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Epidemiological aspects of visceral leishmaniasis in the municipality of Montes Claros-MG

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ABSTRACT. Visceral leishmaniasis (VL), also known as ‘calazar’, is a serious chronic disease caused by *Leishmania* species from *Leishmania (Leishmania) donovani* complex, which the disease is characterized by abdominal swelling (hepatosplenomegaly) and may evolve to death in extreme cases. In this sense, the aim of our study was to assess the epidemiological profile of the cases found in Montes Claros (Minas Gerais state). A retrospective or cross-sectional study was carried out using secondary data provided by Health Information System (SINAN/HM) of Brazil from January 2010 to February 2020. Our data has shown that VL is an endemic disease in Montes Claros region, with 413 VL cases reported, 62.00% (252) male, average age $\pm$ standard deviation (years), and 93.46% (386) lived in Montes Claros city. The presence of comorbidities was observed in 13.70% (54) of the patients and in 7.26% (30). As for the evolution of the disease, 246 (59.56%) were cured, 30 (7.26%) died due to VL. Between 2010 and 2015, Glucantime® stands out, in which 46 (11.13%) patients used the drug, followed by common Amphotericin B 24 (13.48%) and liposomal Amphotericin B 38 (21.34%). In the period between 2016 and 2020, the most prevalent drug was liposomal Amphotericin B, with 71 (29.83%) patients using it, followed by Glucantime® 45 (18.9%). The condition evolved to death. We conclude that Montes Claros is still an endemic area for VL with an increased number of cases over time and a noticeable shift in patient profile towards children and young people. Joint efforts from different areas of scientific knowledge and public health services are needed to improve the effectiveness of visceral leishmaniasis surveillance and control actions. The population can contribute to this process of disease prevention and control, through educational actions in health and the environment.

Keywords: visceral leishmaniasis; zoonoses; epidemiology; communicable diseases.

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Introduction

Visceral Leishmaniasis (VL) is an important disease for public health. It has a high prevalence, incidence and is worldwide distributed with significant mortality rates (Guimarães et al., 2012). Nowadays, according to World Health Organization (WHO, 2020) more than 1 billion people live in areas endemic for leishmaniasis and are at risk of infection. An estimated 30,000 new cases of VL occur annually. It is an anthroponosis caused by *Leishmania* species belonging to the *Leishmania (Leishmania) donovani* complex (Rath et al., 2003).

The etiological leishmaniasis agent in Brazil is *Leishmania (Leishmania) infantum chagasi*. The transmission parasite to man transmission occurs through *Lutzomyia (Lutzomyia) longipalpis* species female bite (Michalsky et al., 2011). When infected, they release metacyclic promastigote forms and spittle (Rath et al., 2003). Differentiation occurs in macrophages, where amastigotes multiply intensely until cell disruption (Malaria Consortium, 2010).

According to Ministry of Health (MH) of Brazil, VL was once considered a rural zoonosis which nowadays affects medium and large urban centers in a phenomenon known as visceral leishmaniasis urbanization. The first epidemic outbreak in Brazil occurred in Teresina from 1981 to 1984 and since then many others have been reported in other cities' periphery: São Luiz, Belo Horizonte, Montes Claros (Minas Gerais) and Rio de Janeiro (Rio de Janeiro) (Carranza-Tamayo et al., 2010).

In recent years, VL lethality has gradually grown in Brazil from 3.6% in 1994 to 6.7% in 2003 and to 8.4% in 2004 (Alvarenga, Escalda, Costa, & Monreal, 2010). Among the hosts, species of wild and domestic

animals are found and the dog is considered the main natural host related to human cases (Silva, 2007). The Brazilian program to combat VL aims to reduce lethality and morbidity rates through epidemiological studies, early diagnosis and treatment of human cases concomitantly to the reservoir populations and vectors control (Souza, Silva, Afonso-Cardoso, Favoreto Junior, & Ferreira, 2005).

The use of tools such as the mapping areas and understanding urban spot spatial dynamics, a phenomenon resulting from urbanization, have been of great value for the study of diseases that present varied transmission patterns, as they allow mapping and identifying areas with high risk for new cases (Bavia, Carneiro, Gurgel Hda, Madureira Filho, & Barbosa, 2005; Desjeux, 2004). Thus, the present study evaluated the epidemiological aspects of notified visceral leishmaniasis cases in Montes Claros, state of Minas Gerais in Southeast Brazil, between the years 2010 to 2020.

Materials and methods

This cross-sectional study was carried out in the city of Montes Claros, northern mesoregion of Minas Gerais in Southeast Brazil (16° 43 '41 "S and 43° 51' 54" W, 638 m sea level). The territory occupies approximately 4,135 km² and a population of 413,487 people (Figure 1). It has an average annual temperature of 24°C with relative humidity ranging from 52-80%. The climate is tropical semi-arid, hot and dry with rainy periods concentrated between October and March. Annual rainfall is around 1029 mm (Monteiro et al., 2005).

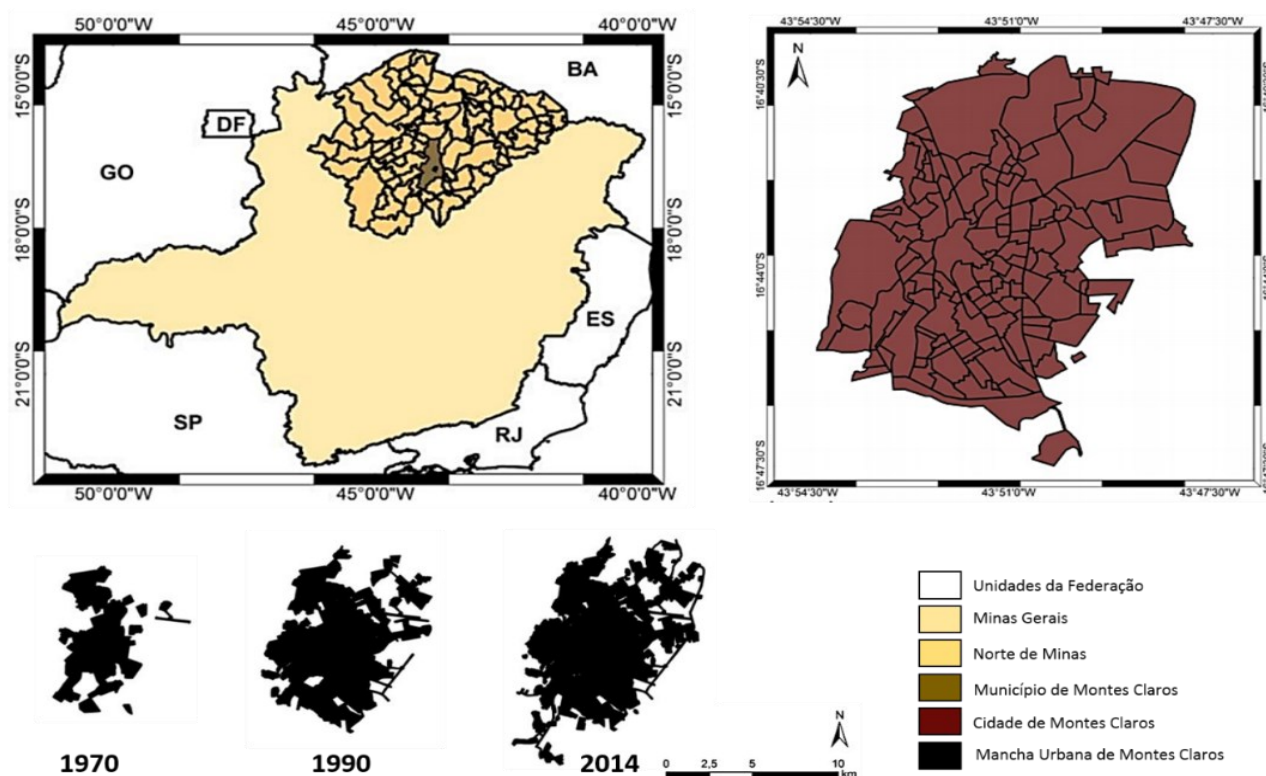


Figure 1. Municipality of Montes Claros (MG, Brazil) and development of the urban area between the years 1970-2014.

Source: Bortolo, Rodrigues and Borges (2018) and Sousa-Gomes et al. (2011).

This study was based on case records notified by “Sistema de Informação de Agravos de Notificação – SINAN” (Diseases Information and Notifications System - DIN) from Ministry of Health (MH) of Brazil, made available by the Epidemiological Surveillance sector of the Municipal Health Department in Montes Claros from January 2010 to December 2020. The notification forms for VL were tabulated in the Microsoft office Excel® 2013 software and later treated in the original 8.0 software, using the Chi-square test (χ^2), with 95% reliability, statistical significance when p value < 0.05. The present work was approved by Ethics Committee on Research with Human being at Plataforma Brasil - Ministry of Health/Brazil, CAAE 69738117.2.0000.5146.

Results

A total of 413 VL notifications were recorded from 2010 to 2020. There was no decrease in notified cases of VL over those ten years (Figure 2A). Male patients represented the overwhelming majority of notified cases 252 (62.00%), accounted for the remaining 161 (38.98%) of notified cases (Figure 2B). Regarding the age group, it was significant ($p < 0.05$) in patients under the age of 19 with 167 (40.43%) of the cases, followed by the age groups from 20 to 49, 130 (31.47%), 50 to 64 years old, 66 (15.9%) and over 65 years old, 50 (12.1%), decreasing with increasing age (Figure 2C). For the local notification variable, a significant number of cases is perceived in the urban area with 386 (93.46%) of cases and the rural area with 27 (6.53%) (Figure 2D).

The initial complaints reported by the patients and the clinical manifestations at the time of diagnosis are summarized in Index 1 (Table 1). The most frequent symptoms were fever (89.83%), followed by splenomegaly (84.26%), pallor (62.92%), hepatomegaly (79.77%) and weakness (60.67%), the most common.

Table 1. Clinical manifestations and initial complaints of patients with visceral leishmaniasis reported in the notification that lead them to seek the health system.

Clinical manifestations	n	%
Fever	371	89.83
Splenomegaly	325	78.69
Pallor	268	64.89
Hepatomegaly	309	74.81
Slimming	226	54.47
Cough	141	34.14
Weakness	287	69.49
Edema	90	21.79
Abdominal pain	5	2.80
Infection	127	30.75
Headache	2	1.12
Vomiting	2	1.12
Hyporexia	5	2.80
Jaundice	57	13.80

Data from DIN/MHS/Montes Claros - MG.

A total of 54 (13.7%) exhibited HIV as a comorbidity, 343 (83.05%) no reported comorbidity, and 45 (10.41%) of the files simply lacked this information (Figure 2E).

About the disease evolution, 246 (59.56%) were cured, 30 (7.26%) died due to VL and 17 (4.11%) died from unrelated causes (Figure 2F), while 120 (29%) did not have reported notifications regarding the evolution.

As for the treatment, the most used drugs of choice during the 10 years of evaluation were Glucantime®, Amphotericin B (AmB), and AmB liposomal. Between 2010 and 2015, Glucantime® was used in 46 (11.13%) of the followed by AmB common 24 (13.48%) and Amphotericin B liposomal 38 (21.34%) (Table 2). From 2016 to 2020, the most prevalent drug used was AmB liposomal with 71 (29.83%), followed by Glucantime® 45 (18.9%) and common AmB (1.68%).

Discussion

The present study in Montes Claros region demonstrated that the presence of VL in the North of Minas Gerais, Brazil, is still a frequent disease. In accordance to previous studies, we found that male individuals represented the vast majority of affected patients (Oliveira et al., 2010; Cavalcante & Vale, 2014; Sousa et al., 2018). Studies indicate that this may be related to the type of occupational activity of men, such as: agriculture, livestock, woodcutters and gardening. In addition, leisure, outdoor sport and housing that predisposes them to greater exposure of the vector, which is suggested to be a possible result from men's occupational activity, leisure and housing that predisposes them to a greater vector exposure. However, this association is not well established and infection can occur equally without gender preference (Oliveira et al., 2008; Theocharidou, Maltezos, Constantinidis, & Papa, 2019).

Urban space corresponded to 96.0% of the cases, a fact that may be linked to environmental conditions in the municipality, which are described in the literature as favorable for VL occurrence demonstrated great adaptability in areas of human occupation, they can coexist with domestic animals in the peri-household

and resist environmental variations, judging by the abundance with which they occurred in these environments. The predominance of these species allows greater contact with humans and justifies the notification of cases of Visceral Leishmaniasis in the region, changing the epidemiological profile of previously wild leishmaniasis (Moraes, Santana, Bandeira, & Rebêlo, 2020). Another factor related to the expansion of the disease in the urban perimeter is the geographical situation. In Montes Claros, as well as in much of Brazil, there was a disorderly population growth caused by the intense migratory flow in the 70s coupled with the lack of planning. This resulted in an intra-urban spatial differentiation across several areas denoted by poverty foci which in turn led to the introduction of the disease in the city, as can be seen in the urban area increase over time until 2015 (Figure 1) (Sherlock, 1996; Rath et al., 2003; Barbosa, 2016). According to (Monteiro et al., 2005) an urban centers expansion process, anthropic action results forest areas invasion and deforestation, thus increasing vector density and direct contact with wild and domestic animals, contributing to the increase leishmaniasis cases. These factors indicate the urbanization process of the disease, which may justify the occurrence of the disease in both sexes and in different age groups.

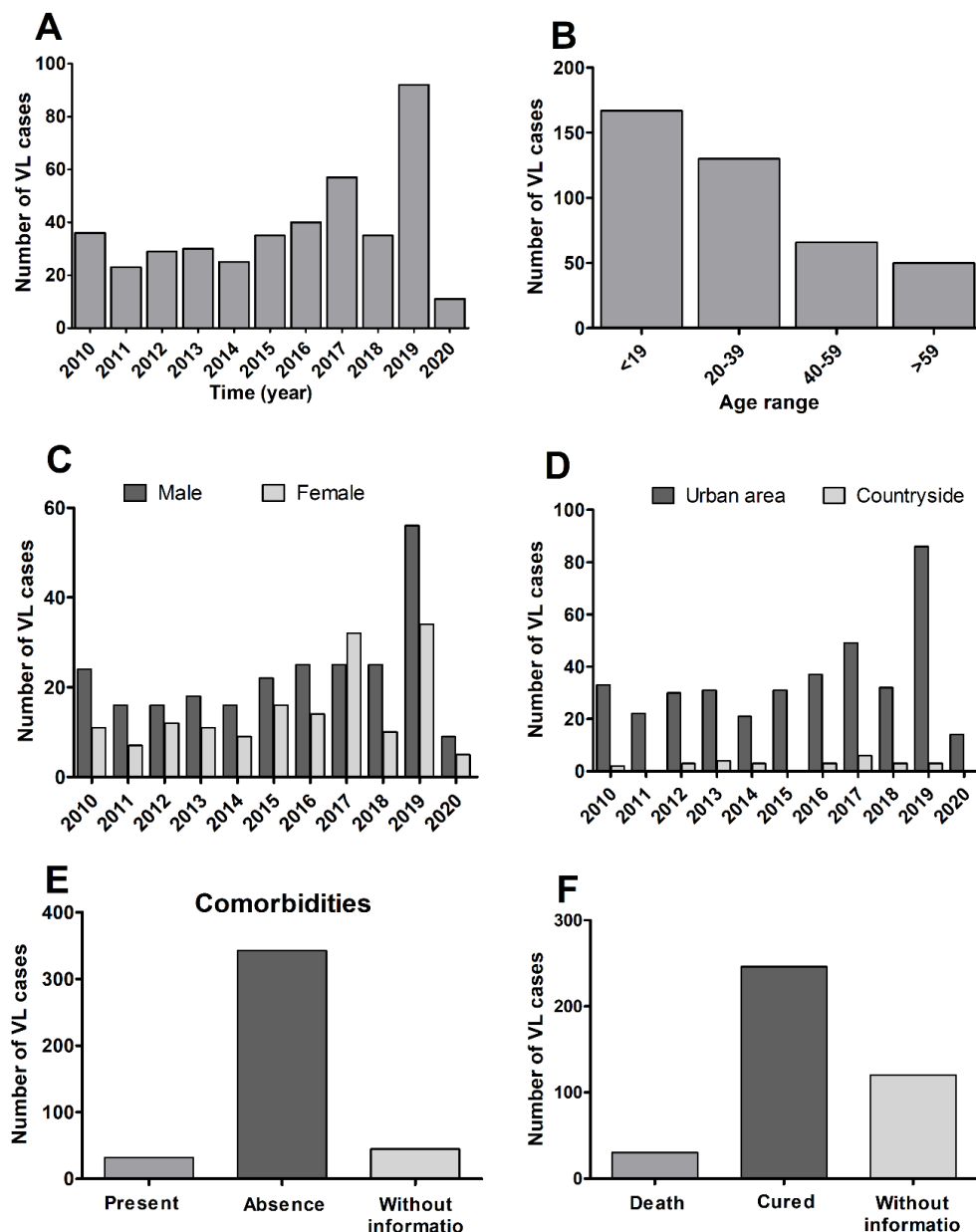


Figure 2. Visceral Leishmaniasis in Montes Claros city from 2010 to 2020. (A) Number of reported cases, (B) VL prevalence by age group, (C) patient informed gender, (D) place of residence of the cases reported, (E) evaluation of comorbidity and (F) number of deaths.

Data from DIN/ Municipal Health Secretariat (MHS) / Montes Claros - MG, 2020).

Table 2. Drugs used in the treatment of VL in patient in the region of Montes Claros-MG between the years 2010-2020.

Year	Drugs					
	Glucantime		AmB		AmB liposomal	
	n (95)	%	n (28)	%	N (97)	%
2010	7	31.81	10	45.45	5	22.72
2011	8	53.33	4	26.66	3	20.0
2012	9	45.0	5	25.0	6	30.0
2013	13	48.14	3	11.11	11	47.74
2014	5	41.66	2	16.66	5	41.66
2015	8	50.0	0	0.0	8	50.0
2016	13	41.93	0	0.0	18	58.06
2017	17	37.77	0	0.0	28	62.22
2018	6	35.29	2	11.76	9	52.94
2019	8	88.88	0	0.0	1	11.11
2020	1	16.66	2	33.33	3	50.0

AmB: Amphotericin. Data from DIN/MHS/Montes Claros - MG.

Regarding the medication choice, there is a high frequency of the use of Glucantime® (28.08%) as the drug of first choice in the period from 2010 to 2020 for treatment of patients with VL. The drug causes rapid regression of clinical and hematological manifestations of the disease, as well as sterilizing the parasite (Rath et al., 2003). However, this drug can be clinically ineffective in some forms of VL which tend to relapse at a later stage and can cause side effects such as myalgia, arthralgia, pancreatitis, leukopenia, kidney and liver problems, as well as toxicity affecting heart rate (Manual de Vigilância e Controle da Leishmaniose Tegumentar Americana, 2007). Its prolonged use in the treatment of VL can cause death to patients diagnosed with diabetes mellitus (DM) and hypertension (Lima, Cerino, Oliveira, Silveira, & Lima, 2007).

Amphotericin B is a second choice treatment in Brazil, and its liposomal formulations and pentamidines are used. VL patients who failed treatment used AmB (3.37%) and AmB liposomal (2.24%). It is observed that the failure of the treatment is related to some factors such as: strain resistance, endemic region, immunological factor and co-morbidity presence. Thus, second-line drugs such as amphotericin B (Fungizone®), have been recommended in cases of patient intolerance and parasites resistance to conventional treatment (Lima et al., 2007). In this sense, from 2016 to 2020 the most used drug was liposomal Amphotericin B, because of its lower acquisition cost. In addition, the Ministry of Health started to advocate in specific cases because the drug has a low toxicity (Caldas, Lisboa, Fonseca Silva, Coutinho, & Silva, 2014). Since then, the drug has been used in groups that were not supposed to be used as the first choice.

A percentage of 13.7% of the patients showed HIV as a co-morbidity. The clinical manifestations in serum-positive HIV patients are similar to the VL of immunocompetent ones, however, their immune system more susceptible to a bad evolution of the disease (Sousa-Gomes et al., 2011), because the patient, when infected with HIV, has a significant decrease in immunity which predisposes to the development of associated comorbidities such as VL.

The investigation of the epidemiological profile of VL in the Northern region of Minas Gerais brought to our knowledge that a possible study weakness is a time gap in updated studies on the disease, as well as the regional data scarcity. In addition, we verified gaps in the notifications through missing data which suggests the education of health professionals to correctly fill out the notification form, for a better detailed analysis of the disease behavior to take preventive measures.

In this sense, we recognize the importance of the present study to the knowledge about VL in view of its impacts on health and quality of life. Such data are indicative to assist health systems and professionals in the control area of the disease, as Montes Claros receives patients from all over the northern region of Minas. Thus, action measures in the transmission chain are recommended such as control of sand flies so that the use of collars with deltamethrin proved to be efficient in controlling the vector in endemic areas, vaccination of dogs, cleaning the environment, avoiding the accumulation of organic matter in backyards, proper cleaning of the shelter of domestic animals, use of products topics with action replete with insects, and walks with dogs during the day, reservoirs and wild hosts. For individual protection, mechanical means are recommended such as the use of mosquito nets, fine screens and repellents on doors and windows as well as appropriate clothing (long-sleeved shirts, long pants, socks and shoes) (Leite et al., 2018; Sousa et al., 2018). In areas with the highest incidence, the teams of the Family Health and Strategy Program showed that the intervention contributes to better organization of health services aimed at the prevention and control of VL. Also, they can play an important role in the active search for cases and in the adoption of

educational activities with the community, advising on the disease and explaining the importance of cleaning backyards (Silva et al., 2019). At the greatest incidence areas, the Family Health Program teams can play an important role in active search for cases and in adoption of educational activities with the community (Barbosa, Guimarães, & Luz, 2016). Political practices employed in urban planning and of fundamental importance as poor quality human housing in inadequate locations, the disordered construction of shelters for domestic animals in home environment and the lack of minimum basic sanitation conditions are common conditions that contribute to the proliferation of the vector and continuity of its cycle (Muniz, Rossi, Neitzke, Monteiro, & Teodoro, 2006).

Conclusion

VL is an important endemic parasitic disease in the Montes Claros municipality. The occurrence of the disease was not related to occupational activity, and this study suggests that the transmission profile in Montes Claros was preferably periurban, which should be taken into account when defining measures to control the disease. Health education works must be carried out with the population who should receive information about epidemiological aspects of the leishmaniasis, as clinical manifestations, reservoir, and vector aiming at controlling vectorial transmission of the disease in the region. Since, transmission occurs through the bite of the infected phlebotomy that attacks the host's immune system, evolving into a severe form of VL. The contagious person has some common symptoms such as fever, splenomegaly, hepatomegaly, pallor, among other symptoms. The treatment is done using chemotherapy, Glucantime, and AmB, the choice of which drug is used in each patient is according to the criteria recommended by the Ministry of Health. In the urban area, the dog (*Canis familiaris*) is the main source of infection. In the wild, the reservoirs are foxes (*Dusicyon vetulus* and *Cerdocyon thous*) and marsupials (*Didelphis albiventris*).

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