnosed with degrees 1 and 2 of physical disability showed a significant increase of 6.5% and 4.9%, respectively (AAPC). As for the evaluation of the overall detection coefficient, in the health regions of *Bico do Papagaio*, *Cantão*, *Capim Dourado* and *Sudeste*, there was stability in the Average Annual Percent Change (AAPC). The *Médio Norte Araguaia*, *Cerrado Tocantins Araguaia* and *Ilha do Bananal* health regions showed a significant downward trend in the AAPC, with 3.1%, 4.6% and 5.3% respectively. Only the *Amor Perfeito* health region showed a significant upward trend of 2.7% in the AAPC. In the evaluation of the Annual Percent Change (APC), the *Bico do Papagaio* health region had a significant increase of 12.1% between 2001 and 2008 (*Trend 1*) followed by a significant decrease of 10.3% between 2008 and 2020 (*Trend 2*). In the *Capim Dourado* health region, the APC had a significant drop of 6.3% between 2001 and 2013 (*Trend 1*) and a significant increase of 34.5% between 2013 and 2018 (*Trend 2*) (Table 2).



**Figure 4. Overall leprosy detection coefficient (per 100,000 inhabitants) according to health regions in the state of Tocantins, Brazil, 2001-2020**

## DISCUSSION

The clinical prevalence of MB and the high burden of leprosy in children under 15 years of age demonstrate late diagnosis and active transmission of the disease in the state of Tocantins. The trend of the analyzed indicators reports that the disease remains in high magnitude with persistence of the hyperendemic *status*. The heterogeneous trend in the eight health regions of the state highlights the need to strengthen surveillance and disease control measures, considering regional differences in the population and health services. In addition to the fluctuations inherent in the prolonged course of the disease, as well as the greater or lesser efficiency of decentralized control actions by health regions, external aspects also impacted the trend of the indicators. The Pandemic Covid-19, declared by the WHO on March 11, 2020, has become a serious and imminent global public health problem, causing severe damage to health systems around the world, and has required a rapid adaptation and adequacy of the Brazilian Unified Health System (SUS, as per its Portuguese acronym), given the spread of infected persons, the seasonality of new case peaks and the absence of specific treatment for the disease. The result was and still is the overburden of health services at the primary, secondary and tertiary levels (Farias, 2020). With 32 years of formal constitution, the state of Tocantins represents a territory of new possibilities and opportunities, attractive to migrants. As it borders states that are also endemic for leprosy, such as Mato Grosso, Bahia and Maranhão, migration is considered a risk factor and a social determinant for the maintenance of significantly high rates of leprosy in the north-central region of Brazil, mainly in the state of Tocantins. Since the distribution of the disease is directly related to the new expansion corridors of the agricultural frontier, the new leprosy cases in this region are mainly related to consanguineous and/or non-consanguineous family contact, close family and other social contact of leprosy (Monteiro, 2017; Murto, 2013).

The search for employment and access to better services, associated with improved traffic conditions and confinement in periurban settlements of migrants may even reflect the higher incidence of the disease in men, a trend that is observed in Brazil as a whole, with predominance of this sex in most age groups and years. The higher frequency in the sociodemographic analysis of leprosy cases in men can also be explained by cultural factors, such as greater exposure to the risk environment, low demand for medical care and failures of health services in the adoption of specific strategies to achieve this audience. Thus, it is predictable to find advanced forms of the disease in male individuals, as well as greater chances of serious complications and mortality (Monteiro, 2016; Souza, 2014; Nery, 2019). The difference in the manifestation of leprosy between the sexes reflects the differences between them in terms of exposure and access to health care (Nery, 2019). Although it is possible to observe a decrease and a trend towards stability in the detection of new leprosy cases in the 20 years evaluated, the proportion of cases with disabilities increased significantly. This highlights the maintenance of bacilliferous sources, late diagnosis and hidden prevalence. This operational indicator is an important indicator of gaps in leprosy control strategies at the population level; and, through efforts to reduce it, it is expected that the delay in diagnosis and the number of new cases will also be reduced (BRAZIL, 2016; World Health Organization, 2020b; World Health Organization, 2020b). Such process is called “pseudo-decline”, considering that the actual number of cases is even higher than those currently registered in official information systems (Salgado, 2016). The drop in the percentage of PB cases is consistent with the increase in the percentage of MB cases and the decrease in the percentage of cases not evaluated in the diagnosis regarding the degree of disability. It is observed that, from 2014, there was a reversal in the diagnosis regarding the operational classification with MB predominance, responsible for cases with physical disabilities.



Table 2. Trend of leprosy indicators, according to joinpoint regression analysis in the state of Tocantins, Brazil, 2001-2020

Indicators	Trend 1			Trend 2			Trend 3			Trend 4			Total Period	
	Period	APC <sup>a</sup>	CI <sup>b</sup>	Period	APC <sup>a</sup>	CI <sup>b</sup>	Period	APC <sup>a</sup>	CI <sup>b</sup>	Period	APC <sup>a</sup>	CI <sup>b</sup>	AAPC <sup>c</sup>	CI <sup>b</sup>
Overall Detection Coefficient	2001-2007	1.4	-2.5to 5.5	2007-2015	-6.2*	-9.2 to 3.2	2015-2018	24.7	-0.8 to 56.6	2018-2020	-28.2*	-44.2 to 7.7	-2.3	-6.3 to 1.9
Detection Coefficient in Children under 15 years old	2001-2020	-1.0	-2.8to 0.8	-	-	-	-	-	-	-	-	-	-1.0	-2.8 to 0.8
<b>Sex</b>														
Detection Coefficient in Men	2001-2015	-3.3*	-4.7to 1.9	2015-2018	14.8	-14.4 to 53.9	2018-2020	-25.1	-45.8 to 3.6	-	-	-	-3.3	-8.2 to 2.0
Detection Coefficient in Women	2001-2006	4.5	-2.3 to 11.8	2006-2015	-6.4*	-9.4 to 3.3	2015-2018	31.1	-0.4 to 72.5	2018-2020	-30.5*	-48.7 to 5.9	-1.5	-6.4 to 3.6
<b>Clinical Form</b>														
% Paucibacillary	2001-2014	-2.7*	-3.7 to 1.6	2014-2020	-25.3*	-30.7 to 19.4	-	-	-	-	-	-	-10.5*	-12.5 to 8.4
% Multibacillary	2001-2014	3.3*	2.4 to 4.3	2014-2017	14.4*	3.0 to 27.2	2017-2020	1.1	-1.7 to 3.9	-	-	-	4.7*	2.9 to 6.4
% Indeterminate	2001-2008	1.7	-0.5 to 4.0	2008-2014	-4.1	-8.0 to 0.0	2014-2017	-29.7*	-47.6 to 5.5	2017-2020	-0.7	-17.4 to 19.4	-6.2*	-10.7 to 1.4
% Tuberculoid	2001-2011	-6.4*	-8.4 to 4.3	2011-2014	5.9	-25.0 to 49.4	2014-2020	-25.4*	-32.1 to 18.0	-	-	-	-11.1*	-16.0 to 6.0
% Borderline	2001-2013	3.7*	2.6 to 4.9	2013-2016	18.3*	1.6 to 37.8	2016-2020	5.1*	2.4 to 7.9	-	-	-	6.2*	3.8 to 8.7
% Virchowian	2001-2012	0.8	-1.6 to 3.2	2012-2020	-6.0*	-10.4 to 1.5	-	-	-	-	-	-	-2.2	-4.3 to 0.0
<b>Health Regions</b>														
Overall Detection Coefficient in the <i>Bico do Papagaio</i> health region	2001-2008	12.1*	3.7 to 21.1	2008-2020	-10.3*	-13.8 to 6.6	-	-	-	-	-	-	-2.6	-6.0 to 0.9
Overall Detection Coefficient in the <i>Médio Norte Araguaia</i> health region	2001-2020	-3.1*	-4.3 to 1.9	-	-	-	-	-	-	-	-	-	-3.1*	-4.3 to 1.9
Overall Detection Coefficient in the <i>Cerrada Tocantins Araguaia</i> health region	2001-2006	6.1	-1.6 to 14.4	2006-2020	-8.2*	-9.9 to 6.4	-	-	-	-	-	-	-4.6*	-6.7 to 2.5
Overall Detection Coefficient in the <i>Cantão Health Region</i>	2001-2020	-1.7	-3.4 to 0.0	-	-	-	-	-	-	-	-	-	-1.7	-3.4 to 0.0
Overall Detection Coefficient in the <i>Capim Dourado</i> health region	2001-2013	-6.3*	-10.4 to 2.1	2013-2018	34.5*	9.9 to 64.5	2018-2020	-31.2	-58.5 to 14.0	-	-	-	-0.3	-7.2 to 7.2
Overall Detection Coefficient in the <i>Amor Perfeito</i> health region	2001-2020	2.7*	0.3 to 5.2	-	-	-	-	-	-	-	-	-	2.7*	0.3 to 5.2
Overall Detection Coefficient in the <i>Ilha do Bananal</i> health region	2001-2020	-5.3*	-6.9 to 3.7	-	-	-	-	-	-	-	-	-	-5.3*	-6.9 to 3.7
Overall Detection Coefficient in the <i>Sudeste</i> health region	2001-2020	-0.6	-3.4 to 2.2	-	-	-	-	-	-	-	-	-	-0.6	-3.4 to 2.2
<b>Operational Indicators</b>														
% Grade 0 at diagnosis	2001-2020	-1.8*	-2.2 to 1.3	-	-	-	-	-	-	-	-	-	-1.8*	-2.2 to 1.3
% Grade 1 at diagnosis	2001-2020	6.5*	5.4 to 7.7	-	-	-	-	-	-	-	-	-	6.5*	5.4 to 7.7
% Grade 2 at diagnosis	2001-2020	4.9*	3.4 to 6.5	-	-	-	-	-	-	-	-	-	4.9*	3.4 to 6.5
% Cases not evaluated at diagnosis	2001-2015	-4.5*	-6.7 to 2.3	2015-2020	-21.9*	-34.7 to 6.5	-	-	-	-	-	-	-9.4*	-13.5 to 5.1
% Contact examined	2001-2009	8.1*	4.6 to 11.6	2009-2020	0.4	-0.7 to 1.5	-	-	-	-	-	-	3.6*	2.2 to 5.0
<b>Education</b>														
% Illiterate	2001-2005	-4.9	-12.8 to 3.7	2005-2008	-20.1	-45.0 to 16.0	2008-2012	11.5	-8.5 to 35.8	2012-2020	-8.6*	-13.1 to 3.9	-5.9	-12.0 to 0.6
% 1-4 years of study	2001-2009	6.4*	2.2 to 10.8	2009-2020	-6.4*	-9.0 to 3.7	-	-	-	-	-	-	-1.2	-3.4 to 1.0
% 4-8 years of study	2001-2003	-12.8	-24.4 to 0.5	2003-2006	5.3	-8.6 to 21.2	2006-2011	-9.8*	-14.5 to 5.0	2011-2020	0.0	-1.9 to 2.0	-3.3*	-5.9 to 0.6
% 9-11 years of study	2001-2020	2.3*	1.6 to 3.1	-	-	-	-	-	-	-	-	-	2.3*	1.6 to 3.1
% 12 or more years of study	2001-2020	4.2*	2.7 to 5.8	-	-	-	-	-	-	-	-	-	4.2*	2.7 to 5.8

<sup>a</sup> Percentage change per year. <sup>b</sup> 95% confidence interval. <sup>c</sup> Average Annual Percent Change. \* Significantly different from 0 (p<0.005).

As leprosy is a disease with a long-lasting course, the fact that the proportion of cases with degrees 1 and 2 of physical incapacity shows a significant increase is worrying and indicates diagnostic difficulty, configuring itself as evidence of late detection and insufficient performance of the health system in its elimination. The high burden and the stationary trend in the detection coefficient in children under 15 years of age highlight the presence of active transmission foci in the family environment, as it signals the presence of an undiagnosed and untreated adult. The existence of considerable juvenile cases diagnosed in MB clinical forms represents the delay in diagnosis by health services; and in the state of Tocantins, these data were only verified due to campaigns and task forces aimed at identifying sick individuals. Despite the greater diagnostic difficulty in children, the active search and evaluation of contacts are essential to halt high rates of infection in the respective age group and the disease transmission chain, as immediate treatment for detection and the effectiveness of MDT reduce the number of infected persons (Santana, 2018; Souza, 2018). Active search allows identifying sources of contagion, while early diagnosis can avoid complications and disabilities. Thus, high leprosy detection coefficients in children signal operational fragility of surveillance by PHC (Monteiro, 2018; Monteiro, 2019). The effectiveness of campaigns to diagnose the repressed demands of leprosy to bring the numbers closer to the actual incidence of the disease has been the subject of studies, and these report the potential of training professionals to diagnose new cases safely and expertly, as well as the appropriate management in the primary care network. In 2016, after 1,000 hours of training in PHC through the project "Palmas Free from Leprosy", a significant increase in the detection coefficient of new cases in adults and children was observed, along with an increase in the detection coefficients by evaluation of contacts, advanced clinical forms, physical disabilities and readmissions (Monteiro, 2002; Santana, 2018). These actions impacted the increase in disease indicators in the pre-pandemic period of Covid-19 in the state. In turn, the chaotic scenario caused by the pandemic spread fear among the Brazilian population regarding the search for health care, reducing the passive search and the continuity of new and ongoing treatments. In order to control the pandemic in Brazil, social isolation protocols were established with the aim of protecting individuals from the SARS-CoV-2 virus and preventing the collapse of SUS. Among the institutional actions proposed for coping this evil, PHC became the gateway to non-serious cases of the disease. Given the need to build a unit around a common work among all professional categories to control the sanitary crisis, several reports from PHC professionals also discuss the reduction in the number of services and suspension of daily schedules, in order to reduce the flow of people in the units (Medina, 2020; Gonçalves, 2021).

As a result, the overall detection rate of new leprosy cases had a significant drop of 28.2% (*Trend 4*) in the period from 2018 to 2020; and, in this analysis, mainly women contributed to the decrease, as they followed the trend with a significant reduction of 30.5% (*Trend 4*) in the detection of new cases in female individuals in the same period. This reflects the reduced demand for health services for fear of contracting SARS-CoV-2 and the adoption of social distancing as a public health measure. Both indicators show the same fluctuations in years of study, which indicates the female gender as a predictor of greater search for health care, being measured with a magnitude of 2.43 times compared to males (Levorato, 2014). In the pandemic scenario, the emergency contribution of financial resources to fight it did not strengthen the PHC services. The CHWs stopped carrying out home visits and active search, thus hampering the investigation and monitoring of leprosy treatment. Accordingly, the power of territorial actions and the family and community approach was limited, both by the fragility of recommendations and policies that would guide and legitimize the extramural work of the Primary Health Care Units and by the inefficiency, oftentimes, of ensuring personal protective equipment to workers (Gonçalves, 2021). The arrival of the pandemic intensified the already existing fragility in the care acute and chronic conditions, the result of limitations of health care models, of the fragmented and reactive operation of the health system and of the insufficient qualification of PHC to fulfill its functions and attributes

in the health system (Gonçalves, 2021; Mendes, 2018). Consequently, the impacts of the pandemic can be even more prolonged and devastating to SUS, as it can set back the control of several chronic diseases that, like leprosy, require comprehensive and longitudinal care, and that had their assistance abruptly and continuously interrupted in the current health scenario. Therefore, it is possible to presume treatment abandonment, increased underreporting, reactivation of cases and loss of progress achieved in major projects that aim at eliminating leprosy in the state of Tocantins.

Another potential factor for fluctuating disease indicators and the growing trend of MB and borderline cases is inadequate treatment, which enables infection foci, in addition to incomplete cure and development of resistance to already used drugs, requiring change in treatment with alternative drugs and, consequently, generating more side effects. In the state of Tocantins, it was identified that the characteristics of the population itself, such as socioeconomic and cultural conditions, contribute to both poor adherence and delay in diagnosis. Even with the exclusive and free offer of MDT by SUS, effective adherence to treatment with multiple drugs is small, and abandonment is attributed to several side effects (Heukelbach *et al.*, 2011). In the 20-year temporal analysis, although in a general downward trend, heterogeneity marks the results found in the indicators of detection of new cases in the state's health regions, capable of signaling better or worse operational capacity of health services in each location, whether in diagnostic capacity or in clinical management. Socioeconomic and ecological advances contribute to reducing the burden of the disease, and regions with greater potential for development in the state, such as *Capim Dourado* and *Amor Perfeito*, positively influence the provision of health services and their access by the population. On the other hand, the limited availability and difficult access to health services, especially in smaller municipalities, where passive detection is the prevalent form, mark regions such as *Bico do Papagaio* and *Cantão Cantão*. Thus, the reduction in the overall detection coefficient points more to the failure of health services, and not to progress in control actions, in such a way that the heterogeneous distribution of the disease may reflect territorial vulnerabilities, due to the presence of sources of transmissibility, income inequalities and poverty (Monteiro, 2017; Souza, 2019). On the other hand, public policies aimed at offering continuing education can change the epidemiological reality, as they boost the detection of cases, the treatment and the management of complications caused by leprosy. The implementation of these policies corroborated with the significant increase trend of 34.5% (*Trend 2*) in the overall detection coefficient in the *Capim Dourado* health region, which encompasses the state capital. The increase in case detection in this region was driven by the implementation of the "Palmas Free from Leprosy" Project, which showed a significantly increasing detection coefficient of 104.6% in 2016 in the state capital, which had repercussions at the state level (Monteiro, 2017; Souza, 2019). Furthermore, the significant increase in the detection of cases in the *Amor Perfeito* health region is a result of the surrounding influence of control actions in the *Capim Dourado* health region. The developed *Médio Norte Araguaia* health region has a greater offer of health care services, as it is a major region and concentrates leprosy diagnoses in the HTD reference service. This reports the need for decentralization of control actions for PHC and, consequently, early diagnosis.<sup>7,23</sup> Thus, in health regions with a lower detection coefficient, it is possible to identify the fragility of surveillance systems for the diagnosis and management of the disease. These deficiencies perpetuate the increase in hidden prevalence and grade 1 and 2 disabilities. Ecological studies have some limitations. It is not possible to state that the conclusions of the study occur similarly at the individual level with an analysis of aggregated data. As a spatial unit of analysis, Tocantins has a large territorial extension and heterogeneity of characteristics; however, as it is an administrative division, its use can facilitate decision-making during the planning and organization of control actions focusing on priority areas. In addition, the data used are secondary, originating from DATASUS, which is fed by case notifications. These data may contain filling gaps and unanswered information. Therefore, analyses must be interpreted with caution.

Incomplete information can make it difficult to really understand who is getting sick and, consequently, interfere with the planning of disease control actions, which can be modified and improved through education, whether during academic training or continuing education of professionals, or even by the qualification of information among the databases used in epidemiological surveillance. In short, the study approach provides data to improve leprosy control measures, adapting them to the epidemiological reality of Tocantins and its health regions, as it was possible to verify operational problems in the execution of epidemiological surveillance by the control programs. Continuing health education must be strengthened, with definition of the program content and training methodology aimed at the actual needs of professionals, users and health regions, and its impact must be regularly evaluated. The identification of the temporal trend of leprosy in a hyperendemic state allowed the identification of areas that need to carry out prevention and control actions aiming at the elimination of the disease and can serve as a scientific support for the organization and planning of actions to improve health services. Furthermore, fluctuations in the trend of indicators by health regions over the last 20 years have helped to identify positive interventions and the challenges to be faced in different geographic areas.

## CONCLUSION

Leprosy remains in high magnitude in Tocantins, indicating active transmission, late diagnosis and persistence of hyperendemicity. There was a heterogeneous trend in case detection in the eight health regions, with necessary strengthening of surveillance and control measures, especially in the pandemic Covid-19. The challenge of the health system after the pandemic Covid-19 will be to manage resources to direct health care towards neglected diseases, taking into account the material and professional fragility in the face of the current epidemiological context. Therefore, it is necessary to establish new goals and public policies, with an emphasis on continuing education in PHC, in order to fight leprosy in countries and regions with extreme social inequality. No funding was paid for this research. The authors report no conflict of interest. No patient consent was required. Lucas Sales Scherr, Marina Piccolo de Almeida, Sara Martins Guarda, Marne Noleto Sales and Lorena Dias Monteiro drafted the work and revised it critically for important intellectual content, gave the final approval of the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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