

Original Article

## Factors associated with multibacillary leprosy in a region of northeastern Brazil

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### Abstract

**Introduction:** The analysis of factors associated with multibacillary leprosy is important for the development of strategies to mitigate the disease, which persists as a public health problem in Brazil and the world. The objective of this study was to verify the associations between sociodemographic and clinical-epidemiological variables and multibacillary leprosy in the state of northeastern Brazil.

**Methodology:** This is a cross-sectional, analytical, and retrospective study, with a quantitative approach, carried out in 16 municipalities in the southwest of Maranhão State, northeastern Brazil. All cases of leprosy reported between January 2008 and December 2017 were considered. Sociodemographic and clinical-epidemiological variables were analyzed using descriptive statistics. The identification of the risk factors associated with multibacillary leprosy was conducted using Poisson regression models. The prevalence ratios and respective 95% confidence intervals were estimated using regression coefficients at a 5% significance level.

**Results:** A total of 3,903 leprosy cases were analyzed. Individuals older than 15 years, males, with less than 8 years of education, with level I, II, or "not evaluated" disability, and with type 1 or 2 or both reactional states were more likely to have multibacillary leprosy. Therefore, these characteristics may be considered risk factors. No protective factors were identified.

**Conclusions:** The investigation revealed important associations between risk factors and multibacillary leprosy. The findings can be considered during the creation of strategies to control and combat the disease.

**Key words:** leprosy, epidemiology, health information systems.

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### Introduction

Leprosy is an infectious disease caused by *Mycobacterium leprae*, which affects the skin, eyes, and peripheral nerves. The disease persists as a public health problem in Brazil and the world. Transmission occurs through upper airways through aerosols and prolonged contact with secretions, especially in the family environment [1,2].

In 2020, the World Health Organization (WHO) reported 127,396 new cases of leprosy in the world, of which 19,195 cases were registered in the Americas, with about 17,979 (93.6%) cases reported in Brazil. Worldwide, 8,629 (6.8%) new cases occurred in children under 15 years of age. The Northeast region of Brazil has the highest number of new cases, with a

proportion of 53,684 thousand, followed by the Midwest region with 27,156 new cases. Mato Grosso is the state with the highest number of reported cases (17,738), followed by Maranhão (14,658) and Pará (11,890) [3].

Given the epidemiological panorama of leprosy in the world, the WHO launched The Global Leprosy Strategy 2020–2031, which has, as its main goal, the reduction of the rate of new cases of leprosy to less than 1 per 10,000 inhabitants through the interruption of the disease transmission chain and the achievement of zero autochthonous cases [4].

Leprosy does not develop linearly. The illness process involves physical, socioeconomic, cultural, and psychological factors in a cause-and-effect relationship.

Given this scenario, it is possible to understand that the occurrence of leprosy is closely related to the low socioeconomic conditions of the affected population, especially in developing countries [5], as reported in recent studies [6,7].

The remarkable relationship of the disease with social conditions demands new ways of approaching and monitoring reported cases in different scenarios to break the disease transmission cycle. Thus, understanding the factors associated with leprosy and the other social determinants closely linked to the disease allows for a reflection on the health determinants and an understanding of how the disease has presented itself, contributing to the elaboration of effective strategies for its control [8].

Scientific investigations on the morbidity and mortality of infectious diseases, including leprosy, have been stimulated because they are considered an important tool for detecting failures in disease control and describing the profile of the affected patients in different stages of the disease, an important surveillance measure [9-11].

The need for knowledge on the factors associated with the spread of the different clinical forms of leprosy in priority regions motivated this study, whose objective was to verify the associations between sociodemographic and clinical-epidemiological variables and multibacillary leprosy in a state of northeastern Brazil.

## Methodology

This is a cross-sectional, analytical, and retrospective study with a quantitative approach. Sixteen municipalities that make up the Imperatriz Regional Health Management Unit (UGRSI in Portuguese) were considered: Amarante do Maranhão, Buritirana, Campestre do Maranhão, Carolina, Davinópolis, Estreito, Governador Edson Lobão, Imperatriz, João Lisboa, Lajeado Novo, Montes Altos, Porto Franco, Ribamar Ficanne, São João do Paraíso, Senador La Rocque, and Sítio Novo. These municipalities have, in total, an estimated population of 546,913 inhabitants, and a territorial area of 1,094,483.081 km<sup>2</sup> [12].

The UGRSI is located in the southwest of Maranhão and is constituted by groups of neighboring municipalities under the influence of large projects such as Serra dos Carajás and Igarapé Salobro mining projects, Carajás/Itaqui and Norte-Sul railways, Guseiras (companies that produce pig iron), and Suzano's paper industries. Thus, this region is considered a major economic, social, cultural, and

communication network hub [13] and has the second highest number of infectious and parasitic diseases (9.5%), behind only the Metropolitan region (28.3%). Of 16 municipalities belonging to the unit, Imperatriz is the only one among the 15 priority municipalities for controlling leprosy in Maranhão State, with the second-highest detection of new cases [14].

This study used secondary data collected in September 2021. Leprosy cases registered in the Notifiable Diseases Information System (SINAN in Portuguese) by the Imperatriz Regional Health Management Unit from January 2008 to December 2017 were considered.

The sociodemographic variables considered in the study were age, sex, race/skin color, education, and area of residence. The clinical-epidemiological variables comprised leprosy operational classification, level of physical disability, number of affected nerves, entry status code (new case, transfer, relapse, other re-entries, and ignored/blank), reactional state, examined contact persons, registered contact persons, and termination status code (death, cure, transfer, treatment abandonment, and ignored/blank). All data were obtained from the SINAN leprosy notification form.

In the exploratory phase, variables were selected to characterize the cases at an individual level. After analyzing the consistency of the collected data, the Statistica 10.0 program was used for data conversion, and the variables were recategorized and analyzed. After checking for errors and inconsistencies, a descriptive analysis was performed using absolute and relative frequencies for all sociodemographic and clinical-epidemiological variables.

It is worth mentioning the exclusion of cases due to duplication and diagnostic errors regarding the operational classification of leprosy. A total of 126 cases with incorrect records in the notification forms were found (paucibacillary patients whose clinical form was classified as borderline or lepromatous and multibacillary patients whose clinical form was classified as indeterminate or tuberculoid).

The identification of the factors associated with multibacillary leprosy was conducted using Poisson regression models with robust variance [15]. Sociodemographic and clinical-epidemiological variables with a *p* value  $\leq 0.20$  were included in the adjusted model. The prevalence ratios (PR) and respective 95% confidence intervals were estimated directly using regression coefficients. On this occasion, the skipped data was deleted.

**Table 1.** Sociodemographic and clinical-epidemiological variables according to the operational classification of leprosy in Imperatriz Regional Health Management Unit, Maranhão, Brazil (2008 to 2017).

Characteristics	Operational Classification			
	Paucibacillary (n = 1,240)		Multibacillary (n = 2,663)	
	N	%	N	%
<b>Age</b>				
< 15 years	173	49.1	179	50.9
15 to 29 years	295	35.0	549	65.0
30 to 59 years	599	31.1	1324	68.9
≥ 60 years	173	22.1	611	77.9
<b>Sex</b>				
Female	703	45.3	850	54.7
Male	537	22.9	1813	77.1
<b>Race/skin color</b>				
Brown	694	30.8	1556	69.2
Non brown	528	32.8	1081	67.2
Ignored/blank	18	41.0	26.0	59.0
<b>Education</b>				
≥ 8 years	439	41.8	610	58.2
< 8 years	652	27.7	1700	72.3
Not applicable	27	54.0	23	46.0
Ignored/blank	122	26.8	330	73.2
<b>Area of residence</b>				
Rural	110	27.6	289	72.4
Urban	1114	32.3	2340	67.7
Ignored/blank	16	32.0	34	68.0
<b>Physical disability</b>				
Level 0	912	40.3	1351	59.7
Level 1	137	18.1	622	81.9
Level 2	17	7.3	215	92.7
Not rated	132	27.0	357	73.0
Ignored/blank	42	26.3	118	73.7
<b>Number of affected nerves</b>				
0	578	39.6	881	60.4
1	103	29.0	251	71.0
2 to 5	58	9.8	539	90.2
> 5	29	17.5	138	82.5
Ignored/blank	472	35.6	854	64.4
<b>Entry status code</b>				
New case	1154	36.6	2002	63.4
Transfer	41	16.1	214	83.9
Relapse	20	14.8	115	85.2
Other re-entries	25	7.0	330	93.0
Ignored/blank	0	0.00	2	100.0
<b>Reactional state</b>				
No reaction	415	31.2	914	68.8
Type I	12	6.7	167	93.3
Type II	1	2.6	37	97.4
Type I and II	3	11.1	24	88.9
Ignored/blank	809	34.7	1521	65.3
<b>Examined contact persons</b>				
≤ 5	953	31.1	2107	68.9
> 5	122	33.2	245	66.8
Ignored/blank	165	34.7	311	65.3
<b>Registered contact persons</b>				
≤ 5	1021	31.8	2194	68.2
> 5	190	32.0	404	68.0
Ignored/blank	29	32.0	65	68.0
<b>Termination status code</b>				
Cure	1098	35.5	1996	64.5
Transfer	53	17.0	259	83.0
Death	9	12.8	61	87.2
Abandonment	60	26.0	172	74.0
Ignored/blank	20	10.5	175	89.5

Data were tabulated in Microsoft Office Excel® in 2019, and the statistical tests were performed in IBM SPSS® 24.0 at a 5% significance level.

### *Ethical approval*

The study was approved by the Ethical Committee of the Federal University of Maranhão (opinion No. 2,965,606, issued on October 17, 2018) and complied with the Brazilian legislation's norms of resolution No. 466/12.

## **Results**

Between January 2008 and December 2017, 4,029 cases of leprosy were reported in Imperatriz, of which 126 cases were excluded due to misdiagnosis, resulting in 3,903 cases included in the study. Regarding the clinical forms of leprosy, the following frequencies were found: indeterminate (557), tuberculoid (613), dimorph (1,975), and virchowian (758).

Among the multibacillary cases, the most common characteristics were age  $\geq 60$  years (77.9%), male sex (77.1%), mixed race (69.2%), education  $< 8$  years (72.3%), living in the rural area (72.4%), level II physical disability (92.7%),  $> 5$  affected nerves (71.8%), "other re-entries" entry code (93.0%), type 2 reaction (97.4%),  $\leq 5$  examined contact persons (68.9%),  $\leq 5$  registered contact persons (68.2%), and "ignored/blank" termination status code (89.5%).

It is important to highlight the significant percentage of ignored fields concerning race/skin color (69.2%), education (73.2%), area of residence (68.0%), level of physical disability (73.7%), number of affected nerves (64.4%), reactional state (65.3%), examined contact persons (65.3%), registered contact persons (68.0%), and termination status code (89.5%) (Table 1).

In the crude analysis, significant associations ( $p \leq 0.20$ ) were found between the following variables and multibacillary leprosy: age above 15, male sex, education below 8 years, level I, II, or "not evaluated" disability, and type 1 or 2 or both reactional states. In the adjusted analysis, all associations remained significant ( $p$  value  $< 0.05$ ), and the variables above continued to be risk factors associated with the outcome, showing prevalence ratio (PR) values greater than one. No protective factors were identified (Table 2).

## **Discussion**

In this investigation, the predominant operational classification of leprosy was multibacillary (2,663 cases), corroborating studies that point to multibacillary

forms as the main responsible for disease transmission [16-18].

All contact persons must be followed up for at least 5 years due to the bacillus's long incubation period and the high risk of illness. The greater circulation of the bacillus linked to multibacillary cases is worrisome [19].

The sociodemographic and clinical-epidemiological characteristics were similar to those of other studies regarding the predominance of the multibacillary form [20-22], brown skin color [23,24], and residence in the urban area [22,25].

Regarding the age variable, the highest percentage of multibacillary cases occurred in the age group of  $\geq 60$  years (77.9%), consistent with studies carried out in the Brazilian territory indicating a direct relationship between multibacillary cases and age [26-27].

Age above 60 was identified as a risk factor for the development of multibacillary leprosy, with prevalence ratios increasing two and a half times in this age group. The compromise of the elderly raises questions not only about stigma, which is intensified when people perceive leprosy as something that segregates the patient from the community but also concerning the feeling of rejection, a major element that affects elderly people [28].

Persons aged from 30 to 59 years corresponded to 68.9% of our sample, and as they are part of the economically active population, it is worrisome that these persons may be excluded from the production chain after getting leprosy in terms of not keeping employed, not finding a job, or having issues involving social exclusion [29].

We found an association between multibacillary leprosy and the male gender (77.1% of the cases occurred in males, and males were twice more likely to have multibacillary leprosy). Several factors may explain this finding, and other studies have also shown men's greater vulnerability to chronic diseases [30,31].

Two factors probably contribute to the worse health status among men. First, women tend to attend to health care more frequently than men, and second, there is still a cultural barrier that leads men not to seek health care, linked to a strong patriarchal ideology in which the disease is perceived as a sign of weakness. In addition, studies highlight that men are less concerned with the body and aesthetics than women [32-34].

A statistically significant association was identified between multibacillary leprosy and low educational level, which behaved as a risk factor with a prevalence ratio about two and a half times superior to that of the

subjects with more than 8 years of education, agreeing with other studies [35-38].

Studies point to low education as a risk factor closely linked to precarious living conditions and an important social determinant for leprosy. Education is an important indicator of social inequalities and is usually linked with precarious housing conditions, nutrition, and hygiene problems, and lack of access to

information and health services, which are determinants of the health and disease process that contribute to the maintenance of the epidemiological chain of leprosy transmission [36,39-42].

Physical disability is classified as 0 when the subject does not show any disability, I when there is a decrease or loss of sensation in the eyes or lower/upper limbs, and II when there are motor changes in the eyes

**Table 2.** Crude and adjusted Poisson regression models of the relationship between sociodemographic and clinical-epidemiological variables according to multibacillary leprosy, Maranhão, Brazil, 2008 to 2017 (n = 3,903).

Characteristics	MULTIBACILLARY OPERATIONAL CLASSIFICATION			
	Crude PR (95%CI)	p value	Adjusted PR (95%CI)	p value
<b>Age</b>				
< 15 years	1			
15 to 29 years	1.45 (1.38 - 1.53)	< 0.001	1.52 (1.33 - 1.71)	< 0.001
30 to 59 years	1.70 (1.43 - 1.97)	< 0.001	2.01 (1.75 - 2.32)	< 0.001
≥ 60 years	1.91 (1.24 - 1.39)	< 0.001	2.50 (2.10 - 2.99)	< 0.001
<b>Sex</b>				
Female	1			
Male	1.75 (1.41 - 2.09)	< 0.001	2.10 (1.79 - 2.57)	< 0.001
<b>Race/Skin color</b>				
Brown	1.02 (0.99 - 1.05)	0.39	-	-
Non brown	1			
<b>Education</b>				
≥ 8 years	1			
< 8 years	2.15 (1.79 - 2.56)	< 0.001	2.50 (2.09 - 2.58)	< 0.001
<b>Area of residence</b>				
Rural	1.05 (0.99 - 1.10)	0.25	-	-
Urban	1			
<b>Physical disability</b>				
Level 0	1			
Level 1	1.25 (1.21 - 1.29)	< 0.001	1.50 (1.09 - 1.72)	< 0.001
Level 2	1.69 (1.54 - 1.85)	< 0.001	2.01 (1.67 - 2.37)	< 0.001
Not rated	1.17 (1.11 - 1.26)	< 0.001	1.45 (1.04 - 1.66)	0.03
<b>Entry status code</b>				
Other re-entries	1			
Transfer	0.97 (0.87-1.08)	0.22		
Relapse	1.05 (0.98-1.13)	0.30		
New case	0.79 (0.65-0.87)	0.25		
<b>Number of affected nerves</b>				
0	1		-	-
1	0.97 (0.92 - 1.02)	0.34	-	-
2 to 5	0.99 (0.95 - 1.04)	0.65	-	-
> 5	1.04 (0.96 - 1.11)	0.35	-	-
<b>Reactional state</b>				
No reaction	1			
Type I	1.28 (1.22 - 1.34)	< 0.001	1.24 (1.18 - 1.31)	< 0.001
Type II	1.33 (1.26 - 1.41)	< 0.001	1.30 (1.22 - 1.39)	< 0.001
Type I and II	1.22 (1.08 - 1.38)	0.001	1.20 (1.05 - 1.37)	0.001
<b>Examined contact persons</b>				
≤ 5	1.02 (0.97 - 1.08)	0.42	-	-
> 5	1		-	-
<b>Registered contact persons</b>				
≤ 5	1.00 (0.96 - 1.04)	0.91	-	-
> 5	1		-	-
<b>Termination status code</b>				
Cure	1			
Transfer	0.97 (0.91 - 1.02)	0.23	-	-
Death	1.10 (0.99 - 1.22)	0.29	-	-
Abandonment	1.00 (0.94 - 1.07)	0.93	-	-

PR: Prevalence Ratio; 95% CI: 95% confidence interval; \*Wald's chi-square test.



or lower/upper limbs, or deformities related with the progression of the disease [43]. We found an association between level II disability (92.7% of the cases) and multibacillary leprosy, with an adjusted prevalence ratio of 2.10. Similar findings have been reported in other studies conducted in Brazil [10,31,39].

The above findings draw attention to the possible negligence regarding the dermato-neurological examination and the role of health professionals in identifying and addressing physical disabilities, as well as the need to carry out an active search to interrupt the chain of transmission in response to the low attendance to health centers [31].

Furthermore, the fact that physical disability was not assessed and that this response variable was associated with the multibacillary clinical forms of the disease is worrying, considering that the service has failed to carry out its role of monitoring and surveillance of the disease and that the guidelines for the prevention of physical disabilities have been gaining prominence in controlling the disease in addition to multidrug therapy. In this sense, it is necessary to transcend care practice and incorporate assertive operational actions into the patient care program [44].

An association between type 1 or 2 or both reactional states and multibacillary leprosy was observed in leprosy reactions. Studies highlighting the distribution of reactions, associating it with smear microscopy, identified a high frequency of type 1 reactions in paucibacillary patients and type 2 reactions in multibacillary patients [45,46].

Multibacillary patients with type 2 reactions present a more severe clinical picture accompanied by signs and symptoms that debilitate and cause disabilities, such as neuritis, edema, pain in the lower and upper limbs, blisters, and ulcers [47].

Type 2 reactions occur more frequently in multibacillary patients during multidrug therapy when the skin lesions are involuting. The reactional episodes are the main responsible for the nerve injuries and disabilities generated by the disease. For this reason, an early diagnosis is critical so that treatment can be started and disabilities can be prevented [48,49].

As this study used secondary data, it is worth mentioning that underreporting of cases in the information system may have happened, making it impossible to know the epidemiological situation of leprosy, which impairs the planning of actions aimed at leprosy control [50,51].

One weakness identified by the study is the incomplete or incorrect filling out of data in the

information system, as some fields were left blank. A total of 126 cases were excluded for not having the operational classification of leprosy properly identified. These data are paramount to health management and planning [9,52].

Given the above, strategies to improve the quality of health records such as the one we used must be employed. Besides, the timely offer of health services with greater resolution and the active search for leprosy patients and their contacts are critical for the reliability of epidemiological data [53].

## Conclusions

The investigation revealed that individuals older than 15 years, males, with less than 8 years of education, with level I, II, or "not evaluated" disability, and with type 1 or 2 or both reactional states were more likely to have multibacillary leprosy. Therefore, these characteristics may be considered risk factors.

These findings may assist policymakers, health managers, and health workers in reducing social inequities through planning, monitoring, and evaluating leprosy control and surveillance strategies.

## Authors' contributions

JCS conceived the study. MSN provided supervision throughout. All authors were involved in the implementation of the study. RAO, LFSS, FSS, and ICCMD extracted data from the Information System. ACVR, LHS, JSML, ASAG, LMP and ILTPR performed statistical analysis. IGF, VMF, JMB, FAASS, and ACPJC analyzed the data. JCS and MSN wrote the manuscript. All authors edited the manuscript. All authors reviewed and approved the final version of the manuscript.

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