

## Epidemiological approach and management of Human Visceral Leishmaniasis in Brazil



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**Alyce Araújo Sabino de Aguiar**

Medical Students of UNITPAC ARAGUAÍNA

**Camila Karielle Sousa Carvalho Pinto**

Medical Students of UNITPAC ARAGUAÍNA

**Gabryella Trindade Vieira**

Medical Students of UNITPAC ARAGUAÍNA

**Gustavo Cardoso Costa**

Medical Students of UNITPAC ARAGUAÍNA

**Hanne Karoline Lopes Oliveira**

Medical Students of UNITPAC ARAGUAÍNA

**Heloisa Cardoso Gomes**

Medical Students of UNITPAC ARAGUAÍNA

**Marlon Cantillo da Luz**

Medical Students of UNITPAC ARAGUAÍNA

**Rebecca Padilha Santos**

Medical Students of UNITPAC ARAGUAÍNA

**Vitor Emanuel Barbosa da Silva**

Medical Students of UNITPAC ARAGUAÍNA

**Yasmin Gondim de Paiva Faria**

Medical Students of UNITPAC ARAGUAÍNA

### ABSTRACT

Human Visceral Leishmaniasis (HVL) is caused by obligate intracellular protozoa of the genus *Leishmania* which, depending on the species, results in different clinical manifestations, treatments, and prognosis. Considered a neglected tropical disease and, because it represents a high severity index and a high lethality rate in humans, in addition to the wide geographic distribution of vector transmission, it is necessary to pay attention to compulsory notifications, health education measures and effective disease prevention, collaborating in the control and eradication of the disease.

**Keywords:** Visceral Leishmaniasis, Tropical diseases, Neglected diseases.

### 1 INTRODUCTION

Human Visceral Leishmaniasis (HVL), also known as Kala-azar, is a serious pathology caused by obligate intracellular protozoa of the genus *Leishmania*, which, depending on the species, results in different clinical manifestations, treatments, and prognosis. Considered an issue of negligence in global public health, especially in countries with tropical climates, it results in high mortality, especially in underdeveloped regions, due to its association with malnutrition and opportunistic infections. In South America, Brazil is responsible for about 96% of the cases, distributed throughout the national territory, with a predominance in the Northeast region.

In Brazil, the etiological agent is *L. chagasi*, a species similar to *L. infantum*, found in Asia and Mediterranean countries. The history of the protozoan's spread around the world is still controversial. Some authors cite its introduction at the time of European colonization, caused by the



species *L. In the first* place, others argue that they appeared millions and millions of years ago with canids, and the first species classified was *L. chagasi*. On the other hand, due to high infection rates in Amazonian canids, many researchers suggest an autochthonous origin.

Regardless of the worldwide appearance, it is known that in Brazil, the first documented case was in 1934, in people who died with suspected yellow fever, and that the disease was only recognized 20 years later, when the first outbreak of HVL occurred in Ceará. However, as early as 1911, Carlos Chagas, on an expedition along the Amazon River, suspected the disease in the region, by diagnosing splenomegaly in some patients who had no apparent cause, or another underlying disease.

Despite decades with a history of comorbidity in Brazil, in 1980 the disease, which was predominantly rural, was taking over the urban area, and spreading even through the less affluent neighborhoods of large centers. The disease, which was previously endemic to the Northeast, spread to the North, and reached the Southeast region in a few years, this fact is mainly due to the expansion of urban processes, and the modification of the habitats of the species involved in the transmission cycle.

It is believed that the movement of dogs between endemic and non-endemic areas of Visceral Leishmaniasis, and adaptive changes of the main vector in Brazil, *Lutzomyia longipalpis*, have contributed to the spread of the disease. Such transformation also occurs due to climate changes that have induced the dispersion of insects, such as sandflies, which were previously predominantly found in the peridomiciliary region, are now dispersed inside homes, especially before dark. The vectors that chose to propagate in humid areas are increasingly resistant and adapted to hot and dry environments, making them live and reproduce in any region of the country.

Likewise, the places with the highest rate of leishmaniasis transmission still predominate in peripheries and sectors where socioeconomic conditions are precarious. With the expansion of urbanization, places with greater precariousness in sanitation, lack of infrastructure and organization, with the presence of potential breeding sites, such as the accumulation of garbage and stagnant water, with the presence of domestic animals, combined with low investments in health and education, bring to light the gaps in actions for prevention and control of the disease. cooperating for the urbanization and endemic of HVL in the country.

## 2 METHODOLOGY

The research was developed and based on the reading and analysis of scientific articles, obtained from the databases: PUBMED, MEDLINE and SciELO, where publications related to the theme were selected, without geographical restriction. The search took place from October 28 to December 9, 2023, using the Descriptors in Sciences and Health (DeCS): "Visceral leishmaniasis", "tropical diseases" and "neglected diseases".



The study was carried out in two moments, where in the first there was an investigation of whether the articles addressed the theme and period in question, reviewing the history of the disease, forms of transmission and involvement of HVL in Brazil, in a total of 64 articles. Secondly, the review was based on the diagnosis and treatment of the disease, in addition to the increasing number of cases in the national territory. It is worth mentioning that we opted for public health journals, focused on the reality of the disease in the country, and since they are the most commonly accessed and updated publications.

Following the two stages, the following criteria were applied to the total of 34 publications found: Only research conducted in humans, available in full, in Portuguese, English or Spanish, published in the last 5 years (2019 to 2023) and which mentioned the comparison of rapid immunochromatographic tests used in the diagnosis of VL, was considered as inclusion criteria. Therefore, there are 14 studies left. Reviews and studies that addressed HVL as secondary data were excluded. After applying these criteria, at the end of the search, 11 scientific studies were read, categorized and evaluated for the interpretation of the results.

### 3 RESULTS AND DISCUSSION

In Brazil, visceral leishmaniasis affects about 3,500 people annually, with a predominance today in the North region, followed by the Midwest and Northeast regions. Until 2006, no cases were found in the Southeast and South regions, such as Santa Catarina, which identified the first case in humans in 2017, so that HVL is currently present in almost all territories.

In recent years, there has been a decrease in the number of new cases of HVL in some Brazilian states, but it is not known whether this decrease is due to increased preventive measures or underreporting. According to Fiocruz, in July 2023, there was a worrying increase in cases of leishmaniasis in dogs in several states of the country, which raises an alert for the increase of the disease in humans, if measures are not taken to prevent it, intensifying surveillance, vector control, and education of the entire population.

Visceral leishmaniasis is a chronic disease with systemic involvement of the body, which, if not treated early, can lead to death in more than 90% of cases. Its transmission occurs in humans, through the bite of females of the sandfly, an insect known in Brazil as straw mosquito, hard-winged mosquito, birigui, tatuquiras, among other regional names. The way in which HVL is transmitted occurs when infected hematophagous females bite dogs or animals, and then bite humans, transmitting the protozoan.

The incubation period of the disease is varied, lasting between 10 days and 24 months, with an average between 2 and 6 months. There is no susceptibility between age groups, however, children under 10 years of age and the elderly over 70 are usually the most affected, due to low immunity.



Because the *Leishmania* parasite is an obligate intracellular phagocytic cell parasite, its presence is characterized by a reversible and specific suppression of cell-controlled immunity, allowing the rapid and uncontrollable multiplication of the parasite in question.

As a highly lethal and endemic disease in Brazil, HVL is a notifiable disease, bringing to light the need for rapid diagnosis and treatment of the disease, due to its severe evolution, and the fact that it is present in the most diverse regions of Brazil. Whenever possible, confirmation of HVL should be performed through laboratory, serological and parasitological tests before proceeding with treatment, since in many cases the clinical manifestations are oligosymptomatic. In situations where there is a delay in the delivery of test results or there is no possibility of performing them, treatment should be started as early as possible in order to avoid the evolution of the zoonosis.

The suspicion of visceral leishmaniasis should be raised when the patient presents fever and splenomegaly, associated or not with hepatomegaly and weight loss. The evolution of the disease occurs in three parts: Initial phase, stage phase and final phase. In the initial or acute phase, symptoms include fever lasting less than four weeks, hepatosplenomegaly, and mucosal skin pallor. In the case of children, the course of the disease can lead to mild manifestations, such as low-grade fever, diarrhea and dry cough, and hepatomegaly of low intensity.

In the phase or period of the state, there is the presence of high fever interspersed with episodes of low fever, progressive weight loss, pallor and hepatosplenomegaly of greater proportion, with prolonged conditions, presenting more than 8 weeks of evolution, with impairment of the individual's general condition.

If there is no diagnosis or treatment until the stage of the disease, the disease progresses to the final phase, with continuous clinical high fever, impairment of the general condition of great intensity, accompanied by edema of the lower limbs, malnutrition, hemorrhages, jaundice and ascites, causing a poor prognosis, progressively evolving to death due to a drop in immunity, serving as a gateway for infections and other opportunistic diseases.

Among the most common complications of Kala-azar are urinary and respiratory tract infections, otitis, pyoderma and all other bacterial infections, which, if not treated quickly with appropriate antibiotics, evolve to sepsis quickly, leading to an often fatal outcome.

The immunological diagnosis of HVL is basically carried out through indirect immunofluorescence (IFAT), with a positive result from a dilution of 1:80. Results with values of 1:40, it is necessary to repeat the test in 30 days to make the diagnosis. And in any case, if the test is positive, but there is not enough clinic to suggest leishmaniasis, treatment should not be carried out. On the other hand, the Montenegro test should not be used for diagnostic purposes, it is positive in most patients from 6 months to 3 years after the end of treatment, being a good indicator of control.



Despite the seriousness of the disease, prevention is still the best way to avoid HVL, and the population has an essential role in the control of leishmaniasis by combating the transmitting insect, through periodic cleaning of yards, proper disposal of organic waste, cleaning of places where domestic animals live, use of a collar impregnated with repellent in dogs (Deltamethrin 4%), The use of insecticides and fine mesh screens on the windows and doors of homes and kennels, as well as individual protection such as the use of repellents, are simple measures that can contribute to the non-spread of the vector.

The prevention of the disease mobilizes various sectors, disciplines and communities, at different levels of society, stimulating joint work to promote social well-being and face the spread of the disease. In addition, this practice stimulates collective work and creates possibilities for the implementation of programs, policies, legislation and research on the subject, in order to achieve positive results in the fight against HVL and enabling, through health education and social participation, a better understanding of the risks to human and animal health, covering a whole and bringing numerous benefits to society.

In Brazil, VL treatment can be performed on an outpatient or in-hospital basis, depending on the severity, and the occurrence of cases should be immediately reported to public health authorities, allowing rapid containment of the spread of Leishmaniasis. The drugs of choice are Meglumine Antimonate, Amphotericin B deoxycholate, and liposomal Amphotericin B. The choice of medication should take into account the patient's clinical condition, age, comorbidities, and pregnancy. Antimonate can be administered on an outpatient basis and is primarily intended to prevent disease progression and reduce hospitalizations.

Amphotericin B is the drug of choice, and the most effective in fighting HVL. The deoxycholate and liposomal forms are compatible, with the latter being less hepatotoxic according to research. For pregnant women, amphotericin B is the only treatment option.

In addition to medications, it is extremely important to provide early nutritional support to patients with HVL, to avoid catabolism and consequent malnutrition. Another relevant support is hemotherapy, which should be individualized according to the needs of each individual, hemodynamic status, bleeding, disseminated intravascular coagulation, and complications such as sepsis.

The criteria for curing the disease are linked to an improvement in the general condition of the patients, with a return of appetite, weight gain, a decrease in the size of the liver and spleen, which can be observed after a few weeks of starting treatment. Full clinical improvement and regression of the disease may take months to occur. The patient, after treatment, should be followed up on an outpatient basis for at least six months, if he remains stable during this period, without and no return of symptoms, he is considered cured. If symptoms return within 12 months after treatment, it is considered a recurrence, requiring a new medical evaluation to return the medication.



#### 4 FINAL THOUGHTS

Effective communication between the spheres of government, society and the SUS is essential to create effective public policies aimed at HVL in Brazil. Without the union of all sectors in favor of the fight against the vector, it is impossible to contain the advances of the disease. In the case of Leishmaniasis, advertisements, health education, government projects, private initiatives, all are welcome to fight the mosquito. Endemic areas, such as the North, Midwest and Northeast regions, need active surveillance in cooperation with the zoonosis sector.

Above all, it is necessary for health professionals to be aware of the importance of correctly reporting cases, since there is still a high number of underreporting in Brazil, especially in areas not yet considered endemic.

Based on the results presented, it is concluded that VL continues to be a neglected disease in the country, with a worrying increasing trend of incidence, mainly due to a decrease in rates in some states and an increase in canine VL. Even in the face of such concern, there are still few current studies analyzing HVL in Brazil.

In this sense, this analysis contributes to the level of information and knowledge of human visceral leishmaniasis and, consequently, alerts to actions to identify areas of risk of vector transmission, entomological and zoonotic surveillance, making it necessary to develop new studies on the subject, identifying the conditioning factors and, subsequently, in order to collaborate for the eradication of the disease in the environment in which it lives.



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