

# Factors associated with neural alterations and physical disabilities in patients with leprosy in São Luis, State of Maranhão, Brazil

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## ABSTRACT

**Introduction:** Leprosy is a chronic infectious disease that is caused by *Mycobacterium leprae*. The objective of this study was to evaluate the risk factors that are associated with neural alterations and physical disabilities in leprosy patients at the time of diagnosis. **Methods:** A prospective cross-sectional study was conducted on 155 leprosy patients who participated in a program that aimed to eliminate leprosy from São Luis, State of Maranhão. **Results:** Patients who were 31-45 years of age, were older than 60 years of age or had a partner were more likely to have a disability. Patients with partners were 1.14 times more likely ( $p = 0.025$ ) to have disabilities of the hands. The frequency of disabilities in the feet among the patients with different clinical forms of leprosy was statistically significant. **Conclusions:** The identification of risk factors that are associated with neural alterations and physical disabilities in leprosy patients is important for diagnosing the disease because this approach enables physicians to plan and prioritize actions for the treatment and monitoring of patients.

**Keywords:** Leprosy. Associated factors. Neural changes. Physical disabilities.

## INTRODUCTION

Leprosy is a chronic, infectious and contagious disease that is caused by the bacillus *Mycobacterium leprae*. This bacterium primarily affects the skin and peripheral nerves and causes significant motor and sensorial impairment. Leprosy is considered a public health problem due to its severe clinical manifestations and potential to cause physical disabilities<sup>1-3</sup>.

A reduction in the prevalence of leprosy has been observed in Brazil; however, a definitive detection rate has not been established. In absolute numbers, Brazil has the second highest prevalence of leprosy in the world<sup>4</sup>. In 2011, the country had a high coefficient of detection (15.88 cases/100,000 inhabitants) and a medium coefficient of prevalence (1.24 cases/10,000 inhabitants)<sup>1,5</sup>; therefore, Brazil accounts for 96% of all cases of

leprosy in Latin America. However, oscillations have occurred in the prevalence rates in several states and regions in the country. In 2011, the State of Maranhão had a general detection rate of 56.0 cases/100,000 inhabitants and 8.5 cases/10,000 inhabitants in people under 15 years of age; therefore, the state was classified as hyperendemic<sup>6</sup>.

The different clinical manifestations of leprosy depend on the relationship between the pathogenicity of the bacillus and the immune response of the host. The main clinical symptoms are as follows: macules, plaques, papules, nodules, infiltrations with a loss of sensitivity, paresthesia, anesthesia, neuritic pain and a thickening of peripheral nerves, mainly in the eyes, hands and feet<sup>3</sup>.

Using multidrug therapy (MDT), the prevention and treatment of physical disabilities should be integrated into the treatment of leprosy. To prevent future disabilities, every health care provider should be attentive to early indications of neural alterations in leprosy patients and should understand the diagnostic and treatment guidelines for neural lesions<sup>7-9</sup>.

The protocol for the prevention of disabilities (PD) recommends frequent exams of the nerve trunks in every patient with leprosy during treatment. According to the Minister of Health of Brazil<sup>5</sup>, the neurological evaluation must be performed in every patient at the beginning of treatment, every three months during treatment when the patient has no complaints, every time the patient has complaints, during the periodic

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use of corticoids, when the patient is in reactive and neuritis states, and after patients complete treatment<sup>10</sup>.

The World Health Organization (WHO)<sup>10</sup> developed *The Enhanced Global Strategy for Further Reducing the Disease Burden Due to Leprosy: 2011-2015*, which aims to reduce the prevalence of grade 2 physical disabilities by 35%, thereby reducing the prevalence rate to 1.19 cases/100,000 inhabitants. These recommendations reinforce the necessity of programs for the control of leprosy to ensure the early detection of the disease before the emergence of physical disabilities.

Identifying neural alterations and physical disabilities in leprosy patients will contribute to our understanding of the epidemiology of the disease. These data are useful for evaluating operational quality in health care settings, the protocols used by health services, delays in diagnosis, actions for patient monitoring, the prevention of disabilities, and patient rehabilitation<sup>11-13</sup>.

In addition, these data reveal the morbidity of leprosy and may be used as a guide for disease control and prevention after diagnosis. Therefore, the aim of this study was to investigate the risk factors that are associated with neural alterations and physical disabilities in leprosy patients at the time of diagnosis.

## METHODS

A cross-sectional study was performed on leprosy patients who participated in the Leprosy Control Program at the University Hospital of the Federal University of Maranhão (*Universidade Federal do Maranhão*).

The study population consisted of 155 cases of leprosy that were diagnosed as new cases based on self-referral from March 2010 to February 2011. The inclusion criteria were as follows: new cases of clinically confirmed leprosy that were registered in patient records for residents of São Luis, MA. Patients who participated in the program because of relapse, transfer or readmission and patients with sequelae due to other neurological disorders, orthopedic trauma, and/or rheumatic disabling diseases were not included.

After a medical screening, the patients were invited to participate in the research and were informed of the objectives and importance of the study and the type of procedure that would be performed. The patients who agreed to participate were required to sign an informed consent form.

The Madrid classification<sup>14</sup>, as defined by the 6<sup>th</sup> International Congress of Leprosy, was used to classify the clinical forms of leprosy into indeterminate (I), tuberculoid (T), borderline (B) and lepromatous (L). A survey was used to collect socioeconomic, demographic and clinical data from the participants. The severity of physical disabilities was based on a physical examination of the eyes, hands, and feet. The examinations were performed according to the parameters that were adopted by the Minister of Health of Brazil<sup>15,16</sup>.

The eye examinations were performed according to the technique described by Vieth et al.<sup>17</sup>. The hand and foot examinations were performed according to the techniques

used by Lehman et al.<sup>18</sup> and Rodrigues et al.<sup>19</sup>. To assess the sensitivity of the hands and feet, an esthesiometer was used (Semmes-Weinstein kit (Bauru, SP, Brazil) with monofilaments for sensitivity testing).

The association between the presence of neural alterations and the level of physical disability was investigated in addition to the variables of gender, age, educational level, marital status, and household income. A univariate analysis was performed using the chi-squared test for linear tendency. This analysis served as a comparison using an ordinal variable that was presented as a response variable. The proportional odds ratios and 95% confidence intervals were calculated for the estimate. The chi-squared test was utilized to analyze the association between the presence of neural alterations and the degree of physical disability using a nominal variable that represented the clinical forms of leprosy.

## Ethical considerations

The study was approved by the Research Ethics Committee of the Federal University of Maranhão (UFMA - *Universidade Federal do Maranhão*) (opinion number 23115-003005/2009-36).

## RESULTS

Of the 155 individuals evaluated, 55.5% were female, 29.7% were 16-30 years of age, 42.6% were single, 32.9% had only a middle school education, and 36.1% had a household income of one to two minimum wage salaries.

The analysis of the association between the socio-demographic variables and the presence of a physical disability indicated that gender, marital status, educational level and household income were not statistically significant (**Table 1**).

To evaluate the risk factors for physical disabilities, the age groups were compared. The group of patients 31-45 years of age was associated with an odds ratio (OR) 5.2 times higher than that of the other age groups [ $p=0.04$ ; 95% confidence interval (95%CI) 1.06-25.7] regarding the presence of disabilities. **Table 1** shows that the individuals over 60 years of age were associated with an OR of 19.8 ( $p=0.001$ ; 95%CI 3.45-114.09).

The patients with partners were 1.14 times more likely [ $p=0.025$ ; 95%CI 1.10-4.20] to have neural alterations in the hands when compared with the patients without partners. Gender, age, educational level and household income were not associated with any risk of neural alterations in the hands, eyes, nose and feet (**Table 2** and **Table 3**).

A predominance of alterations was observed in the hands (66.7%) of the patients who presented the lepromatous clinical form; however, no statistical significance was detected ( $p=0.070$ ). The patients with the lepromatous form (91.7%) or the borderline form (52.8%) presented alterations in the feet. By contrast, more than half of the patients with the tuberculoid, borderline and lepromatous forms (51.1%, 54.2% and 58.3%, respectively) presented alterations in the eyes; however, no statistical significance was found ( $p>0.05$ ). **Table 4** shows that the frequency of alterations in the nose was low, and

**TABLE 1 - Evaluation of the association between the sociodemographic variables and the presence of physical disabilities in leprosy patients, São Luis, State of Maranhão, 2012.**

Variable	Physical		Disabilities		Total		OR	p value	95% CI
	n (Grade 1 or 2)	%	n	%	n	%			
<b>Gender</b>									
female	23	47.9	63	58.9	86	55.5	1		
male	25	52.8	44	41.1	69	44.5	1.5	0.206	0.78-3.09
<b>Age group (years)</b>									
up to 15	2	4.2	17	15.9	19	12.3	1		
16-30	12	25.0	34	31.8	46	29.7	3.00	0.18	0.60-14.95
31-45	16	33.3	26	24.3	42	18.1	5.23	0.04	1.06-25.70
46-60	7	14.6	21	19.6	28	18.1	2.83	0.23	0.52-15.46
>60	11	22.9	9	8.4	20	12.9	10.39	0.007	1.88-57.42
<b>Schooling</b>									
higher education	6	12.5	18	16.8	24	15.5	1		
uneducated	1	2.1	4	3.7	5	3.2	0.75	0.81	0.07-8.09
middle school	19	39.6	32	29.9	51	32.9	1.78	0.30	0.60-5.27
high school	22	45.8	53	49.5	75	48.4	1.25	0.68	0.43-3.56
<b>Marital status</b>									
without a partner	15	31.3	51	47.7	66	42.6	1		
with a partner	33	68.7	56	52.3	89	57.4	2.00	0.06	0.98-4.11
<b>Household income (minimum wage salaries)</b>									
≥3	28	58.3	53	49.5	81	52.3	1		
≥1 - 2	13	27.1	43	40.2	56	36.1	0.57	0.156	0.26-1.24
<1	7	14.6	7	14.6	18	11.6	1.20	0.729	0.42-3.45
Total	48	100.0	107	100.0	155	100.0			

**OR:** odds ratio; **95% CI:** confidence interval of 95%.

the highest frequency of patients with this type of alteration had the borderline clinical form (9.7%), but no statistical significance was observed ( $p=0.348$ ).

In a comparison of the percentages of patients with and without physical disabilities (**Table 5**), the lepromatous form was associated with a physical disability in the eyes ( $p=0.020$ ), hands ( $p<0.001$ ) and feet ( $p<0.001$ ). The tuberculoid and borderline forms were associated only with physical disabilities in the feet ( $p<0.05$ ).

## DISCUSSION

Leprosy in Maranhão continues to be an important public health problem because the persistence of cases acts as a reservoir to feed the transmission cycle of the disease. This study did not find any association between gender and the level of

disability, similar to the studies by Sharma et al.<sup>20</sup> and Ribeiro<sup>21</sup>. However, Gonçalves<sup>22</sup> (OR=2;  $p<0.05$ ) and Moschioni<sup>23</sup> (OR=1.83;  $p<0.05$ ) found higher grades of physical disability among male individuals with leprosy. The frequency of leprosy cases was similar between genders. Cultural characteristics may explain the difference between the studies because women may be more likely to seek health assistance than men.

Educational level was not a risk factor for physical disabilities and neural alterations in the hands, feet, eyes and nose ( $p>0.05$ ). Similarly, Bernardes et al.<sup>24</sup> did not find a significant association between the level of education and the degree of disability. However, Moshioni<sup>23</sup> found that patients with no education were 5.69 times more likely to have physical disabilities than patients with 12 or more years of education. Additionally, Ribeiro<sup>21</sup> observed that 33.9% of patients who had a lower educational level were diagnosed with a

**TABLE 2 - Evaluation of the association between the sociodemographic variables and the presence of neural alterations in the hands and feet of leprosy patients, São Luis, State of Maranhão, 2012.**

Variable	Alterations in the hands						OR	p value	95% CI
	yes		no		total				
	n	%	n	%	n	%			
<b>Marital status</b>									
without a partner	18	31.6	48	49.0	66	42.6	1		
with a partner	39	68.4	50	51.0	89	57.4	2.08	0.04	1.04-4.12
<b>Household income (minimum wage salaries)</b>									
≥3	25	43.9	56	57.1	81	52.3	1		
≥1-2	22	38.6	34	34.7	56	36.1	1.45	0.308	0.71-2.96
<1	10	17.5	8	8.2	18	11.6	2.80	0.053	0.99-7.94
Total	57	100.0	98	100.0	155	100.0			
Variable	Alterations in the feet						OR	p value	95% CI
	yes		no		total				
	n	%	n	%	n	%			
<b>Educational level</b>									
higher education	6	8.7	18	20.9	24	15.5	1		
uneducated	1	1.5	4	4.7	5	3.2	0.75	0.813	0.07-8.09
middle school	27	39.1	24	27.9	51	32.9	3.38	0.027	1.15-9.89
high school	35	50.7	40	46.5	75	48.4	2.63	0.066	0.94-7.35
<b>Household income (minimum wage salaries)</b>									
≥3	34	49.3	47	54.7	81	52.3	1		
≥1-2	25	36.2	31	36.1	56	36.1	1.11	0.757	0.56-2.21
<1	10	14.5	8	9.3	18	11.6	1.73	0.298	0.62-4.84
total	69	100.0	86	100.0	155	100.0			

**OR:** odds ratio; **95% CI:** confidence interval of 95%.

grade 2 disability ( $p=0.032$ ). Corrêa et al.<sup>25</sup> observed that education, an indirect indicator of social conditions, was a determinant factor for the incidence of disabilities because the incidence worsened when the patient was uneducated.

Household income was not a risk factor for physical disabilities or neural alterations in the hands, feet, eyes and nose ( $p>0.05$ ). By contrast, a statistically significant association was found between a low income and a higher risk of physical disabilities in the study by Bernardes et al.<sup>24</sup>, a study in which the patients generally had a low income.

Patients 31-45 years of age ( $p=0.04$ ) and patients >60 years of age ( $p=0.007$ ) were at a higher risk for the emergence of physical disabilities but not for alterations in the hands, feet, eyes and nose ( $p>0.05$ ). Similar results were obtained in the study by Ribeiro Junior et al.<sup>26</sup> in which a higher frequency of physical disabilities was found in individuals older than 45 years of age

( $p=0.001$ ). Gonçalves<sup>22</sup> demonstrated that older individuals (43 years of age and older) were 3.3 times more likely to experience physical disabilities than younger individuals.

In contrast to the findings in this study, Bernardes et al.<sup>24</sup> did not find an association between age and a higher frequency of physical disabilities. According to Corrêa et al.<sup>25</sup> and Trindade and Nemes<sup>27</sup>, age may be associated with increased physical impairment over time due to the chronicity of the disease, which leads to a worsening of sensitivity and motor conditions. Notably, the risk of physical disabilities increased in individuals older than 60 years of age. This high risk has not been previously reported in the literature. In this study, patients older than 60 years of age were analyzed separately from the patients up to 45 years of age in contrast to other studies that evaluated both age groups together, which may explain this discrepancy.

**TABLE 3 - Evaluation of the association between the sociodemographic variables and the presence of neural alterations in the eyes and nose of leprosy patients, Sao Luis, State of Maranhão, 2012.**

Variable	Alterations in the eyes						OR	p value	95% CI
	yes		no		total				
	n	%	n	%	n	%			
Marital status									
without a partner	34	49.3	32	37.2	66	42.6	1		
with a partner	35	50.7	54	62.8	89	57.4	0.61	0.132	0.32-1.16
Household income (minimum wage salaries)									
≥3	37	53.6	44	51.2	81	52.3	1		
≥1-2	24	34.8	32	37.2	56	36.1	0.89	0.744	0.44-1.77
<1	8	11.6	10	11.6	18	11.6	1.95	0.924	0.34-2.65
total	69	100.0	86	100.0	155	100.0			
Variable	Alterations in the nose						OR	p value	95% CI
	yes		no		total				
	n	%	n	%	n	%			
Marital status									
without a partner	4	40.0	62	42.8	66	42.6	1		
with a partner	6	60.0	83	57.2	89	57.4	1.12	0.87	0.30-4.14
Household income (minimum wage salaries)									
≥3	5	50.0	76	52.4	81	52.3	1		
≥1-2	5	50.0	51	35.2	56	36.1	1.49	0.544	0.41-5.41
<1	0	0.0	18	12.4	18	11.6	0.89	--	--
total	10	100.0	145	100.0	155	100.0			

OR: odds ratio; 95% CI: confidence interval of 95%.

The patients who had partners had a higher risk of neural alterations in the hands (OR=1.14; p=0.025). Marital status was not a risk factor for physical disabilities or alterations in the feet, eyes and nose. Most of the patients in this study had a partner, and the hand is more prone and exposed to traumas and injuries, which may explain this finding. No other studies have demonstrated an association between marital status and physical disabilities in leprosy patients; therefore, new studies are needed.

The presence of neural alterations in the hands and feet were not significantly associated with gender, age, educational level or family income. However, patients older than 60 years of age were 2.17 times more likely to have alterations in the feet, most likely because the ability to walk in a supportive structure is affected by sensitivity and motor disorganization, predominantly in older patients.

No significant differences were detected in the analysis of socio-economic variables (gender, age, educational level, marital status and income) and neural alterations in the eyes and nose. However, Moreno et al.<sup>28</sup> found that an age of 40 years

and older was a determinant in the occurrence of alterations in the eyes of leprosy patients (p<0.003). Julio et al.<sup>29</sup> found that the male gender and an age of 33-54 years was associated with alterations in the nose. These results are important because few studies have evaluated nasal alterations caused by complications of leprosy according to Martins<sup>30</sup> and Silva et al.<sup>31</sup>

The lepromatous clinical form was associated with neural alterations in the feet. The high rates of neural alterations that were observed in the borderline and lepromatous clinical forms may be explained by the pattern of disease progression over time. In borderline leprosy, the nerves are affected more extensively than in the tuberculoid form. In the lepromatous type, the neural effect becomes intense and spreads after several years of exposure to the disease. The nerves become fibrous and paralyzed, which results in most of the observed neural alterations<sup>32,33</sup>.

An association was found between the lepromatous type and the presence of disabilities in the eyes, hands and feet (66.7%, 41.7% and 33.3%, respectively). Similar results were found in the study by Bernardes et al.<sup>24</sup> in which the distribution between



**TABLE 4 - Evaluation of the association between the clinical forms of leprosy and the presence of neural alterations in the hands, feet, eyes and nose of leprosy patients, São Luis, State of Maranhão, 2012.**

Clinical forms	Alterations in the hands						p value
	yes		no		total		
	n	%	n	%	n	%	
Tuberculoid	14	31.1	31	68.9	45	100.0	0.122
Borderline	35	48.6	37	51.4	72	100.0	0.060
Lepromatous	8	66.7	4	33.3	12	100.0	0.070
Total	57	36.8	98	63.2	155	100.0	

  

Clinical forms	Alterations feet						p value
	yes		no		total		
	n	%	n	%	n	%	
Tuberculoid	20	44.4	25	55.6	45	100.0	0.213
Borderline	38	52.8	34	47.2	72	100.0	0.904
Lepromatous	11	91.7	1	8.3	12	100.0	0.005
Total	69	44.5	86	55.5	155	100.0	

  

Clinical forms	Alterations eyes						p value
	yes		no		total		
	n	%	n	%	n	%	
Tuberculoid	23	51.1	22	51.1	45	100.0	0.936
Borderline	39	54.2	33	45.8	72	100.0	0.553
Lepromatous	7	58.3	5	41.7	12	100.0	0.628
Total	69	44.5	86	55.5	155	100.0	

  

Clinical forms	Alterations nose						p value
	yes		no		total		
	n	%	n	%	n	%	
Tuberculoid	3	6.7	42	93.3	45	100.0	1.000
Borderline	7	9.7	65	90.3	72	100.0	0.348
Lepromatous	0	0.0	12	100.0	12	100.0	1.000
Total	10	6.5	145	93.5	155	100.0	

the clinical form and the degree of physical disability was shown as follows: tuberculoid, 13.8%; borderline, 25%; and lepromatous, 33.3%. For the evaluated variables, a statistically significant association was found between the clinical form and the degree of physical disability. Carvalho and Alvarez<sup>34</sup> obtained a similar distribution for the classification of grade 2 physical disabilities: 11.1% for the tuberculoid type, 28.6% for the borderline group and 30% for the lepromatous type. Corrêa et al.<sup>25</sup> found a significantly higher percentage ( $p < 0.001$ ) of patients with a physical disability (grades 1 or 2) among patients in a multibacillary therapeutic scheme, which confirms the results in this study.

In this study, a higher frequency of physical disabilities was observed in patients with the borderline and lepromatous

clinical forms, which is in agreement with the studies by Ribeiro Junior et al.<sup>26</sup>, Miranzi et al.<sup>35</sup>, Silva et al.<sup>36</sup> and Resende et al.<sup>37</sup>. This finding has important implications for the early diagnosis of leprosy by health professionals because these clinical forms are associated with high transmissibility and a high grade of residual disability.

Few studies have evaluated the frequency and potential risk factors for physical disabilities and neural alterations in the eyes, nose, hands, and feet of patients with leprosy; therefore, this study is important. Most studies have only evaluated the degree of physical disabilities; however, this study performed neurological examinations of patients in addition to assessing physical disabilities. A limitation of this study is the investigation

**TABLE 5 - Evaluation of the association between the presence of disabilities in the eyes, hands and feet of leprosy patients, São Luis, State of Maranhão, 2012.**

Clinical forms	Alterations in the eyes						p value
	yes		no		total		
	n	%	n	%	n	%	
Tuberculoid	3	6.7	42	93.3	45	100.0	0.175
Borderline	10	13.9	62	86.1	72	100.0	0.564
Lepromatous	4	33.3	8	66.7	12	100.0	0.020
Total	17	11.0	138	89.0	155	100.0	

  

Clinical forms	Alterations in the hands						p value
	yes		no		total		
	n	%	n	%	n	%	
Tuberculoid	2	4.4	43	95.6	45	100.0	0.096
Borderline	9	12.5	63	87.5	72	100.0	0.570
Lepromatous	5	41.7	7	58.3	12	100.0	< 0.001
Total	16	10.3	139	89.7	155	100.0	

  

Clinical forms	Alterations feet						p value
	yes		no		total		
	n	%	n	%	n	%	
Tuberculoid	5	11.1	40	88.9	45	100.0	0.007
Borderline	25	34.7	47	65.3	72	100.0	0.018
Lepromatous	8	66.7	4	33.3	12	100.0	0.001
Total	38	24.5	117	75.5	155	100.0	

method that was adopted from the Minister of Health to evaluate the degree of physical disabilities. The threshold of sensitivity in this commonly used tool, which assigns a grade of 0-1, varies significantly.

Patients 31-45 years of age and patients older than 60 years of age had an increased risk of physical disabilities. The patients who had partners had an increased risk of developing alterations in the hands.

Of the patients who had the lepromatous clinical form, 66.7% presented disabilities in the eyes. The frequencies of disabilities in the feet were significantly associated with the different clinical forms.

The lepromatous clinical form was significantly associated with physical disabilities in the eyes, hands and feet.

These results suggest that identifying the factors that are associated with the presence of neural alterations and physical disabilities in leprosy patients is important for the early diagnosis of the disease because these data enable physicians to plan and prioritize actions for the treatment and monitoring of patients who have a high risk of developing physical disabilities.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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