

# Clinical and Epidemiological Profile of Visceral Leishmaniasis Patients Treated at a Reference Unit in Campo Grande, State of Mato do Grosso do Sul, Brazil

## Perfil Clínico e Epidemiológico de Portadores de Leishmaniose Visceral Tratados em uma Unidade de Referência em Campo Grande, Mato Grosso do Sul, Brasil

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### Abstract

Visceral leishmaniasis is the most severe form of leishmaniasis. In Brazil, the importance of visceral leishmaniasis lies not only in its high incidence and wide distribution, but also in the possibility of assuming severe and lethal forms when associated with malnutrition and concomitant infections. There are still few studies carried out in the search to better deal with these cases, in order to avoid aggravations and deaths due to the disease. The objective of this study was to describe the clinical and epidemiological characteristics of patients undergoing treatment in the period between January 2010 and December 2013 for visceral leishmaniasis at a reference unit in the city of Campo Grande, MS. It consists of a retrospective and documentary study of biological, demographic, clinical and laboratory data. This is a descriptive and cross-sectional study with a quantitative approach. The study was conducted at the Day Hospital (Municipal Health Department) in Campo Grande, MS. All records of any age group and sex were analyzed, provided they were completed, referring to the period from January 2010 to December 2013. The variables age, gender, residence status, area, clinical manifestations, diagnosis, type treatment, hematological data, comorbidities and evolution of the condition were analyzed. The results obtained are expected to verify the clinical-epidemiological characteristics of the visceral leishmaniasis patients, contributing to an earlier and prognostic diagnosis with a greater chance of cure and improvement in the quality of life of these patients.

**Keywords:** Epidemiology. Leishmaniasis, Visceral. Endemic Diseases.

### Resumo

*A leishmaniose visceral é a forma mais grave das leishmanioses. No Brasil, a importância da leishmaniose visceral reside não somente na sua alta incidência e ampla distribuição, mas também na possibilidade de assumir formas graves e letais quando associada ao quadro de má nutrição e infecções concomitantes. Ainda são poucos os estudos realizados na busca para melhor atender esses casos, a fim de evitar agravos e mortes pela doença. Foi objetivo deste estudo descrever as características clínico-epidemiológicas dos pacientes em tratamento no período entre janeiro de 2010 a dezembro de 2013, para leishmaniose visceral em uma unidade de referência na cidade de Campo Grande, MS. Consiste em um estudo retrospectivo e documental dos dados biológicos, demográficos, clínicos e laboratoriais. Trata-se de um estudo descritivo e transversal de abordagem quantitativa. O estudo foi realizado no Hospital Dia (Secretaria Municipal de Saúde) em Campo Grande, MS. Foram analisados todos os prontuários de indivíduos de qualquer faixa etária e sexo, desde que se encontrassem devidamente preenchidos, referentes ao período de janeiro de 2010 a dezembro de 2013. Foram analisadas as variáveis idade, gênero, estado de residência, zona, manifestações clínicas, diagnóstico, tipo de entrada, tratamento, dados hematológicos, comorbidades e evolução do quadro. Por meio dos resultados obtidos espera-se verificar as características clínico-epidemiológicas dos portadores de leishmaniose visceral contribuindo para um diagnóstico mais precoce e prognóstico com maiores chances de cura e melhora na qualidade de vida desses pacientes.*

**Palavras-chave:** Epidemiologia. Leishmaniose Visceral. Doenças Endêmicas.

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## 1 Introduction

It is estimated that 350 million people worldwide are exposed to the risk of developing visceral leishmaniasis (VL) and approximately 12 million people may be infected. The incidence of visceral form reaches 500,000 annual cases, leading to death around 75 thousand people per year throughout the world<sup>1,2</sup>.

According to the World Health Organization (WHO), leishmaniasis is present in 88 countries, of which 72 are developing countries, with compulsory notification in just 32<sup>3</sup>. The disease is widely disseminated in Brazil and is currently

notified in all the states. It is an endemic disease with records of frequent outbreaks, in expansion in the main Brazilian capitals, and that, when left untreated can be fatal in 90% of the cases<sup>4,5</sup>.

LV is considered a disease of great impact on public health, characterized by systemic weakness, lethality and opportunist character with high incidence in children, elderly and individuals with comorbidities 6,7. In Brazil, the importance of visceral leishmaniasis lies not only in its high incidence and wide distribution, but also in the possibility of assuming severe and lethal forms when associated with malnutrition and concomitant infections<sup>8</sup>.

In the period from 2001-2016 55,530 human cases of LV were reported in the Americas with an annual average of 3,457 cases. In 2016, it was observed a reduction of 67% in the number of cases of LV in Paraguay compared to 2013. In this same period, the cases of Colombia and Venezuela had an increase from 13 to 37 and from 7 to 33 cases per year, respectively<sup>9</sup>.

In 2016, in Brazil, a total of 3,354 cases of LV were recorded, with an incidence of 4.51 and 1.04 cases per 100,000 inhabitants, considering the population of transmission areas and the total population of the country, respectively. The cases were reported in seven countries, distributed in 54 departments/states and 935 municipalities (1-89 cases).

In the state of Mato Grosso do Sul, according to the National Systems of Case Reports (SINAN), from January 2008 until December 2017 1,942 were notified and confirmed human cases of LV. In the same period 147 deaths from the disease were recorded. From 2002, it is noted great expansion and urbanization of the disease in municipalities in the State with a significant increase in the incidence in new transmission areas. In 2012 300 cases of LV were notified in SINAN, distributed in 26 municipalities in the State. Of the total of these cases, 205 (68.33%) were from the city of Campo Grande<sup>10</sup>.

LV is a generalized chronic illness characterized by irregular and of long duration fever, hepatosplenomegaly, lymphadenopathy, anemia with leukopenia, hypergammaglobulinemia and hypoalbuminemia, dry cough, weight loss, edema and condition of progressive weakness, leading to cachexia, and even to death. Caused in the Americas by *Leishmania infantum* and transmitted by the bite of females of dipterous *Lutzomyia longipalpis* and *Lutzomyia cruzi*<sup>5,11,12</sup>. The evolution of the clinical forms is varied, and the individual may present since spontaneous cure, asymptomatic and oligosymptomatic forms, up to severe manifestations, and may reach lethality between 10% and 98% in cases inadequately treated and not treated, respectively<sup>13</sup>. It is observed for Brazil in the years 2001 to 2008, that the lethality reaches patients aged less than 1 year and with 50 or more years of age<sup>14</sup>.

The association of comorbidities such as malnutrition, late diagnosis of the disease and the presence of complications, such as bacterial infections mainly caused by *Staphylococcus aureus* and *Pseudomonas aeruginosa* and hemorrhage also contribute to the increase of mortality cause by this disease<sup>5,16</sup>. The identification of these factors in the initial care to the patient with LV is of fundamental importance, since prophylactic and therapeutic actions can be initiated for the reduction of mortality<sup>14</sup>.

The diagnosis of LV can be done by parasitological examination, culture or direct immunofluorescence reaction, immunochromatographic tests, commonly known as rapid test or molecular test by PCR (Polymerase Chain Reaction)<sup>14</sup>.

In Brazil, the drugs used for the treatment of the LV are the pentavalent antimoniate and amphotericin B. The choice of each one of them should consider age, presence of comorbidities and pregnancy<sup>14</sup>. However, since 1940, pentavalent antimony is taken as first-choice therapy for treatment of LV<sup>17</sup>. The N-methylglucamine antimoniate has the advantage of being able to be administered in an outpatient level, which decreases the risks related to hospitalization<sup>18</sup>. However, it should be administered with caution in patients with heart diseases, kidney diseases, liver diseases and Chagas disease. During the treatment, regardless the comorbidities, monitoring should be done with electrocardiogram (minimum twice a week) and weekly serum dosage of creatinine, urea transaminases, bilirubin, and alkaline phosphatase, in addition to leukogram<sup>17</sup>.

Amphotericin B is indicated as first choice for treatment of LV only in those patients with signs of gravity, is the only option in the treatment of pregnant women<sup>14</sup>. It must be considered severe LV all patients below the age of six months or more than 65 years, severe malnutrition, comorbidities or one of the following clinical manifestations: jaundice, hemorrhagic phenomena (except epistaxis), generalized edema, signs of toxemia (lethargy, poor perfusion, cyanosis, tachycardia or bradycardia, hypoventilation or hyperventilation and hemodynamic instability), according to the Manual of the Ministry of Health<sup>19</sup>.

There are still few studies carried out in the search to better deal with these cases, in order to avoid aggravations and deaths due to the disease. Therefore, it is important the clinical and epidemiological analysis of cases for a more efficient and suitable diagnosis and treatment for the patient, aiming at a correct approach of cases in order to prevent future injuries by the disease.

In the same context, retrospective studies of medical records of patients with LV can provide useful epidemiological and clinical data, particularly in endemic areas, and should, therefore, be held periodically<sup>20</sup>.

Due to all explained above the objective of this study was to describe the clinical and epidemiological characteristics of patients undergoing treatment in the period between January 2010 and December 2013 for visceral leishmaniasis at a reference unit in the city of Campo Grande, MS..

## 2 Material and Methods

### 2.1 Study site

The study was conducted in the Specialties Center for Infectious and Parasitic Diseases (CEDIP), in Campo Grande, Mato Grosso do Sul. Location which is a reference to care and outpatient treatment for LV among other parasitic diseases throughout the state.

## 2.2 Method

It consists of a retrospective and documentary study of biological, demographic, clinical and laboratory data. It is a retrospective and documentary study of quantitative approach.

All records were analyzed relating to the period from January 2010 to December 2013 of patients treated for LV in Specialties Center for Infectious and Parasitic Diseases (CEDIP) of any age and sex, since these were duly completed.

The variables age, gender, residence status, area, clinical manifestations, diagnosis, type treatment, hematological data, comorbidities and evolution of the condition were evaluated

The study was performed after approval by the Ethics and Research Committee of University Anhanguera Uniderp, according to the Resolution 466/2012 of the National Health Council (Opinion 546.561 /2014). After data collection, the same were tabulated using the program Epi-info 3.5.

## 3 Results and Discussion

In the period from January 2010 to December 2013 127 patients with confirmed diagnosis for LV were recorded in CEDIP. Regarding the distribution by sex, there was a prevalence of male sex (69.62%) (Table 1).

**Table 1** - Demographic variables of participants with visceral leishmaniasis, Campo Grande/MS, period from 2010 to 2013 (n=127)

Variables	N	%
<b>Sex</b>		
Female	50	39.37
Male	77	69.62
<b>Age range (years)</b>		
From 0 to 5	43	33.85
6 to 12	11	8.66
12 to 17	04	3.14
18 to 34	26	20.47
35 to 55	22	17.32
Above 55	21	16.53
<b>State of origin</b>		
Mato Grosso do Sul	126	99.21
Rondônia	01	0.79
<b>Residence Zone</b>		
Rural	10	7.87
Urban	117	92.13

Source: Research Data.

The most frequently affected age range in the analyzed period was 0-5 years (33.85%) (Table 1). In Brazil, the classic Visceral Leishmaniasis affects individuals of all ages, but in endemic areas 80% of the cases occur in children aged less than 10 years, being 41% of registered cases in children under 5 years<sup>21</sup>.

The reason for the increased susceptibility in children is related to the state of relative cell immunological immaturity, since lasting immunity develops progressively with age. And this susceptibility is aggravated by malnutrition, common factor in endemic areas, plus a greater exposure to the vector in the peridomicile<sup>22</sup>.

As to the State of origin of the patients, the state of Mato Grosso do Sul prevailed with 126 (99.21%) of the cases. In this research only an imported case was recorded (0.79%) coming from the state of Rondônia. The residence zone speaks very much in favor of the urbanization process of the infection transmission. 117 (92.13%) patients reside in the urban area and 10 (7.87%) residing in the rural zone (Table 1).

Several studies suggest that the opening of new roads and avenues along the course of streams, and the deforestation for construction of popular houses, led to an increase of the vector density in the urban area of the municipality<sup>17,23</sup>.

In the present study 104 (81.88%) immunological diagnosis were registered, compared to 11 parasitological diagnosis (8.66%). Still, in 12 cases (9.45%) the two types of diagnosis were used, and in 8 cases (6.29%) were clinical signs added to parasitological or immunological analysis (Table 2).

**Table 2** - Number and percentage of the types of diagnoses used and input profile of patients with visceral leishmaniasis, according to new cases or relapses, Campo Grande/MS period from 2010 to 2013 (n=127)

Types of diagnosis and input profile	N	%
<b>Diagnosis</b>		
Parasitological	11	8.66
Immunological	104	81.88
Parasitological + immunological	12	9.45
Clinical+immunological or parasitological	08	6.29
<b>Input Type</b>		
Recurrence	4	3.14
New Case	123	96.86

Source: Research Data.

The present study showed that the parasitological test is being performed with less frequency in recent years, giving rise to the immunological test, presenting good sensitivity and specificity in the diagnosis. The most used immunological diagnosis exam was the indirect immunofluorescence test (IIF), being in agreement with the reported by the Ministry of Health<sup>19</sup>.

Evaluating the input type, the majority of patients admitted were new cases of visceral leishmaniasis totaling 123 (96.86%) individuals and 4 (3.14%) recurrences. This is because when the individual is immunocompetent the disease rarely returns (Table 2).

As to the signs and symptoms found, the most frequent were the fever that affected 111 (87.40%), increase of the spleen 90 (71%), increase of the liver, 81 (64%). Other symptoms associated with infection were less frequent (Table 3).

**Table 3** - Number and percentage of the main signs and symptoms presented by patients with visceral leishmaniasis, Campo Grande/MS in the period from 2010 to 2013 (n=127)

Major signs and symptoms	N	%
Fever	111	87.40
Increase of spleen	90	71.00
Increase of liver	81	64.00
Paleness	46	36.22
Losing weight	48	38.00
Weakness	32	25.20
Cough and/or diarrhea	27	21.25
Jaundice	15	11.81
Edema	14	11.00
Secondary infections	16	12.60
Bleeding episodes	05	4.00
Hyporexia	17	13.40
Pneumonia	15	11.81
Abdominal pain	13	10.23
Pancytopenia	40	31.50
Nausea and vomiting	15	11.81

Source: Research Data.

The signs and symptoms presented by patients are in line with those found in the literature, when one considers the classic LV. Fever, increased liver and spleen, paleness, hyporexia, cough and abdominal pain are classic symptoms of the disease present in almost all cases at the time of admission due to the fact that it is during this stage that the majority looks for medical assistance<sup>22</sup>.

In a study conducted in MS, fever that was present in 97.3% of the individuals who developed LV, splenomegaly in 85.9%, 75.8% anemia and pneumonia in 21.5%<sup>17</sup> are pointed out as the most frequent symptoms in the studied population.

The most frequent complications of leishmaniasis are edema of the lower limbs (that can evolve to anasarca) and bacterial infectious nature, highlighting acute otitis media, piodermites, infections of the urinary tract and respiratory tract. If these infections are not treated, the patient can develop a septic shock with fatal evolution. The digestive hemorrhage, ascites and jaundice when present indicate severity of the case<sup>24</sup>.

In the present study, as already highlighted in others, the presence of secondary infections occurred, probably due to the leukopenia and immunosuppression due to the disease itself, or by the presence of comorbidities.

The main comorbidities found in this study were systemic arterial hypertension, 18 (14.17%), acquired immunodeficiency syndrome 10 (8%), diabetes mellitus 8 (6.3%) (Table 4). The comorbidities are factors that can alter the course of the disease development. LV in recent years eventually assume a character of opportunistic disease in people infected with HIV (Human Immunodeficiency Virus)<sup>4</sup>, this fact observed in the present study where 8% of the participants were co-infected. It is known that the presence of LV in individuals infected by the HIV virus accelerates the progression of infection to promote viral replication, further

aggravating the condition of immunosuppression<sup>25</sup>.

**Table 4** - Number and percentage distribution of 127 cases of LV, concerning the comorbidities found. Campo Grande/MS (from 2010 to 2013)

Associated Comorbidities	N	%
HIV	10	8.0
HAS	18	14.17
DIA	08	6.3
HEP C	03	2.36
Leprosy	03	2.36
None	94	74

Source: Research Data.

Hemorrhage and generalized infection are the main causes of death by the disease. With the emergence of AIDS (Acquired Immunodeficiency Syndrome), LV gained importance due to the susceptibility of HIV carriers.

As to the treatment used, one can verify that the Pentavalent Antimony was the most used, with a total of 62 patients (48.81%), followed by amphotericin B with 34 patients (26.77%) and Liposomal Amphotericin B with 31 (24.4%) (Table 5). Amphotericin B was used in some cases of reaction, toxicity and side effects caused by the pentavalent antimony. Pentavalent Antimoniate N-methylglucamine (Glucantime®) is still being considered the drug of first choice, and the patients treated have demonstrated good evolution.

**Table 5** - Number and percentage of medications used in the treatment and evolution of cases of visceral leishmaniasis, Campo Grande/MS in the period from 2010 to 2013 (n=127)

Treatment and evolution	N	%
<b>Treatment Performed</b>		
Pentavalent antimony	62	48.81
Amphotericin B	34	26.77
Liposomal amphotericin B	31	24.40
<b>Case Evolution</b>		
Cure	123	96.85
Completion of the treatment	04	3.15

Source: Research Data.

Through the analysis of the data of 116 children treated at University Hospital Maria Aparecida Pedrossian (HU/UFMS), Campo Grande, in the period from January 1998 to February 2005, it was identified that the main effects of treatment with N-methylglucamine were: increase in aminotransferases (22.5%); electrocardiographic alterations (18%); an increase of amylase (17.5%); fever, cyanosis and tremors (6.3%); arthralgia, allergic conjunctivitis and nystagmus (0.9%). When amphotericin B was administered, hypokalemia was observed in 72.2% of cases, cardiac alterations in 16.6% and fever, cyanosis and shivering during the infusion in 22.2% of patients. Of the patients analyzed in this study, 123 (96.85%) evolved to cure, and 04 (3.15%) were in the final phase of the treatment (Table 5).

In the present study deaths were not recorded, which may be due to the fact of care having been carried out in a reference

center which contributes so that the diagnosis and initiation of treatment occurs early. The early recognition of the disease, as well as the clinical and laboratory monitoring of patients during the treatment of LV and the introduction of antibiotics to the least sign of infection, reduces potential complications and consequently deaths caused by the disease.

Hematological data regarding the red, white and

platelet series are presented in Table 6. The data show that, statistically, 68% of patients present hematological values within the normal range, and when we broaden the analysis, 95% are with values considered very close to the reference values. Therefore, the data are distributed within the standards of normality.

**Table 6** - Laboratory exams parameters in patients with visceral leishmaniasis, Campo Grande/MS (2010-2013)

Laboratory exams	Minimum	Maximum	Mean $\pm$ sd*	V reference
Hemoglobin	5.6	16.3	10.5 $\pm$ 2.0 g/dl	(12.3-17.5) g/dl
Red blood cells	2.3x10 <sup>6</sup>	8.1x10 <sup>6</sup>	(4.3 $\pm$ 0.9)x10 <sup>6</sup> / $\mu$ L	(4.1 -5.9)x10 <sup>6</sup> / $\mu$ L
Hematocrit	8.1	47.0	32.7 $\pm$ 5.9	36% - 50%
Leukocytes	10 <sup>3</sup>	17.9x10 <sup>3</sup>	(6.0 $\pm$ 3.8)x10 <sup>3</sup> / $\mu$ L	(4.4-11.3)x10 <sup>3</sup> / $\mu$ L
Platelets	29x10 <sup>3</sup>	737x10 <sup>3</sup>	(200 $\pm$ 125)x10 <sup>3</sup> / $\mu$ L	(172-450)x10 <sup>3</sup> / $\mu$ L

sd\*: Standard Deviation

Source: Research Data.

Hemorrhagic phenomena occurred in 4% of cases. It should be emphasized that thrombocytopenia is a common finding in patients with LV, and can be a predictive factor for severe hemorrhage in patients in which the platelet count is less than 150,000/mm<sup>3</sup>.

In patients with LV the complete blood count may reveal pancytopenia, erythropenia, leukopenia and thrombocytopenia, relative lymphocytosis; the dosage of proteins demonstrates strong reversal of the albumin/globulin ratio. In oligosymptomatic form, the laboratory tests do not usually change, except the speed of erythrocyte sedimentation rate (High) and hyperglobulinemia<sup>24</sup>.

LV is characterized by a marked polyclonal stimulation of B lymphocytes, which results in hypergammaglobulinemia and large-scale production of antibodies<sup>9</sup>.

With the progress of the disease, anemia is accentuated and there is a marked tendency to hemorrhages. The evolution of the disease can be quickly, leading the patient to cachexia and death within a few weeks or a few months, or take a chronic course. The outcome ensues, many times, by intercurrent diseases, since the immunological mechanisms are already definitively affected<sup>21</sup>.

#### 4 Conclusion

Still with the passing of years, and the constant notification of new cases of Leishmaniasis in the state of Mato Grosso do Sul, the disease is still proving to be neglected.

A good diagnosis, followed by a safe and proper treatment is fundamental for the referral of patients to a good prognosis, even with the presence of comorbidities.

The nursing professional, who spends more time in contact with the patient should be attentive and keep in constant update regarding the clinical signs of the disease, as the bearers of leishmaniasis need a systemized nursing assistance, in order to contribute to a better quality in the care and treatment of this infection.

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