ORIGINAL ARTICLE

SOCIODEMOGRAPHIC, CLINICAL, AND THERAPEUTIC CHARACTERISTICS OF PATIENTS WITH VISCERAL LEISHMANIASIS IN SOUTHWESTERN MARANHÃO, BRAZIL

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Highlights: (1) VL remains highly endemic in southwestern Maranhão. (2) Porto Franco shows the highest HVL incidence; Lajeado Novo the lowest. (3) Predominant HVL profile: male, mixed-race, urban residents aged 1–9 years.

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ABSTRACT

Introduction: Human Visceral Leishmaniasis (HVL) remains a significant public health issue in Brazil, with an estimated 400,000 cases and 20,000 to 40,000 deaths annually. Over the past three decades, the disease has rapidly expanded, primarily due to urbanization, resulting in a shift in its epidemiological profile toward urban centers. Despite this trend, regional data on the sociodemographic, clinical, and therapeutic characteristics of HVL cases remain limited, particularly in Maranhão. This study aimed to fill this gap by characterizing HVL cases in the southwestern region of the state. Methods: A descriptive, cross-sectional, and retrospective study was conducted using data from the Notifiable Diseases Information System (SINAN). HVL cases reported from 2009 to 2018 across sixteen municipalities within the macro-region of the 10th Health Regional Management Unit of Maranhão were analyzed. Results: A total of 623 HVL cases were recorded, with 95% classified as new cases. The incidence rate was 1.15 cases per 100,000 inhabitants over the ten-year period. Most cases involved male children from urban areas, revealing key sociodemographic patterns. Conclusions: The study confirmed the region's high endemicity and the predominance of new HVL cases. These findings highlight the need for enhanced surveillance efforts and underscore the clinical significance of early diagnosis.

Keywords: Visceral Leishmaniasis; Epidemiology; Clinical Profile; Therapeutic Profile; Prevention and Control.

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INTRODUTION

Leishmaniases are a group of diseases caused by protozoa of the genus *Leishmania*, family Trypanosomatidae, transmitted to humans through the bite of infected phlebotomine sandflies. These diseases are present in 97 countries; however, over 90% of new cases reported in 2014 occurred in just six countries: Brazil, Ethiopia, India, Somalia, Sudan, and South Sudan [(1)]. Leishmaniases present in different clinical forms: cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis (MCL), and visceral leishmaniasis (VL) [(2)].

Visceral leishmaniasis presents a broad clinical spectrum, with symptoms ranging from fever to leukopenia. As a disease affecting the reticuloendothelial system, patients typically present with fever, hepatosplenomegaly, and lymphadenopathy. Other common symptoms include weight loss, asthenia/adynamia, and ochrodermia. Due to hypoalbuminemia, some patients may also exhibit pedal edema and ascites [(3)].

The disease often begins with a sudden onset of moderate to high fever, accompanied by chills. Fever may last for weeks and diminish in intensity, with possible afebrile intervals before recurring peaks. Hemolysis frequently results in anemia. The infection also causes leukopenia, compromising immune defense, while thrombocytopenia may lead to hemorrhagic events such as epistaxis, enterorrhagia, and retinal bleeding [(3)].

Currently, the primary treatment for VL in humans (HVL) involves pentavalent antimonial drugs, in use since the 1920s. Amphotericin B, including its lipid formulations, along with paromomycin, miltefosine, and pentamidine, are also employed; however, these drugs are associated with significant toxicity, similar to antimonials [(4)].

Tropical and subtropical regions are the most affected by VL, making it a major public health issue. Being endemic in several parts of the world, VL has an estimated global incidence of 400,000 cases annually, with a mortality ranging between 20,000 and 40,000 deaths per year [(5,7)]. However, due to deficiencies in mandatory reporting systems, surveillance, investigation, and data management in several countries, these figures are likely underestimated. In contrast, since 1984, HVL has been a notifiable disease in Brazil, integrated into the Notifiable Diseases Information System (SINAN) [(8,9)].

In Brazil, rural-to-urban migration has led to the emergence of diseases previously restricted to rural areas in urban environments. This shift is closely linked to poor living

conditions in urban peripheries, such as limited access to public services, which facilitates the adaptation and spread of vectors like *Lutzomyia longipalpis*. Consequently, a transmission cycle once confined to rural areas now also occurs in urban settings [10].

In Brazil, approximately 50% of VL cases are reported in the Northeast region, which remains the most affected. Between 1990 and 2014, the number of reported cases increased from 1,944 to 3,453. In 1990, the Northeast accounted for 85% of cases, and even in 2014—despite the disease's spread to other regions—it was still responsible for 58.5% of national notifications [10,12].

Between 1999 and 2005, the state of Maranhão led Brazil in reported cases of VL. Within the state, the city of Imperatriz recorded the highest incidence between 2000 and 2009 (30.8 cases per 100,000 inhabitants). According to the Brazilian Ministry of Health, Imperatriz is classified as a high-transmission zone [13]. Therefore, quantitative studies addressing the disease's sociodemographic, clinical, and therapeutic aspects are essential, as these indicators reflect the effectiveness of public health policies.

This study aims to characterize the southwestern region of Maranhão in terms of HVL cases, focusing on sociodemographic factors, clinical presentation, diagnosis, treatment, and outcomes, using data from SINAN for the period 2009-2018.

METHODS

The research consisted of a descriptive, cross-sectional, and retrospective study (14) of Human Visceral Leishmaniasis (HVL) cases in the 16 municipalities that comprise the macro-region of the 10th Health Regional Management Unit of Maranhão, spanning the period from 2009 to 2018. Data were obtained through the Notifiable Diseases Information System (SINAN), a service managed by the Epidemiological Surveillance of the Municipal Health Department.

For this study, demographic data were collected based on the 2010 census by the Brazilian Institute of Geography and Statistics (IBGE) and divided into two groups: the eight most populous municipalities and the eight least populous within the macro-region. The most populous municipalities are: Imperatriz, the largest and most populated city among the sixteen in the macro-region, with a territory of 1,368.988 km² and a population of 247,505; João Lisboa,

with a territory of 1,135.211 km² and 20,381 inhabitants; Amarante do Maranhão, with 7,438.217 km² and 37,932 inhabitants; Sítio Novo, with 3,114.871 km² and 17,002 inhabitants; Senador La Rocque, with 738.548 km² and 17,998 inhabitants; Porto Franco, with 1,417.493 km² and 21,530 inhabitants; Estreito, with 2,718.978 km² and 35,835 inhabitants; and Carolina, with 6,441.603 km² and 23,959 inhabitants—all with more than 17,000 inhabitants.

Meanwhile, the municipalities with fewer than 16,000 inhabitants are: Montes Altos, with 1,488.336 km² and 9,413 inhabitants; Lajeado Novo, with 1,064.455 km² and 6,923 inhabitants; São João do Paraíso, with 2,053.843 km² and 10,814 inhabitants; Campestre do Maranhão, with 615.384 km² and 13,369 inhabitants; Governador Edison Lobão, with 615.860 km² and 15,895 inhabitants; Ribamar Fiquene, with 733.830 km² and 7,318 inhabitants; Davinópolis, with 335.767 km² and 12,579 inhabitants; and Buritirana, with 818.424 km² and 14,784 inhabitants. The total population of the macro-region was 513,237.

All reported cases (autochthonous, transferred, and relapses) within the municipalities of the 10th Health Regional Management Unit were included. Cases of visceral leishmaniasis were defined as notifications with a confirmed diagnosis by bone marrow aspiration, indirect immunofluorescence (≥ 1:80), or those with clinical-epidemiological suspicion. Cases reported outside the macro-region, as well as those without clinical suspicion and/or laboratory confirmation (by bone marrow or immunofluorescence), were excluded.

Secondary disease data were obtained from the Ministry of Health's DATASUS system, covering the period from January 2009 to December 2018. The standard data collection form includes eight components: general information, individual notification, residential data, epidemiological history, clinical data, laboratory data/case classification, treatment, and outcome.

The independent variables collected included: year of notification; sex (male or female); race/skin color (White, Black, Asian, Mixed-race, or Indigenous); age (in whole years); educational level (illiterate, incomplete or complete elementary school, incomplete or complete high school, incomplete or complete higher education); area of residence (urban or rural); neighborhood; occupation; clinical manifestations (fever, weakness, edema, weight loss, cough and/or diarrhea, pallor, splenomegaly, infectious syndrome, hemorrhagic events, hepatomegaly, jaundice); HIV co-infection (yes, no, or unknown); parasitological diagnosis (positive, negative, or not performed); immunological diagnosis (positive, negative, or not

performed); type of case entry (new case, transfer, relapse, or unknown); treatment received (pentavalent antimonial, amphotericin B, liposomal amphotericin, or pentamidine); confirmation criteria (laboratory or clinical-epidemiological); autochthonous case from the municipality of residence (yes, no, or undetermined); and case outcome (cure, death, or treatment abandonment).

Initially, data normality for each parameter was tested using the Kolmogorov–Smirnov test. Data were tabulated and analyzed using SPSS Statistics® version 19. Absolute and relative frequencies were calculated for all variables. Annual incidence and prevalence rates for the total study period were determined. The incidence rate was calculated by dividing the number of reported cases by the resident population of the exact location and time and then multiplying by 100,000. This rate was standardized by area of residence, sex, and age, as these variables are available from SINAN/MS and IBGE. A bivariate descriptive analysis was conducted to identify relationships and potential associations between the data and the variables that influence it.

This study complied with the guidelines of Resolution 466/12 of the National Health Council, and data collection only began after approval by the Research Ethics Committee involving Human Subjects (Platform Brazil: CAAE No. 06472118.6.0000.5087, approval No. 3.294.331, dated August 30, 2017). To access the required data in accordance with ethical principles, a declaration of custodianship was submitted to the Epidemiological Surveillance of Imperatriz to obtain permission.

This study followed the basic principles of bioethics: beneficence, ensuring benefits to society, and non-maleficence, ensuring no intentional harm. All information collected was used exclusively for this research. Data privacy was guaranteed, with no individual identification of records, and data handling was the researcher's sole responsibility in compliance with ethical standards.

RESULTS

Between January 2009 and December 2018, 35 deaths from Human Visceral Leishmaniasis (HVL) were recorded out of 623 reported cases in the sixteen municipalities that comprise the macro-region of the 10th Health Regional Management Unit of Maranhão. The

overall incidence rate was 115.15 cases per 100,000 inhabitants, and the case fatality rate over the ten-year period was 5.61%. The municipality with the highest incidence was Porto Franco, with 301.9 cases per 100,000 inhabitants, while the lowest incidence was observed in Lajeado Novo, with 28.8 cases per 100,000 inhabitants.

As shown in Table 1, 66% of the reported HVL cases were male. The municipality with the highest proportion of male cases was Davinópolis (79%). Regarding age, a priori categorization was performed using 10-year intervals, along with separate groups for individuals under 1 year of age and those over 50, in line with IBGE census standards and the typical age profile for disease susceptibility. It was observed that, apart from infants under 1 year, there were no substantial differences among the affected age groups. Nonetheless, the most affected group was children aged 1 to 9 years, accounting for 29% of cases. The municipality with the highest proportion in this age group was Amarante (50%), while Lajeado Novo reported no cases in this group. In contrast, the least affected group was infants under 1 year, with only one case reported in Buritirana.

About ethnicity, there was a notable disparity: 73% of cases occurred in individuals identifying as mixed-race (pardo), followed by White individuals (15%) and Black individuals (8%). The municipality with the highest proportion of mixed-race cases was Lajeado Novo, where all reported cases fell into this category, while the lowest was in Ribamar Fiquene (55%). Only three individuals (1%) identified as Asian. It is also important to note that the majority of HVL cases (86%) occurred in residents of urban areas. Lajeado Novo had the highest percentage of urban residents among HVL cases, whereas Amarante had the lowest (56%).

Table 1 – Sociodemographic Characteristics of Confirmed Human Visceral Leishmaniasis Cases in the Municipalities of the macro-region of the 10th Health Regional Management Unit of Maranhão, from 2009 to 2018.

	TOTAL		IMPERATRIZ		JOÃO LISBOA		AMARANTE		MONTES ALTOS		SÍTIO NOVO		LAJEADO NOVO		SÃO JOÃO DO PARAÍSO		CAMPESTRE	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sex																		
Female	213	34%	89	39%	21	39%	16	24%	4	40%	3	27%	1	50%	5	38%	4	40%
Male	410	66%	140	61%	33	61%	50	76%	6	60%	8	73%	1	50%	8	62%	6	60%
Age Group																		
< 1 year	1	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
1 to 9 years	179	29%	55	24%	7	13%	33	50%	2	20%	2	18%	0	0%	5	38%	3	30%
10 to 19 years	130	21%	24	10%	23	43%	14	21%	0	0%	2	18%	0	0%	2	15%	2	20%
20 to 49 years	167	27%	46	20%	17	31%	13	20%	8	80%	5	45%	2	100%	4	31%	3	30%
> 50 years	146	23%	104	45%	7	13%	7	11%	0	0%	2	18%	0	0%	2	15%	2	20%
Ethnicity																		
Asian	3	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
White	94	15%	37	16%	8	15%	13	20%	1	10%	2	18%	0	0%	1	8%	0	0%
Indigenous	14	2%	1	0%	0	0%	10	15%	0	0%	0	0%	0	0%	0	0%	2	20%
Mixed race	452	73%	166	72%	40	74%	40	61%	7	70%	7	64%	2	100%	12	92%	6	60%
Black	52	8%	24	10%	6	11%	3	5%	1	10%	2	18%	0	0%	0	0%	2	20%
Area of Residence*																		
Rural	74	12%	2	1%	7	13%	25	38%	4	40%	4	36%	0	0%	4	31%	3	30%
Urban	536	86%	225	98%	47	87%	37	56%	6	60%	7	64%	2	100%	9	69%	7	70%
Peri-urban	3	0%	0	0%	0	0%	3	5%	0	0%	0	0%	0	0%	0	0%	0	0%

Table 1 (cont.) – Sociodemographic Characteristics of Confirmed Human Visceral Leishmaniasis Cases in the Municipalities of the macro-region of the 10th Health Regional Management Unit of Maranhão, from 2009 to 2018.

	TOTAL		GOVERNADOR EDISON LOBÃO		RIBAMAR FIQUENE		SENADOR LA ROQUE		DAVINÓPOLIS		BURITIRANA		PORTO FRANCO		ESTREITO		CAROLINA	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sex																		
Female	213	34%	14	33%	8	73%	8	33%	3	21%	4	25%	18	26%	13	30%	2	25%
Male	410	66%	29	67%	3	27%	16	67%	11	79%	12	75%	50	74%	31	70%	6	75%
Age Group																		
< 1 year	1	0%	0	0%	0	0%	0	0%	0	0%	1	6%	0	0%	0	0%	0	0%
1 to 9 years	179	29%	13	30%	6	55%	5	21%	5	36%	5	31%	19	28%	15	34%	4	50%
10 to 19 years	130	21%	12	28%	3	27%	8	33%	2	14%	4	25%	25	37%	8	18%	2	25%
20 to 49 years	167	27%	14	33%	2	18%	8	33%	6	43%	4	25%	18	26%	15	34%	2	25%
> 50 years	146	23%	4	9%	0	0%	3	13%	1	7%	2	13%	6	9%	6	14%	0	0%
Ethnicity																		
Asian	3	1%	2	5%	0	0%	0	0%	0	0%	0	0%	0	0%	1	2%	0	0%
White	94	15%	4	9%	4	36%	3	13%	5	36%	3	19%	6	9%	6	14%	1	13%
Indigenous	14	2%	0	0%	0	0%	0	0%	0	0%	1	6%	0	0%	0	0%	0	0%
Mixed race	452	73%	31	72%	6	55%	19	79%	8	57%	11	69%	57	84%	33	75%	7	88%
Black	52	8%	2	5%	1	9%	2	8%	1	7%	1	6%	4	6%	4	9%	0	0%
Area of Residence*																		
Rural	74	12%	3	7%	2	18%	9	38%	1	7%	2	13%	5	7%	2	5%	1	13%
Urban	536	86%	36	84%	8	73%	15	63%	13	93%	13	81%	62	91%	42	95%	7	88%
Peri-urban	3	1%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%

Regarding the clinical profile presented in Table 2, the most prevalent symptoms among patients were fever (96%), weakness (87%), weight loss (84%), pallor (81%), splenomegaly (84%), and hepatomegaly (62%). The municipalities with the highest proportion of these symptoms were Lajeado Novo (100%), along with Ribamar Fiquene (100% – spleen), Buritirana (100% – fever), and Campestre (100%).

On the other hand, the municipalities with the lowest proportions of these symptoms were, respectively: Campestre, Davinópolis (weakness and weight loss), Estreito, and São João do Paraíso (hepatosplenomegaly). It was also found that 5% of these cases had HIV co-infection, with the highest percentage observed in Campestre (20%)

The method of diagnostic confirmation was also analyzed. It was found that most cases were diagnosed through immunological tests (44%), followed by parasitological diagnosis (23%). The municipality with the highest proportion of diagnoses by immunology was Montes Altos (80%), while the lowest proportions were observed in Gov. Edson Lobão and Amarante (both 23%).

Table 2 – Clinical Profile of Patients Confirmed with Human Visceral Leishmaniasis in the Municipalities of the macro-region of the 10th Health Regional Management Unit of Maranhão, from 2009 to 2018.

	TOTAL		IMPERATRIZ		JOÃO LISBOA		AMARANTE		MONTES ALTOS		SÍTIO NOVO		LAJEADO NOVO		SÃO JOÃO DO PARAÍSO		CAMPESTRE	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Clinical																		
Fever	595	96%	224	98%	51	94%	64	97%	9	90%	10	91%	2	100%	12	92%	8	80%
Weakness	540	87%	211	92%	46	85%	58	88%	8	80%	10	91%	2	100%	12	92%	8	80%
Edema	253	41%	110	48%	15	28%	40	61%	3	30%	2	18%	0	0%	2	15%	5	50%
Weight loss	524	84%	202	88%	48	89%	56	85%	7	70%	9	82%	2	100%	11	85%	6	60%
Cough	293	47%	142	62%	24	44%	28	42%	3	30%	3	27%	1	50%	2	15%	4	40%
Paleness	506	81%	200	87%	39	72%	61	92%	7	70%	10	91%	2	100%	10	77%	7	70%
Enlarged Spleen	523	84%	202	88%	38	70%	61	92%	6	60%	10	91%	2	100%	5	38%	8	80%
Infectious condition	218	35%	76	33%	11	20%	42	64%	2	20%	4	36%	1	50%	7	54%	3	30%
Hemorrhagic phenomenon	39	6%	20	9%	1	2%	3	5%	1	10%	1	9%	0	0%	0	0%	0	0%
Enlarged Liver	384	62%	137	60%	24	44%	54	82%	4	40%	8	73%	2	100%	5	38%	5	50%
Jaundice	177	28%	52	23%	11	20%	40	61%	4	40%	5	45%	1	50%	2	15%	3	30%
Others	65	10%	33	14%	0	0%	11	17%	0	0%	0	0%	0	0%	1	8%	0	0%
HIV Co-infection**	33	5%	22	10%	1	2%	0	0%	1	10%	0	0%	0	0%	2	15%	2	20%
Diagnostic Confirmation																		
Parasitological	145	23%	17	7%	6	11%	33	50%	5	50%	7	64%	0	0%	3	23%	0	0%
Immunological	275	44%	115	50%	32	59%	15	23%	8	80%	3	27%	1	50%	4	31%	4	40%

Table 2 (cont.) – Clinical Profile of Patients Confirmed with Human Visceral Leishmaniasis in the Municipalities of the macro-region of the 10th Health Regional Management Unit of Maranhão, from 2009 to 2018.

	TOTAL		GOVERNADOR EDISON LOBÃO		RIBAMAR FIQUENE		SENADOR LA ROQUE		DAVINÓPOLIS		BURITIRANA		PORTO FRANCO		ESTREITO		CAROLINA	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Clinical																		
Fever	595	96%	42	98%	9	82%	22	92%	13	93%	16	100%	64	94%	41	93%	8	100%
Weakness	540	87%	38	88%	8	73%	19	79%	8	57%	14	88%	53	78%	39	89%	6	75%
Edema	253	41%	23	53%	2	18%	7	29%	3	21%	6	38%	19	28%	12	27%	4	50%
Weight loss	524	84%	39	91%	10	91%	20	83%	8	57%	11	69%	55	81%	35	80%	5	63%
Cough	293	47%	19	44%	6	55%	10	42%	4	29%	9	56%	24	35%	11	25%	3	38%
Paleness	506	81%	33	77%	9	82%	21	88%	12	86%	14	88%	55	81%	19	43%	7	88%
Enlarged Spleen	523	84%	39	91%	11	100%	19	79%	8	57%	14	88%	53	78%	41	93%	6	75%
Infectious condition	218	35%	16	37%	5	45%	7	29%	4	29%	3	19%	30	44%	5	11%	2	25%
Hemorrhagic phenomenon	39	6%	5	12%	3	27%	2	8%	0	0%	0	0%	1	1%	2	5%	0	0%
Enlarged Liver	384	62%	28	65%	8	73%	12	50%	6	43%	6	38%	45	66%	36	82%	4	50%
Jaundice	177	28%	13	30%	7	64%	2	8%	4	29%	7	44%	14	21%	10	23%	2	25%
Others	65	10%	3	7%	1	9%	1	4%	5	36%	1	6%	3	4%	5	11%	1	13%
HIV Co-infection**	33	5%	2	5%	0	0%	0	0%	1	7%	0	0%	0	0%	2	5%	0	0%
Diagnostic Confirmation																		
Parasitological	145	23%	24	56%	2	18%	8	33%	5	36%	5	31%	18	26%	11	25%	1	13%
Immunological	275	44%	10	23%	8	73%	13	54%	8	57%	5	31%	20	29%	27	61%	2	25%

As shown in Table 3, there was a clear predominance of new cases as the type of case entry, accounting for 95% of all reports. Only a small fraction (5%) represented relapses or patient transfers. The municipalities with the highest proportions of relapses were Montes Altos and Campestre (10%), while Sítio Novo reported the highest percentage of transferred cases (18%).

The therapeutic profile was based on the use of three drugs: N-methylglucamine antimoniate, amphotericin B deoxycholate, and liposomal amphotericin B. Among these, N-methylglucamine antimoniate was the most widely administered, used in 78% of cases. Liposomal amphotericin B accounted for 8%, while amphotericin B deoxycholate was used in only 4% of treatments. The highest usage rates for these drugs were observed in Amarante (94% – Glucamine), Montes Altos (20% – Amphotericin B deoxycholate), and Buritirana (19% – Liposomal amphotericin B).

Case outcome analysis considered two main endpoints: cure and death from HVL. Cure was the most frequent outcome, recorded in 73% of cases, whereas HVL-related death occurred in 6% of closed cases. Lajeado Novo had the highest cure rate (100%), while Campestre had the lowest (20%) and simultaneously presented the highest case fatality rate (30%).

Table 3 – Therapeutic Profile of Confirmed Human Visceral Leishmaniasis Patients in the Municipalities of the macro-region of the 10th Health Regional Management Unit of Maranhão, from 2009 to 2018

	TOTAL		IMPERATRIZ		JOÃO LISBOA		AMARANTE		MONTES ALTOS		SÍTIO NOVO		LAJEADO NOVO		SÃO JOÃO DO PARAÍSO		CAMPESTRE	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Type of Admission																		
New cases	591	95%	221	97%	47	87%	65	98%	8	80%	9	82%	2	100%	12	92%	8	80%
Relapses	15	2%	7	3%	4	7%	0	0%	1	10%	0	0%	0	0%	1	8%	1	10%
Transfer	13	2%	1	0%	2	4%	1	2%	0	0%	2	18%	0	0%	0	0%	0	0%
Initial Drug																		
N-methyl glucamine antimoniate	489	78%	195	85%	30	56%	62	94%	5	50%	8	73%	1	50%	6	46%	6	60%
Amphotericin B deoxycholate	25	4%	13	6%	2	4%	1	2%	2	20%	0	0%	0	0%	0	0%	1	10%
Liposomal amphotericin B	47	8%	19	8%	4	7%	1	2%	0	0%	2	18%	0	0%	2	15%	0	0%
Case Outcome																		
Cure	455	73%	195	85%	30	56%	52	79%	7	70%	8	73%	2	100%	8	62%	2	20%
Deaths due to Visceral Leishmaniasis	35	6%	14	6%	2	4%	2	3%	0	0%	1	9%	0	0%	2	15%	3	30%

Table 3 (cont.) – Therapeutic Profile of Confirmed Human Visceral Leishmaniasis Patients in the Municipalities of the macro-region of the 10th Health Regional Management Unit of Maranhão, from 2009 to 2018

	TOTAL		GOVERNADOR EDISON LOBÃO		RIBAMAR FIQUENE		SENADOR LA ROQUE		DAVINÓPOLIS		BURITIRANA		PORTO FRANCO		ESTREITO		CAROLINA	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Type of Admission																		
New cases	591	95%	40	93%	11	100%	24	100%	14	100%	15	94%	65	96%	43	98%	7	88%
Relapses	15	2%	1	2%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Transfer	13	2%	2	5%	0	0%	0	0%	0	0%	1	6%	3	4%	0	0%	1	13%
Initial Drug																		
N-methyl glucamine antimoniate	489	78%	37	86%	8	73%	19	79%	10	71%	9	56%	57	84%	29	66%	7	88%
Amphotericin B deoxycholate	25	4%	0	0%	0	0%	1	4%	0	0%	1	6%	1	1%	3	7%	0	0%
Liposomal amphotericin B	47	8%	4	9%	2	18%	3	13%	0	0%	3	19%	1	1%	5	11%	1	13%
Case Outcome																		
Cure	455	73%	30	70%	6	55%	12	50%	9	64%	7	44%	54	79%	31	70%	2	25%
Deaths due to Visceral Leishmaniasis	35	6%	3	7%	1	9%	2	8%	0	0%	1	6%	1	1%	3	7%	0	0%

Over the 10-year analysis period, the municipality most affected by HVL was Porto Franco, with an incidence rate of 301.9 cases per 100,000 inhabitants. The most affected age group was individuals over 50 years, followed by children aged 1 to 9 years. The predominant ethnic group was mixed-race (pardo). A clear predominance of urban residents was observed, accounting for 98% of patients. The clinical profile observed in Imperatriz closely reflects the general pattern: patients typically presented with fever, weakness, pallor, weight loss, and hepatosplenomegaly. HIV co-infection was identified in 10% of patients, and half of the cases were diagnosed through immunological testing. With the exception of 3% relapse cases, all others were classified as new cases (97%). N-methylglucamine antimoniate was used in 85% of treatments, and 85% of patients achieved cure.

In contrast, the municipality least affected by the disease was Lajeado Novo, with an incidence of 28.8 cases per 100,000 inhabitants and zero lethality, meaning all cases progressed to cure. Both sexes were equally affected, and all patients were between 20 and 49 years old, identified as mixed-race (pardo), and resided in urban areas. The clinical presentation mirrored both the general profile and that observed in Imperatriz, with fever, weakness, pallor, weight loss, and hepatosplenomegaly. No HIV co-infection was reported. Immunological methods diagnosed half of the cases. All were classified as new cases, and the only drug used was N-methylglucamine antimoniate.

DISCUSSÃO

In Brazil, VL is considered an endemic and neglected disease. In 2017, the state of Maranhão led national notification statistics, with an incidence of 10.66 cases per 100,000 inhabitants, accounting for 34.73% of all cases reported in the Northeast region [15]. This finding, combined with the incidence of 115.15 cases per 100,000 inhabitants recorded from 2009 to 2018 in the 10th Regional Health Management Unit of Maranhão, indicates that the macro-region studied presents alarmingly high numbers within the state context.

Consistent with other studies, this research revealed a predominance of HVL among males. This trend may be attributed to increased male exposure to environments where the vector is present, such as agricultural areas, engineering projects, or rural settlements in deforested zones. However, there is no strong scientific evidence to support the hypothesis of

greater physiological susceptibility or higher morbidity and mortality among males. HVL can occur and progress similarly in both sexes [13,16].

The pediatric age group is commonly associated with high morbidity and mortality rates, as well as elevated disease prevalence. In line with this, our study found that children aged 1 to 9 years were the most affected group across all sixteen municipalities. In Amarante, 50% of cases fell within this age group, possibly reflecting the population's nutritional and socioeconomic status. These findings may be justified by the immaturity of the immune system in children; in addition, malnutrition is a known risk factor for immunosuppression and is frequently observed among children in northeastern Brazil [17,19].

Most cases occurred in individuals self-identified as mixed-race (pardo), which may reflect the ethnic composition of the studied municipalities. For example, in Lajeado Novo, 100% of patients were reported as mixed-race, though this may also be due to the low absolute number of cases (only two). Furthermore, a study by Bruhn et al. (2018) in Belo Horizonte (MG) showed increased susceptibility to HVL among mixed-race and Black populations, likely due to lower socioeconomic status and greater social vulnerability [19].

Over the ten years analyzed, 86% of patients reported living in urban areas. This proportion may be explained by the adaptation of the Lutzomyia longipalpis vector to peridomestic environments, and reinforced by the presence of domestic dogs, which are the primary non-human reservoirs of the disease. Conversely, Amarante had the lowest proportion of urban-dwelling patients, though still significant (56%). This may reflect regional sociocultural factors and the vector's high adaptive capacity. Even with urban adaptation, the vector remains viable in rural environments. Additionally, the attraction and maintenance of the vector can be influenced by poor sanitation conditions, particularly the inadequate disposal of organic waste from domestic animals, which is relevant in both urban and rural settings[6].

The symptoms of fever, weakness, pallor, weight loss, and hepatosplenomegaly characterized the clinical profile of patients in this study. This presentation, along with ochrodermia, aligns with the classical clinical picture described in the literature [3,5], representing the pre-hospital phase of the disease. Initial symptoms may hinder diagnosis due to their nonspecific nature.

During the study period, 33 cases of HIV co-infection were reported across the sixteen municipalities, representing 5% of total HVL cases. The highest number was recorded in

Imperatriz, with 22 co-infected patients (10% of the city's total HVL cases). However, in proportional terms, Campestre was the most affected, with 2 out of 10 HVL cases (20%) presenting HIV co-infection. Although these numbers may appear modest, HIV-HVL co-infection is known to significantly increase lethality, for two key reasons: the high toxicity of HVL treatments—including liposomal amphotericin B, considered the least toxic—and the reduced treatment response due to HIV-related immunosuppression, which prolongs exposure to toxic drug effects [9,20].

Immunological testing accounted for 44% of case confirmations, underscoring its role as the primary method in public health programs. Montes Altos had the highest rate of immunological diagnoses, indicating effective implementation of Ministry of Health protocols [21].

The analysis also showed that 95% of cases were classified as new, while only 2% were relapses (defined as the reappearance of symptoms more than 12 months after cure). On one hand, the low relapse rate may reflect the high efficacy of the medication used. On the other hand, the high number of new cases may indicate continued exposure to risk factors. Porto Franco had the highest incidence during the study period, with 301.9 cases per 100,000 inhabitants. This may indicate ineffective epidemiological surveillance and a lack of preventive strategies, particularly when compared to other municipalities [13].

The most widely used drug was N-methylglucamine antimoniate (78%), while the remaining 22% included amphotericin B deoxycholate, its liposomal formulation, and other medications. This predominance is likely due to Ministry of Health guidelines recommending N-methylglucamine antimoniate as the first-line treatment. Amarante had the highest usage rate of this drug (94%), while São João do Paraíso had the lowest (46%). These differences may be related to adherence to Ministry of Health protocols, drug availability, and the number of untreated patients [8,13].

CONCLUSION

The findings show that the region remains highly endemic, with most cases classified as new (95%) and predominantly affecting males, children aged 1–9 years, and urban residents.

The municipality of Porto Franco presents the highest incidence rate, while Lajeado Novo shows the lowest and reports no deaths during the study period. The clinical presentation is consistent across municipalities, commonly involving fever, weakness, pallor, weight loss, and hepatosplenomegaly. Immunological testing is the primary diagnostic method, and N-methylglucamine antimoniate is the most frequently used treatment.

The predominance of new cases suggests ongoing exposure to risk factors and underscores the need to strengthen surveillance and prevention efforts. These findings contribute to understanding the local dynamics of HVL and support public health interventions in similar endemic settings.

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SOCIODEMOGRAPHIC, CLINICAL, AND THERAPEUTIC CHARACTERISTICS OF PATIENTS WITH VISCERAL LEISHMANIASIS IN SOUTHWESTERN MARANHÃO, BRAZIL

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