Factors associated with cure and abandonment of leprosy treatment: A reflective analysis

Fatores associados à cura e ao abandono do tratamento da hanseníase: Uma análise reflexiva

Factores asociados a la cura y el abandono del tratamiento de la lepra: Un análisis reflexivo

Thayane Santos Siqueira
ORCID: https://orcid.org/0000-0001-8370-0544
Federal University of Sergipe, Brazil
Email: thayane_siqueira@live.com
Ariel Oliveira Celestino
ORCID: https://orcid.org/0000-0003-3907-187X
Federal University of Sergipe, Brazil
Email: biomédica.ariel@gmail.com
José Rodrigo Santos Silva
ORCID: https://orcid.org/0000-0002-1918-7122
Federal University of Sergipe, Brazil
Email: rodrigo.ufs@gmail.com

Abstract

To analyze trends, and the main socioeconomic and clinical factors related to treatment abandonment and the cure of leprosy in Sergipe. For the present study, data from all new cases of cure and abandonment of leprosy treatment notified by the health centers of the municipalities to the SINAN (Information System on Notifiable Diseases) in the state of Sergipe, Brazil, from 2007 to 2017, were used. This is an ecological study of cases of cure and abandonment of leprosy treatment, rates were calculated based on the "Guidelines for surveillance, care and elimination of leprosy as a public health problem".using time-series analysis and multivariate logistic regression. Concerning multivariate regression, the young age group presents a higher risk for quitting the treatment (p = 0.429; OR = 2.75). Blacks/browns/indigenous were more likely to abandon treatment (p = 0.482; OR = 1.69), as well as multibacillary individuals (p = 0.541; OR = 2.26). Regarding the cure, the young age group has less chances of cure (OR = 0.34). The same happens for the operational classification; the multibacillary patients have a lower chance of cure (OR = 0.35). Finally, individuals with grade 2 of physical disability are less likely to be cured (OR = 0.54). Health services are noticeably weak, especially when it comes to clinical factors associated with treatment abandonment and a low proportion of cure. Multibacillary (Borderline and Lepromatous) are responsible for the active transmission of leprosy.
Keywords: Primary health care; Public health; Epidemiology; Leprosy.

Resumo

Analisar as tendências e os principais fatores socioeconômicos e clínicos relacionados ao abandono do tratamento e à cura da hanseníase em Sergipe. Para o presente estudo, foram utilizados os dados de todos os casos novos de cura e abandono do tratamento da hanseníase notificados pelos centros de saúde dos municípios ao SINAN (Sistema de Informação de Agravos de Notificação) do estado de Sergipe, Brasil, de 2007 a 2017. . Trata-se de um estudo ecológico de casos de cura e abandono do tratamento da hanseníase, cujas taxas foram calculadas com base nas "Diretrizes para vigilância, atenção e eliminação da hanseníase como problema de saúde pública", utilizando análise de séries temporais e regressão logística multivariada. Em relação à regressão multivariada, a faixa etária jovem apresenta maior risco para abandono do tratamento (p = 0,429; OR = 2,75). Negros / pardos / indígenas apresentaram maior chance de abandonar o tratamento (p = 0,482; OR = 1,69), assim como multibacilares (p = 0,541; OR = 2,26). Em relação à cura, a faixa etária jovem tem menos chances de cura (OR = 0,34). O mesmo acontece para a classificação operacional; os multibacilares têm menor chance de cura (OR = 0,35). Por fim, indivíduos

com grau 2 de incapacidade física têm menor probabilidade de cura (OR = 0,54). Os serviços de saúde são visivelmente frágeis, principalmente quando se trata de fatores clínicos associados ao abandono do tratamento e baixa proporção de cura. Os multibacilares (Borderline e virchowianos) são os responsáveis pela transmissão ativa da hanseníase.

Palavras-chave: Atenção Primária à Saúde; Saúde pública; Epidemiologia; Lepra.

Resumen

Analizar las tendencias y los principales factores socioeconómicos y clínicos relacionados con el abandono del tratamiento y la curación de la lepra en Sergipe. Para el presente estudio se utilizaron datos de todos los nuevos casos de curación y abandono del tratamiento de la lepra notificados por los centros de salud de los municipios al SINAN (Sistema de Información de Enfermedades Notificables) del estado de Sergipe, Brasil, de 2007 a 2007. 2017. Se trata de un estudio ecológico de casos de cura y abandono del tratamiento de la lepra, cuyas tasas se calcularon con base en las "Directrices para la vigilancia, atención y eliminación de la lepra como problema de salud pública", utilizando análisis de series de tiempo y regresión logística. multivariante. En relación con la regresión multivariante, el grupo de edad joven tiene mayor riesgo de abandonar el tratamiento (p = 0,429; OR = 2,75). Los negros / pardos / indios tuvieron más probabilidades de abandonar el tratamiento (p = 0,482; OR = 1,69), así como los multibaciliarios (p = 0,541; OR = 2,26). En cuanto a la cura, el grupo de edad joven tiene menos posibilidades de cura (OR = 0,34). Lo mismo ocurre con la clasificación operativa; es menos probable que se curen los multibaciliarios (OR = 0,35). Finalmente, las personas con grado 2 de discapacidad física tienen menos probabilidades de curarse (OR = 0,54). Los servicios de salud son visiblemente frágiles, especialmente cuando se trata de factores clínicos asociados con el abandono del tratamiento y una baja tasa de curación. Los multibacilarios (Borderline y Virchowian) son responsables de la transmisión activa de la lepra.

Palabras clave: Atención primaria de salud; Salud pública; Epidemiología; Lepra.

1. Introduction

Leprosy is still a relevant public health problem due to its heterogeneous character in the Brazilian territory. Its importance lies not only in its persistence in developing countries but also in the physical and psychosocial damage that this disease causes (Souza, Luna & Magalhães, 2019). Brazil has shown, over the years, a decreasing trend both in the prevalence and in the incidence of leprosy, however, the maintenance of the disease in the territory is linked to the socioeconomic and health conditions of the population. Regional disparities, as well as the effectiveness or not of the health system, corroborate for the persistence of the disease in the country (Ribeiro, Silva & Oliveira, 2018).

The National Leprosy Control Program, (NLCP), is based on disease control through early diagnosis and treatment, aiming to eliminate sources of infection and the appearance of sequelae in affected individuals (Loyal, Cazarin & Bezarra, 2014). Despite the existence of effective diagnostics for leprosy, in addition to the availability and efficacy of polychemotherapy, operational failures at different points in the health care network play a fundamental role in the persistence of the *Mycobacterium leprae* transmission chain (Noriega et al., 2016)

In this perspective, it is necessary to qualify health professionals to better monitor the treatment of the patients until discharge, since the treatment abandonment is one of the main causes for the development of resistance to antibiotics, physical disabilities, and continuity of the transmission chain (Lira, Silva & Gonçalves, 2017). Comprehensive analysis of operational indicators, including treatment abandonment and cure, permits inferring problems related to the universalization of access and comprehensive health care concerning leprosy (Souza et al., 2018)

There are few studies of the epidemiological line that pay attention to factors associated with the abandonment of treatment and cure of leprosy within the panorama of operational health indicators. Based on this assumption, the present study

aimed to analyze the trend and the main socioeconomic and clinical factors related to treatment abandonment and the cure of the disease in Sergipe, taking into account that they express the effectiveness of services in ensuring treatment adherence until the discharge.

2. Methods

2.1- Study design

This is a descriptive study with the individual characterization of cases of cure and abandonment of leprosy treatment; and also ecological of the retrospective type of time- series, with the use of multivariate logistic regression techniques. In the present study, data from all new cases of cure and abandonment of leprosy treatment notified by the health centers of the municipalities to the SINAN (Notifiable Diseases Information System) in the state of Sergipe, Brazil, from 2007 to 2017, were used. This system consists of a database of the Health Secretariat of all states in Brazil, to report information on sociodemographic and clinical characteristics and the address of mandatory reporting diseases (Santos et al., 2019)

The study took place in the state of Sergipe (Figure 1). Sergipe is one of the nine states located in the Northeast region of Brazil whose capital city is Aracaju. It is the smallest Brazilian state with a territory of 21,962.10 km2, equivalent to 0.26% of the national territory, and an estimated population of 2,288,116, in the year 2017. In its administrative political organization, it has 75 municipalities grouped in three mesoregions and 13 microregions (IBGE, 2019)

Figure 1: A) Map of Brazil with emphasis on the Northeast region. B) Map of the state of Sergipe with the municipal divisions.
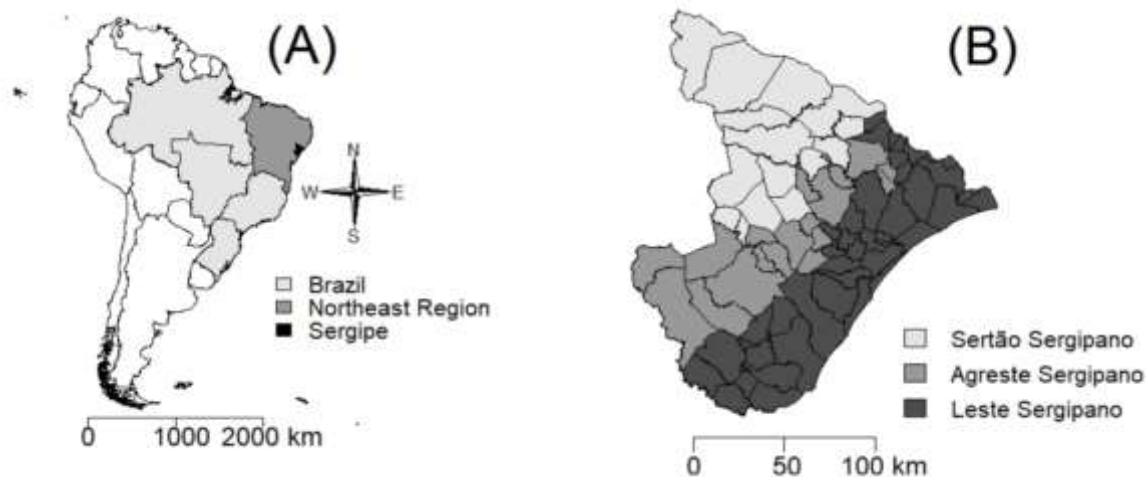
Source: Authors.

For the analysis of the tendency of leprosy cure and treatment abandonment, the percentage of cases cured and treatment abandonment among the cases reported in the year was calculated, and these rates were calculated based on the "Guidelines for surveillance, care and elimination of leprosy as a public health problem". For the percentage of cure, the numerator was the number of new leprosy cases, residing in a specific place, diagnosed in the years of the cohorts, and cured until 12/31 of the year of evaluation. The denominator was the total number of new leprosy cases residing in the same place and diagnosed in the years of the cohorts. This proportion is multiplied by 100 to obtain an indicator in percentage terms. The parameters adopted by the Ministry of Health vary between: Good: $\geq 90\%$; Regular: ≥ 75 to 89.9%; Precarious: $<75\%$ (Brazil, 2016 A).

The formula used to calculate the percentage of treatment abandonment consists of new cases of leprosy diagnosed in the years of the cohorts who abandoned treatment until 12/31 of the year of assessment, divided by the total of new cases diagnosed in the years of the cohorts, and multiply by 100. The parameters adopted by the Ministry of Health vary between Good <10%; Regular 10 to 24.9%; Precarious ≥25% (Brazil, 2016 A).

2.2 Statistics analysis

Polynomial regression was utilized to calculate the annual variation of the indicator, between 2007 and 2017. This method of analysis consists of a segmented linear regression, using dummy variables, to identify points where there is a change in the trend and estimate the Annual Percentage Change (APC), and the Average Annual Percentage Change (AAPC), considering the entire period of the series and with a 95% confidence interval. The trend was classified as increasing, decreasing, and stationary (Monteiro, Martins, Brito, Alencar & Heukelbah, 2015)

The variables chosen for the analysis of the factors associated with the cure of leprosy and the treatment abandonment were: sex, age group, race, schooling, zone, operational classification, clinical form, degree of physical disability and bacilloscopy. The association of these variables with the dependent variables was verified using the Chi-Square test and the Odds Ratio (OR). The significant variables in the bivariate analysis were used as independent in a multivariate logistic regression model to adjust the occurrence or not of treatment abandonment and cure. All statistical analyzes were performed using software R 3.6.1, and the level of significance adopted was 5%.

2.3 Ethical aspects

The study was submitted to the Research Ethics Committee (CEP) of the Federal University of Sergipe and approved with the following approval opinion (No. 3,151,215), of February 18, 2019.

3. Results

In the analyzed period of 2007-2017 in Sergipe, 179 individuals abandoned the treatment. There were variations in the percentages of this indicator for the entire period, in 2007 the dropout percentage was (4%), in 2011 it decreased to (1.4%), in 2016 it increased to (5.8%) (Figure 2A). From the analysis it was noticed the occurrence of two trends in the period, a decreasing in 2007-2011 (APC = -28.30 and p-value = 0.045) and another increasing between 2011-2017 (APC = 21.33 and p-value = 0.011). Regarding the percentage of cure, 4706 people were cured of leprosy between 2007 and 2017. The cure indicator showed fluctuations in the period studied; in 2007, it presented a percentage of (88.52%), in 2013 (91.53%) and 2017 (79.07%), varying between Good and Regular percentage, according to Brazilian parameters. Two trends were observed, one stationary from 2007 to 2013 (p-value = 0.073), and the second decreasing between the years 2013 and 2017 (APC = -3.61 and p-value <0.001) (Figure 2B). The results of the trend in operational health indicators showed a reduction in adherence to treatment and, consequently, a decrease in the proportion of cured patients, as shown in (Figure 2).

Figure 2: (A) Proportion of abandonment of leprosy treatment among new cases, in the period from 2007 to 2017. Decreasing trend from 2007 to 2011 (APC = -28.30; p-value = 0.045). Increasing trend from 2011 to 2017 (APC = 21.33; p-value = 0.011). (B) Proportion of leprosy cure among new cases, in the period 2007-2017. Stationary trend from 2007 to 2013 (p-value = 0.073). Downward trend from 2013 to 2017 (APC = -3.61; p-value < 0.001).
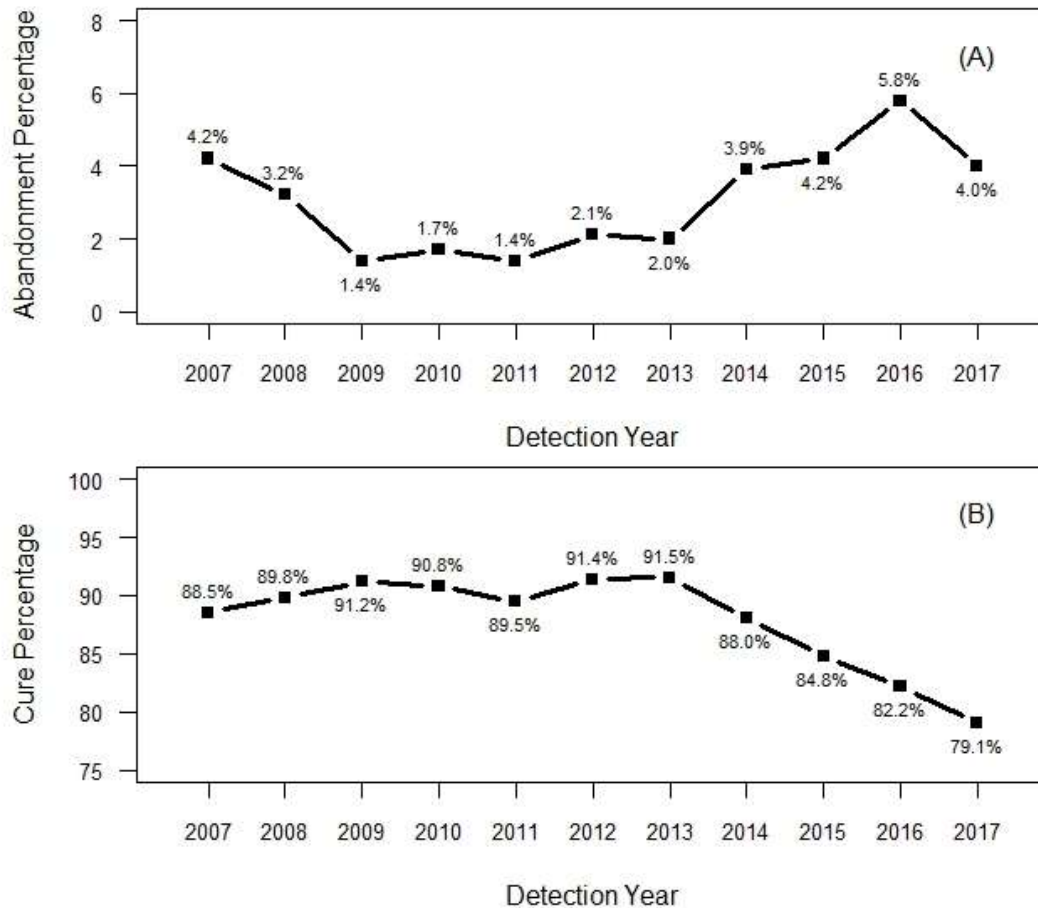
Source: Research data.

The variables sex (p-value = 0.0963), schooling (p-value = 0.3688), zone (p-value = 0.4149) and bacilloscopy (p=0,1459), did not show statistical significance to the percentage of treatment abandonment (Table 1). Concerning the age group, young people had 2.65 chances (p-value = 0.0004; OR = 2.65) to abandon treatment when compared to children under 15 years old. Black, browns and indigenous people had 1.74 more chances (p-value = 0.0156; OR = 1.74) to abandon treatment in regard to white people. When it comes to clinical characteristics, it was observed that multibacillary individuals are 2 times more likely to abandon treatment (p-value < 0.0001; OR = 2.02) than paucibacillary ones. Another important point is that individuals with the Borderline and Lepromatous clinical forms manifested 1.74 and 1.91 more chances of abandoning the treatment (p-value = 0.0028; OR = 1.74; OR = 1.91, respectively) when compared to individuals who have an indeterminate form. Individuals with grade 2 of physical disability were twice as likely to abandon treatment (p-value = 0.0013; OR = 2.20) when compared to grade 0 disability.

Table 1: Odds ratio (OR) for abandonment of leprosy treatment in Sergipe, according to

sociodemographic and clinical characteristics from 2007 to 2017.

Variable / Category	Abandonment of Treatment		OR (CI 95%)	P-value
	Yes (%)	No (%)		
Gender				
Female	76 (3.08)	2388 (96.92)	0.77 (0.57; 1.04)	0.0963
Male	103 (3.99)	2478 (96.01)	1.00	
Age group				
Elderly	26 (2.37)	1070 (97.63)	1.12 (0.49; 2.55)	0.0004
Adult	36 (2.76)	1269 (97.24)	1.30 (0.58; 2.90)	
Young Adult	78 (4.47)	1666 (95.53)	2.11 (0.98; 4.53)	
Young	32 (5.61)	538 (94.39)	2.65 (1.18; 5.93)	
Under 15 years	7 (2.12)	323 (97.88)	1.00	
Ethnicity				
Black/Mixed/Indigenous	146 (3.81)	3686 (96.19)	1.74 (1.12; 2.69)	0.0156
White/Yellow	24 (2.23)	1054 (97.77)	1.00	
Schooling				
Illiterate	20 (3.85)	499 (96.15)	1.71 (0.65; 4.50)	0.3688
Elementary School	94 (3.52)	2576 (96.48)	1.56 (0.64; 3.80)	
High school	20 (2.53)	772 (97.47)	1.12 (0.43; 2.95)	
University education	5 (2.25)	217 (97.75)	1.00	
Region				
Periurban	4 (5.33)	71 (94.67)	1.46 (0.56; 3.85)	0.4149
Countryside	26 (3.03)	832 (96.97)	0.83 (0.55; 1.26)	
Urban	137 (3.64)	3623 (96.36)	1.00	
Operational Classification				
Multibacillary	122 (4.65)	2501 (95.35)	2.02 (1.47; 2.78)	0.0001
Paucibacillary	57 (2.35)	2364 (97.65)	1.00	
Clinical form				
Lepromatous	53 (4.65)	1088 (95.35)	1.91 (1.22; 3.00)	0.0028
Borderline	48 (4.23)	1087 (95.77)	1.74 (1.10; 2.75)	
Tuberculoid	31 (2.49)	1213 (97.51)	1.02 (0.62; 1.70)	
Indeterminate	28 (2.43)	1123 (97.57)	1.00	
Physical disability degree				
G2	24 (5.99)	377 (94.01)	2.20 (1.41; 3.43)	0.0013
G1	39 (3.82)	981 (96.18)	1.41 (0.97; 2.05)	

Zero	81 (2.72)	2901 (97.28)	1.00	
Bacilloscopy				
Positive	52 (3.80)	1315 (96.20)	1.37 (0.92; 2.04)	0.1459
Negative	49 (2.81)	1696 (97.19)	1.00	

Source: Research data.

Adjustments were made to logistic regression models, assuming abandonment as a dependent variable (adopting a value of 1 for cases in which treatment was abandoned). The independent variables in each model were significant in the previous bivariate tests (Table 1). It is noted by the multivariate regression (Table 2) that the young age group presents a higher risk for treatment abandonment (p-value = 0.0429; OR = 2.75), compared to the other age groups that were significant only in the bivariate analysis. Blacks, Browns and Indigenous were more likely to abandon treatment (p-value = 0.0482; OR = 1.69) regarding white people, as well as individuals with a multibacillary operational classification had a greater chance of abandoning treatment (p-value = 0.0541; OR = 2.26) when compared to paucibacillary ones.

Table 2: Multivariate analysis of the association between socioeconomic and clinical risk variables and abandonment of leprosy treatment.

Variables	Estimate	OR (CI 95%)	S.E.	P-value
Intercept	-4.83		0.53	<0.0001
Age Group (Elderly)	-0.19	0.83 (0.32; 2.57)	0.52	0.7154
Age Group (Adult)	0.06	1.07 (0.43; 3.22)	0.50	0.8971
Age Group (Young Adult)	0.64	1.89 (0.82; 5.49)	0.48	0.1810
Age Group (Youth)	1.01	2.75 (1.12; 8.28)	0.50	0.0429
Race (Black/Mixed race/Indigenous)	0.52	1.69 (1.03; 2.94)	0.27	0.0482
Operational Classification (Multibacillary)	0.82	2.26 (0.92; 4.91)	0.42	0.0541
Clinical Form (Lepromatous)	0.04	1.05 (0.44; 2.77)	0.46	0.9239
Clinical Form (Borderline)	-0.13	0.87 (0.37; 2.30)	0.46	0.7724
Clinical Form (Tuberculoid)	0.13	1.14 (0.63; 2.07)	0.30	0.6659
Physical disability degree (G 1)	0.13	1.14 (0.73; 1.75)	0.22	0.5488
Physical disability degree (G 2)	0.45	1.56 (0.86; 2.71)	0.29	0.1227

Source: Research data.

The grade 2 of physical disability did not show statistical significance in a regression model with multiple variables, different from what occurred in the bivariate. We can then point out that race, age, and operational classification are important variables regarding the risk of abandoning leprosy treatment.

The odds ratio for curing the disease was calculated for sociodemographic variables. The data show that women are more likely to be cured when compared to men (p-value = 0.0016; OR = 1.44). Regarding the age group, children under 15 are more likely to be cured, when compared to other age groups. The race (p-value = 0.2890) and the zone (p-value = 0.3809) did

not obtain statistical significance. Regarding schooling, people with higher education had a higher percentage of cure (96.85%) when compared to the illiterate (91.52%); to elementary school (93.60%); and to high school (94.82%) (Table 3).

Concerning clinical variables, paucibacillary patients (96.98%) had a higher percentage of cure when compared to multibacillary ones (89.90%) (p-value < 0.0001). Individuals with the Lepromatous form and Borderline (OR = 0.93, OR = 0.95, p-value < 0.0001) were less likely to be cured when compared to individuals who developed the indeterminate form of the disease. Regarding the degree of disability, the percentage of cure was higher in individuals with grade 0 of disability (95.47%) when compared to grade 1 (92.65%) and grade 2 (86.78%) (p-value < 0.0001). Negative intradermal bacilloscopy was considered a protective factor for healing (p-value < 0.0001), and this was evidenced by higher percentages of cure in individuals with negative test results (95.59%). (Table 3).

Table 3. Chance ratio (OR) for leprosy cure in Sergipe, according to sociodemographic and clinical characteristics from 2007 to 2017.

Variable / Category	Leprosy Cure		OR (CI 95%)	P-value
	Yes (%)	No (%)		
Gender				
Female	2327 (94.44)	137 (5.56)	1.44 (1.15; 1.80)	0.0016
Male	2379 (92.17)	202 (7.83)	1.00	
Age group				
Elderly	996 (90.88)	100 (9.12)	0.94 (0.91; 0.96)	0.0002
Adult	1233 (94.48)	72 (5.52)	0.97 (0.95; 1.00)	
Young Adult	1632 (93.58)	112 (6.42)	0.97 (0.94; 0.99)	
Young	525 (92.11)	45 (7.89)	0.95 (0.92; 0.98)	
Under 15 years	320 (96.97)	10 (3.03)	1.00	
Ethnicity				
Black/Mixed/Indigenous	3571 (93.19)	261 (6.81)	0.85 (0.64; 1.13)	0.2890
White/Yellow	1015 (94.16)	63 (5.84)	1.00	
Schooling				
Illiterate	475 (91.52)	44 (8.48)	0.95 (0.91; 0.98)	0.0214
Elementary School	2499 (93.60)	171 (6.40)	0.97 (0.94; 0.99)	
High school	751 (94.82)	41 (5.18)	0.98 (0.95; 1.01)	
University education	215 (96.85)	7 (3.15)	1.00	
Region				
Periurban	67 (89.33)	8 (10.67)	0.96 (0.88; 1.03)	0.3809
Countryside	801 (93.36)	57 (6.64)	1.00 (0.98; 1.02)	

Urban	3511 (93.38)	249 (6.62)	1.00	
Operational Classification				
Multibacillary	2358 (89.90)	265 (10.10)	0.28 (0.21; 0.36)	<0.0001
Paucibacillary	2348 (96.98)	73 (3.02)	1.00	
Clinical form				
Lepromatous	1018 (89.22)	123 (10.78)	0.93 (0.90; 0.95)	<0.0001
Borderline	1044 (91.98)	91 (8.02)	0.95 (0.93; 0.97)	
Tuberculoid	1207 (97.03)	37 (2.97)	1.01 (0.99; 1.02)	
Indeterminate	1110 (96.44)	41 (3.56)	1.00	
Physical disability degree				
G2	348 (86.78)	53 (13.22)	0.91 (0.87; 0.95)	<0.0001
G1	945 (92.65)	75 (7.35)	0.97 (0.95; 0.99)	
Zero	2847 (95.47)	135 (4.53)	1.00	
Bacilloscopy				
Positive	1234 (90.27)	133 (9.73)	0.43 (0.32; 0.57)	<0.0001
Negative	1668 (95.59)	77 (4.41)	1.00	

Source: Research data.

Source: Research data.

It is noted by the multivariate regression, that the young age group has less chance of cure (OR = 0.34) when compared to children under 15 years old. The same happens for the operational classification; the multibacillary individuals have a lower chance of cure (OR = 0.35) when analyzed together with other independent variables (Table 4).

Lastly, individuals with grade 2 of physical disability are less likely to be cured (OR = 0.54) in opposition to the grade 1. It is inferred, then, that the young age group, the multibacillary operational classification, and the degree of physical disability were the main factors associated with the risk of not obtaining a cure from the analyzes (Table 4).

Table 4. Multivariate analysis of the association between socioeconomic and clinical risk variables and leprosy cure.

Variables	Estimate	OR (CI 95%)	S.E.	P-value
Intercept	5.00		0.69	<0.0001
Sexo (Feminino)	-0.16	0.85 (0.63; 1.16)	0.16	0.3043
Age Group (Elderly)	-0.68	0.51 (0.19; 1.14)	0.45	0.1306
Age Group (Adult)	-0.37	0.69 (0.26; 1.55)	0.45	0.4062
Age Group (Young Adult)	-0.58	0.56 (0.21; 1.23)	0.44	0.1857
Age Group (Youth)	-1.07	0.34 (0.13; 0.80)	0.47	**0.0216**
Schooling (Illiterate)	-0.95	0.39 (0.11; 1.03)	0.55	0.0852
Schooling (Elementary School)	-0.85	0.43 (0.13; 1.05)	0.52	0.1022
Schooling (High school)	-0.57	0.56 (0.16; 1.47)	0.54	0.2926
Operational Classification (Multibacillary)	-1.06	0.35 (0.17; 0.74)	0.37	**0.0039**
Clinical Form (Lepromatous)	-0.04	0.96 (0.43; 1.98)	0.39	0.9203
Clinical Form (Borderline)	0.24	1.27 (0.57; 2.61)	0.39	0.5431
Clinical Form (Tuberculoid)	0.24	1.27 (0.73; 2.22)	0.28	0.3926
Physical Disability Degree (G 1)	-0.27	0.77 (0.55; 1.08)	0.17	0.1254
Physical Disability Degree (G 2)	-0.62	0.54 (0.36; 0.83)	0.22	**0.0044**

Source: Research data.

4. Discussion

The results of this study demonstrate a vulnerability related to leprosy operational indicators, treatment abandonment, and cure, in the state of Sergipe, in Brazil. Some studies indicate that the organizational structure of the health system has a greater influence on the epidemiological situation of leprosy than the socioeconomic disparities, given that, greater coverage of the *Estratégia Saúde da Família* (The Family Health Strategy) effectively contributes to the promotion of greater adherence to treatment (Lapa et al.,2006; Brito et al., 2015)

In this study, it was possible to observe a growing trend in Sergipe of people who abandoned treatment between 2011 and 2017. Sousa (2015) emphasize that the abandonment / non-adherence of leprosy treatment can be related to several reasons, such as lack of motivation, lack of knowledge about the disease and the norms, and non-credibility of the cure. In other epidemiological studies, such as de Souza et al. (2018) the leprosy operational indicators in Bahia, from 2001 to 2014, were analyzed, from a gender perspective; in this study, there was a reduction in the number of people who abandoned the treatment of leprosy in the aforementioned historical series.

Another epidemiological study, carried out by Oliveira et al. (2015) in the state of Paraná, from 2001 to 2010, also observed a decreasing trend in people who abandoned leprosy treatment. It is noteworthy that in Sergipe, unlike other locations in Brazil, there is a tendency to increase the proportion of people who abandoned treatment. These high rates may reflect the fragility that exists in the relationship between the user and the health services, as the same must project credibility with the treatment adopted by the patient.

It is important to emphasize that there is a difference between non-adherence and treatment abandonment. Non-adherence is configured when the diagnosed user fails to regularly attend appointments at the Health Unit that are previously

scheduled. In this case, the health team must make an active search, aiming to rescue the user from treatment. Whereas treatment abandonment is when people who have not completed the number of doses within the scheduled time and who have not attended the health service in the last 12 months, are discharged for abandonment (Lira, Silva & Gonçalves, 2017).

Concomitant to the increase in the proportion of people who abandoned leprosy treatment, in 2013, the proportion of people cured decreased considerably until 2017. In an epidemiological study in Brazil conducted by Ribeiro et al. (2018) it was observed that between 2010 and 2015 there was a general reduction in the percentage of cure, thus showing a weakness in the health system. From these data, it is possible to infer that the Ministry of Health, over the years, has been concerned with early diagnosis, and in the active search for cases in children under 15, and in the general population; however, there is a notable weakness in treatment follow-up of leprosy, evidenced by national and local studies that reinforce the decreasing trend in the percentage of cure.

It is worth mentioning that in Sergipe, in the last epidemiological bulletin carried out from 2012 to 2016, the rate of new cases was 17.59 per thousand people, thus expressing high levels of incidence for the state (Brazil, 2018 B). A hypothesis for maintaining this high rate is precisely the failure to monitor the treatment of patients, as it has been seen that diagnosed and not cured individuals inflame the prevalence and contribute to the maintenance of active transmission of the disease (Barbosa et al.,2014). Another problem is that people who are not cured can evolve to a state of permanent physical disability, thus leading to an increase in social inequities and public spending.

Our study also proposed to analyze the factors connected to treatment abandonment and the cure of leprosy in Sergipe. Regarding treatment abandonment, in the bivariate analysis, the variables sex, education and zone did not show statistical significance, however, a study by Sousa et al.(2013) in the state of Maranhão, Brazil, analyzed the factors that influenced or not the abandonment of leprosy treatment; in this study, women, and people with low education had the highest percentage of treatment abandonment.

Although the zone factor did not show statistical significance in our study, both for treatment abandonment and for the cure. Other studies claim that the permanence of users in the treatment regime depends on the access to health services. Many users when receiving the diagnosis, do not adhere to therapy because they live far from the health unit, which requires a greater intervention from the teams, especially concerning the active search for these absentees (Ignotti, et al.,2001). Travel costs and the time spent going to the health care unit are also factors that contribute to a higher dropout rate, since most of these patients prefer to remain anonymous, due to the stigmas created culturally around this disease (Luna et al., 2010)

By giving feedback on factors related to healing, women and people with higher education are more likely to be cured when compared to other groups. The fact that women have a greater chance of cure is related to greater detection of cases in this group, because culturally, the female sex has a greater concern with health and aesthetics, and therefore, there is a greater demand for health services by this group (Souza et al., 2018)

Regarding education, as stated by other researches, leprosy affects people with less education, which often interferes with the understanding of the technical language used by health professionals. In other words, there's difficulty in understanding the information related to the treatment which leads to lower adherence and lower cure rate. Thus, people with higher education are more likely to be cured due to the greater ease in understanding the various aspects related to leprosy (Monteiro et al., 2017)

Young people and blacks, browns, and indigenous had a greater chance of abandoning treatment when compared to other groups. In a study by Araújo et al. (2014) in the state of Piauí, Brazil, it was found that the age group of 15-59 years is responsible for about 79.41% of cases of abandonment of leprosy treatment. These data corroborate other studies that affirm that the economically active population is the most affected by the disease, consequently the most prone to abandonment. The opening hours of the health services are not always compatible with the patients' working hours, which in itself is a

contributing factor to greater treatment abandonment in this age group. This data is relevant because, as leprosy is a disabling and stigmatizing disease, there is a tendency for people to abandon their work functions and isolate themselves for fear of social judgment (Heukelbach, Chichava & Oliveira, 2011). In the same study by Araújo et al. (2014) children under 15 years old, corresponded to only 2.9% of the cases that abandoned treatment. In our study, this same group had a greater chance of cure when compared to other age groups.

Black, brown, and indigenous races were associated in this study as a risk factor for abandoning treatment. In the last Census Bureau, the majority of the Brazilian population defined themselves as brown and black (50.7%). Studies indicate that a detailed analysis of this factor is necessary as a contributor to treatment abandonment, since the analysis of color/race is subjective; which requires a more detailed study of the association of this variable related to the treatment abandonment and the cure (Ignotti et al., 2001),

Regarding the studied clinical variables, multibacillary individuals with the Borderline and Lepromatous clinical forms, and with a grade 2 of physical disability, are more likely to abandon treatment. These results are similar to that of Araújo et al.(2014) in which 61.76% of patients who abandoned treatment belonged to the multibacillary operational classification. These data are remarkable since the multibacillary form is responsible for the active transmission of the disease. Ignotii et al.(2001) reinforce that the abandonment of treatment by patients with the most severe clinical forms is not only related to the durability of the treatment, which is greater when compared to paucibacillary individuals, but also, to the perception that the individual has about the signs and symptoms related to the most complicated forms, resulting in disbelief in the prognosis of the cure.

In our analysis, the clinical characteristics related to the cure of leprosy were assessed. Multibacillary individuals with a grade 2 of physical disability are less likely to be cured, which reinforces the results of the bivariate and multivariate analysis of these same groups regarding treatment abandonment. It is worth stressing the importance of the first contact of the Family Health Team with patients with the most severe forms of leprosy; the reception, and monitoring of this patient are of fundamental importance for better understanding and motivation regarding the credibility of the treatment and cure disease (Luna et al.,2010; Araújo et al., 2014).

5. Conlusion

This study reveals that although leprosy has treatment and cure, the proportion of people who abandon treatment has grown, and accordingly, the proportion of cure has decreased. Through the results described, it is possible to observe the weakness of health services, especially when it comes to the clinical factors associated with treatment abandonment and the low proportion of cure. Multibacillary individuals with the most severe forms of the disease (Borderline and Lepromatous) are responsible for the active transmission of leprosy, and the most likely to abandon treatment. Therefore, the need for a more structured follow-up of these patients is emphasized, aiming at the integrality and the concretization of the bond as a fundamental principle of Primary Care.

Besides, the main sociodemographic factors associated with a higher rate of treatment abandonment and a lower proportion of cure were highlighted. It is up to the managers a greater concern with individuals who have less education, who are in the young age group, and who belong to the black/brown or indigenous races. The greater the social vulnerability, the greater the spread and emergence of diseases such as leprosy, and the barriers to effective treatment. The opening of new protocols targeting the most vulnerable population in health services could contribute to a lower rate of treatment abandonment for people with leprosy.

In conclusion, this study aims to encourage further research that better elucidates how sociodemographic and clinical factors can contribute to a lower cure rate and greater treatment abandonment.

Funding

Support for the project was provided by Support Foundation for Research and Technological Innovation of the State of Sergipe fellowships.

Competing interests

None declared

Ethical approval

The study protocols were reviewed and approved by the Ethical Research Committee of Federal University of Sergipe, o, Brazil (protocols n°. 3.151.215

References

Alencar, C. H. M., Ramos Jr, A. N., Sena Neto, S. A., Murto, C., Alencar, M. J. F., Barbosa, J. C., et al.(2012). Diagnosis of leprosy outside the municipality of residence: a spatial approach, 2001 to 2009. *Cad Saude Publica*. 28 (9), 1685-98

Araújo, M. M., Silva, J. H. S., Gomes, A. C. S. (2014). Clinical and epidemiological profile of patients who dropped out leprosy treatment. *Hansen Int* . 39 (2), 55-63.

Barbosa, J. C., Junior, A. N. R., Alencar, O. M. (2014). Leprosy after release from treatment in the Brazilian Unified Health System: aspects for access in the Northeast region. *Cad. Saúde Colet*.22 (4): 351-8.

Boygni, R. N., Souza, E. A., Romanholo, H. S. B,, et al. (2019). Persistence of leprosy in household social networks: overlapping cases and vulnerability in endemic regions in Brazil. *Cad. Saúde Pública*, 35(2), 14.

Brazil. (2016) A. Ministry of Health, Secretariat of Health Surveillance, Department of Communicable Diseases. Guidelines for surveillance, care and elimination of leprosy as a public health problem: technical-operational manual [Internet]. Brasília

Brazil (2018) B. Ministry of Health. Health Surveillance Secretary. Characterization of the epidemiological situation of leprosy and differences by sex, Brazil, 2012-2016. Epidemiological bulletin. 49(4), 1-12.

Brazilian Institute of Geography and Statistics (IBGE) (2019). Cities @ Sergipe. 2019

Brito, A. L., Monteiro, L. D., Ramos Junior, A. N., Heukelbach, J., Alencar, C. H. (2018). Temporal trends of leprosy in a Brazilian state capital in Northeast Brazil: epidemiology and analysis by joinpoints, 2001 to 2012. *Rev Bras Epidemiol*.19(1):194-204.

Cabral-Miranda, W., Chiaravalloti, N. F., & Barrozo, L. V. (2014). Socioeconomic and environmental effects influencing the development of leprosy in Bahia, northeastern Brazil. *Trop Med Int Health.* 19(12), 1504-14

Heukelbach, J., Chichava, A. O., & Oliveira, A. R. (2011). Interruption and Defaulting of Multidrug Therapy against Leprosy: Population-Based Study in Brazil's Savannah Region. *Plos. Neglected Tropical Diseases*. 5(5), 1-9

Ignotti, E., Andrade, V. L. G., Sabroza, P. C., & Araújo, A. J. G. (2001). Study of adherence to leprosy treatment in the city of Duque de Caxias / RJ. "Abandonment or Abandoned". *Hansenologia Internationals*. 26(11), 23-30

Lapa, T. M., Albuquerque, M. F. P. M., Carvalho, M. F., et al.(2006). Spatial analysis of leprosy cases treated at public health care facilities in Brazil. *Cad. Saúde Pública.* 22(12):2575-2583

Lira, R. M. N., Silva, M. V. S., & Gonçalves, G. B. (2017). Factors related to abandonment or interruption of leprosy treatment: an integrative literature review. *Rev Enferm UFPI*, 6(4),53-8

Loyal, D. R., Cazarin, G., Bezerra, L. C. A., et al. (2017). Leprosy Control Program: Assessment Of Implementation In Districts. *Health Debate.* 41, 209-228.

Luna, I. T., Beserra, E. P., Alves, M. D. S., & Pinheiro, P. N. C. (2010). Adhesion to Leprosy treatment: inherent difficulties of the patients. *Rev Bras Enferm.* 63(6), 983-90.

Monteiro, L. D., Martins-Melo, F. R., Brito, A. L., Alencar, C. H., Heukelbah, J. (2015). Spatial patterns of leprosy in a hyperendemic state in Northern Brazil, 2001-2012. *Rev Saúde Pública* 49(84), 1-8.

Monteiro, L. D., et al.(2017). Social determinants of leprosy in a hyper-endemic state in northern Brazil. *Rev Saude Publica*, 51(70), 1-12

Naaz, F., Mohanty, P. S., Bansal, A. K., et al.(2017) Challenges Beyond Elimination in Leprosy. *Int J Mycobacteriol.* 6(3), 222-228.

Noriega, L. F., Chiacchio, N. D., Noriega, A. F., Pereira, G. A., & Vieira, M. (2016). Leprosy: ancient disease remains a public health problem nowadays. *An Bras Dermatol* .91, 547-8

Oliveira, K. S., Souza, J., Zilly, A., Silva-Sobrinho, R. A. (2015). Evaluation of leprosy epidemiological and operational indicators in priority municipalities in the state of Paraná, 2001 to 2010. *Epidemiol Serv Saude*. 24(3), 507-16

Ribeiro, M. D. A., Silva, J. C. A., Oliveira, S. B. (2018) Epidemiologic study of leprosy in Brazil: reflections on elimination goals. *Rev Panam Salud Publica*. 42(7), 7.

Rodrigues, A. L. P., Almeida, A. P., Rodrigues, B. F., et al.(2000). Occurrence of late lepra reaction in leprosy pacients: subsidies for implementation of a specific care program. *Hansen. Int.*. 25(1), 7-16.

Santos, M. B., Santos, A. D., Barreto, A. S., et al.(2019). Clinical and epidemiological indicators and spatial analysis of leprosy cases in patients under 15 years old in an endemic area of Northeast Brazil: an ecological and time series study. *BMJ Open*. 9(7): e023420.

Sousa, A. A., Oliveira, F. J. F., Costa, A. C. P. J, et al.(2013). Adhesion to Hansen's Disease Treatment for Patients monitored at basic Health Units in Impertatriz-MA. *Sanare, Sobral*, 12(1), 06-12

Souza, C. D. F., Luna, C. F., & Magalhães, C. A. F. (2019). Leprosy transmission in Bahia, 2001-2015: modeling based on Joinpoint regression and spatial scan statistics. *Epidemiol. Serv. Saude*. . 28(1). e2018065

Souza, E. A., Ferreira, A. F., Boigny, R. N., et al. (2018). Leprosy and gender in Brazil: trends in an endemic area of the Northeast region, 2001–2014. *Rev. Saúde Pública*. 52, 20.