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CUTANEOUS LEISHMANIASIS AND THE BRAZILIAN POPULATION IN THE LAST DECADES

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Abstract: **Introduction**: Leishmaniasis is a parasitic disease related to poverty and considered a neglected disease by the World Health Organization, responsible for affecting about 100 endemic countries. Its most common presentations are visceral leishmaniasis and cutaneous leishmaniasis (CL). CL is a tropical disease that has significantly increased the number of people affected in recent decades, with an increase in global prevalence from 1990 to 2013 of 174.2%. Objective: To describe the incidence of hospitalizations for CL according to the different regions of Brazil between 2007 and 2021, analyzing the most affected groups, as well as the health policies implemented to control the disease in this period. Methodology: This is a descriptive observational study, whose data were collected by the DataSUS platform, as well as epidemiological bulletins from the Pan American Health Organization. The collection started from the Hospital Information System (SIH), through hospital morbidity data by place of residence between January 2007 and December 2021. Results and Discussion: Cutaneous leishmaniasis is a disease still present and neglected in society Brazilian affecting mainly the North and Midwest regions; regions with higher incidence of cases and higher mortality rate. The region with the highest number of hospitalizations in the last decade is the Southeast with 36.4% of all cases. CL is characterized by affecting more men than women at a rate of 1.9:1, respectively. Furthermore, the peak of cases by age group affected is generally between 50 and 69, with a peculiarity for the Northeast that presents another peak in children aged 1 to 4 years. Conclusion: CL remains a neglected disease, affecting the most vulnerable population in the country, especially regions with little access to health and awareness of the severity of the disease.

Keywords: Leishmaniasis; Cutaneous

leishmaniasis; neglected diseases.

INTRODUCTION

Leishmaniasis is caused by agents of the genus Leishmania, a group of protozoa that transmit the disease to mammals, including humans, through sandflies.1 Currently, there are approximately 12 million people infected with leishmaniasis in 88 countries.2 WHO lists leishmaniasis as one of the neglected tropical diseases for which the development of new treatments is a priority.3

The 2 main forms of clinical presentation of leishmaniasis are: visceral leishmaniasis, the most prevalent and severe form, and cutaneous leishmaniasis (CL). CL is a tropical disease that has significantly increased the number of people affected in recent decades, with an increase in global prevalence from 1990 to 2013 of 174.2%.4 Furthermore, CL can be divided into ulcerative skin lesions that develop in the sandfly bite site, which is localized cutaneous leishmaniasis (LCL) or multiple non-ulcerative nodules; diffuse cutaneous leishmaniasis (DCL).1 Lesions that heal with scars, often in aesthetically apparent and perceptible locations, leave those affected with some degree of disfigurement.4

Cutaneous leishmaniasis is endemic in more than 70 countries worldwide, and 90% of cases occur in Afghanistan, Pakistan, Algeria, Syria, Peru, Saudi Arabia and Brazil. Currently, in Brazil, the incidence of CL is 15.4 cases/100,000 inhab.5 These increases can be explained in part by better diagnosis and case reporting, but they are also a result of inadequate control of the vector or reservoir, increased detection of cutaneous leishmaniasis associated with opportunistic infections (eg HIV/AIDS) and the emergence of resistance to anti-leishmanial drugs.6-8 However, as many infections are asymptomatic or misdiagnosed, the global burden of cutaneous leishmaniasis is likely to be underestimated.9 Thus form,

METHODOLOGY

This is a descriptive observational study, whose objective is to understand the epidemiological distributionof hospitalizations for cutaneous leishmaniasis in Brazil. Data were collected by the DataSUS platform, through information collected by the Notifiable Diseases Information System (SINAN). The collection started from the Hospital Information System (SIH), through hospital morbidity data by place of residence between January 2007 and December 2021.

The information was characterized by regions of Brazil according to hospitalizations per year of care. The indicators used were: sex, age, color/race, deaths and mortality rates. In addition, incidence and epidemiological prevalence data were taken from data made available by the Pan American Health Organization. The study was carried out in line with the principles of Resolution 466/2012 of the National Health Council of Brazil.

RESULTS AND DISCUSSION

In the last 20 years, 1,067,759 cases of cutaneous (CL) and mucosal (LM) leishmaniasis were reported to the Pan American Health Organization (PAHO), with an average of 53,387 per year. During this period, there is a downward trend in the number of cases and, in 2020, the lowest number was recorded (39,705). In 2020, the countries that reported the highest number of cases were Brazil (16,432), Colombia (6,161), Peru (4,178), Nicaragua (3,443) and Bolivia (2,059), which together represented 81% of the cases in the Region. The regional incidence rate was 18.37 cases per 100,000 inhabitants.10

In Brazil, the agents responsible for causing cutaneous leishmaniasis are Leishmania amazonensis, Leishmania braziliensis, Leishmania guyanensis, Leishmania lansoni, Leishmania lindembergi, Leishmania naiffi

and Leishmania shawi. The main vectors are: Lutzomyia amazonensis, Lutzomyia ayrozai, Lutzomyia complex, Lutzomyia davisi, Lutzomyia fischeri, Lutzomyia flaviscutellata, Lutzomyia intermedia, Lutzomyia migonei, Lutzomyia neivai, Lutzomyia ovallesi, Lutzomyia paraensis, Lutzomyia Pessoai, Lutzomyia shaquital, Lutzomyia salesi, Lutzomyia shawiis, Lutzomyia umbrallis, Lutzomyia wellcomei and Lutzomyia whitmani.11

The incidence of hospitalizations for CL varied in the last decade in Brazil. Between 2007 and 2021, 6,489 cases of hospitalization were registered in the country Table 1.0. The region with the highest number of hospitalizations was the Southeast, with 2,360 patients representing 36.4% of all cases, which may be related to greater access to diagnostic procedures and hospital ne2rks. The second region with the most cases was the Northeast with 2,187, followed by the North, Midwest and South, respectively.

Interestingly, if we divide the period 2007 and 2021 into 2 periods (2007-2013 and 2014-2021), a significant change in the epidemiological profile of the affected population is noticeable. Until 2013, the Northeast led the ranking of the highest number of hospitalizations with 44.6% of all cases. The second region was the Southeast with 26.1% of cases. Until that moment, with the exception of 2013 itself, in none of the previous years, the number of hospitalizations in the Southeast surpassed the Northeast. As of 2013, the Southeast led every year as the region with the highest number of cases in the country. Thus, analyzing the second moment, from 2014 to 2021, the Southeast led the ranking with 44.9% of cases, followed by the Northeast with 24.6%. The third, fourth and fifth place were occupied by the North, Midwest and South regions, respectively, in both moments.

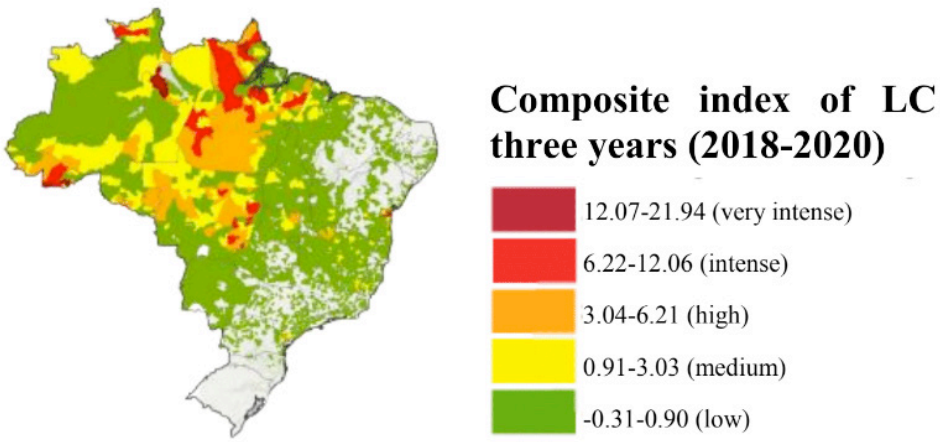

Figure 1.0Incidence of cases of cutaneous and mucosal Leishmaniasis in 2020 in Brazil expressed in number of cases per 100,000 inhabitants

Source: Pan American Health Organization. Regional information system on leishmaniasis. Washington, DC: PAHO; 2021

Region/Unit of the Federation	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total
TOTAL	**43**	**567**	**512**	**576**	**482**	**407**	**368**	**360**	**308**	**269**	**394**	**486**	**678**	**504**	**535**	**6,489**
North region	**9**	**95**	**72**	**54**	**61**	**52**	**85**	**79**	**79**	**44**	**65**	**86**	**118**	**72**	**70**	**1,041**
Rondônia	-	3	1	2	-	5	35	25	42	21	15	23	31	8	10	221
Acre	1	7	16	12	10	3	-	7	3	7	11	10	5	3	7	102
Amazonas	1	3	1	2	-	3	1	4	2	1	5	16	14	9	15	77
Roraima	1	5	14	11	6	11	7	7	6	-	4	5	1	2	9	89
Pará	5	51	27	12	29	11	16	13	12	7	11	11	23	16	11	255
Amapá	-	1	-	-	1	-	1	2	1	-	-	1	-	-	-	7
Tocantins	1	25	13	15	15	19	25	21	13	8	19	20	44	34	18	290
Northeast Region	**17**	**251**	**248**	**265**	**234**	**191**	**111**	**114**	**95**	**89**	**110**	**111**	**134**	**116**	**101**	**2,187**
Maranhão	3	37	22	33	23	24	17	25	18	15	19	26	16	20	14	312
Piauí	1	15	29	34	57	55	26	41	19	15	13	15	21	10	13	364
Ceará	4	60	48	48	15	10	10	12	19	14	18	24	20	21	29	352
Rio Grande do Norte	-	7	3	4	6	-	5	4	2	1	2	4	-	1	2	41
Paraíba	2	14	23	16	9	5	4	7	11	13	7	12	18	4	8	153
Pernambuco	2	67	83	90	77	51	16	3	4	7	12	8	25	37	13	495
Alagoas	-	-	1	-	2	2	-	-	1	-	-	2	-	-	1	9
Sergipe	-	3	23	2	3	5	1	-	1	2	4	3	8	4	1	60
Bahia	5	48	16	38	42	39	32	22	20	22	35	17	26	19	20	401
Southeast region	**10**	**122**	**106**	**164**	**138**	**117**	**115**	**123**	**107**	**100**	**179**	**224**	**347**	**213**	**295**	**2,360**
Minas Gerais	6	57	56	101	89	65	73	66	54	60	119	185	259	174	220	1,584
Espírito Santo	1	2	1	5	-	1	-	1	-	-	2	-	2	5	3	23
Rio de Janeiro	1	7	6	4	-	2	1	3	2	-	1	2	8	-	6	43
São Paulo	2	56	43	54	49	49	41	53	51	40	57	37	78	34	66	710
South region	**3**	**10**	**10**	**10**	**8**	**12**	**6**	**5**	**3**	**9**	**7**	**14**	**23**	**20**	**12**	**152**
Paraná	-	3	8	9	6	12	6	3	2	4	4	10	14	9	7	97
Santa Catarina	2	-	-	-	-	-	-	-	-	3	3	2	8	7	3	28
Rio Grande do Sul	1	7	2	1	2	-	-	2	1	2	-	2	1	4	2	27
Midwest region	**4**	**89**	**76**	**83**	**41**	**35**	**51**	**39**	**24**	**27**	**33**	**51**	**56**	**83**	**57**	**749**
Mato Grosso do Sul	-	34	43	43	9	12	12	5	3	2	4	3	4	8	14	196
Mato Grosso	-	18	7	6	10	7	20	14	6	11	12	18	19	14	5	167
Goiás	1	7	6	17	11	11	14	8	13	8	14	24	28	54	32	248
Federal District	3	30	20	17	11	5	5	12	2	6	3	6	5	7	6	138

Table 1.0 Number of patients hospitalized for cutaneous leishmaniasis according to each Brazilian region and state between 2007 and 2021

Source: Ministry of Health - SUS Hospital Information System (SIH/SUS). 2022.

Region	Deaths	Mortality rate
TOTAL	**119**	**1.83**
North region	30	2.88
Northeast Region	45	2.06
Southeast region	25	1.06
South region	3	1.97
Midwest region	16	2.14

Table 2.0Mortality indicators population hospitalized for visceral leishmaniasis in Brazil between the years 2007 and 2021 according to regions of the country by place of residence

Source: Ministry of Health - SUS Hospital Information System (SIH/SUS). 2022.

Region	Under 1 year	1 to 4 years old	5 to 9 years old	10 to 14 years old	15 to 19 years old	20 to 29 years old	30 to 39 years	40 to 49 years old	50 to 59 years old	60 to 69 years old	70 to 79 years old	80 years and more	Total
TOTAL	**209**	**590**	**330**	**227**	**206**	**474**	**633**	**713**	**1,026**	**1,040**	**735**	**306**	**6,489**
North region	37	95	47	27	33	100	108	101	192	168	98	35	1,041
Northeast Region	125	337	149	108	94	170	215	247	215	243	188	96	2,187
Southeast region	15	121	95	73	59	132	201	250	472	475	334	133	2,360
South region	2	2	6	7	3	12	19	27	25	27	15	7	152
Midwest region	30	35	33	12	17	60	90	88	122	127	100	35	749

Table 3.0Distribution by age group of the population hospitalized for cutaneous leishmaniasis in Brazil between the years 2007 and 2021 according to the regions of the country by place of residence.

Source: Ministry of Health - SUS Hospital Information System (SIH/SUS). 2022.

Region	White	black	brown	Yellow	Indigenous	No information	Total
TOTAL	**1,172**	**204**	**3,020**	**134**	**53**	**1906**	**6,489**
North region	51	20	676	31	24	239	1,041
Northeast Region	111	35	1,097	42	9	893	2,187
Southeast region	741	122	945	49	7	496	2,360
South region	105	9	13	-	-	25	152
Midwest region	164	18	289	12	13	253	749

Table 4.0Distribution by color/race of the population hospitalized for cutaneous leishmaniasis in Brazil between the years 2007 and 2021 according to the regions of the country by place of residence

Source: Ministry of Health – SUS (Unified Health System), Hospital Information System (SIH/SUS). 2022.

Although the regions with the highest number of hospitalizations are the Southeast and

Northeast, the regions with the highest incidence of CL cases are the North and Midwest Figure 1.0. This may reflect a lack of an assistance ne2rk for people in that region or a lack of awareness on the part of the population to seek an assistance service. Proof of this is that the highest mortality rates are in the North and Midwest regions, with values of 2.88 and 2.14, respectively Table 2.0.

The age group affected by the disease across the country also does not show a uniform pattern. In general, there is a peak of cases between 50 and 69 years old, which starts to decrease after 70 years old Table 3.0. However, this relationship is not true in all regions of the country. In the Northeast, specifically, there is another peak of cases in the range of 1 to 4 years. The data from this study also showed that the most affected population is formed by men in a ratio of approximately 1.9:1 man/woman Table 5.0.

As for the color/race of the patients, it was noticed that the brown population was the most affected, representing 46.5% of the total hospitalizations, and, if patients without this information are excluded, the percentage goes to 65.9%. Despite this, in the southern region of the country, the white population represented 69% of cases. This finding is probably related to the history of colonization of the region by European immigrants, not representing a significant epidemiological change, since approximately 76% of the inhabitants declare themselves white.

Region/Gender	Masculine	Female	Total
TOTAL	**4,258**	**2,231**	**6,489**
North region	762	279	1,041
Northeast Region	1,327	860	2,187
Southeast region	1,523	837	2,360
South region	109	43	152
Midwest region	537	212	749

Table 5.0Distribution by gender of the population hospitalized for cutaneous leishmaniasis in Brazil between the years 2007 and 2021 according to regions of the country by place of residence

Source: Ministry of Health – SUS (Unified Health System) Hospital Information System (SIH/SUS). 2022.

Although not fatal, cutaneous leishmaniasis is treated to speed healing, reduce scarring, especially in cosmetic sites, and prevent parasite spread or recurrence. The main goal of CL treatment is to reduce morbidity.1 Most lesions heal slowly without specific therapy; however, therapy must be considered, especially when the lesions are distressing to the patient, the lesion is complex, or if there is a risk of mucosal disease. Although most of these lesions heal spontaneously, without significant consequences, in addition to the disfiguring scar, some species of the subgenus Viannia are associated with SCI, which can cause a relevant increase in morbidity and mortality.12

There is no drug of choice for the general treatment of CL, because available systemic treatments have significant toxicities and are not equally effective against all Leishmania species, thus differing the choice geographically. Local treatment modalities include cryotherapy, thermotherapy, topical therapy, creams/ointments, and intralesional (IL) medications.

A recent systematic review of IL antimony showed an overall efficacy of 75%.13 The combination of cryotherapy and IL antimony was evaluated in a systematic review and found cure rates of 82% versus 53% with IL antimony

alone.13,14 Intralesional amphotericin may support further research as an alternative to SbV.15 If systemic therapy is required, options are limited and several have the potential for significant adverse effects. In addition, there are special cases. In recent years, an increasing trend has been observed in the number of cases of co-infection by cutaneous and mucosal leishmaniasis with HIV, with a decrease in 2016 and 2019. However, in 2020, the highest proportion of co-infected cases since 2012 was recorded (229 cases). Four countries reported cases of co-infection in 2020: Argentina (1), Colombia (63),

Therefore, the decision of which drug to use needs to be individualized, based on the patient, the infecting species and regionally observed susceptibilities to drugs with a view to drug resistance. For systemic therapy, oral options are an azole (fluconazole, itraconazole, and ketoconazole) and miltefosine. In Brazil, the drugs available for treatment are: Meglumine anmoniate, liposomal amphotericin B, amphotericin B deoxycholate and pentamidine iseonate.11

The average hospitalization cost of a patient with CL is R$428.33, costing the public coffers approximately R$200,000 annually Table 6.0. Most of this cost is due to medications, especially Amphotericin B; high purchasing power medication made available only in the most severe cases or with contraindication to other drugs. Thus, the best way to reduce costs is prevention.

Region	Average value per hospitalization	Number of admissions from 2008-2021	Average admissions per year from 2008-2021	Average annual expenses with hospitalizations
TOTAL	**BRL 428.33**	**6,489**	**463.5**	**BRL 198,530.96**
North region	BRL 466.64	1,041	73.71428571	BRL 34,398.03
Northeast Region	BRL 461.81	2,170	155	BRL 71,580.55
Southeast region	BRL 387.58	2,360	167.8571429	BRL 65,058.07
South region	BRL 361.32	152	10.64285714	BRL 3,845.48
Midwest region	BRL 419.37	749	53.21428571	BRL 22,316.48

Table 6.0Average hospitalization cost of the Brazilian population diagnosed with cutaneous leishmaniasis between the years 2008 and 2021 according to regions of the country by place of residence

Source: Ministry of Health – SUS (Unified Health System) Hospital Information System (SIH/SUS). 2022.

CONCLUSION

Cutaneous leishmaniasis is a disease that is still present and neglected in Brazilian society, affecting mainly the North and Midwest regions; regions with higher incidence of cases and higher mortality rate. This may reflect a lack of assistance ne2rk for people in this region or the lack of awareness on the part of the population to seek an assistance service. The region with the highest number of hospitalizations in the last decade is the Southeast with 36.4% of all cases; This situation changed from 2013 onwards, when the Southeast overtook the Northeast every year in cases of hospitalization. In addition, CL is characterized by affecting more men than women at a rate of 1.9:1, respectively. Furthermore, the peak of cases by age group affected is generally between 50 and 69,

CONFLICT OF INTERESTS

None

FINANCING

Researchers

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