

Epidemiological aspects of visceral leishmaniasis in Brazil and in international border regions

Aspectos epidemiológicos da leishmaniose visceral no Brasil e em regiões de fronteira internacional

Aspectos epidemiológicos de la leishmaniasis visceral en Brasil y en las regiones fronterizas internacionales

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Abstract

Objectives: To verify the number of visceral leishmaniasis (VL) cases in Brazil and its states and twin cities, with a focus on the state and twin city with the highest number of cases. We investigated social, demographic, laboratory and clinical aspects of these cases. **Methodological design:** We performed a descriptive study using a quantitative approach and data from 2010 to 2019 that were obtained through a public domain website, the Informatics Department of the Unified Health System. The incidence rate of VL cases was calculated per 100,000 inhabitants. **Results:** In Brazil, 35,886 VL cases were reported, with 2,834 cases in international border states and 148 cases in twin cities. The state and twin city with the highest number of cases were Mato Grosso do Sul (1,834 cases) and Corumbá (94 cases), respectively, with annual mean incidence rates of 6.4 and 8.3 cases per 100,000 inhabitants. In Mato Grosso do Sul and Corumbá, the disease was more frequent in male and brown-skinned individuals who had up to 8 years of education (age range: 1 to > 80 years old). Most of the cases occurred in urban areas, was diagnosed by laboratory tests and evolved to cure ($p < 0.05$). **Conclusions:** A high number of VL cases in Brazil was found during the period of study. The cases were distributed in 10 states with international borders and eight twin cities. These findings draw attention to the greater need for management programs to control and prevent VL.

Keywords: Visceral leishmaniasis; Brazil; Border areas; Health on the border; Epidemiology.

Resumo

Objetivo: verificar o número de casos de leishmaniose visceral (LV) no Brasil e estados e cidades gêmeas do país, com enfoque no estado e na cidade gêmea com maior número de casos. Investigamos aspectos sociais, demográficos, laboratoriais e clínicos desses casos. **Percurso metodológico:** Estudo descritivo e com abordagem quantitativa, realizado no período de 2010 a 2019, por meio do site de domínio público do Departamento de Informática do Sistema Único de Saúde. A taxa de incidência de casos de LV foi calculada por 100.000. **Resultados:** No Brasil foram notificados 35.886 casos de LV, 2834 casos foram em estados de fronteira internacional, sendo 148 em cidades gêmeas. O estado e cidade gêmea com maior número de casos foi Mato Grosso do Sul (MS) (1834) e Corumbá (94), com taxa média anual de 6,4 e 8,3 casos/100.000 habitantes. No MS e em Corumbá, a doença foi mais frequente no sexo masculino, pessoas de cor parda, escolaridade até 8 anos de estudo, faixa etária entre menores de um ano a maiores de 80 anos, a maioria dos casos ocorreu na zona urbana, foi diagnosticado por exames laboratoriais e com evoluiu para a cura ($p < 0,05$). **Conclusão:** Foi encontrado um elevado número de casos de LV no Brasil durante o período do estudo. Os casos foram distribuídos em 10 estados com fronteiras internacionais e oito cidades gêmeas. Esses achados chamam a atenção para a maior necessidade de programas de manejo integrado para controlar e prevenir a LV.

Palavras-chave: Leishmaniose visceral; Brasil; Áreas de fronteira; Saúde na fronteira; Epidemiologia.

Resumen

Objetivo: Verificar el número de casos de leishmaniasis visceral (LV) en Brasil y en los estados y ciudades gemelas del país, enfocándose en el estado y en la ciudad gemela con mayor número de casos. Investigamos aspectos sociales, demográficos, de laboratorio y clínicos de estos casos. **Trayectoria metodológica:** Estudio descriptivo con abordaje cuantitativo, realizado de 2010 a 2019, a través del sitio web de dominio público del Departamento de Informática del Sistema Único de Salud. La tasa de incidencia de casos de LV se calculó por 100.000. **Resultados:** En Brasil se reportaron 35,886 casos de LV, 2834 casos ocurrieron en estados fronterizos internacionales, siendo 148 en Twin Cities.

El estado y ciudad hermanada con mayor número de casos fueron Mato Grosso do Sul (1834) y Corumbá (94), con una tasa promedio anual de 6,4 y 8,3 casos/100.000 habitantes. En Mato Grosso do Sul y Corumbá, la enfermedad fue más frecuente en varones, gente morena, educación hasta 8 años de estudio, grupo de edad desde menos de un año hasta más de 80 años. La mayoría de los casos ocurrieron en áreas urbanas, fueron diagnosticados mediante pruebas de laboratorio y progresaron hasta la curación ($p < 0.05$). Conclusión: Se encontró un alto número de casos de LV en Brasil durante el período de estudio. Los casos se distribuyeron en 10 estados con fronteras internacionales y ocho ciudades gemelas. Estos hallazgos destacan la mayor necesidad de programas de gestión integrados para controlar y prevenir la LV.

Palabras clave: Leishmaniasis visceral; Brasil; Zonas fronterizas; Salud fronteriza; Epidemiología.

1. Introduction

Leishmaniasis is the second most important group among vector-borne diseases in Brazil, second only to dengue in terms of the number of cases and emergence of epidemics (Brasil, 2014). Leishmaniasis is considered a neglected disease because it is endemic among more vulnerable populations, with unacceptable morbidity and mortality and lower investments in research, drug production, and control interventions (Valverde, 2021).

Visceral leishmaniasis (VL) is the most severe clinical form of leishmaniasis. It is classified as a chronic and systemic disease that, when undiagnosed and untreated, is fatal in more than 95% of cases (Maia-Elkhoury et al., 2021). Transmission to humans and dogs, the latter of which is the main reservoir (Dantas-Torres et al., 2019), occurs through bites of infected females of the vector species *Lutzomyia longipalpis* (because of its ease of adaptation to peridomestic areas and a wide range of temperatures) and *Lutzomyia cruzi* (Brasil, 2017).

Even with actions of the Visceral Leishmaniasis Surveillance and Control Program (Brasil, 2016a) that targets entomological and animal reservoirs and the treatment of diagnosed human cases, Brazil still has approximately 96% of VL cases in Latin America (Maia-Elkhoury et al., 2021). Thus, one can question whether these actions are indeed sufficiently effective to reduce the incidence of VL in Brazil (Costa et al., 2018; Salomón et al., 2015; Oliveira et al., 2016; Lopez et al., 2021).

The continual increase in the incidence of VL in several Brazilian regions can be attributed to the migration of people from rural to urban areas, deforestation, and the construction of large projects that impact the environment and cause the resettlement of people from one place to another. These people often take their pets with them, leading to a disorderly increase in deficient sanitary conditions where the vector *L. longipalpis* has successfully settled (Costa et al., 2018; Salomón et al., 2015). This situation represents a major challenge to controlling VL in urban areas.

Additionally, sandflies and dogs (specifically dogs that live on the street) circulate freely with no restrictions, thereby favoring the spread of VL. Several studies have reported the presence of sandflies in the border region, especially the species *Lutzomyia cruzi* (Oliveira et al., 2016), and dogs that are diagnosed with leishmaniasis (Lopez et al., 2021). Therefore, international border areas (i.e., areas with at least two international territories) can generate situations of vulnerability to health of the population (Pêgo & Moura, 2018). These areas require further study to contribute to the implementation of preventive measures that specifically target VL and control vectors (e.g., dogs).

The geographical environment that best characterizes a border area consists of “twin cities” (i.e., municipalities, cities, or towns with corresponding cities in a neighboring country). Depending on how these twin cities are connected (e.g., by land, a bridge over a river, or a river without a bridge), the flow of people between these cities and their interactions can increase or decrease (Brasil, 2016b).

Understanding the spread of human VL cases and possible factors that contribute to its spread in Brazil and in border regions is important for implementing more effective strategies, including joint policies and actions with neighboring countries (Costa et al., 2018). The present study sought to verify the number of human VL cases in Brazil and its states and twin cities, with a focus on the state and twin city with the highest number of cases and social, epidemiological, demographic, laboratory

and clinical aspects.

2. Methodological design

Type of study

This was an epidemiological, observational, descriptive, retrospective, cross-sectional study that was designed based on secondary data (Silva, 2014) on the number of human VL cases in Brazil and its states and twin cities that were collected from 2010 to 2019, with a focus on the state and twin city with the highest number of cases.

Data source

The data were obtained through the public domain website of the Information Technology Department of the Unified Health System (DATASUS), at the electronic address (<http://www.datasus.gov.br>). After accessing the address, the steps are as follows: epidemiological and morbidity; notification diseases and injuries - 2007 onwards; in this case, visceral leishmaniasis; Brazil by region, Federative Unit and municipality, where different options appear according to the objectives of the study, as well as the years to be considered in the research.

Characterization of the study area

Brazil is located in Latin America. It is the fifth largest country in the world and has a territory of approximately 8,510,345.538 km², an estimated population of approximately 211,755,692 inhabitants in 2020, and a demographic density of 22.43 inhabitants/km² (IBGE, 2020). The country has 33 twin cities that are distributed in the states of Acre, Amazonas, Amapá, Mato Grosso do Sul, Paraná, Rondônia, Roraima, Rio Grande do Sul, Santa Catarina, and Mato Grosso (Brasil, 2019).

Inclusion criteria

We included human VL cases in Brazil and its states and twin cities, with a focus on the state and twin city with the highest number of cases, in the period from 2010 to 2019.

Study variables

The dependent variable was number of human VL cases in Brazil and its states and twin cities, with a focus on the state and twin city with the highest number of reported cases. The independent variables were gender, race/skin color, education, age group, autochthony of the case, urban/rural area, laboratory and clinical aspects (i.e., case evolution).

Data analysis

The data were collected, imported into Microsoft Excel, organized into tables and graphs, and expressed as absolute frequency and relative frequency for better visualization of the results.

The incidence rate of VL cases between 2010 and 2019 was calculated for the state and twin city with the highest number of cases, dividing the number of new cases by the exposed population, multiplied by 100,000. For this purpose, population data obtained from information from population censuses in Mato Grosso do Sul and Corumbá 2010 were considered, through the website of the Brazilian Institute of Geography and Statistics (www.ibge.gov.br) (Instituto Brasileiro de Geografia e Estatística [IBGE], 2010).

All variables surveyed were statistically analyzed. Therefore, the distribution of data was initially verified with the Shapiro-Wilk test. Since the data presented an unspecified distribution, the non-parametric Mann-Whitney test was used (Ayres et al., 2003). A significance level of 5% and the Minitab 18 program were used.

Ethical aspects

Because this was a secondary data analysis, no registration from any research ethics committee was required, with a waiver of consideration according to ethical standards that were established by Resolution No. 510 of 2016, of the National Health Council of Brazil, which determines specific ethical guidelines for the human and social sciences (Brasil, 2016c).

3. Results

According to the time series of VL in Brazil between January 2010 and December 2019, 35,886 human VL cases were reported in the Notifiable Diseases Information System (Sistema de Informações dos Agravos de Notificação [SINAN]), of which 2,834 cases were in states with international borders. The state of Mato Grosso do Sul had the highest number of notifications (Table 1).

Table 1. Distribution of human visceral leishmaniasis cases in Brazilian states with international borders (2010-2019).

Notification location	
State	No. of cases
Mato Grosso do Sul	1,834
Pará	347
Mato Grosso	317
Roraima	217
Paraná	50
Rio Grande do Sul	34
Santa Catarina	14
Amazonas	9
Rondônia	9
Amapá	3
Acre	-
Total	2,834

Source: Based on data from the Notifiable Diseases Information System, Ministry of Health, Brazil.

Among the 2,834 VL cases in states with international borders, 148 were in twin cities (0.4%). The city of Corumbá had the highest number of notifications (Table 2).

Table 2. Distribution of human visceral leishmaniasis cases in Brazilian twin cities in each Brazilian state with an international border (2010-2019).

Notification location		
State	Twin city	No. of cases
Mato Grosso do Sul	Corumbá	94
	Ponta Porã	14
	Bela Vista	4
Paraná	Foz do Iguaçu	23
Rio Grande do Sul	São Borja	6
	Uruguaiana	3
	Itaqui	2
Roraima	Pacaraíma	2
Total		148

Source: Based on data from the Notifiable Diseases Information System, Ministry of Health, Brazil.

Table 3 shows that the number of human VL cases in Mato Grosso do Sul from 2010 to 2013 was higher, followed by a subsequent reduction. The same happened with incident rates: 8.0, 9.9, 10.5, and 8.3 cases per 100,000 inhabitants, with an annual mean incidence rate of 6.4 cases/100,000 inhabitants (Table 3).

In Corumbá, the number of VL cases remained constant between 2010 and 2013, fluctuated with little variability between 2014 and 2016, was the highest between 2017 and 2018, and then slightly decreased in 2019 (Table 3). Of the total number of notified cases, 91 were autochthonous. The annual mean incidence rate was 8.3 cases/100,000 inhabitants. In 2017 and 2018, the mean incidence rates were 16.9 and 13.3 cases per 100,000 inhabitants (Table 3).

Table 3. Number of cases and incidence rate* of visceral leishmaniasis according to notification year in the state of Mato Grosso do Sul and municipality of Corumbá (2010-2019).

Notification year	Notification location			
	Mato Grosso do Sul		Corumbá	
2010	225	8.0	6	5.3
2011	280	9.9	8	7.1
2012	297	10.5	5	4.4
2013	235	8.3	4	3.5
2014	170	6.0	11	9.8
2015	125	4.4	6	5.3
2016	141	5.0	9	8.0
2017	140	4.9	19	16.9
2018	110	3.9	15	13.3
2019	111	3.9	11	9.8
Total	1,834	64.8	94	83.4

Source: Based on data from the Notifiable Diseases Information System, Ministry of Health, Brazil. *Per 100,000 inhabitants.

The disease was more frequent in males ($n = 1,175$ and 61), corresponding to 64.0% of cases in Mato Grosso do Sul and 65.0% of cases in Corumbá ($p < 0.05$). With regard to race/skin color, 8.7% and 1.0% of the research forms ($n = 160$ and 1) were blank or marked unknown, with a higher proportion of self-declared brown-skinned people ($p = 0.0001$), representing 52.9% ($n = 972$) and 76.7% ($n = 72$) of VL cases. No difference was found in the comparison between the number of people who self-declared as white- and brown-skinned ($n = 972/547$, $p > 0.05$) in Mato Grosso do Sul (Table 4).

With regard to education, 26.8% ($n = 492$) and 45.7% ($n = 43$) were in the “not applicable” group at the time of notification in Mato Grosso do Sul and Corumbá, respectively, possibly because of the high number of cases in children under 4 years old (25.2% and 42.5% , respectively). Among VL patients, 2.0% ($n = 37$) and 2.1% ($n = 2$) declared themselves illiterate, 34.0% ($n = 624$) and 29.7% ($n = 28$) had up to 8 years of education, 13.9% ($n = 256$) and 12.7% ($n = 12$) had more than 8 years of education, and 23.3% ($n = 425$) and 9.8% ($n = 9$) were “unknown.” A greater number of human VL cases was observed in the group who had up to 8 years of education ($p = 0.0001$; Table 4).

Human VL cases ranged from under 1 year old ($n = 141$) to over 80 years old ($n = 41$) in Mato Grosso do Sul and from under 1 year old ($n = 18$) to 79 years old ($n = 4$) in Corumbá, with 25.2% ($n = 461$) and 42.5% ($n = 40$) of the patients aged up to 4 years old and 48.1% ($n = 884$) and 33.9% ($n = 32$) aged between 20 and 59 years old ($p < 0.05$). No difference was found in the comparison between the number of people aged 1-4 years old and 40-59 years old ($n = 320/469$, $p > 0.05$) or between those aged under 1-4 years old ($n = 18/22$) and 20-59 years ($n = 17/15$) in Mato Grosso do Sul and Corumbá (Table 4).

With regard to the area of residence, most cases occurred in urban areas, representing 93.3% ($n = 1,711$) of the total in Mato Grosso do Sul and 85.1% ($n = 80$) of the total in Corumbá ($p = 0.0001$). Only 4.1% ($n = 76$) and 3.1% ($n = 3$) were recorded in rural areas (Table 4).

Table 4. Characteristics of people with visceral leishmaniasis in the state of Mato Grosso do Sul and municipality of Corumbá (2010-2019).

Variable	Notification location					
	Mato Grosso do Sul			Corumbá		
	AF	RF (%)	<i>p</i>	AF	RF (%)	<i>p</i>
Gender			0.014*			0.039*
Female	658	36.0		33	35.1	
Male	1,175	64.0		61	65.0	
Race/Skin color			0.0001*			0.0001*
White	547 ^a	30.0		16	17.0	
Black	123	6.7		5	5.3	
Brown	972 ^a	52.9		72	76.7	
Indigenous	17	0.9		-	-	
Asian	15	0.8		-	-	
Unknown/Blank	160	8.7		1	1.0	
Education			0.0001*			0.0001*
Illiterate	37	2.0		2	2.1	
≤ 8 years	624	34.0		28	29.7	
> 8 years	256	13.9		12	12.7	
Unknown/blank	425	23.3		9	9.8	
Not applicable	492	26.8		43	45.7	
Age group			0.0001*			< 0.05*
< 1 year	141	7.6		18 ^a	19.1	
1-4 years	320 ^a	17.6		22 ^a	23.4	
5-9 years	75	4.0		3	3.1	
10-14 years	45	2.8		4	4.2	
15-19 years	83	4.5		4	4.2	
20-39 years	415	22.6		17 ^a	18.0	
40-59 years	469 ^a	25.5		15 ^a	15.9	
60-64 years	79	4.3		5	5.3	
65-69 years	69	3.7		2	2.1	
70-79 years	94	5.1		4	4.2	
≥ 80 years	41	2.2		-	-	
Unknown/White	3	0.1		-	-	
Area			0.0001*			0.0001*
Rural	76	4.1		3	3.1	
Urban	1,711	93.3		80	85.1	
Peri-urban	3	0.2		2	2.1	
Unknown/blank	44	2.4		9	9.5	

AF, absolute frequency; RF, relative frequency; **p* < 0.05 (Mann-Whitney test). Values with the same letter (^a) indicate no significant difference (*p* > 0.05, Mann-Whitney test). (-), not calculated. Source: Data from the Notifiable Diseases Information System, Ministry of Health, Brazil.

The diagnosis of VL cases reported in Mato Grosso do Sul and in Corumbá was performed by means of parasitological examination, with positivity of 26.7% (n = 491) and 41.5 (n = 39) (*p* < 0.05) and of the immunological exam, indirect immunofluorescence (IIF), with positivity of 43.7% (n = 801) (*p* = 0.0003) and 45.7% (n = 43) (*p* > 0.05), being that, 88.8% (n = 1629) and 77.7% (n = 73) of the cases were confirmed by laboratory examination and 11.2% (n = 205) and 22.3% (n = 21) by criteria clinical-epidemiological (*p* < 0.05) (Table 5).

With regard to clinical evolution, most of the cases evolved to a cure (80.9% (n = 1,484) in Mato Grosso do Sul and 76.5% (n = 72) in Corumbá; *p* = 0.0001; Table 5).

With regard to the number of deaths that were attributable to VL, 6.7% (n = 124) were reported in Mato Grosso do Sul, and 15.9% (n = 15) were reported in Corumbá (*p* = 0.0001; Table 5).

Table 5. Laboratory and clinical characteristics of people with visceral leishmaniasis, in the state of Mato Grosso do Sul and municipality of Corumbá (2010-2019).

Variable	Notification location					
	Mato Grosso do Sul			Corumbá		
	AF	RF (%)	<i>p</i>	AF	RF (%)	<i>p</i>
Parasitological diagnosis			0.0019*			0.0003*
Positive	491	26.7		39	41.5 ^a	
Negative	197	10.7		11	11.7	
Unrealized	1141	62.3		44	46.8 ^a	
Ignored/white	5	0.3		-	-	
Immunological diagnosis^b			0.0003*			0.1212
Positive	801	43.7 ^a		43	45.7	
Negative	199	10.8		14	14.9	
Unrealized	829	45.2 ^a		37	39.4	
Ignored/white	5	0.3		-	-	
Confirmation criteria for LV			0.0002*			0.0019*
Laboratory	1629	88.8		73	77.7	
Clinical-epidemiological	205	11.2		21	22.3	
Clinical evolution			0.0001*			0.0001*
Cure	1.484	80.9		72	76.5	
Abandonment	25	1.3		-	-	
Death due to VL	124	6.7		15	15.9	
Death due to other disease	100	5.7		5	5.3	
Transfer	42	2.2		2	2.1	
Unknown/blank	59	3.2		-	-	

AF, absolute frequency; RF, relative frequency; ^bIndirect immunofluorescence technique. * $p < 0.05$ (Mann-Whitney test). Values with the same letter (^a) indicate no significant difference ($p > 0.05$, Mann-Whitney test). (-), not calculated. Source: Data from the Notifiable Diseases Information System. Ministry of Health. Brazil.

4. Discussion

Visceral leishmaniasis is the most severe form of leishmaniasis and almost always fatal if not diagnosed and treated. It is endemic in 12 countries on the South American continent. From 2001 to 2017, 59,769 new cases were recorded in these countries, with an average of 3,516 cases annually (Maia-Elkhoury et al., 2021). Approximately 96% (57,582) of the cases were concentrated in Brazil, thus corroborating the high number of cases in 2010-2019 that were identified in the present study, with an annual average of 3,588 cases. However, geographical expansion has been observed in other South American countries, including Argentina, Colombia, Paraguay, and Venezuela (Maia-Elkhoury et al., 2021).

According to a bibliographic review of the profile of VL in Brazil (Lemos, Sousa & Silva, 2019), the high percentage of cases in Brazilian regions is attributable to a progressive increase in urban areas. Leishmaniasis is associated with anthropogenic environmental transformations that allow the adaptation and formation of mosquito breeding sites that are encouraged by socioeconomic factors that direct a significant proportion of the population to migrate to urban peripheries that have relatively precarious housing and sanitary infrastructure conditions. Deforestation and large fires also favor displacement of the transmission vector to urban centers, consequently exposing the population to vector transmission (Costa et al., 2018; Salomón et al., 2015; Ortiz & Anversa 2015).

International border areas can also generate situations of vulnerability to the health of populations (Pêgo & Moura, 2018), especially in the presence of sandflies and dogs (specifically those that live on the street) (Oliveira et al., 2016; Lopez et al., 2021). Thus, understanding the epidemiological profile of VL in border regions provides better knowledge about the disease and supports managers and health professionals in the construction of measures, as well as in directing and prioritizing areas to

be worked (Maia-Elkhoury et al., 2021).

In the present study, the most affected state with an international border and twin city were Mato Grosso do Sul and Corumbá, respectively. According to epidemiological evidence, the presence of the parasite in these regions can be attributed to the construction of a railway that originated in Bolivia, a highway that was built between Três Lagoas and Corumbá, and a natural gas pipeline that was built between Bolivia and Brazil (Lopez et al., 2021).

Consequently, VL became urbanized through changes in the vector's behavior that resulted from socioenvironmental changes, specifically deforestation and the migration process. Deforestation reduced access to animals that were normally a source of food for the vector insect. Dogs and humans then emerged as the most accessible alternative food sources for the vector. The migratory process took human and canine populations from rural areas where the disease was endemic to cities' peripheral areas (Costa et al., 2018; Salomón et al., 2015; Oliveira et al., 2016). Consequently, the state of Mato Grosso do Sul began to be considered a new Brazilian endemic region for VL (Lopez et al., 2021).

According to an epidemiological bulletin on VL in Mato Grosso do Sul between 2011 and July 2020, 1,741 cases were confirmed, with an annual average of 174.1 cases and 124 deaths (Bogiani & Oliveira, 2020). In the municipality of Campo Grande, Mato Grosso do Sul, from 2001 to 2018, 1,855 VL cases were reported, with an annual average of 103.0 cases and annual average incidence rate of 13.23 cases/100,000 inhabitants, demonstrating the rapid transition from epidemic to endemic (Oliveira et al., 2020). These data corroborate the present findings. From 2010 to 2019, the annual average was calculated to be 183.4 human cases, with an incidence rate that ranged from 3.9 to 10.5 cases per 100,000 inhabitants in the state. From 2010 to 2013, the number of human VL cases was higher, which subsequently decreased.

For the municipality of Corumbá, the present study found an annual average of 9.4 cases, with incidence rates that ranged from 3.5 to 16.9 cases per 100,000 inhabitants in the region. The number of cases remained constant between 2010 and 2013, fluctuated with little variability between 2014 and 2016, was the highest between 2017 and 2018, and slightly decreased in 2019. Calculations of the incidence rate of cases remains an important tool for surveillance because it provides better knowledge about VL and guides health managers and professionals in adopting actions that may be useful (Maia-Elkhoury et al., 2021).

We cannot definitively explain the variations in incidence rates that were found in the present study. The *Leishmania* parasite presents wide complexity in transmission dynamics (Courtenay et al., 2017). Various factors can be involved and various hypotheses can be posited, including the cyclical nature of the disease, particularities of its pathogenesis (e.g., its indeterminate incubation period and asymptomatic and subclinical forms) (Toledo et al., 2017; Zuben & Donalísio, 2016). Furthermore, the high adaptability of the vector insect that is responsible for transmission of the disease should also be considered (Rocha, 2019).

Visceral leishmaniasis is transmitted through bites of infected female sandflies, especially *Lutzomyia longipalpis* and *Lutzomyia cruzi* (Rocha, 2019). A study in the municipality of Corumbá that evaluated the seasonal distribution of sandflies over a 2-year period (from April 2012 to March 2014) found that the monthly distribution of sandflies was 93.9% for *L. cruzi* (Oliveira et al., 2016).

Additionally, an epidemiology research study of VL in the municipality of Três Lagoas, Mato Grosso do Sul, investigated 6,469 dogs for the presence of canine VL between 2016 and 2019, of which 52.6% were positive¹⁰. In the border area of Corumbá and in Paraguay and Bolivia (Corumbá, 2021), sandflies and dogs (specifically those that live on the street) circulate freely between the borders. Therefore, there is no barrier to where they may roam, which contributes to spread of the disease in these areas (Pêgo & Moura, 2018).

As for VL preventive measures, the Surveillance and Control Program determines the following actions when directed at the human population: use of mosquito nets, screens on doors and windows and use of repellents; vector-directed: environmental management and sanitation, through urban cleaning, disposal and proper disposal of organic solid waste,

elimination of a source of moisture and non-permanence of domestic animals in the home; directed to dogs: control of the errant canine population, in cases of animal donation, perform a serological test for VL before donation, use of screens in individual or collective kennels and collars impregnated with 4% deltamethrin for dogs (Brasil, 2016a).

However, the number and incidence of human cases of VL reported in Mato Grosso do Sul and Corumbá, the high percentage of sandfly *L. cruzi*, in Corumbá (Lopez et al., 2021) and the positivity found for canine VL in Três Lagoas (Pêgo & Moura, 2018), indicate failure in the realization of preventive measures and require actions effective measures to combat and eliminate the disease.

With regard to sociodemographic aspects, according to the Epidemiological Bulletin on VL that was published in 2020, the most affected age group in the state of Mato Grosso do Sul was 35-49 years old (22.9%), followed by 1-4 years old (17.1%), most of whom were male (65.0%) (Bogiani & Oliveira, 2020). In Campo Grande, the most affected age groups were children up to 5 years old and adults over 40 years old, and the highest incidence was in males (Oliveira et al., 2020). In the present study, the most affected age groups in Mato Grosso do Sul and Corumbá were up to 5 years old and 20-59 years old, and the most affected were also male ($p < 0.05$).

The frequency of cases in children compared with adults may be related to the fact that children have more direct contact with reservoir and vector animals and have immature immune function and nutritional deficits (Oliveira et al., 2014). The predominance of males may be attributable to behavioral differences relative to females, given the higher presence of men in areas with a higher risk of sandfly bites (Araújo et al., 2016).

As for to race/skin color, most cases were brown-skinned individuals in the state of Mato Grosso do Sul and municipality of Corumbá ($p = 0.0001$), which is consistent with observations in Palmas-Tocantins, Brazil, between 2002 and 2013, where 71.4% of people declared themselves to be brown-skinned (Silva et al., 2017).

With regard to education, most people in Mato Grosso do Sul and Corumbá had up to 8 years of education ($p = 0.0001$), suggesting socioeconomic vulnerability that is usually associated with VL (Luz et al., 2018). This finding shows that a low level of education can influence knowledge and health practices related to prevention (Menezes et al., 2016).

As for to the place of residence, the wide distribution of VL in urban areas ($p = 0.0001$) in Mato Grosso do Sul and Corumbá has been an epidemiological reality that requires a new rationale for disease surveillance and control systems. The present findings corroborate other studies, in which the predominance of VL cases also occurred in urban areas as a result of destruction of the vectors' natural habitats and environmental conditions that were favorable to spread of the disease, such as a precarious sanitary infrastructure and high population density with lower purchasing power (Silva et al., 2017; Barbosa, 2016; Cardim et al., 2016).

With regard to laboratory, parasitological and immunological tests used to diagnose VL cases reported in Mato Grosso do Sul and Corumbá, the IIF serological test and the bone marrow and spleen aspirate that usually shows the presence of amastigotes of the parasite, are generally recommended for diagnosing VL (Brasil, 2016a; Rey, 2010), which provided confirmation of 88.8% and 77.7% of cases, and only 22.3% of case by criteria clinical-epidemiological ($p < 0.05$).

As for the drug used for treatment, this information was not available on SINAN, however, in Brazil, the drug of first choice is the pentavalent antimonial (Sb^{+5}), n-methyl-glucamine antimoniate, distributed by the Ministry of Health in 1 ml ampoules, containing 81mg of Sb^{+5} . It is recommended to treat VL with a dose of 20mg of Sb^{+5} kg/day, with intravenous-IV or intramuscular-IM application, for 20 to 40 days, using the maximum limit of 2 to 3 ampoules/day of product with favorable cure rates (Brasil, 2016a).

With regard to clinical and epidemiological profiles, the frequencies of cure above 81.0% and 72.0% in Mato Grosso do Sul and Corumbá, respectively, and frequencies of death of 7.4% and 16.0% ($p = 0.0001$) are consistent with a study of the epidemiology of VL in the municipality of Três Lagoas, Mato Grosso do Sul, where 84.8% of 211 human cases diagnosed

between 2000 and 2019 evolved to a cure and 10.4% evolved to death (Lopez et al., 2021), indicating that among the actions of the VL Surveillance and Control Program, the treatment is being carried out effectively (Brasil, 2016a).

The present study has limitations. The use of retrospective secondary data and quality of the information that was collected on the notification forms are possible weaknesses. Nonetheless, studies of the epidemiological profile of VL that use retrospective designs and secondary data (Araújo et al., 2016; Silva et al., 2017; Barbosa, 2016; Cardim et al., 2016; Cavalcanti et al., 2017; Cavalcante et al., 2020; Graepp-Fontoura et al., 2020) can indeed support the planning of expanded and structured public policies that can guide current strategies to control the disease and identify possible high-risk areas, with the goal of preventing leishmaniasis.

5. Conclusions

A high number of human VL cases was reported in Brazil between 2010 and 2019, with a wide distribution in 10 states with international borders and an emphasis on eight twin cities. Of the states with international borders and twin cities, Mato Grosso do Sul and Corumbá were the most affected by the disease in the period of study, with an annual mean incidence rate of 6.4 and 8.3 cases/100,000 inhabitants.

In Mato Grosso do Sul and Corumbá, the disease was more frequent in males, in children under 4 years of age, and in adults 20-59 years of age. The highest frequency was found among people who self-identified as brown-skinned and who had 8 years of education.

Most cases occurred in urban areas, was diagnosed by laboratory tests and progressed to cure. However, the high number of notified VL cases requires greater attention from integrated disease management programs. Visceral leishmaniasis is difficult to control and prevent and has a rapid and wide geographic dispersion, mainly in border areas where vectors and dogs (specifically those that live on the street) move freely between countries.

Thus, works about spatial analysis to identify the places with the highest occurrence of VL in Mato Grosso do Sul and Corumbá, with the objective of guiding the implementation of prevention and control policies aimed at needy regions, are important.

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