

Visceral Leishmaniasis Associated with HIV Coinfection in Pará, Brazil

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Introduction: Human visceral leishmaniasis (VL) is a zoonosis of great importance to public health due to its epidemiological diversity, with emphasis on the possibility of aggravation by coinfection with the human immunodeficiency virus (HIV).

Objective: The aim was to study the epidemiological characteristics of VL cases associated with HIV coinfection in Pará. Methods. Reported cases of VL from January 2006 to December 2016 were investigated. A descriptive epidemiological method related to age, gender, area of residence and coinfection with HIV was used. To calculate variance and test equity, the *F*-test (Fisher) was performed. To observe the influence of one aspect on another, the chi-square was used to verify if there was dependence or independence between the variables.

Results: A total of 1171 cases of VL were reported during the study period. There was an annual mean of LV of 94.9, with a statistical difference ($p < 0.05$) between age groups, with the highest number of cases being observed in children aged 1 to 4 years (27.16%). Males and the urban area had a higher number of cases. There were 57 cases of VL/HIV coinfection, with emphasis on the year 2013 and the municipality of Santarém, which had the highest number of cases. During the ten years studied, there was a correlation between coinfection VL/ HIV, with significant differences between patients with and without HIV who contracted VL ($p < 0.001$).

Conclusion: The data reveal the endemic nature of VL in the region, with a high percentage of infection in children living in urban areas. Although the studied region is not identified as a predominant area of HIV cases, this study showed a high annual average (10.3) of cases of VL/HIV coinfection being the first time that cases of VL/HIV coinfection were reported in the Mesoregion of the Lower Amazon and Southwest Pará.

Keywords: age group, male, children, analytical epidemiology

Introduction

Human visceral leishmaniasis (VL) known as calazar^{1,2} or kala-azar^{3,4} ("black fever"), is a chronic zoonosis,⁵ of great importance for public health⁶ due to its epidemiological diversity,⁷ and in the absence of adequate treatment, results in fatal cases for humans.⁸ VL has high mortality, especially in untreated people and malnourished children, is also seen developing in individuals with acquired immunodeficiency virus (HIV) infection.

It is estimated that around 350 million people worldwide live in areas at risk for leishmaniasis, having been diagnosed in 88 countries, of which 72 are developing.⁹ Approximately 94% of the world's cases of calazar are concentrated in the South Asian region, South and Central America.¹⁰ In Brazil, the disease is endemic, there has been an expansion, becoming a growing public health problem in rapid geographical expansion.¹¹⁻¹³

Regardless of the care in the management of vectors and tanks, the disease is in vertiginous growth, so it characterizes a threat to individuals and worries the health authorities. Although there have been resources in certain routines for the

precise treatment of visceral leishmaniasis, the country has been notifying an increase in mortality in numerous regions, one of the main factors contributing to the increase of this lethality is the late diagnosis.^{14,15}

So many socioeconomic aspects, such as environmental aspects, influence the distribution of VL, and hinder disease control strategies.¹⁶ Environmental transformations have occurred intensely, and for this reason, knowledge of the epidemiological profile and understanding of the local evolution of the disease are necessary to guide more effective actions aimed at surveillance, prevention, and control of this disease.^{17,18}

Cases of leishmaniasis associated with coinfection with HIV are worrisome, as they involve complications and usually present in the most aggressive forms of the disease.¹⁹ In addition, impaired immune function in patients with VL coinfecting with HIV may favor the reactivation of latent *Leishmania* infection, cause a worse therapeutic response, and increase the risk of relapse after treatment.^{20,21}

The first report of VL/HIV coinfection occurred in southern Europe and currently coinfection is documented in 45 countries, highlighting the high rates reported in Brazil, Ethiopia and the state of Bihar in India.^{22–24} Recent studies reveal VL/HIV coinfection in adult males,^{25,26} pregnant women,^{27–29} and childrens.^{30,31} Given the above, the objective of this work was to describe relevant epidemiological aspects of human visceral leishmaniasis in the Lower Amazon and Southwest Paraense - Pará, Brazil.

Materials and Methods

Location and Series Analyzed

A study of cases of Visceral Leishmaniasis in Humans (VL) was conducted in nineteen municipalities in Pará (Figure 1). Of these, 13 are part of the Lower Amazon mesoregion, namely: Santarém, Alenquer, Almerim, Belterra, Curuá, Juruti, Mojuí dos Campos, Monte Alegre, Óbidos, Oriximiná, Prainha, Placas and Terra Santa. The other 6 municipalities

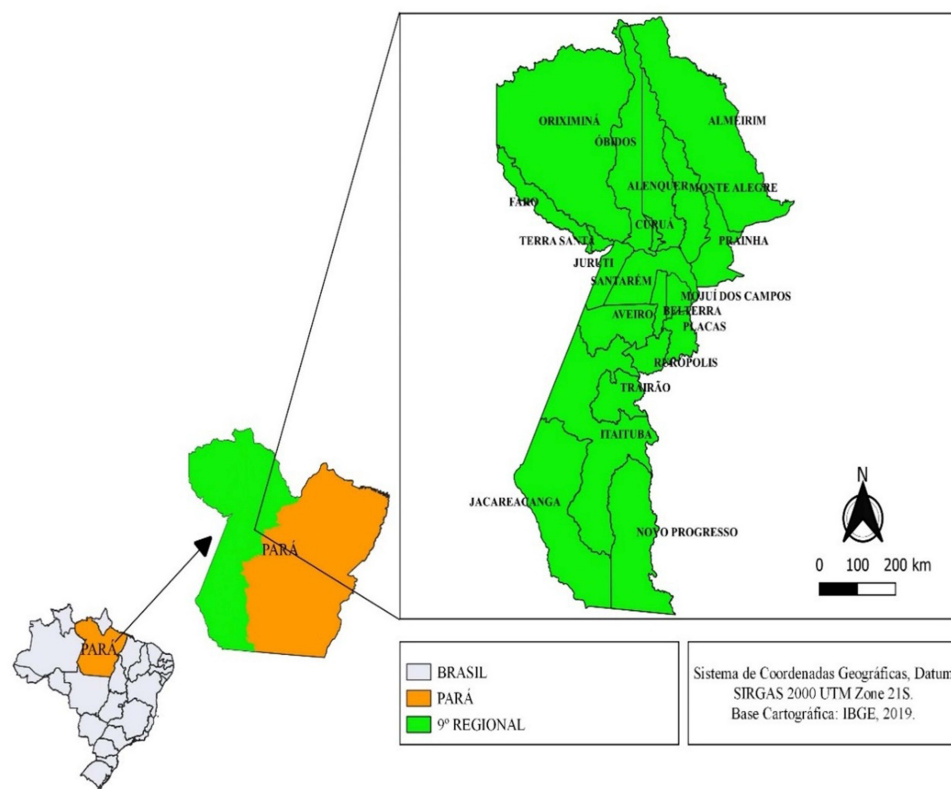


Figure 1 Location of the studied area.

Notes: Adapted from Silva WCD, Santos FB, Costa JWS et al. Epidemiological characteristics of pregnant patients accidented by fish in the Brazilian Amazon. *International Journal of Development Research*. 2022/01/30 2022;12(1):53,379–53,381. Copyright © 2022, Wellington Conceição da Silva et al. This is an open access article distributed under the Creative Commons Attribution License.⁵⁸

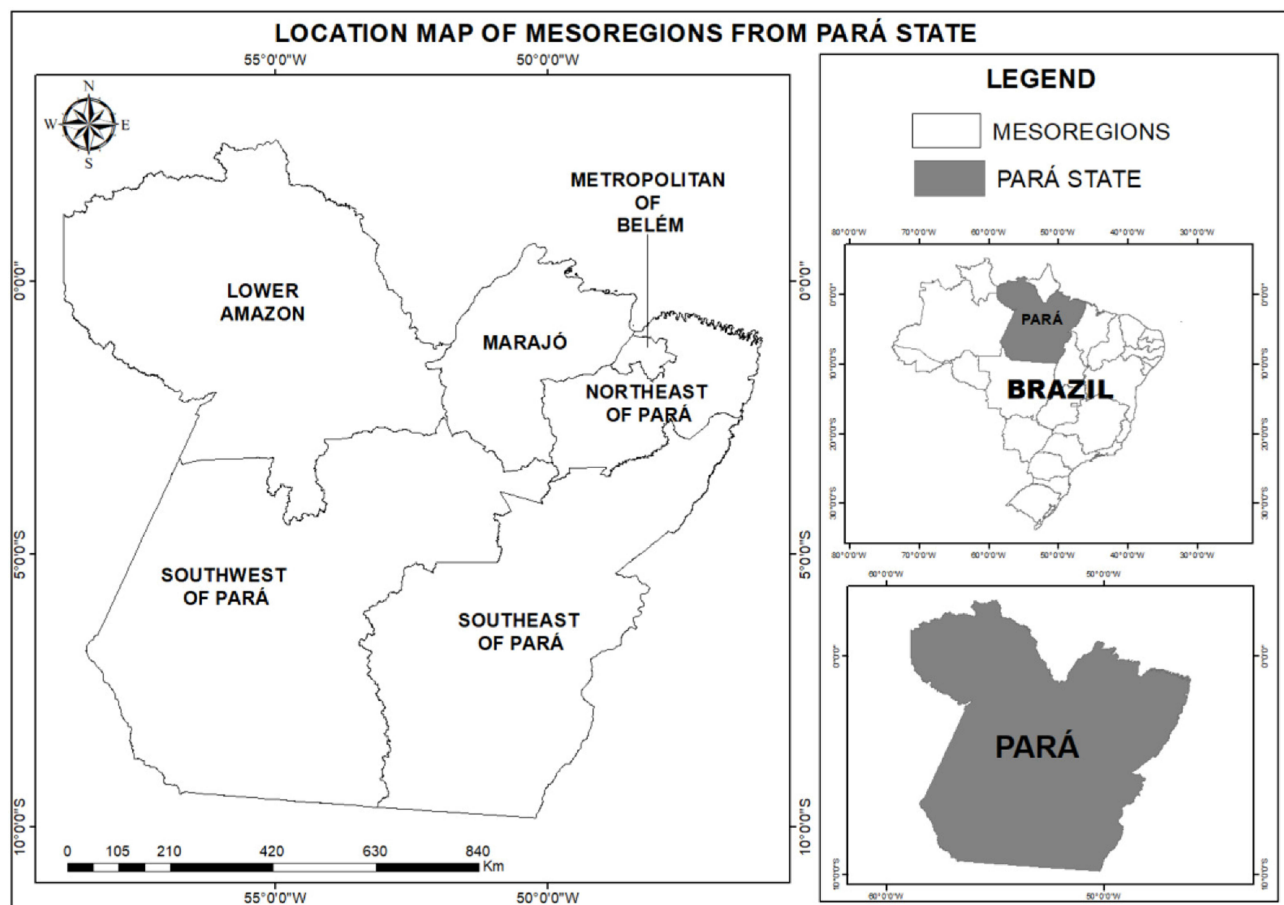


Figure 2 Mesoregions from Pará state.

Notes: Adapted from Andrade FVC, Pinto TI, Moreira LdS et al. The Legal Roundwood Market in the Amazon and Its Impact on Deforestation in the Region between 2009 and 2015. *Forests*. 2022;13(4):558. © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).⁵⁹

studied belong to the Southwest Paraense mesoregion, that is: Aveiro, Itaituba, Jacareacanga, Novo Progresso, Rurópolis and Trairão (Figure 2). The occurrence of cases was verified within a ten-year historical series, from January 2006 to December 2016, in which the notification of 1171 cases in humans with an annual average of 97.5 cases was analyzed.

Data Collection

The data from this research were obtained from the Notifiable Diseases Information System (SINAN),^{32,33} provided by the Endemic Division, the 9th Regional Health Center, the State Department of Public Health - Endemic Division/9^oCRS/SESPA. Data were collected from June 1 to 20, 2017.

Variables Studied

The descriptive epidemiological method was used, based on the study of variables related to age, gender, residence zone and confirmed cases of VL coinfecting with HIV.

The variables studied were: age, with age groups divided as follows: group 1: less than one year old, group 2: from one to four years old, group 3: from five to nine years old, group 4: ten to fourteen years old, group 5: fifteen to nineteen years old, group 6: twenty to thirty-four years old, group 7: thirty-five to forty-nine years old, group 8: fifty to sixty-four years old, group 9: sixty-five to seventy-nine years old, group 10: eighty years old or more.

As for the gender variable, both female and male were considered. Finally, for the residence zone variable, rural and urban areas were considered. The variable coinfection with the HIV virus admitted only yes or no values.

Statistical Analysis

Descriptive statistics were performed to obtain the means and standard deviation. To calculate variance and test equity, the *F*-test (Fisher) was performed, useful for using data when the size of your samples is small. To observe the influence of one aspect on another, qui-quadrado was used to verify whether there was dependence or independence between the variables, which were tabulated and analyzed and thus obtained if the results were obtained.

Ethical Aspects

The data used in this study were free, secondary and the names of the different patients involved in the study were not mentioned, respecting, therefore, the ethics of the study in Resolution No. 510 of the National Health Council of April 7, 2016, and it is not necessary to approve the Ethics Committee in the Research Committee.

Results

In cases of human VL, 1171 cases were reported in 19 municipalities in the Mesoregion of Western Pará. There was a statistical difference ($p < 0.05$) between age groups (Figure 3), and the highest number of cases was observed in children aged 1 to 4 years old (27.16%), later in individuals aged between 20 and 34 years old (13.92%), followed by people aged between 35 and 49 years old (13.66%), and by elderly purposes aged between 50 and 64 years old (11.53%).

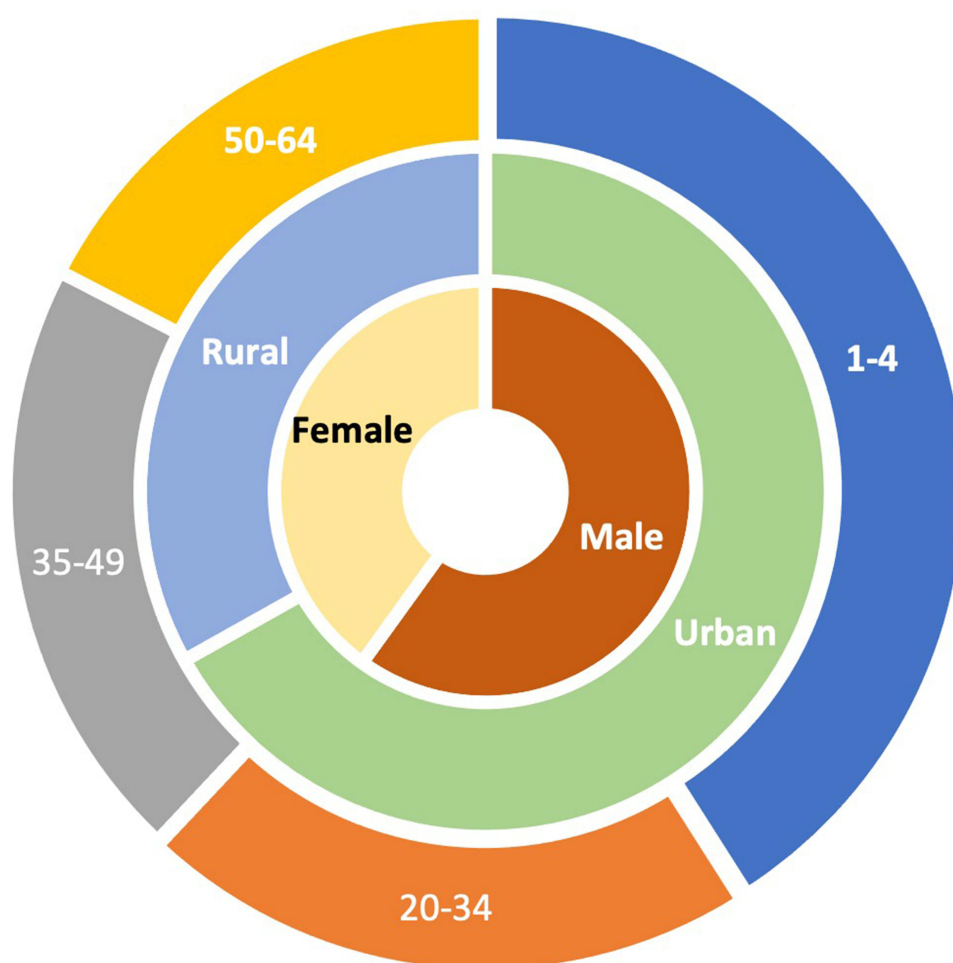


Figure 3 Number of VL cases observed by age group ($p < 0.05$). Occurrence of VL cases according to age group ($p < 0.05$), residence zone and gender.

Notes: 1-4: age group 2 (1-4 years old; 27.16%); 20-34: age group 6 (20-34 years old; 13.92%); 35-49: age group 7 (35-49 years old; 13.66%); 50-64: age group 8 (50-64 years old; 11.53%); Urban: residence zone urban (66.52%); Rural: residence zone rural (32.96%); Male: male gender (59.94%); Female: female gender (40.06%).

Table 1 Absolute and Relative Values of HIV and VL Cases in Municipalities with Positive Cases

Municipalities	Absolute	Relative (%)
Santarém	41	71.92982
Itaituba	6	10.52632
Novo Progresso	3	5.263158
Juruti	2	3.508772
Óbidos	2	3.508772
Belterra	1	1.754386
Oriximiná	1	1.754386
Trairão	1	1.754386

Regarding the occurrence of the disease according to the area of residence, many of the affected cases are resident in urban areas (66.52%) and the rural area was with the minority (32.96%) of the reported cases (Figure 3).

It was also observed in the cases studied that the most relevant was male (59.94%), accompanied by (40.06%) belonging to females (Figure 3).

During the ten years studied, a correlation was observed between HIV coinfection and visceral leishmaniasis. According to the data obtained, there were significant differences between patients with and without HIV who contracted Leishmaniasis ($p < 0.001$).

We reported 57 cases of VL/HIV coinfection during the study period, with an average of 10.3 cases per year reported, especially in 2013 and 2010, with the highest (13) and lower number (1), respectively.

In this study, only 8 municipalities had cases of VL/HIV coinfection. Santarém presented the highest number of cases (41), followed by Itaituba (6) and Novo Progresso (3) (Table 1), being the first time that cases of VL/HIV coinfection were reported in the Mesoregion of the Lower Amazon and Southwest Pará.

Discussion

For VL, there is no distinction of susceptibility between age, sex, and race. However, children and the elderly are more predisposing to VL infection corresponding to the state of relative cellular immunological prematurity.³⁴ In relation to the age group with the greatest involvement, VL refers especially to children, especially malnourished children.³⁵

In this study, a higher prevalence was found between 1 and 4 years of age. The disease in its traditional form affects individuals of all ages, 80% of the cases cataloged occur in children under 10 years. In some urban areas there is a predisposition to change in the ordering of cases by age group, with incidence of high rates also in the group of young adults.³⁶ A situation observed in the study in question, which among adults describes a higher frequency in the age group between 20 and 34 years.

The preference for childhood is justified, the fact that malnutrition is frequent in groups of people with low socioeconomic status and in whom the disease is frequent to another factor to collaborate in this genesis.³⁷

Visceral leishmaniasis mainly affected male people, which was also evidenced in Bahia,³⁸ this may be related to increased exposure to environments in which natural transmission of infection occurs.³⁹ However, there are genetic and hormonal factors related to the greater susceptibility of males to infection, but it is not properly explained.⁴⁰

In the present study, the urban area presented a higher record of occurrence of VL, which shows that in the municipalities studied the urban profile of the disease prevailed, although there is also occurrence in the rural area. VL is undergoing changes in the epidemiological pattern of transmission in some regions of Brazil,⁴¹ changing from

a profile that was initially characterized as rural,⁴² for a profile characterized as urbanized.⁴³ There is overcoming the paradigm of being VL a typically rural disease.⁴⁴

A recent study shows that there is no change in the epidemiological pattern in the process of transmission of the disease,⁴⁵ the change has been happening in the geographic expansion of VL, to an area designated as an urban area, which has environments very similar to the rural environment,^{46–48} providing a better adaptation of the vector to the place.

Brazil today challenges the expansion and urbanization of VL with human cases and many positive dogs in several regions, which are large and medium-sized. The transmission cycle that used to take place in a wild and rural environment, today intensifies in urban centers.⁴⁹

The highest risk of this infection occurs due to instability as poor sanitary infrastructure, breeding of animals that act as deposit of the parasite, climatic conditions favorable to vector multiplication, disordered development in urban areas with accumulation of organic matter and diligence of the first indications of this pathology.^{50,51}

A correlation was noted between cases of VL and HIV. Acquired immunodeficiency syndrome (AIDS) is a relevant cause of immunodeficiency worldwide and HIV contamination significantly intensifies the possible complications of VL coinfection. Regardless of whether it is a mandatory notification disease, the information presented is based on passive perception of cases. The number of individuals exposed to infection or asymptomatic infected in some areas is much higher than the number of cases detected.⁵²

The occurrence of subclinical infections in urban areas is the result, among other factors, of the greater exposure of man to infectious bites of sandfly already adapted to the environment, which indicates a serious problem associated with areas of greater HIV circulation; can turn VL into opportunistic parasites.⁵³

VL exhibits different management in HIV coinfection, which is mainly reflected in the irregular response to treatment and alteration of the diagnostic pattern. The increasing number of Leishmania/HIV cases in urban areas of Brazil has been verified, leading to the emergence of a new form of propagation by the sharing of contaminated needles, with risk of propagation of the artificial anthroponotic cycle.⁵⁴

VL can change the follow-up of HIV disease and immunodepression caused by this virus, simplifying the progression of leishmaniasis. The opinion of the set of clinical occurrences of VL in HIV-infected individuals indicates that there is no definite description of symptoms that can be unquestionably aggregated with coinfection.⁵⁵

There are few studies of the epidemiological aspects of VL/HIV coinfection cases in Brazil^{56,57} and there are no studies developed in the studied region, making this study the pioneer in the research of cases of VL/HIV coinfection in the studied region and produced worrying results regarding the concomitant occurrence of the two infections. Although the occurrence of AIDS or aids has not been evaluated, the annual mean VL/HIV coinfection of approximately 10 patients leads to the need for further investigations into the epidemiology of these coinfection cases.

Conclusion

This is the first study to report cases of VL/HIV coinfection in the Mesoregion of the Lower Amazon and Southwest Pará, with emphasis on the occurrence of coinfection in the municipalities of Santarém, Itaituba, Novo Progresso, Juruti, Óbidos, Belterra, Oriximiná, Trairão.

VL was endemic in this study, affecting mainly boys from 1 to 4 years old living in the urban area. Although the studied region is not identified as the predominant area of AIDS cases, this study showed cases of coinfection in individuals with HIV.

Studies conducted in other countries indicate higher lethality for VL-HIV coinfecting patients when compared to those with VL. This alone should make the obligation of the HIV test to patients with VL routine with a view to the early diagnosis of coinfection and, consequently, the probable reduction of lethality.

However, in this research, many epidemiological records in the SINAN evaluated did not contain concrete information in the variable “HIV coinfection”, which implied the white/ignored attribution to this field of notification, which by the results presented here refers to a probable underreporting of cases of coinfection.

Among the limitations encountered while carrying out this research, the neglect of adequate investigation of the possibility of VL/HIV coinfection in cases of VL was poignant, as well as the lack of filling out this information in many epidemiological forms.

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Disclosure

The authors report no conflicts of interest in this work.

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