American Tegumentary Leishmaniasis in Montes Claros: an epidemiological study

Leishmaniose Tegumentar Americana em Montes Claros: um estudo epidemiológico

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Abstract
Introduction: American Tegumentary Leishmaniasis (ATL), or kala azar, is a serious chronic disease caused by *Leishmania spp*. It is an infectious and non-contagious disease that affects both humans and several species of wild and domestic animals, presenting the clinical forms of cutaneous, mucocutaneous and diffuse cutaneous. ATL is classified as a generalized zoonotic disease that has a global impact. It is caused by protozoa of the genus *Leishmania* and is considered a serious public health problem. Objective: To describe the epidemiological profile of cases found in Montes Claros-MG. Methodology: An epidemiological assessment was performed based on secondary data from SINAN/MS from January 2010 to December 2015. Results: From 2010 to 2015, 286 cases of ATL were registered, with the majority of cases occurring in children under 19 years of age (31.81%) and patients over 59 years (17.83%) had a lower percentage of disease involvement. The first choice drug used by patients was Glucantime (87.06%). The most affected gender was male (52.44%) and most patients had no comorbidities (76.96%). Conclusion: In Montes Claros, Minas Gerais, ATL presented high cases during the research period. In this sense, this study guides the development of new researches that address and monitor the spread of the disease by monitoring urban areas concomitantly with the capture of animals for the presence of the parasite, thus assisting in public health decision-making in controlling the disease.
Keywords: Visceral leishmaniasis; Zoonoses; Neglected diseases.

Resumo

Introdução: A leishmaniose tegumentar (LTA), ou calazar, é uma doença crônica grave causada por Leishmania spp. É uma doença de caráter infeccioso e não contagiosa que afeta tanto o homem como diversas espécies de animais silvestres e domésticos, apresentando as formas clínicas cutânea, mucocutânea e cutânea difusa. A LTA se classifica como uma doença zoonótica generalizada que tem impacto global. É causada pelos protozoários do gênero Leishmania e é considerada um grave problema de saúde pública. Objetivo: Descrever o perfil epidemiológico dos casos encontrados em Montes Claros-MG. Metodologia: Foi realizada avaliação epidemiológica com base em dados secundários do SINAN/MS de janeiro de 2010 a dezembro de 2015. Resultados: De 2010 a 2015, 286 casos de LTA foram registrados, sendo que a maioria dos casos ocorreu em menores de 19 anos (31,81%) e os pacientes com mais de 59 anos (17,83%) apresentaram menor percentual de acometimento da doença. A droga de primeira escolha utilizada pelos pacientes foi o Glucantime (87,06%). O gênero mais afetado era o masculino (52,44%) e a maioria dos pacientes não apresentava comorbidades (76,96%). Conclusão: Em Montes Claros, Minas Gerais a LT apresentou elevados casos no período da pesquisa. Nesse sentido, este estudo orienta o desenvolvimento de novas pesquisas que abordem e monitorem a disseminação da doença por meio do monitoramento de áreas urbanas concomitante à captura de animais para a presença do parasita, auxiliando assim na tomada de decisão em saúde pública no controle da doença.

Palavras-chave: Leishmaniose visceral; Zoonoses; Doenças negligenciadas.

Resumen

Introducción: La Leishmaniasis Tegumentaria Americana (LTA), o kala azar, es una enfermedad crónica grave causada por *Leishmania spp*. Es una enfermedad infecciosa y no contagiosa que afecta tanto al ser humano como a varias especies de animales silvestres y domésticos, presentando las formas clínicas cutánea, mucocutánea y cutánea difusa. La TLA está clasificada como una enfermedad zoonótica generalizada que tiene un impacto global. Es causada por protozoos del género *Leishmania* y se considera un grave problema de salud pública. Objetivo: Describir el perfil epidemiológico de los casos encontrados en Montes Claros-MG. Metodología: Se realizó una evaluación epidemiológica con base en datos secundarios del SINAN / MS de enero de 2010 a diciembre de 2015. Resultados: de 2010 a 2015 se registraron 286 casos de LTA, la mayoría de los casos ocurrieron en menores de 19 años (31,81%) y los pacientes mayores de 59 años (17,83%) tenían un menor porcentaje de afectación de la enfermedad. El fármaco de primera elección utilizado por los pacientes fue Glucantime (87,06%). El sexo más afectado fue el masculino (52,44%) y la mayoría de los pacientes no presentaron comorbilidades (76,96%). Conclusión: En Montes Claros, Minas Gerais, LTA presentó casos elevados durante el período de investigación. En este sentido, este estudio orienta el desarrollo de nuevas investigaciones que abordan y monitorean la propagación de la enfermedad a través del monitoreo de áreas urbanas de manera concurrente con la captura de animales para detectar la presencia del parásito, ayudando así en la toma de decisiones de salud pública en el control. la enfermedad.

Palabras clave: Leishmaniasis visceral; Zoonosis; Enfermedades desatendidas.

1. Introduction

American Tegumentary Leishmaniasis (ATL) is popularly known as Bauru ulcer and wild wound. This disease is caused by *Leishmania (viannia) brasiliensis, Leishmania (leishmania) amazonensis*, and *Leishmania (viannia) guyanensis* (Figueira et al., 2017), which are species of protozoa of the order Kinetoplastida, family Trypanomatidae and genus *Leishmania.* (Lyra et al., 2015).

According to the World Health Organization, TL is a public health problem in 85 countries, affecting four continents (Americas, Europe, Africa, and Asia), with an annual record of 0.7 to 1.3 million new cases. TL is one of the six most important infectious diseases due to its high detection rate and ability to produce deformities (Guerra et al., 2015).

In Brazil, ATL is one of the dermatological conditions that deserves the most attention due to its magnitude, its risk of causing deformities in humans, and its psychological involvement. In the last 20 years, ATL incidence in Brazil has increased in practically all States (Brazil, 2017).

Endemic outbreaks have occurred in the Southeast, Midwest, Northeast, and more recently in the Amazon region, the latter being related to the predatory process of colonization (Gontijo & de Carvalho Mde, 2003). Over the last years, the Ministry of Health registered an annual average of 35,000 new cases of ATL in Brazil. In the state of Minas Gerais, American Tegumentary Leishmaniasis (ATL) was first reported in 1940 and its transmission has been reported in rural and peri-urban areas. Minas Gerais is a state in which 1,000-2,000 LTA cases are reported annually (Miranda et al., 2011).

In the metropolitan region of Belo Horizonte, capital of the State of Minas Gerais, autochthonous cases of ATL have been registered by official health institutions since 1987 (Miranda et al., 2011). In this sense, this study aimed to carry out a descriptive study of ATL in the municipality of Montes Claros, state of Minas Gerais, between 2010 and 2015.

As a disease neglected by many countries, the need for epidemiological knowledge is necessary (Romero, 2016; Torres-Guerrero, Quintanilla-Cedillo, Ruiz-Esmenjaud, & Arenas, 2017) with the aim of promoting public policies favorable to the citizen.

2. Methodology

2.1 Study area

The present study was conducted in the Municipality of Montes Claros (16º 43 '41"S and 43º51'54"W, 638 m sea level), located in the north of the state of Minas Gerais, Brazil. Montes Claros has 413,487 inhabitants, with a population density of 3,568,941 inhabitants/km². The region has a semi-arid tropical climate, hot and dry seasons with rainy periods between October and March. It constitutes an endemic area, with a high number of cases, which motivated our studies.

2.2 Study design and data collection

We performed a cross-sectional study based on notification forms of patients with an epidemiological and laboratory diagnosis of ATL registered between 2010 and 2015. Data were obtained from the database of the National, free public agencies and, System of Notifiable Diseases (SINAN) and provided by the Health Department in force. We collected sociodemographic (gender, age, place of residence) and epidemiological (probable site of infection, comorbidities, start of treatment, type of drug) data (Schneider, Fujii, & Corazza, 2017). In compliance with ethnic principles, the present work was submitted to the Ethics Committee for Research with Human Beings at Plataforma Brasil - Ministry of Health, CAAE 69738117.2.0000.5146.

2.3 Georeferencing

For the elaboration of the mappings where the technical procedures were carried out, processes were performed using data in loco, database of free public agencies and software. All steps will be described in chronological order. In the first step, the geographic coordinates of the collection sites were confirmed using the Google Earth software. After manually entering the collection locations in the program, the collection location was visually confirmed by extracting the geographic coordinates.

After completion of the first step, the second step proceeded by converting the coordinates to kml format, for better management of the ArcGIS 10.6.1 software. Data input in this software was from the databases of the Brazilian Institute of Geography and Statistics – IBGE, after data input and then superimposing the collected points on the database, we selected and cut the municipality of Montes Claros using the tools to select and to extract selects.

Subsequently, we opened the ArcTool Box toolbox: Analysis Tools - Overlay folder. After the union between the collected points and the delimitation of the area is made, this process allows the generation of the location of the area of the collected points.

Following the aforementioned procedures. We navigated through the following options: ArcTool Box - Spatial Analyst Tools - Density - Kernel Density, to generate the kernel map. Kernel Map is an alternative for geographic analysis of pattern behavior. On the map, the punctual intensity of a given phenomenon in the entire study region is plotted using interpolation methods. As a result, we generated an overview of the intensity of the process in all regions of the map. Kernel Map is an alternative for geographic analysis of pattern behavior. On the map, the punctual intensity of a given phenomenon in the entire study region is plotted using interpolation methods. Thus, we have an overview of the intensity of the process in all

regions of the map.

2.4 Data analysis

Notification forms for ATL were tabulated in Microsoft office Excel® 2013 software (2013 version) and later treated in Origin 8.0 software, using the Chi-square test (X2), with a confidence interval of 95% and significance at p<0.05.

3. Results and Discussion

From 2010 to 2015, 286 cases of ATL were registered and confirmed in Montes Claros area, according to data obtained by SINAN. The presence of ATL was verified in different parts of the municipality, with a greater density in the suburbs (Figure 1). However, the advance of cases to the central region stands out. Between the analyzed period, there was a significant reduction (p<0.05) of 50% of the registered cases (Figure 2A). Regarding the age variable, ATL occurred in all age groups (Figure 2B). However, the distribution of patients showed that the number of cases increased significantly (p<0.05) in patients under 19 years old (31.81%, n=91), followed by the age group 20 to 39 years old (25.52%, n= 73), 40 to 59 years old (24.82%, n=71) and over 59 years old (17.83%, n=51). In addition, most of those affected by ATL were male (52.44%, n=150), while 47.55% (136) were female (Figure 2C). Of this total, 84.26% (n=241) and 15.73% (n=45) of patients lived in urban and rural areas of Montes Claros, respectively (Figure 2D). The presence of comorbidities was observed in 5.61% (3) of the patients, whereas 76.96% (n=116) had no comorbidities, and 17.41% (n=167) did not disclose this information on their files (Figure 2E). As to fatality due to TL (0.7%) notified and confirmed by SINAN, the two patients who died were male aged over 62 years. The drug of first choice used by both patients was Glucantime®. The presence of comorbidities was observed in only one of the patients who died (Figure 2F). The rate of initial lesions reported by patients at the time of diagnosis are presented in Table 1. Cutaneous injuries were the most prevalent manifestation, being reported by 98.25% of patients.

As for the type of drug, 87.06% (n=249) of the patients used antimoniate-N-methyl glucamine (Glucantime®) as the first choice, 10.13% (n=29) used the common amphotericin B and 2.97% (n=8) patients used pentamidine and other drugs. Of these patients, 14 relapsed, and 10 patients used Glucantime and the rest were treated with amphotericin b (Table 2).
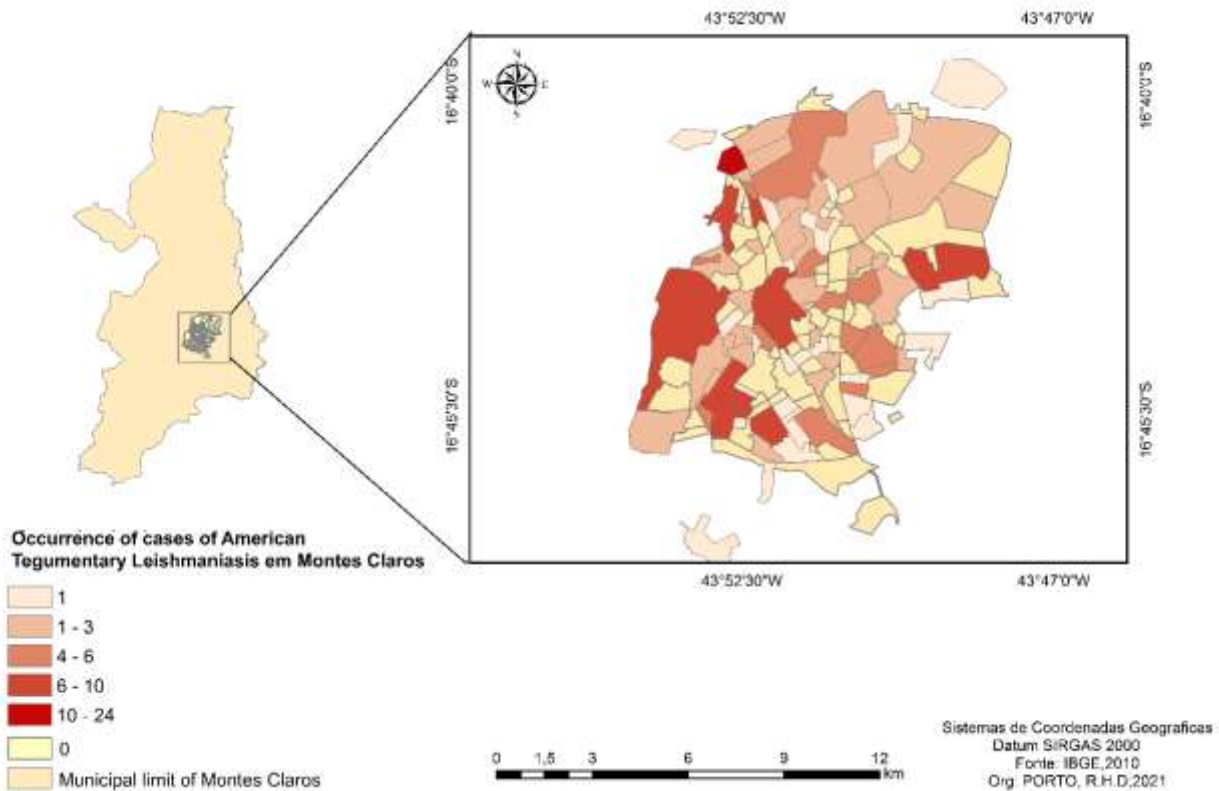
Tegumentary leishmaniasis (TL) mainly affects the skin and mucous membranes and can also be fatal in the absence of treatment (de Souza, da Silva, Afonso-Cardoso, Favoreto, & Ferreira, 2005). The results presented in this study regarding the gender of the patients showed a greater predominance of males. The literature indicates the male sex as more susceptible to illness (JCF., 2009; Murback, Hans Filho, Nascimento, Nakazato, & Dorval, 2011; Ribeiro, Roewer, & Nascimento, 2014)

This is also a common feature found in several published studies, which can be attributed to genetic factors and exposure to the etiological agent (Lima, Porto, Motta, & Sampaio, 2007). In Brazil, integument affects people of all ages, but mostly in endemic areas, 80% of recorded cases occur in children under 10 years of age (CUNHA, OLIVEIRA, & POMPEU, 2006). In some urban areas studied, there is a tendency to change the distribution of cases by age group, with the occurrence of high rates also in the group of young adults (Abraão et al., 2020; Silva et al., 2021).

As for the clinical manifestations, they were similar to epidemiological studies, with the most frequent symptoms being fever, splenomegaly, pallor and hepatomegaly (Oliveira, Figueiredo, & Braga, 2014) In The types of lesions were verified, the most frequent lesion was the skin lesion, as it is the area of the body that is most exposed, it occurs through the bite of the sand fly, the mucosal lesion occurred in 14 patients and the classic form is secondary to skin lesion (Pinto, Paiva, Queiroz, Rapela, & Oliveira, 2010) The presence of comorbidity, regardless of sex, demonstrates that the clinical manifestations are similar to TL in immunocompetent patients, however, the immune system of HIV carriers is more susceptible to poor disease evolution (Sampaio, Salaro, Resende, & de Paula, 2002).

The most used treatment was Glucantime® 87.06%, 10.13% used amphotericin B and 21.97% used pentamidine and other drugs. Methylglucamine antimoniate is especially effective in the treatment of cutaneous, mucocutaneous leishmaniasis. The drug causes rapid regression of the clinical and hematological manifestations of the disease, as well as sterilization of the parasite (Pelissari, Cechinel, Sousa-Gomes, & Júnior, 2011).

Figure 1. Tegumentary Leishmaniasis georeferencing in Montes Claros city from 2010 to 2015. Distribution of ATL cases by neighborhoods in Montes Claros, showing distribution throughout the territory, highlighting the peripheral regions and an increase in cases towards the urban center.

Source: Authors.

Table 1. Initial lesions of 286 patients with tegumentary leishmaniasis according to the site of the lesion.

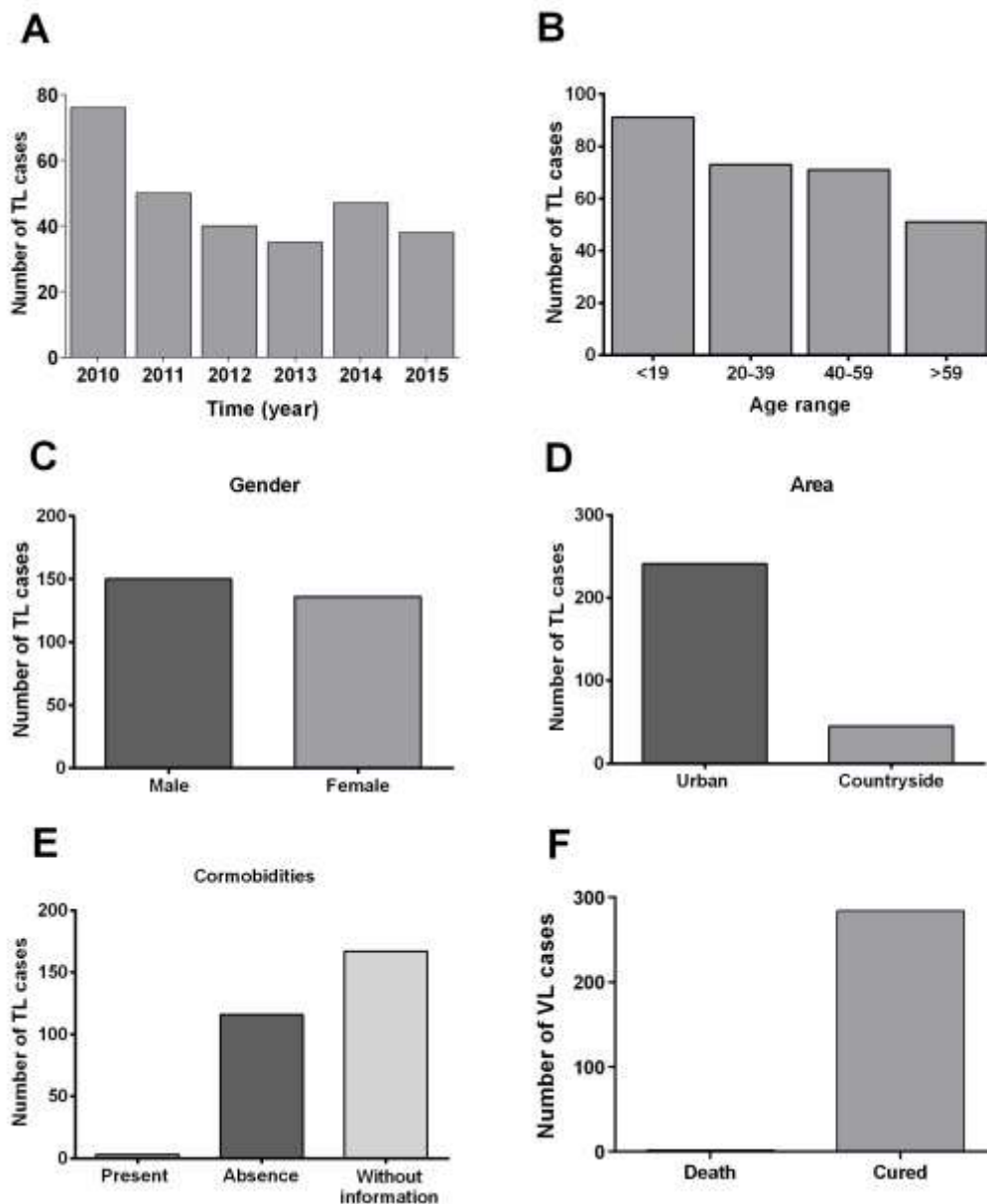| Tegumentary Leishmaniasis	Presence of Injuries		Presence of Scars	
	N	%	N	%
Cutaneous	281	98.2	-	-
mucous	14	4.8	7	2.4
Total	295	100	7	2.4

Source: Authors.

Table 2. Use of 1st and 2nd choice drugs in the treatment of patients with tegumentary leishmaniasis registered by SINAN.

Type of drug	1st choice		2nd choice	
	N	%	N	%
Glucantime®	249	87,06		
Anfotericina B	29	10,14	15	5,24
Pentamidina	8	2,80	8	2,79
Total	**286**	**100**	**23**	**8,03**

Source: Authors.

Figure 2. Tegumentary Leishmaniasis in Montes Claros city from 2010 to 2015. (A) Number of reported cases, (B) TL prevalence by age group, (C) patient informed gender, (D) place of residence of the reported cases, (E) evaluation of comorbidity and (F) number of deaths. For all variables there was a statistical difference ($p<0.05$).

Source: SINAN/ Municipal Health Secretariat (MHS)/ Montes Claros - MG, 2020).

4. Conclusion

Studies that verify the profile of this disease should be carried out more frequently, with the intention of generating characteristics of local populations with a higher incidence of the disease, consequently providing a greater possibility of rapid intervention in the diagnosis, thus the influence on inserting data in information systems, such as SINAN, provide a variety of exceptional bases in the evaluation of epidemiological profiles, so this tool is extremely important in the preventive care of communities, in relation to American Tegumentary Leishmaniasis, among others. In this sense, this study guides the development of new studies that address and monitor the spread of disease through monitoring of urban areas concomitant with the capture of animals for the presence of the parasite, thus helping in public health decision-making in the control of vector and shells.

Acknowledgments

References

Abraão, L. S. d. O., José, B. M. P. A., Gomes, C. B. d. S., Nunes, P. C., Santos, D. R. d., Varela, A. P. A. d. S., & Lima, C. d. S. (2020). Perfil epidemiológico dos casos de leishmaniose tegumentar americana no estado do Pará, Brasil, entre 2008 e 2017. *Revista Pan-Amazônica de Saúde,* 11.

Brazil. (2017). Manual de vigilância da leishmaniose tegumentar.

Cunha, J. C. d. L., Oliveira, J. W. d., & Pompeu, L. M. (2006). Transmissão domiciliar de leishmaniose tegumentar e associação entre leishmaniose humana e canina, durante uma epidemia na Serra de Baturité, no estado de Ceará, Brasil. 9, 425-435.

de Souza, M. A., da Silva, A. G., Afonso-Cardoso, S. R., Favoreto, S. J., & Ferreira, M. S. (2005). [Immunoglobulin isotype and IgG subclass profiles in American tegumentary leishmaniasis]. *Rev Soc Bras Med Trop, 38*(2), 137-141. 10.1590/s0037-86822005000200002.

Figueira, L. d. P., Soares, F. V., Naiff Júnior, R. D., Vinhote-Silva, A. C., Silva, S. S. d., Espir, T. T., & Franco, A. M. R. (2017). New human case reports of cutaneous leishmaniasis by Leishmania (Viannia) naiffi in the Amazon region, Brazil. Brazil. *Acta Amazonica* 47, 47-52. 10.1590/1809-4392201601484.

Gontijo, B., & de Carvalho Mde, L. (2003). [American cutaneous leishmaniasis]. Rev Soc Bras Med Trop, 36(1), 71-80. 10.1590/s0037-86822003000100011.

Guerra, J. A., Maciel, M. G., Guerra, M. V., Talhari, A. C., Prestes, S. R., Fernandes, M. A., . . . Barbosa, M. (2015). Tegumentary leishmaniasis in the State of Amazonas: what have we learned and what do we need? *Rev Soc Bras Med Trop*, 48 Suppl 1, 12-19. 10.1590/0037-8682-0268-2013.

JCF., S. (2009). Leishmaniose tegumentar americana (LTA), nos municípios de Crato, Juazeiro do Norte e Barbalha, Estado do Ceará, Brasil, 2003-2005 [dissertação]. Fortaleza (CE). Universidade Federal do Ceará, Faculdade de Medicina.

Lima, E. B. d., Porto, C., Motta, J. O. C., & Sampaio, R. N. R. (2007). Tratamento da Leishmaniose Tegumentar Americana. *An Bras Dermatol,* 111-124. 10.1590/S0365-05962007000200002.

Lyra, M. R., Pimentel, M. I., Madeira Mde, F., Antonio Lde, F., Lyra, J. P., Fagundes, A., & Schubach Ade, O. (2015). First Report Of Cutaneous Leishmaniasis Caused By Leishmania (Leishmania) infantum chagasi IN AN Urban Area Of Rio De Janeiro, Brazil. *Rev Inst Med Trop* 57(5), 451-454. 10.1590/S0036-46652015000500016.

Miranda, T. M. d., Malaquias, L. C. C., Escalda, P. M. F., Ramalho, K. C., Coura-Vital, W., Silva, A. R. d., & Reis, A. B. (2011). Descriptive study of American tegumentary leishmaniasis in the urban area of the Municipality of Governador Valadares, Minas Gerais State, Brazil. *Revista Pan-Amazônica de Saúde, 2,* 27-35.

Murback, N. D., Hans Filho, G., Nascimento, R. A., Nakazato, K. R., & Dorval, M. E. (2011). American cutaneous leishmaniasis: clinical, epidemiological and laboratory studies conducted at a university teaching hospital in Campo Grande, Mato Grosso do Sul, Brazil. *An Bras Dermatol,* 86(1), 55-63. 10.1590/s0365-05962011000100007.

Oliveira, D. A. d. S., Figueiredo, M. F., & Braga, P. E. T. (2014). Perfil Epidemiológico Dos Casos De Leishmaniose Tegumentar Americana Na Serra Da Meruoca, Ceará, No Período De 2001 A 2012. 13(2), 36-41.

Pelissari, D. M., Cechinel, M. P., Sousa-Gomes, M. L. d., & Júnior, F. E. F. d. L. (2011). Treatment of Visceral Leishmaniasis and American Cutaneous Leishmaniasis in Brazil. Epidemiol. *Serv. Saúde, Brasília,* 20(1), 107-110.

Pinto, B. F., Sinval, P. C., Milena Paiva, Queiroz, B., Waldir de Queiróz, R., M., Ângela C. R., & Oliveira, G., J. A. de O. (2010). Caracterização de Leishmania spp em amostras isoladas de pacientes portadores de leishmaniose tegumentar americana em área endêmica da região Norte, Brasil. Tese (Saúde pública) - Centro de Pesquisas Aggeu Magalhães.

Ribeiro, J., Roewer, S., & Nascimento, M. (2014). Prevalência de leishmaniose tegumentar americana no município de Barra do Garças-MT. *Interdisciplin Univar,* 11(1), 71-76.

Romero, G. A. (2016). O controle de leishmaniose visceral no Brasil: transformar é preciso. *Cad Saude Publica,* 32(6), S0102-0311X2016000600402. 10.1590/0102-311XCO010616.

Sampaio, R. N., Salaro, C. P., Resende, P., & de Paula, C. D. (2002). [American cutaneous leishmaniasis associated with HIV/AIDS: report of four clinical cases]. *Rev Soc Bras Med Trop,* 35(6), 651-654. 10.1590/s0037-86822002000600017.

Schneider, E. M., Fujii, R. A. X., & Corazza, M. J. (2017). Pesquisas quali-quantitativas: contribuições para a pesquisa em ensino de ciências. *Revista Pesquisa Qualitativa,* 5(9), 569-584.

Silva, F. S. d., Silva, J. O., Aguiar, M. F. F., José, J., Neto, L. d. S., Rocha, R. G. d., & Guimarães, V. H. D. (2021). Epidemiological aspects of visceral leishmaniasis in the municipality of Montes Claros-MG. *Acta Scientiarum. Health Sciences,* 43, 8.

Torres-Guerrero, E., Quintanilla-Cedillo, M. R., Ruiz-Esmenjaud, J., & Arenas, R. (2017). Leishmaniasis: a review. F1000Res, 6, 750. 10.12688/f1000 research .11120.1.