

## Epidemiological characteristics and trends of leprosy in children and adolescents under 15 years old in a low-endemic State in Southern Brazil

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### ABSTRACT

Leprosy is an infectious and contagious disease affecting skin and nerves. The number of cases in individuals under 15 years old is one of the parameters used in Brazil as an indicator of endemic permanence of the disease and its continuous transmission. Rio Grande do Sul State, in Southern Brazil, is low-endemic to leprosy. However, the disease remains a public health problem. This is a retrospective, observational and analytical study of a historical series of new cases of leprosy in children under 15 years old diagnosed in the period from 2000 to 2019, in all health units in Rio Grande do Sul State. Seventy-seven new cases were notified. The male gender was predominant in 53.2% of the cases (n=41). The average age was 10.4 years (standard deviation of 2.9), with predominance of the age group between 10 and 15 incomplete years old. The most frequent operational classification was multibacillary, in 62.3% of cases (n=48), and the most common clinical form was borderline, in 38.9% of cases (n=28). The predominant disability degree in the sample was grade zero, in 80.0% of the cases (n=60), but in 4.0% (n=3) the grade assessed was 2. In 54.0% of cases (n=27), bacilloscopy was performed, with positive results in 36.0% (n=9) of the exams. Multibacillary cases, with physical disability and/or positive bacilloscopy, draws attention that the diagnosis is frequently not made in early stages.

**KEYWORDS:** Leprosy. Public health. Children. Adolescents. Epidemiology.

### INTRODUCTION

Leprosy is an infectious disease mainly affecting skin and nerves, it has high infectivity and low pathogenicity<sup>1</sup>. The transmission occurs through the upper airways and contact between an untreated patient and a person with a predisposition to the disease<sup>2</sup>. The etiological agent of leprosy is the bacillus *Mycobacterium leprae*, which has slow growth, making the incubation period long, with an average of three to five years. However, in children, this period can be reduced to weeks<sup>1</sup>.

The late diagnosis of the disease is a potential factor for the generation of physical disability and emotional damage, affecting the patient's quality of life<sup>3</sup>. Thus, the early diagnosis is essential, especially in individuals under 15 years old.

In Brazil, the World Health Organization guidelines are followed for operational treatment purposes. Thus, leprosy cases are classified as paucibacillary (PB) when they present up to five skin lesions, and as multibacillary (MB) when they present six or more skin lesions and/or there is a positive intradermal bacilloscopy (if it is possible to perform this exam)<sup>4</sup>. However, for patients who do not have visible skin lesions, such as the cases of primarily neural leprosy, and also in cases in which

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skin lesions only appear during treatment, the Ministry of Health indicates the use of the Madrid classification (1953): indeterminate (PB), tuberculoid (PB), borderline (MB) and lepromatous (MB)<sup>5</sup> leprosy.

For operational purposes, patients classified as indeterminate or tuberculoid are paucibacillary and must receive six doses of multidrug therapy within a maximum of nine months, while those classified as borderline or lepromatous are multibacillary and must receive 12 doses of multidrug therapy within a maximum of 18 months<sup>5</sup>. As a fundamental complementary exam for verifying neural integrity, a simplified neurological assessment is performed, which evaluates the face, upper and lower limbs, assigning a degree for the verified physical disabilities. Grade zero is characterized by the total preservation of sensitivity and strength in the regions evaluated, grade 1 is characterized by loss or decrease of sensitivity or strength in one of the evaluated regions, and grade 2 is characterized by visible deficiencies caused by leprosy, such as lagophthalmos, claws, bone resorption and wounds<sup>5</sup>.

The number of cases in individuals under 15 years old is one of the parameters chosen in Brazil as an indicator of endemic permanence of the disease and its continuous transmission<sup>6,7</sup>. Between 2008 and 2016, the country recorded 301,322 cases of leprosy, of which 21,666 (7.2%) were in children under 15 years old. In this group, there was the presence of grade 2 physical disability in 2.7% of the cases. In the period from 2009 to 2018, Rio Grande do Sul State had an average detection rate of 1.20 cases per 100,000 inhabitants. Among children under 15 years old, the average rate of detection of the disease was 0.33 cases per 100,000 inhabitants in the same period, with 1.68 new cases diagnosed with grade 2 physical disability per 1 million inhabitants<sup>8</sup>.

Rio Grande do Sul State, over time, remains classified as a low-endemic region for new cases of leprosy<sup>8</sup>. However, the disease is still a public health problem in the State, mainly due to the late diagnosis in all age groups, a fact observed by the expressive number of new cases with physical disabilities at the time of diagnosis, which also suggests the occurrence of hidden cases<sup>9-11</sup>.

This study aims to present the trend of leprosy diagnosis, socioeconomic, clinical and epidemiological characteristics in individuals under 15 years old in Rio Grande do Sul State, Southern Brazil, in the period from 2000 to 2019.

## MATERIALS AND METHODS

Retrospective, observational and analytical study of a historical series of new cases of leprosy in children under 15 years old, from 2000 to 2019, in all health units in Rio

Grande do Sul State (32°1'60" South, 52°5'55" West). The research project was submitted to the Research Ethics Committee of the Hospital de Clínicas de Porto Alegre, and the Ethics Committee of the School of Public Health of Rio Grande do Sul (CAAE: 31959120.6.0000.5327/3195120.6.5312), being approved according to the process 4.075.445/4.121.621, respecting the resolutions 466/2012 and 510/2016 of the National Health Council that regulates research with human beings.

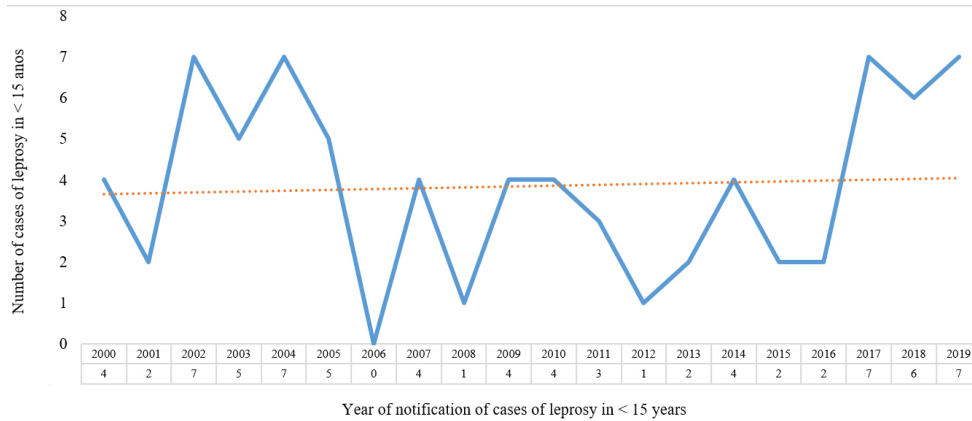
The data were obtained through the Notifiable Diseases Information System (SINAN), stored at the State Health Surveillance Center (CEVS) in Rio Grande do Sul State. The selection was carried out by the CEVS database, including all individuals under 15 years old diagnosed with leprosy in the period from 2000 to 2019. The variables of interest were sex, age, clinical form, operational classification, mode of entry of the new case, disability degree and bacilloscopy results.

Data were grouped by variables in an Excel 365 spreadsheet, distributed in columns, and the database was individually entered in the rows. The descriptive statistical measures used were frequencies, percentages, means and standard deviations. Bivariate analyses were made using the Fisher's Exact Test for categorical variables, assuming a statistical significance level of 5% (bilateral). Analyses were conducted using the SPSS program Statistical Package for the Social Sciences 26 (SPSS) software (IBM, Armonk, NY, USA).

## RESULTS

From 2000 to 2019, 4,233 new leprosy cases were reported, with 1.88% (n=77) of cases in individuals under 15 years old. In the surveyed period, the average was 3.8 cases/year. However, in the period from 2002 to 2005, the average was 6 cases/year, from 2006 to 2016 it was reduced to 2 cases/year, and from 2017 to 2019, it has increased again to 6.6 cases/year (Figure 1), suggesting a return to the 2000s level.

The predominance of the sample regarding gender was male for 53.2% of the cases (n=41), and the average age was 10.4 years (standard deviation=2.9). The predominant age group was between 10 and 15 years old at the time of diagnosis, in 63.6% (n=49) of the cases. The majority (77.4%) of the patients lived in urban areas of Rio Grande do Sul (Table 1). The predominant operational classification was multibacillary, in 62.3% of cases (n=48), and the most common clinical form was borderline, in 38.9% of cases (n=28). In four cases, there was no classification of the clinical form. Twenty percent of the sample already had a degree of physical disability at the time of diagnosis,



**Figure 1** - Number of notified leprosy cases in children under 15 years old in the period 2000 to 2019, Rio Grande do Sul, Brazil.

**Table 1** - Socioeconomic characteristics of individuals under 15 years old diagnosed with leprosy from 2000 to 2019 in Rio Grande do Sul, Brazil.

Characteristic	number (total = 77*)	Percentage
<b>Sex</b>		
Male	41	53.2
Female	36	46.8
<b>Age group (years)</b>		
0 – 4	3	3.9
5 – 9	25	32.5
10 – 15	49	63.6
<b>Ethnicity/skin color</b>		
White	41	59.4
Black	5	7.3
Mixed (black and white)	23	33.3
<b>Residence</b>		
Urban	58	77.4
Rural	16	21.3
Periurban	1	1.3

\*Total data may vary depending on the possibility of absent information.

and 18.0% (n=9) of the cases had positive bacilloscopy (Table 2).

In the bivariate analysis, an association was found between the operational classification and the clinical form with the degree of physical disability ( $p < 0.001$ ). For bacilloscopy, no association was found ( $p = 1.000$ ) (Table 3).

## DISCUSSION

This study showed that, even in low-endemic regions for leprosy, occurrences in children under 15 years old are

present and suggest the permanence of the disease as a public health problem in Brazil<sup>8,9,12</sup>. Some authors consider that it is essential to monitor cases in this population, as they reflect the spreading force of *Mycobacterium leprae*. In addition, this age group is the most vulnerable due to a continuous exposure to the etiological agent<sup>13-15</sup>.

The trend and intensity of the disease in the population under 15 years old is used as one of the main parameters for monitoring and determining the level of the bacterium circulation<sup>13-15</sup> to assess the endemic level in each region. In low endemic regions, this parameter is associated with the clinical form of the disease and the degree of physical disability and may also suggest undiagnosed cases in adults<sup>10,11</sup>. In previous studies, the authors have presented a rate between 2.9 up to 9 of hidden cases for each diagnosis made in children under 15 years old<sup>9-11</sup>.

In other studies carried out in Brazil, the average age at diagnosis was similar to that found here<sup>16</sup>. There was variation regarding sex and clinical forms, with some studies showing a predominance of females and multibacillary patients<sup>16-18</sup>, and others with a predominance of males and paucibacillary forms, especially the tuberculoid clinical form<sup>19,20</sup>.

The number of cases with physical disability and positive bacilloscopy found in our study suggests a late diagnosis. In other studies, there is a fluctuation in the percentage of cases with physical disability ranging from 9% to 23% and, in most of them, there is no report of bacilloscopy results<sup>20-24</sup>. When performed, its percentage varied from 10.3% to 23% of the total sample<sup>20,22,25</sup>. In our sample, this examination was performed in 54.0% (n=27) of the cases. If only this number is considered, the percentage with a positive result increases to approximately 33%, which is in accordance with other studies<sup>26-28</sup>. In Rio Grande do Sul State, bacilloscopy is performed only at the Leprosy Reference Center in Porto Alegre, the State capital. Due to the invasive nature of bacilloscopy, this

**Table 2** - Clinical and epidemiological characteristics of individuals under the age of 15, diagnosed with leprosy in the period from 2000 to 2019, in Rio Grande do Sul, Brazil.

Characteristic	number (total= 77*)	Percentage
<b>Operational classification</b>		
Paucibacillary	29	37.7
Multibacillary	48	62.3
<b>Clinical form</b>		
Indeterminate	16	22.2
Tuberculoid	16	22.2
Borderline	28	38.9
Lepromatous	8	11.1
Unclassified	4	5.6
<b>Therapeutic scheme</b>		
Paucibacillary multidrug therapy	30	39.5
Multibacillary multidrug therapy	38	50.0
Substitute regimes	8	10.5
<b>Case entry mode</b>		
New case	62	81.6
Transfer from another municipality	8	10.5
Transfer from another State	5	6.6
Transfer from another country	1	1.3
<b>Case detection mode</b>		
Forwarding	17	27.0
Spontaneous demand	14	22.2
Contact exams	32	50.8
<b>Degree of physical disability at the time of diagnosis</b>		
Zero degree	60	80.0
Grade 1	12	16.0
Grade 2	3	4.0
<b>Bacilloscopy</b>		
Positive	9	18.0
Negative	18	36.0
Not performed	23	46.0

\*Total data may vary depending on the possibility of missing information.

exam is not performed frequently in the analyzed age group. Ruiz-Fuentes *et al.*<sup>29</sup>, in their study, showed that less than 4% of the cases had a degree of physical disability at the time of diagnosis, even though most cases were multibacillary.

In order to facilitate the diagnosis and treatment of leprosy, the Ministry of Health has determined the following guidelines: paucibacillary patients are those who have indeterminate or tuberculoid clinical forms and are treated with the paucibacillary therapeutic scheme. In contrast, multibacillary patients present the borderline or lepromatous clinical forms and are treated with the

multibacillary therapeutic scheme<sup>5</sup>. In certain situations, it is possible to notice that the notifications inserted in SINAN do not allow the logical sequence indicated by the Ministry of Health to happen. Records with ignored fields or the excess of missing data are frequent and confuse or preclude the correct analysis according to the reality of each case<sup>20</sup>.

In the present study, a significant number of missing data was observed, in addition to inconsistent data with the treatment guidelines recommended by the Ministry of Health. For example, while 29 cases had the paucibacillary operational classification, the therapeutic scheme of these forms of leprosy was applied in at least 30 cases

**Table 3** - Quantitative cross distribution with respect to the following characteristics: operational classification, clinical forms and bacilloscopy with degree of physical disability caused by leprosy, in the period 2000-2019, in Rio Grande do Sul, Brazil.

Characteristic*	Degree of physical disability		p-value <sup>1</sup>
	Grade 0 n = 60	Grade 1-2 n = 15	
<b>Operational Classification</b>			<0.001
Paucibacillary	29 (100)	0 (0)	
Multibacillary	31 (67.4)	15 (32.6)	
<b>Clinical Form</b>			<0.001
Indeterminate	16 (100)	0 (0)	
Tuberculoid	0 (0)	0 (0)	
Borderline	28 (100)	0 (0)	
Lepromatous	0 (0)	8 (0)	
<b>Bacilloscopy</b>			1.000
Negative	18 (100)	0 (0)	
Positive	9 (100)	0 (0)	

<sup>1</sup>Fisher's exact test; \*Total data may vary depending on the possibility of missing information.

(Table 2). In the literature review, several studies were found with data in accordance with the diagnostic and treatment guidelines<sup>20,22,23,25</sup>. However, it is also possible to find studies in which diagnostic and treatment are not suitable<sup>21,24</sup>. Inadequate treatment deserves attention due to their potential to generate relapses.

About 81% (n=62) of the analyzed data were classified as “new cases”, and the examination of “household/social contacts” was the most frequent detection mode. Leprosy cases in individuals under 15 years old demonstrate that the disease remains latent and contaminating, indicating that it will continue to be a public health problem if more effective measures are not taken<sup>14,16,17,19,20,25</sup>.

Regarding the association of the operational classification with the degree of physical disability, there was a significant relationship ( $p < 0.001$ ) for the presence of physical disability at the time of diagnosis in cases classified as multibacillary. In more robust studies in which the odds ratio was available, a ratio of 1.3 to 2.7 times was more likely to have grade 1 or 2 in multibacillary cases<sup>26,27</sup>. The sample of the present study indicates that, in order to avoid the presence of a degree of physical disability at the time of diagnosis, it is necessary to diagnose leprosy earlier to avoid cases classified as multibacillary<sup>5</sup>.

In the association of the clinical form with the degree of physical disability, it was found that the most severe cases of leprosy, the lepromatous forms, are also those with the greatest impairment ( $p < 0.001$ ). Although it was not observed in the present study, the occurrence of physical disability in patients with borderline leprosy is also expected, as this is a group with the highest number

of reactional outbreaks<sup>30</sup>. However, in low endemic regions and in cases in which late diagnosis occurs, it is possible to expect that these reactional outbreaks will not be noticed. This leads to the evolution of the disease to the most severe form and to the presence of physical disability. In addition, the occurrence of silent neuritis, which is not common in the age group studied, but which causes the appearance of physical disability, must also be considered<sup>31,32</sup>. The lack of perception of family members and health professionals regarding the early diagnosis of leprosy can also contribute to the significant result found in the studied sample.

Regarding bacilloscopy, no statistically significant association was found with the degree of physical disability in the sample ( $p = 1.000$ ). Bacilloscopy is not routinely performed in the studied age group, in addition to being a complementary diagnostic test that often becomes unnecessary in view of the clinical manifestations present in cases of leprosy in children and adolescents<sup>5</sup>.

The present study showed that, despite Rio Grande do Sul State being historically a low endemic region, diagnoses of new cases in individuals under 15 years old that are multibacillary and present with a high average of physical disability continues to occur. These data are also found in studies in other regions of Brazil, showing that it is necessary to maintain active care and disease control measures, such as: promote training/updates on leprosy to health workers, so that they will think about the diagnosis of leprosy, especially in the early stages of the disease, and continue the annual monitoring of leprosy cases in all Brazilian States<sup>16,19,20,33</sup>. Especially in the studied age group, physical disabilities produce social isolation, discrimination



and will negatively impact the adult life of these individuals. The early-stage disease diagnosis is essential to avoid these physical and psychological sequelae<sup>23,34</sup>. It is the government's responsibility to deploy in its territory services capable of receiving, identifying, diagnosing, treating, and rehabilitating people affected by leprosy. In this scenario, those under 15 years old stand out since they are a source of infection and a confounding factor in terms of operational classification and clinical form, which may in the future become cases of recurrence.

## CONCLUSION

We conclude that the occurrence of cases in individuals under 15 years old in multibacillary clinical forms with a degree of physical disability and/or positive bacilloscopy, even if in small numbers, is enough reason to speculate that leprosy will continue to be present in Rio Grande do Sul State and even though, as it is a low-endemic region it will not be possible to avoid new cases in this age group.

## AUTHORS' CONTRIBUTIONS

PCM: data curation, formal analysis, investigation, methodology, writing of the original draft; LME: supervision, writing of the review, editing; AK: validation, visualization, writing of the review, editing; DMP: writing of the review, editing; MLS: conceptualization, project administration, supervision.

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