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Original Article

Clinical variables associated with disability in leprosy cases in northeast Brazil

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Abstract

Introduction: The clinical outcomes of leprosy include complications such as physical disabilities and deformities that vary according to the degree of impairment of nerve trunks. Knowledge of the factors that lead to the development of these complications is important for disability prevention programs. This study aimed to evaluate clinical factors associated with the occurrence of physical disability in leprosy cases.

Methodology: This was a retrospective study of 2,358 cases of leprosy in Aracaju, northeast Brazil, between 2001 and 2011. Analysis was done using the Chi-square test and logistic regression model.

Results: Significant factors associated with disability were found to be male gender, having more than two affected nerves, multibacillary leprosy classification, leprosy reaction, and lepromatous leprosy. The multivariate analysis revealed that the associated factors included having more than two affected nerves, leprosy reaction (adjusted odds ratio [aOR]: 2.02, 95% confidence interval [CI]: 1.36 to 3.01), the multibacillary form (aOR: 2.74, 95% CI: 1.84 to 4.08), and lepromatous leprosy (aOR: 4.87, 95% CI: 2.86 to 16.08).

Conclusions: The number of affected nerves, leprosy reaction, operational classification, and clinical presentation were identified as the main factors associated with the development of disability in leprosy patients.

Key words: leprosy; physical disability; epidemiology.

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Introduction

Leprosy is considered an important public health problem due to its morbidity and socioeconomic impact, both of which are consequences of complications (*e.g.*, physical disabilities and deformities) that develop during the clinical outcome of the disease [1-3]. Approximately 200,000 new cases are diagnosed annually worldwide, with the highest prevalence in intertropical developing countries such as India, Brazil, Myanmar, Madagascar, Nepal, and Mozambique [4].

Leprosy is a chronic and infectious granulomatous disease caused by *Mycobacterium leprae* that affects nerve fibers in the skin and peripheral nerves [5]. The impairment of nerve trunks has the potential to cause physical disabilities due to the immune system's action against the bacillus [6]. Its extent depends on the clinical form of the disease and the exacerbation phenomena during leprosy reaction episodes [7,8]

Information on the number of people with disabilities/deformities due to leprosy remains limited. Only estimates of the number of individuals living with disabilities are available. Approximately two million people worldwide are currently living with physical disabilities due to leprosy [9], and it is estimated that there will be one million more over the next decade [10].

The prevalence of disabilities related to leprosy varies among countries [11]. Brazil has increased its detection of new cases with physical disability at diagnosis. In 2001, there was a 17.8% proportion of grade 1 physical disability and 6% of grade 2. In 2008,

the proportion of grade 1 was 20.7% and grade 2 was 7.7% [12]. The distribution of cases with physical disability in Brazil is uneven among regions. In 2008, the northeast region presented an average percentage of new leprosy cases with disabilities. The states of Alagoas, Sergipe, and Paraiba had the most significant values, with 12.4%, 8.9%, and 8.5%, respectively. The first of these states was classified as high, and the last two were classified as average/moderate for Brazilian parameters [13].

Disabilities/deformities can lead to problems such as decreased ability to work, limited social life, and psychological problems, and they are responsible for stigma and prejudice against the disease [14,15].

In an attempt to reduce the disease burden and its disability prevalence by 35% by the end of 2015, the World Health Organization (WHO) launched the Enhanced Global Strategy for Further Reducing the Disease Burden due to Leprosy (2011–2015) [16]. Thus, knowledge of the main risk factors for the development of physical disability is important for disability prevention programs because this knowledge provides access to important predictors of better surveillance.

The aim of this study was to evaluate clinical factors associated with the occurrence of disability in leprosy cases in northeast Brazil.

Methodology

Overall design

This was a retrospective study of leprosy cases in the city of Aracaju, northeast Brazil, from 2001 to 2011.

Setting

Aracaju, the capital of Sergipe State, is a coastal city (10º54'40"S and 37º04'18"W) four meters above sea level and with an area of 181.8 km^2. In 2010, the city had 571,149 inhabitants, with a density of 3,140.67 inhabitants per km^2. In 2007, Aracaju's leprosy detection rate was 49.22 cases per 100,000 inhabitants [17]. Aracaju has 43 basic health units serving leprosy patients distributed throughout its territory. Cases with difficult treatment are referred to a central reference center of the municipality.

Study subjects

Data were obtained from Notifiable Diseases Information System (SINAN – abbreviation in Portuguese) of the Municipal Health Secretariat of Aracaju. This database has information on all leprosy cases reported and confirmed since 2001. All patients reported with assessment for disability degree were included in this study.

Variables

The variables of age, sex, education (number of grades completed), number of skin lesions, number of affected nerves, operational classification, clinical form of the disease, and disability degree (grades 0, 1, and 2) were considered. An affected nerve in leprosy occurs when there are signs of pain or nerve thickening on palpation of the nerves, when there is loss of sensitivity according to the monofilament test, or when any motor impairment is observed [18].

The assessment of the degree of disability was performed according to the current classification system of WHO, using the following criteria: grade 0 indicates no loss of sensitivity or visible deformity; grade 1 is defined by a loss of sensitivity without visible deformity; and grade 2 indicates the presence of visible deformity [18]. Grades 1 and 2 were considered as disability for statistical analysis.

Data analysis

A descriptive analysis of the data was performed to determine absolute frequencies and percentages for categorical variables. Factors associated with the disability were analyzed via the calculation of prevalence ratio (PR). For the multivariate analysis, a logistic regression and a purposeful selection of covariates were used to identify predictors associated with disability. These variables were explored in a multivariate analysis using the step-by-step model. Covariates that were not statistically significant were removed to avoid a confounding effect on other models' parameters. The significance level for all analyses was 5% ($p < 0.05$). The analysis was performed using SPSS version 20.

Ethical considerations

The study was approved by the Human Research Ethics Committee of Federal University of Sergipe (Protocol 10691812.7.0000.5546).

Results

During this ten-year study, 2,358 (79.6%) cases of leprosy were assessed for disability degree, including 1,196 (50.7%) females and 1,162 (49.3%) males. The mean age of the patients was 39.35 years (± 18.70), with a median age of 37 years. Over three-quarters of patients (1,819; 77.1%) were between 15 and 60 years of age. The majority of patients had low education: 674 (35.1%) had between zero and four years of

education, and 973 (50.7%) had between five and nine years. Of the patients with nerve impairment, 745 (55.5%) had more than two affected nerves. According to the operation classification, there was a prevalence of paucibacillary (PB) leprosy, with 1,300 cases (55.1%). In most cases (2,043; 86.7%), patients had no leprosy reaction. The most frequent clinical forms were tuberculoid (689; 31.2%) and indeterminate (567; 25.7%). Regarding the degree of disability, 1,692 (71.8%) had leprosy grade 0, 492 (20.9%) had grade 1, and 172 (7.3%) had grade 2. The prevalence of disability (grade 1 + grade 2) was 28.2% (Table 1).

The highest prevalence was observed for disability in the age group above 60 years (PR: 3.17; 95% CI: 2.10–4.79), in male patients (PR: 1.47; 95% CI: 1.28–1.68), in patients who had more than two affected nerves (PR: 2.45, 95% CI: 2.08–2.89), in cases of multibacillary (MB) leprosy (PR: 2.93; 95% CI: 2.53–3.39), in cases of leprosy reaction (PR: 2.14, 95% CI: 1.87–2.44), and in cases of lepromatous leprosy (PR: 3.97; 95% CI: 3.15–4.99). It was observed that more education was a protective factor for disability (Table 2).

Table 3 summarizes all of the multivariate analysis results. The presence of two or more affected nerves proved to be a protective factor against the development of disability (aOR: 6.79; 95% CI: 2.86–16.09). Regarding the operational classification, the MB form increased the risk of disability (aOR: 2.74; 95% CI: 1.84–4.08). The presence of a leprosy reaction was associated with a higher likelihood of disability (aOR: 2.02; 95% CI: 1.36–3.01). Lepromatous leprosy patients had a greater likelihood of disability when compared to undetermined forms of leprosy (aOR: 4.87; 95% CI: 2.86–16.08).

Table 1. Characteristics of leprosy cases in Aracaju, northeast Brazil, 2001–2011

Variables	N	n	%
Age group (years)	2,358		
< 15		176	7.5
15 to 60		1,819	77.1
> 60		363	15.4
Sex	2,358		
Female		1,196	50.7
Male		1,162	49.3
Educational level (years)	1,919		
0 to 4		674	35.1
5 to 8		973	50.7
≥ 9		272	14.2
Skin lesions	2,353		
≤ 5		1,608	68.3
> 5		745	31.7
Affected nerves	1,343		
≤ 2		598	44.5
> 2		745	55.5
WHO classification	2,358		
Paucibacillary		1,300	55.1
Multibacillary		1,058	44.9
Leprosy reaction	2,357		
No		2,043	86.7
Yes		314	13.3
Clinical forms	2,205		
Indeterminate		567	25.7
Tuberculoid		689	31.7
Borderline		473	21.5
Lepromatous		476	21.6
Degree of disability	2,358		
Grade 0		1,692	71.8
Grade 1		492	20.9
Grade 2		172	7.3

[a] The number of patients in each category may not add up to 2,358 due to missing information.

Table 2. Clinical factors associated with the occurrence of disability in leprosy patients in Aracaju, northeast Brazil, 2001–2011

Variable	Disability			PR	95% CI
	N	Yes (%)	No (%)		
Age group (years)					
< 15	176	22 (12.5)	154 (87.5)	1	
15 to 60	1,819	490 (26.9)	1,329 (73.1)	2.15	1.45–3.21
> 60	363	144 (39.7)	219 (60.3)	3.17	2.10–4.79
Sex					
Female	1,196	270 (22.5)	926 (77.5)	1	
Male	1,162	386 (33.2)	776 (66.8)	1.47	1.28–1.68
Educational level (years)					
0 to 4	674	231 (34.7)	443 (65.3)	1	
5 to 8	973	258 (26.5)	715 (73.5)	0,77	0.67–0.89
≥ 9	272	69 (25.4)	203 (74.6)	0,74	0.59–0.93
Skin lesions					
≤ 5	1,608	333 (20.7)	1,275 (79.3)	1	
> 5	745	318 (42.7)	427 (57.3)	2.06	1.82–2.34
Affected nerves					
≤ 2	598	207 (34.6)	391 (65.4)	1	
> 2	745	39 (84.8)	7 (15.2)	2.45	2.08–2.89
WHO classification					
Paucibacillary	1,300	194 (14.9)	1,106 (85.1)	1	
Multibacillary	1,058	462 (43.7)	596 (56.3)	2.93	2.53–3.39
Leprosy reaction					
No	2,043	493 (24.1)	1,550 (75.9)	1	
Yes	314	162 (51.6)	152 (48.4)	2.14	1.87–2.44
Clinical forms					
Indeterminate	567	73 (12.9)	494 (87.1)	1	
Tuberculoid	689	118 (17.1)	571 (82.9)	1.33	1.02–1.74
Borderline	473	170 (35.9)	303 (64.1)	2.79	2.18–3.57
Lepromatous	476	243 (51.1)	233 (48.9)	3.97	3.15–4.99

PR: prevalence ratio; 95% CI: 95% confidence interval

Table 3. Independent risk factors for disability in patients with leprosy in Aracaju, northeast Brazil, 2001–2011

Risk factors for disability	aOR	95% CI	p value
Affected nerves			
≤ 2	1		
> 2	6,79	2.86–16.09	0.000
WHO classification			
Paucibacillary	1		
Multibacillary	2.74	1.84–4.08	0.000
Leprosy reaction			
No	1		
Yes	2.02	1.36–3.01	0.000
Clinical forms			
Indeterminate	1		
Tuberculoid	2.02	1.09–3.73	0.024
Borderline	3.22	1.77–5.82	0.000
Lepromatous	4.87	2.86–16.08	0.000

aOR: adjusted odds ratio; 95% CI: 95% confidence interval

Discussion

In general, a high frequency of patients with disabilities was found in Aracaju, northeast Brazil, in the ten-year study. The main factors associated with the development of disability in patients with leprosy were the number of affected nerves, leprosy reaction, operational classification, and clinical form of leprosy. Other studies [3,19-22] have shown incidence rates ranging from 2.8% to 24.3%.

Individuals who exhibit reactive outbreaks of leprosy are more susceptible to neural damage and possible sequelae [6,20,23]. In this study, although only 13.3% of the samples had a leprosy reaction, this variable was significant for the development of disability. This association was also observed by Gonçalves *et al*. (2008) [24]. Peripheral nerve injury has been associated with physical disability and is considered to be the most serious complication of leprosy [2,8,25]. Studies conducted in India [3,19], Bangladesh [26], and Brazil [24] have shown that patients with three or more affected nerves are more likely to develop disabilities.

Early identification combined with the proper treatment of leprosy reaction can be an effective strategy to prevent disability in leprosy. The daily administration of prednisone (1 to 2 mg/kg for at least 90 days) has been recommended to prevent the development of neuropathy and consequently disability [23].

Regarding the operational classification, there was a high rate of MB patients, as observed in other studies [22,25,27]. These high numbers suggest a late diagnosis, which may be due to difficult access to health care. In situations where patients have access to a health system, they are diagnosed and classified as MB [28]. Another factor that contributes to high rates of disability may be inadequate treatment, which is often due to a lack of professional knowledge [29].

Although tuberculoid leprosy is more prevalent [30,31], the lepromatous form has a major impact on the development of disabilities, as described in other studies [2,3,32]. Thus, the correct classification is important for appropriate treatment, so it is necessary to perform smear microscopies for classification [30].

The variables of sex, education level, and age were not associated with the occurrence of disability in the multivariate analysis. However, in endemic regions, men have shown physical disability due to leprosy two to three times more frequently than women [2-4]. Social behavior and difficult access to health services have been cited as reasons for this difference [33,34].

Studies have demonstrated an association between a high prevalence of leprosy and low socioeconomic status, social inequality, population growth, poor housing conditions, low income, and low level of education [35-37]. Higher levels of education have been considered a determining factor for disease improvement as well as a protective factor for the occurrence of disability among leprosy cases [2]. Thus, level of education and the ability to understand guidelines regarding treatment are reflected in the development of disease and associated with the population's socioeconomic status. However, based on the results of the multivariate analysis, this study demonstrated that low educational level was not associated with the development of disability in leprosy. The lack of association of this factor may be due to the homogeneity of the population involved in this study.

The present study had some limitations. The data were collected from clinical and surveillance records, leading to a loss of some information. Furthermore, it was not possible to obtain the time evolution of the disease due to failures in the registry. However, the loss of this information occurred randomly, and the study had an excellent sample size, suggesting that the results obtained here are convincing. These results can be explained by treatment discontinuity and the fragility of disability prevention. Furthermore, the development of physical disability is proportional to the disease progression. This finding provides strong evidence that patients are being diagnosed late [3], though this variable was not analyzed in this study due to a lack of data. This delay is often associated with difficult access to health services by the population [38].

Conclusions

Our results showed that the number of affected nerves, leprosy reaction, operational classification, and clinical presentation were the main factors associated with the development of physical disabilities. Better knowledge of the factors associated with the onset of disability due to leprosy is useful for disability prevention programs and can allow the progression of this disease to be monitored more closely.

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