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Epidemiological aspects of Human Visceral Leishmaniasis in the state of Piauí, Brazil (2007-2017)

Aspectos epidemiológicos da Leishmaniose Visceral Humana no estado do Piauí, Brasil (2007-2017)

Aspectos epidemiológicos de la Leishmaniasis Visceral Humana en el estado do Piauí, Brasil (2007-2017)

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ABSTRACT

Background and Objectives: Visceral leishmaniasis presents considerable expansion in urban centers in the state of Piauí and its occurrence is marked by successive records of outbreaks. To analyze the reported cases of Human Visceral Leishmaniasis in Piauí, between 2007 and 2017. **Methods**: The data about the number of cases and variables such as distribution in time, space and some characteristics of the affected people, deaths and diagnosis were obtained from Notifiable Diseases Information System (SINAN-Datasus) **Results**: 2,447 cases were reported, of which 2,265 autochthonous cases (92.56%). The conclusive diagnosis was made in 86.6% of the cases. The year with the highest record (283 cases) was 2014, also the annual lethality rate was 14.1%. Positive cases were registered in residents of 183 municipalities (81.7%). The capital Teresina presents the highest number of cases in residents (734.30%) and notification (1,859, 75.97%). Males (66.30%) were the most affected and individuals under 10 years old (43.44%). Regarding education, the classification "does not apply" (39.84%) was the most prevalent, as well as brown race/color (88.27%) and the urban residential area (67.63%). **Conclusion**: Epidemiological assay provides knowledge about the real epidemiological situation in the state of Piauí, such as profile characterization, frequency of cases occurrence, assisting in actions for control and eradication of the disease in the state.

Keywords*: Leishmania (Leishmania) infantum; Public Health; Epidemiological Monitoring.*

RESUMO

Justificativa e Objetivos: A leishmaniose visceral apresenta considerável expansão em centros urbanos no Piauí, e a sua ocorrência é marcada por sucessivos registros de surtos. O objetivo deste estudo foi analisar os casos notificados de Leishmaniose Visceral Humana no Piauí, entre os anos de 2007 e 2017. **Métodos**: Os dados sobre

os números de casos e variáveis, como a distribuição no tempo, no espaço e algumas características das pessoas atingidas, óbitos e diagnóstico, foram através do Sistema de Informação de Agravos de Notificação (SINAN-Datasus). **Resultados**: Foram notificados 2.447 casos, com 2.265 casos autóctones (92,56%), e o diagnóstico laboratorial conclusivo foi realizado em 86,6% dos casos. O ano de 2014 foi o ano com maior registro (283 casos) e maior coeficiente de letalidade anual de 14,1%. Ao todo, 183 municípios (81,7%) apresentaram casos positivos em residentes. Na capital, Teresina, ocorreu o maior número de casos em residentes (734 casos, 30%) e foi o município que mais notificou em todo o estado (1.859 casos, 75,97%). Os mais acometidos foram indivíduos do sexo masculino (66,30%) e faixa etária menor que 10 anos (43,44%). Em relação à escolaridade, a classificação "não se aplica" foi mais prevalente (39,84%), assim como a raça/cor parda (88,27%) e a zona residencial urbana (67,63%). **Conclusão**: A realização destas análises fornece informações sobre a situação epidemiológica da leishmaniose visceral no Piauí em uma série histórica de 2007 a 2017, como a distribuição espacial dos casos, municípios com maiores incidências, a dificuldade de acesso ao diagnóstico, grupos sociais mais acometidos e óbitos, podendo auxiliar no direcionamento das ações para o controle da doença no estado.

***Descritores**: Leishmania (Leishmania) infantum; Saúde Pública; Monitoramento Epidemiológico.*

RESUMEN

Justificación y Objetivos: La Leishmaniasis visceral presenta una expansión considerable en los centros urbanos de Piauí, y su aparición está marcada por sucesivos registros de brotes. Analizar los casos reportados de Leishmaniasis Visceral Humana en Piauí, entre los años 2007 a 2017. **Métodos**: Datos sobre el número de casos y variables como distribución en tiempo, espacio y algunas características de las personas afectadas, defunciones y diagnóstico fueron obtenido mediante el Sistema de Información de Enfermedades Notificables (SINAN-Datasus). **Resultados**: Fueron notificados 2.447 casos, con 2.265 casos autóctonos (92,56%). El diagnóstico de laboratorio concluyente se realizó en el 86,6% de los casos. 2014 fue el año con el récord más alto (283 casos) y la tasa de letalidad anual del 14,1%. 183 municipios (81,7%) presentó casos positivos en residentes. La capital Teresina tuvo el mayor número de casos en residentes (734 casos, 30%) y fue el municipio que más reportó en todo el estado (1.859 casos, 75,97%). Los más afectados pertenecían al sexo masculino (66,30%) y los menores de 10 años (43,44%). En cuanto a la educación, la clasificación "no aplica" fue más prevalente (39,84%) y la zona residencial urbana (67,63%). **Conclusión**: La realización de estos análisis aporta conocimiento sobre la situación epidemiológica en Piauí en una serie histórica de 2007 a 2017, como la caracterización de los casos, las fallas en los registros y la frecuencia de ocurrencia de los casos, ayudando a orientar las acciones para el control en el estado.

***Palabras clave**: Leishmania (Leishmania) infantum; Salud Pública; Monitoreo Epidemiológico.*

INTRODUCTION

Leishmaniasis is a group of parasitic diseases caused by the infection of protozoa of the genus Leishmania spp., transmitted to humans through the bite of hematophagous insects, sandflies female. Its present in four clinical forms: visceral leishmaniasis (VL); post-kala azar dermal leishmaniasis (PKDL); cutaneous leishmaniasis (CL); mucocutaneous leishmaniasis (MCL).[1] VL is considered the most serious and can be fatal in humans when left untreated, especially in vulnerable groups such as malnourished children and individuals with human immunodeficiency virus (HIV) infection.[2]

The World Health Organization (WHO) considers a disease with increasing notification in worldwide; however, more than 90% of new cases are concentrated in six countries, Bangladesh, Brazil, Ethiopia, India, Sudan, and South Sudan, with approximately 350 million people exposed to the risk of infection[1]. In the Americas, its etiological agent is the protozoan *Leishmania (Leishmania) infantum chagasi*.[3] *Lutzomyia longipalpis* is the most relevant sandfly species in Brazil.[4]

VL are a dynamic disease with transmission in areas wild/rural and urban. In Brazil, the urbanization process of Human Visceral Leishmaniasis (HVL) can be related to different factors, namely: environmental changes caused by anthropic actions, associated with the rapid process of human occupation in peri-urban areas; the interaction between wild and urban reservoirs and the mobilization of infected animals to areas without transmission; the adaptation of the vector *L. Longipalpis*, with feeding eclecticism and presence in the peridomicile; and the domestic dog (*Canis lupus familiaris Linnaeus*, 1758), considered the main urban reservoir host of *L. (L.) infantum chagasi*.[1,3]

For infection diagnosis, the Ministry of Health (MoH) recommends the application of rapid screening tests (immunochromatographic TR-DPP-Bio-Manguinhos) and confirmatory test, which can be serological tests (Indirect Immunofluorescence Assay - IFA and Enzyme Linked Immunosorbent Assay – ELISA), direct parasitological examination (finding the parasite in bone marrow, spleen, liver or lymph node tissue), culture, PCR test or real-time PCR.[2] When there is no possibility of diagnosis laboratory, clinical and epidemiological findings are considered for notify the cases.[5]

The clinical manifestations of HVL are considered

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nonspecific, and are characterized by presenting signs and symptoms of chronic disease, making clinical diagnosis difficult for early treatment. The severity of clinical manifestations can be associated with patients' age, nutritional status and immunogenetic characteristics. In severe cases, the evolution of the clinical condition occurs for voluminous hepatosplenomegaly, persistence of fever, pallor and progressive weight loss.[2,6]

Compulsory notification combined with surveillance of human and canine cases is considered essential for directing control actions. Currently, the MoH and the Ministry of Agriculture, Livestock and Food Supply (MAPA - *Ministério de Agricultura, Pecuária e Abastecimento*), through the State and Municipal Health Departments, conduct the Visceral Leishmaniasis Control Program (VLCP)[2,7,8]

Control measures are turned at dogs and vector insects. For the dog, topical insecticides and repellents can be used, collars impregnated with 4% deltamethrin, vaccination, treatment with miltefosine for positive cases and canine euthanasia in positive cases, with the guardian's consent.[2,9] For the insect vector, the use of chemical insecticides is still one of the most used measures. Despite continuous and intensive control campaigns, many difficulties are found throughout Brazil, such as the difficulty in obtaining a quick and effective diagnosis in epidemiological surveys, especially with regard to dogs and the population's refusal to chemical control, which is considered ineffective due to the probable resistance of *L. longipalpis* to the chemical compounds used.[2,10]

The Northeast Region is the one that most notifies cases of HVL throughout Brazil, corresponding 77% of cases. Notification is carried out by health surveillance departments and collected by SINAN (Disease and Notification Information System - *Sistema de Informação de Agravos de Notificação*).[4] In the state of Piauí, the occurrence of HVL has been known since 1934, with the record of successive epidemic outbreaks in the capital Teresina from the 1980s onwards. Since then, it has been considered a priority area for control measures, which despite this, has not impeded its advance in urban areas and occurrence in a lot municipalities.[11,12]

Therefore, the aim of this study was to analyze the reported cases of HVL in Piauí between 2007 and 2017, with identification of epidemiological aspects of the disease in the state.

METHODS

This is a retrospective epidemiological study about the occurrence of HVL cases in the state of Piauí, notified by SINAN through the virtual public domain platform Datasus provided by the MoH.

The state of Piauí is located in northeastern Brazil, has an approximate area of 251.756 km² and 224 municipalities, with an estimated population of 3.273.227 inhabitants, a demographic density of 12.40 inhabitants/km² in 2019 and more than 2 million people living in urban area, with an average nominal per capita income of R$ 827.00. The capital, Teresina, has a territorial area of 1.391.046 km² and a demographic density of 584.94 hb/km², with an estimated population of 864.845 inhabitants.[13]

The state is in areas belonging to the Caatinga (a type of desert vegetation in Brazil), Cerrado (a vast tropical savanna ecoregion of Brazil) biomes and transition areas between Caatinga/Cerrado, with an average temperature of approximately 27.6ºC and an average annual precipitation of less than 800 mm.[14]

The data included in this study correspond to the 2007-2017 period, obtained with TabWin 32 and tabulated in Microsoft Office Excel 2016. The mapping of notified cases was prepared using QGIS 3.10.

Variables were analyzed according to SINAN registration, number of autochthonous cases, confirmatory criterion, municipality of notification and residence of the case, death, gender, age, education, race/skin color and area of residence (urban or rural). Annual coefficients of incidence per 10,000 inhabitants and lethality per 100,000 inhabitants were calculated, by dividing the absolute number of deaths by the number of reported cases, multiplied by 100. To perform this study, it was not necessary to be submitted to an Institutional Review Board, as the data used are freely accessible.

RESULTS

Between 2007 and 2017, 2,447 cases of HVL in the state of Piauí were notified, 2,265 autochthonous cases (92.56%) and laboratory diagnosis. For confirmation, there were performed in 2,119 cases (86.6%) (Table 1).

Table 1. Autochthonous cases and confirmatory criterion of Human Visceral Leishmaniasis reported in the state of Piauí from 2007 to 2017.

Autochthonous cases	Total	(%)
Yes	2.265	92,56
Not	61	2,49
No answer	1	0,04
Indeterminate	120	4,91
Confirmatory criterion		
Laboratorial	2.119	86,6
Clinical-epidemiological	328	13,4

Source: Ministry of Health/SVS - Information System for Notifiable Diseases – SINAN

The highest register of cases occurred in 2007, 2008 and 2014, with 253, 279 and 283 cases respectively, while 2010 was least reported cases (157), followed by 2009 and 2016, both with notification of 158 cases. Thus, 161 cases evolved to death between 2007 and 2017, with a total lethality rate of 6.64% in state. The highest numbers of death occurred in 2009 (12.5%), 2014 (14.1%) and 2017 (12.5%). Especially, 2014 was the year with the highest notification (283 cases) and the highest lethality rate (14.1%). The lower lethality rate was recorded in 2012 (4.4%) (Figure 1).

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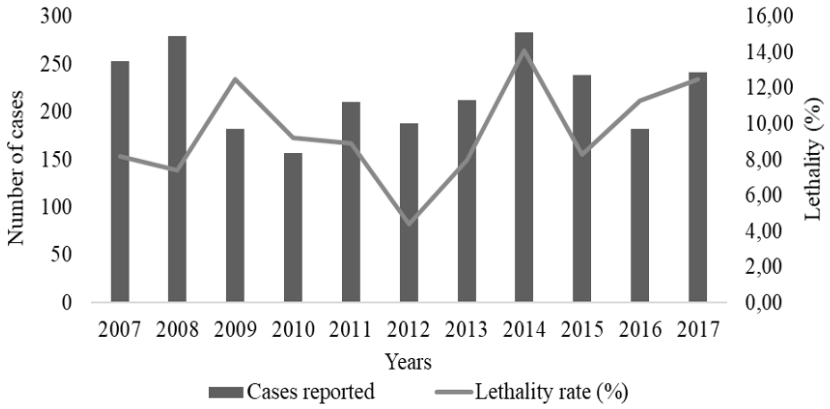

Figure 1. Reported cases of Human Visceral Leishmaniasis and lethality rates (per 100,000 inhabitants) in the state of Piauí from 2007 to 2017.
Source: Ministry of Health/SVS - Information System for Notifiable Diseases – SINAN.

In state, cases of HVL occurred in 183 municipalities (81.7%). In relation to the municipality of residence, in Teresina, the highest number of cases was notified, 734 cases (30%), followed by municipalities of Parnaíba, 123 cases (5.02%) and Miguel Alves, 102 (4.16%), being the only municipalities that registered more than 100 cases of HVL in residents in 2007-2017 (Figure 2).

Among the municipalities with the highest number of cases, the highest concentration of notification was observed in the capital Teresina (Table 2), representing 75.97%, with incidence of 9.01/10,000 inhabitants. In the capital, the lethality rates were 8.86%, with 65 deaths of residents, representing the higher concentration of notification of deaths by HVL in the state. However, the higher incidence of cases occurred in the municipality of Miguel Alves (31.58) and the mortality coefficient of 8.82%, close to result in Teresina.

The most affected with HVL were males (66.30%). The age that prevailed among the notifications was in children under 10 years old (43.44%) and people aged between 20 to 59 years old (41.60%), the lowest incidence was observed in the elderly over 80 years old, which represented 0.86% of reported cases (Table 3).

Education was the variable that showed the most di-

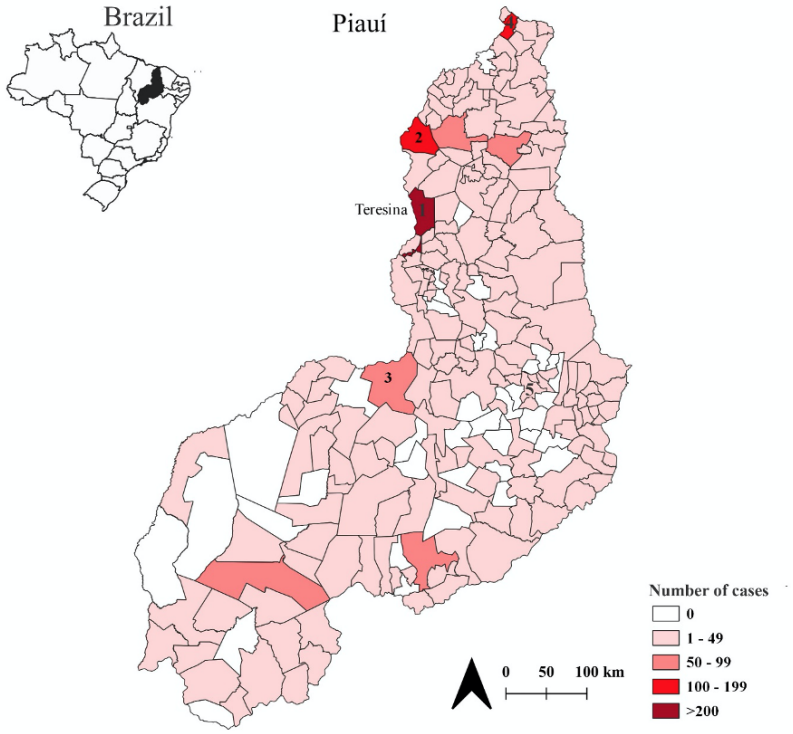

Figure 2. Reported cases of Human Visceral Leishmaniasis (n=2,447) according to the municipality of residence, Piauí, from 2007 to 2017. Municipalities with the highest number of notifications: 1. Teresina; 2. Parnaíba; 3. Floriano; 4. Miguel Alves; 5. Picos.
Source: Ministry of Health/SVS - Information System for Notifiable Diseases – SINAN.

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Table 2. Cities with the highest notifications of Human Visceral Leishmaniasis with data about the incidence, number of deaths in residents and mortality rate in the state of Piauí from 2007 to 2017.

City	N. of reported cases (%)	Incidence per 10,000 inhab.	Deaths in residents	Lethality rate (%) per 100,000 inhab.
1. Teresina	1.859 (75,97)	9,01	65	8,86
2. Parnaíba	132 (5,4)	8,44	6	4,79
3. Floriano	68 (2,78)	12,83	4	5,2
4. Miguel Alves	45 (1,84)	31,58	9	8,82
5. Picos	36 (1,47)	6,13	3	6,7

Source: Ministry of Health/SVS - Information System for Notifiable Diseases – SINAN. Abbreviations: N. - number; inhab. - inhabitants.

Table 3. Reported cases of Human Visceral Leishmaniasis in the state of Piauí, from 2007 to 2017, according to the variables gender, age, education level, race/skin color and residence area.

Variables	Total (n=2.447)	(%)
Gender		
Male	1,621	66.3
Female	824	33.7
Age		
< 10 years old	1,063	43.44
10 to 19 years old	201	8.21
20 to 59 years old	1,018	41.6
60 to 79 years old	144	5.88
> 80 years old	21	0.86
Education		
Ignored/white	193	7.89
Illiterate	84	3.43
Incomplete basic level	212	8.66
Complete basic level	61	2.49
Incomplete elementary school	399	16.31
Complete elementary school	293	11.97
Incomplete high school	148	6.05
Complete high school	65	2.66
Incomplete higher education	6	0.25
Complete higher education	11	0.45
Not applicable	975	39.84
Race/skin color		
Ignored/white	60	2.45
White	109	4.45
Black	93	3.80
Yellow	19	0.78
Brown	2,160	88.27
Indigenous	6	0.25
Residence area		
Ignored/white	83	3.39
Urban	1,655	67.63
Rural	700	28.61
Peri-urban	9	0.37

Source: Ministry of Health/SVS - Information System for Notifiable Diseases – SINAN.

vergences in notification, 39.84% of them were classified as "not applicable", not presenting necessary information to understand the profile of affected individuals. However, it was possible to observe the notification of 16.31% of cases for patients with incomplete elementary school and 11.97% for complete elementary school. In individuals with incomplete or complete higher education, an occurrence percentage of 0.25% and 0.45%, respectively, was observed.

Brown race/skin color had the highest incidence (88.27%), while other in this variable were below 5% of occurrence among the notified cases. The main residence area notified for HVL was the urban (67.63%), while the rural area registered 28.61%. It is worth highlighting the notification of ignored/white cases in this variable as being 3.39% (Table 3).

DISCUSSION

In this study, it was possible to verify the notification of 2,447 cases of HVL in the state of Piauí between 2007-2017, with a total lethality rate of 6.64% (161 deaths). In 2014, 283 cases were notified with a lethality rate of 14.1%, the highest number. The year 2010 was the year that least notified cases of HVL (157 cases), and in 2012 there was the lowest lethality rate.

In Piauí, 2014, had a higher lethality rate than the Northeast region (7.9%) and Brazil (8%), as well as in 2009 and 2017, when rates of 5.6% and 9.6% were registered, respectively, while for the Northeast the records were 6.9% and 8.8%, respectively.[15]

Mortality from VL, in most cases, is related to the absence of treatment and greater occurrence is in groups considered vulnerable and affected by other comorbidities, e.g., malnourished children, the elderly and people with HIV.[4] Another factor that can be highlighted for the occurrence of deaths in the state is the inequality in distribution of care services, leading to late diagnosis and difficulty in accessing healthcare services for less favored social groups and people living in cities in the state countryside, resulting in late treatment.[16]

Laboratory diagnosis was performed in 86.6% of cases in the state of Piauí and clinical and epidemiological criteria were considered for diagnosis in 13.4% of cases. It can be noted that the adoption of more accurate confirmatory methods is being used for diagnosis, e.g., direct parasitological examination and IFA, which have increased significantly in Brazil in recent years.[17]

As for the municipality of residence, it can be seen that HVL is well distributed in the state, occurring in 81.7% of the municipalities. About this aspect, it was possible to observe the spatial distribution of HVL, highlighting areas with a high number of cases in residents, and, therefore,

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a higher risk of transmission. This classification of areas is important from the point of view of epidemiological monitoring for directing control actions. [18]

Municipalities without notification, or even with few cases, may have underreporting, due to the difficulty in accessing diagnosis, which may happen throughout the state as a result of failures in healthcare services.[19]

In Teresina, there were 75.97% of notifications and 30% of cases resided in the capital, with an incidence of 9.01. This result can be associated with the greater offer of healthcare services in Teresina compared to other municipalities in the state. The number of services provided to the population in interior cities is insufficient, requiring the displacement of residents to other municipalities in search of healthcare services. [13] Regarding the fact that 30% of cases are residents of Teresina, it can be attributed to its population density, the municipality of Teresina is one of the most populous in the state, concentrating 26.42% of the total population of Piauí, followed by the municipality of Parnaíba (4.67%), the second in relation to the number of affected residents with HVL (5.4%) in the state.

The high number of cases in Teresina, presented in this historical series, may be mainly related to the occupation of land close to forests and pastures.[20] In this case, the accelerated urbanization process resulted in the adaptation of the vector, sandflies, to the peridomicile and in precarious living conditions, resulting in the high occurrence of HVL in the capital.

In Piauí, the profile of affected by HVL is mostly represented by males (66.3%), patients under 10 years old (43.44%), of brown race/skin color (88.27%) and with incomplete elementary school education (16.31%), despite the classification "not applicable" being predominant in the notifications (39.84%), which may be associated with preschool children. Similar results were observed throughout Brazil in recent years.[17]

According to data from the IBGE Social Indicators Synthesis released in 2017, Piauí ranks 6th, compared to other states, about the number of people living in poverty, is represented by 45.3% of the population in the state.[21] Sanitation in Teresina, assessed by *Instituto Trata Brasil*, through the Brazilian National Survey of Continuous Household Sample (PNAD - *Pesquisa Nacional por Amostra de Domicílios Contínua*), found that 76.5% of households do not have adequate sanitation with drinking water supply, garbage collection, sewage, street cleaning and rainwater management. These aspects may be high in other municipalities in the state.[22] These socioeconomic and environmental data point to social groups that live in conditions of poverty, lack of basic sanitation and deprived of access to information as being those at greatest risk of contracting the infection.

Regarding the insect vector, in Teresina, its habitats are related to places close to homes with animal husbandry and accumulation of organic matter.[23] From this vector behavior, it can be inferred that *L. longipalpis* is found adapted to urban conditions throughout the state, mainly related by cases reported in urban residents (67.63%) and autochthonous cases (92.56%). Furthermore, more investigative studies about the conditions the establishment of *L. longipalpis* in the state are still needed.

The epidemiological data presented in this study may differ from reality, given the difficulty of accessing healthcare services in many municipalities, failures in diagnosis, incomplete notification and heterogeneity in the municipality's epidemiological surveillance actions, which results in possible failures and reduction the reliability of information contained in SINAN.[23] Thus, a more serious situation than the one presented here may be occurring, requiring further analysis of the underreporting of cases in the state. The constant epidemiological surveillance of canine and human cases is one of the most used strategy when it comes to contribute to information to guide VL control, which leads to considering the importance of epidemiological studies in the area to predict future outbreaks and their territorial dissemination.[24]

Therefore, the results of this historical series are important for providing relevant information on the epidemiological situation of HVL in the state of Piauí, such as the spatial distribution of cases, municipalities with higher incidences, difficulty in accessing diagnosis, social groups more affected and deaths, serving to direct actions to control the disease. But for these actions to be effective and efficient, it is necessary to overcome the challenges posed by barriers to accessing real information about the disease, improvements in sanitation and effective systematization of health surveillance in the state. It is also worth the importance of assessing and reviewing the actions used for diagnosis, making it timelier and more accessible, as well as sandfly control, which must be monitored frequently to prevent future outbreaks, especially in urban centers.

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Henrique Rafael Pontes Ferreira, Ana Carolina Landim Pacheco e Marcia Maia Mendes Marques contributed to the conception, design of the article, analysis and writing of the article; **Henrique Rafael Pontes Ferreira, Ana Carolina Landim Pacheco e Marcia Maia Mendes Marques** contributed to the planning and design of the article, review and final approval of the article. All authors have approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and completeness.