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Epidemiological and spatial clinical profile of visceral leishmaniasis in an endemic area of the state of Maranhão, Brazil

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Abstract

Visceral leishmaniasis is a serious systemic disease that represents a challenge for public health because it is part of the list of reemerging diseases in Brazil. Thus, it is important to know the epidemiological profile and the spatial distribution of cases so that health planning may be supported. The present study aimed to analyze the clinical, epidemiological and spatial profile of cases of visceral leishmaniasis in the municipality of Aldeias Altas, Maranhão. This was a retrospective, descriptive study with a quantitative approach. The data were collected by the epidemiological surveillance of the municipality, through the survey of the visceral leishmaniasis notification forms in the database of the Notifiable Diseases Information System of the cases notified and confirmed in the period from 2014 to 2018. With the technology of the Global locator, the position coordinates of the case addresses were collected, and with the Quantum GIS program, the maps were built. 31 cases were notified, 12 cases were confirmed, 13 cases were discarded, and 6 cases did not have a final classification. There was a higher frequency of the disease in females, living in urban areas, aged between 1 and 9 years old, of the brown race and with a low education. Paleness, fever, weakness were the most frequent clinical manifestations. In the spatial analysis, the central area towards the east of the municipality presented the highest concentration of cases. Knowledge of the epidemiological profile and understanding of the evolution of the disease in the municipality.

Keywords: Visceral Leishmaniasis. Epidemiology. Public health.

INTRODUCTION

Visceral Leishmaniasis (VL) is a zoonosis characterized by systemic involvement that affects millions of people in tropical and subtropical regions of the globe and is among the six endemic diseases considered to be priorities in the world¹. It is estimated that about 500,000 new cases and 50,000 deaths from VL occur worldwide each year. In addition, about 350 million people are exposed to the risk of infection, with a prevalence of 12 million infections². With the expansion of the disease coverage area and the significant increase in the number of cases, the disease started to be considered by WHO as one of the priorities among the tropical diseases³. The estimate of the world population at risk for the acquisition of VL reaches 182 million people⁴.

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DOI: 10.15343/0104-7809.202044171182



In Brazil, and especially in endemic areas, such as the state of Maranhão, the importance of VL lies not only in its high incidence and wide distribution, but also in the ability to assume serious and lethal forms when associated with the malnutrition and concomitant infections. Thus, creating projects that act directly on early diagnosis, timely treatment and the population's role in the management and control of the disease are relevant⁵.

This expansion has occurred in space and time, with an increase in the number of affected municipalities and in the number of cases and deaths^{6,7}. Health georeferencing has become an essential tool for the epidemiology of diseases that impact public health8. The use of Geographic Information Systems (GIS) and spatial analysis tools allows for analyzation of this process, making it possible to understand the spatial patterns of the distribution of the disease and to identify areas with high risk for the occurrence of new cases of the disease, whose purpose is to direct actions and public health policies^{6,7,8,9}.

From this point of view, geoprocessing is a set of computational techniques that are fundamental for the management of spatially collected information¹⁰. In the health sphere, the study of spatial distributions of event incidence has been essential to investigate and suggest hypotheses that can determine the causes of disease in a region. Therefore, studies of health problems with the help of georeferencing are enriched with this type of description, as they can provide fundamental information for the understanding, prediction, etiological search, prevention and monitoring of diseases and evaluation of the impact of health interventions in a population¹¹.

According to DATASUS data, in the period from 2010 to 2015, Brazil registered 21,519 new cases of VL, while Maranhão registered 3,126 cases, representing 14.5% of the total cases in the country. The data found for Aldeias Altas are out of date, making it impossible to recognize the real number of cases, death records and infestation in the urban area by vectors in the municipality¹². This study aimed to analyze the epidemiological clinical profile and perform spatial analysis of the reported cases of visceral leishmaniasis in the municipality of Aldeias Altas, Maranhão, with the intention of proposing and encouraging actions and measures for monitoring the disease, as well as early recognition, to contribute to the decrease of the disease's lethality in this locality.

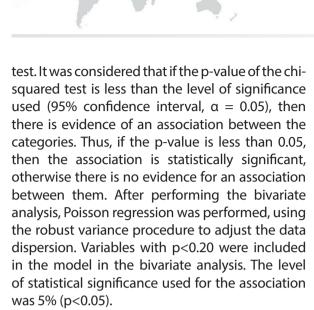
METHODS

This was а retrospective, descriptive, exploratory study, with a quantitative approach, carried out from 2014 to 2018. The study population consisted of notified cases of VL in residents of Aldeias Altas, Maranhão, Aldeias Altas is a Brazilian municipality in the state of Maranhão. It is located in the micro-region of Coelho Neto, mesoregion of Leste Maranhense. Its population is 26,115 (estimated in 2016) with a territorial area of 1,942,121 km2 and demographic density at 12.33 (inhab/km2) with an incidence of poverty in 57.41% of the population 13.

The notification forms in the municipality's epidemiological surveillance of the notified cases were requested. The data collection instrument was a form adapted according to the information present in the Ministry of Health's VL notification form of the following variables: sex, age group, race, education, area of residence, occupation, clinical manifestations, HIV infection, immunological diagnosis, parasitological diagnosis, type of entry, prescribed doses, confirmation criteria, autochthonous case, work-related illness and case evolution.

The data were tabulated and analyzed using the Epi Info statistical software, version 7.2.1.0. A descriptive analysis was carried out, using absolute and relative frequencies for the sociodemographic and economic variables of the cases. To check the associations between the variables, a bivariate analysis was performed, using the chi-squared





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For the spatial analysis of the cases, the addresses contained in the leishmaniasis notification forms were used. In geoprocessing, the GPS (Global Positioning System) locator was used, with an accuracy of 10m in homes with positive cases to map the areas classified as Probable Infection Sites (PIS). Simultaneously with GPS marking, identification was carried out by taking notes of each point (number and geographic coordinates) generated by GPS, in numerical order, from a marker at the beginning of the community boundary (point one).

The study preceded the approval of the research by the Ethics and Research Committee (CEP) of the State University of Maranhão (UEMA) under the opinion number 3.235.493.

RESULTS

It was found that a total of 31 cases of VL were reported in the period from 2014 to 2018 in Aldeias Altas, MA. There were 12 confirmed cases, 13 discarded cases, and 6 did not report a final classification in the notification forms. It is pointed out that the years 2015 (8.3%), 2016 (8.3%) and 2018 (8.3%) were the years with the lowest number of notifications of confirmed cases, and the highest number of notifications occurred in

the year 2017 (58.4%) (Figure 1).

There was a higher frequency of confirmed cases of the disease in the female sex (66.7%), aged between 1 to 9 years old (58.3%) and in the brown race (83.3%). The highest frequency of VL was observed in individuals with incomplete primary education (25.0%), residents of the urban area (75.0%) and agricultural workers (58.3%). With regard to clinical manifestations, it was possible to observe that the symptoms most frequently reported and the most frequently notified in the forms were: paleness (100%), fever (91.66%), weakness (91.66%), hepatomegaly (91.66%), splenomegaly (100%). It was possible to identify that there was no case of patients with Leishmania - HIV/AIDS coinfection (Table 1).

It was found that the parasitological examination was positive in most of the confirmed cases (58.3%), and in most of the cases the immunological diagnosis was not carried out (75.0%). The predominant type of data entry was of new cases (91.7%). It was measured that most of the confirmed cases were classified by laboratory criteria (83.34%), were autochthonous cases (100%), and were not related to work (91.7%). It was found that most of the cases were cured (75.0%) (Table 1).

The final classification of leishmaniasis cases showed a statistical association (p<0.05) with the parasitological diagnosis, the type of confirmation criterion, autochthonous cases and no relationship between the disease and work. In the criterion for confirmation of positive cases, the highest percentage was of the laboratory type and in discarded cases, the highest percentage was in the ignored option. In the variable "autochthonous case", as well as in the confirmation criterion, the most relevant percentage in discarded cases occurred in the ignored option, whereas in confirmed cases, the fact of having autochthonous disease was significantly associated with confirmed cases of leishmaniasis. Finally, in confirmed cases, the most relevant percentage was in the option of not related to work. In discarded cases, a higher





percentage occurred in the ignored option (Table 1).

It was observed that the variables that showed significant prevalence were parasitological diagnoses and work-related illness. Those who presented a positive parasitological diagnosis are 2.8 times more likely to have a positive outcome for leishmaniasis. In relation to workrelated illness, those who were not related to work were 10.154 times more likely to have a final confirmed leishmaniasis classification (Table 2).

The prevalence of cases was observed in residents of the central area towards the east of the municipality, totaling 21 cases reported in the urban area, where we emphasize that the neighborhoods that compose these areas are: Centro, São Francisco and Subestação. It was possible to notice that these areas had unhealthy environments, such as: deficit of hygiene, disordered spatial growth, low socioeconomic level, a population with low level of education, neighborhoods close to the area of deforestation and precarious basic sanitation (Figure 2).

It was observed that the geographical points of the rural zone of notified cases of VL, there was a prevalence of cases in the villages located in the northern zone of the municipality, totaling 10 cases. These villages most affected by VL have the following factors in common: low socioeconomic status, deforestation and precarious basic sanitation, which contribute to the onset of the disease (Figure 3).

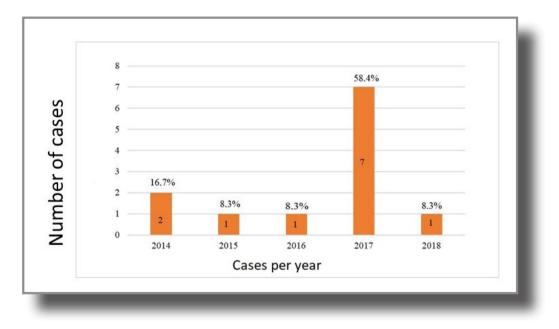


Figure 1 – Distributions of confirmed cases by year of visceral leishmaniasis in Aldeias Altas - MA, from 2014 to 2018.





Table 1 – Epidemiological and clinical data andanalysis of the association between the variables andthe reported cases of visceral leishmaniasis in themunicipality of Aldeias Altas - MA, 2018.

Variables (N=25)	Final classification			
-	Confirmed	Discarded	X ² (p-value*)	
Sex	33.3 (4)	61.5 (8)	1.998 (0.158)	
Male	66.7 (8)	38.5 (5)		
Female				
Age Range	0.0 (0)	7.7 (1)		
<1 year	58.3 (7)	38.5 (5)		
From 1 to 9 years	0.0 (0)	7.7 (1)	2.631 (0.757)	
10 to 19 years	25.0 (3)	23.1 (1)		
From 20 to 39 years	8.3 (1)	15.4 (2)		
From 40 to 59 years	8.3 (1)	7.7 (1)		
≥ 60 years				
Race	8.3 (1)	7.7 (1)		
White	8.3 (1)	7.7 (1)		
Black	83.3 (10)	84.6 (11)		
Brown				
Education	25.0 (3)	38.5 (5)		
Incomplete Primary School	8.3 (1)	0.0 (0)	0.008 (0.996)	
Completed Primary School	8.3 (1)	7.7 (1)	5.287 (0.382)	
Incomplete Highschool	0.0 (0)	7.7 (1)		
Completed Highschool	0.0 (0)	15.4 (2)		
Not applicable	58.3 (7)	30.8 (4)		
Ignored				
Zone	75.0 (9)	69.2 (9)		
Urban area	25.0 (3)	23.1 (3)		
Countryside	0.0 (0)	7.7 (1)		
Suburban				
Occupation	25.0 (3)	15.4 (2)		
Student	33.3 (4)	15.4 (2)		
Agricultural worker	8.3 (1)	15.4 (2)	0.962 (0.618)	
Other	33.3 (4)	53.8 (7)		
Ignored				

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Variables (N=25)	Final classification			
-	Confirmed	Discarded	X ² (p-value*)	
Clinical manifestations	100.0 (12)	92.3 (12)		
Yes	0.0 (0)	7.7 (1)		
Not				
HIV co-infection	75.0 (9)	61.5 (8)		
No	25.0 (3)	38.5 (5)	1.981 (0.576)	
Ignored Parasitological	58.3 (7)	7.7 (1)		
diagnosis				
Positive	41.7 (5)	84.6 (11)		
Not Performed Ignored	0.0 (0)	7.7 (1)	0.962 (0.327)	
Immunological diagnosis	16.7 (2)	0.0 (0)		
Positive	8.3 (1)	7.7 (1)	0.520 (0.471)	
Negative	75.0 (9)	92.3 (12)		
Not Performed				
Input Type	91.7 (11)	100.0 (13)		
New Case	8.3 (1)	0.0 (0)	7.772 (0.021 **)	
Relapse				
Prescribed Doses	41.7 (5)	0.0 (0)		
Greater than or equal to 10 and less than 15	8.3 (1)	0.0 (0)	2.392 (0.302)	
Greater than or equal to 15 and less than 20	33.3 (4)	8.3 (1)		
Greater than or equal to 20	16.7 (2)	91.7 (11)		
Ignored				
Confirmation criteria	83.4 (10)	15.4 (2)		
Laboratory	16.6 (2)	0.0 (0)	1.128 (0.288)	
Epidemiological clinic	0.0 (0)	84.6 (11)		
Ignored				
The autochthonous case	100.0 (12)	15.4 (2)	1.923 (0.212)	

to be continued...

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Variables (N=25)	Final classification			
_	Confirmed	Discarded	X ² (p-value*)	
Yes	0.0 (0)	84.6 (11)		
Ignored				
Work-related illness	91.7 (11)	15.4 (2)		
No	8.3 (1)	84.6 (11)		
Ignored				
Evolution of the case	75.0 (9)	100.0 (13)	17.409 (0.000 **)	
Cured	8.3 (1)	0.0 (0)		
Death from other causes	16.7 (2)	0.0 (0)		
Ignored				
*Chi-squared test (95% conf	idence). ** Sta	tistical significa	ance	

*Chi-squared test (95% confidence). ** Statistical significance Source: Author.

 Table 2 – Analysis of the association between variables and confirmed cases of visceral leishmaniasis in the municipality of Aldeias Altas - MA, 2018.

	Final Confirmation	- Positive	PR (CI95%)	p-value*
Variables	Ν	%		
Sex				
Male	4	33.33%	1	
Female	8	66.67%	1.846 (0.744 - 4.578)	0.186
Parasitological diagnosis				
Positive	7	58.33%	2.800 (1.293 - 6.063)	0.009 **
Not Performed	5	41.67%	1	
Confirmation criteria				
Laboratory	10	83.34%	1,222 (0.925 - 1.615)	0.158
Epidemiological clinic	2	16.66%		
Work-related illness				
No	11	91.67%	10.154 (1.533 – 11.283)	0.016 **
Ignored	1	8.33%	1	
Evolution of the case				
Cured	9	75.00%	8.123 (0.123 - 9.123)	0.321
Death from other causes	1	8.33%	1	
Ignored	2	16.67%	1.833 (0.843 – 3.984)	0.222

*Poisson regression with robust variance. ** Statistical significance. Source: Author.



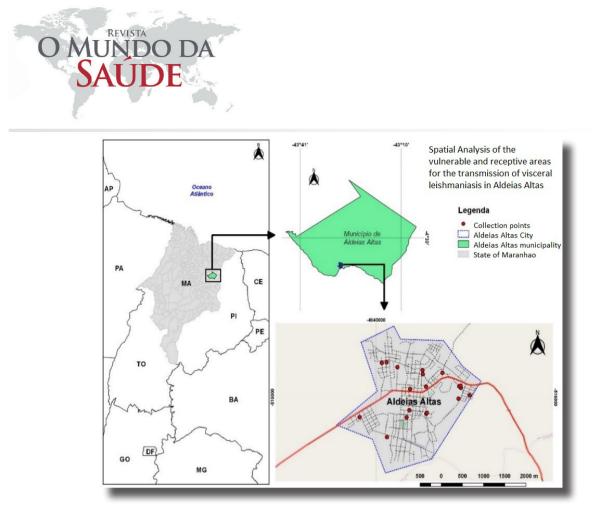
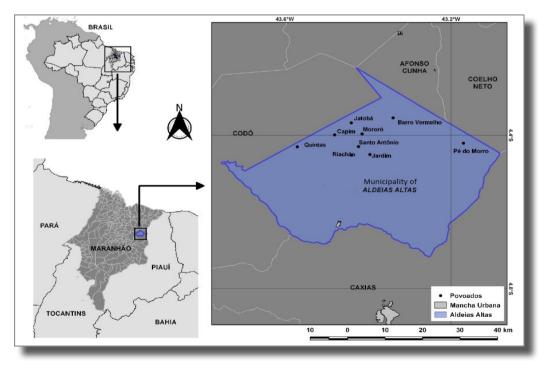
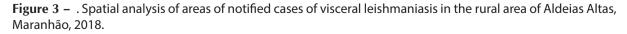


Figure 2 – Spatial analysis of notified areas of visceral leishmaniasis in the urban area of Aldeias Altas, Maranhão. 2018.





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DISCUSSION

VL is the most severe form of leishmaniasis, due to frequent complications and high mortality rates, if left untreated. In 2015, in Brazil alone, 3,289 cases of the disease were reported, representing 95.1% of the cases in the Americas¹⁴.

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In the period covered in the present study, a decrease in the number of cases is observed, followed by a period with a sharp increase in the number of cases of VL. This increase in cases of VL in the municipality of Aldeias Altas has at least two explanations. First, it can be justified by the ecological changes caused by man, which facilitates the proliferation of the vector, that is, the anthropic action contributes to devastating the natural habitats of the pathological agents that cause VL infection in man, promoting a greater impact on the epidemiology of VL in the municipality¹⁵. Second, it must be considered that the disease prevention measures, especially against the vector, have shown unsatisfactory results; or that the tracking of cases on behalf of health professionals has become more effective¹⁶.

Regarding gender, there was a higher incidence of VL on females compared to males, contrary to most studies found in the literature. In the northeast of Minas Gerais, there was a greater predominance of males with leishmania infection, identifying that 62.6% of cases were in men, diverging from our study¹⁷. The disease can affect all ages and both sexes, however, the prevalence of the disease in men can be justified by the greater exposure to sand fly vectors¹⁸. A study conducted in Campo Grande, from 2002 to 2009, showed that men are more affected by VL than women¹⁹. The predominance of leishmania infection occurs in males with an average age of 46.7 years, and a variation of six months to 93 years18. The female predominance in the present study may be related to the fact that men seek the health system less frequently to prevent or treat their illnesses; behavior that can worsen their clinical condition²⁰.

The age distribution coincides with most published studies. Classical VL affects people of all ages, but in some studied urban centers, there is a tendency to change the distribution of cases by age group, with high rates also occurring in the group of young adults. Additionally, the data from the present study are similar to data from studies developed in Pernambuco and Belo Horizonte, whose children also had the highest infection rates²¹.

A study conducted in Ceará, between 2007 and 2011, concerning age groups, VL also had a bimodal distribution, where it is possible to separate the population into two groups: children (0-14 years old) and adults (15 years and older). The main group affected among children is from one to four years old and, among adults, from 20 to 39 years old, a finding similar to the present study²². This higher incidence in the child population is possibly due to the more frequent contact of children with animals, in addition to the greater nutritional deficiency and immune status still developing. More specifically, in this study there was a greater confirmed notification of children between 1 and 9 years old, corresponding to 58.33% of the entire sample. Susceptibility to the disease remains universal, reaching people of all ages and genders, however, it occurs more frequently in children23. On the other hand, adult involvement has a significant impact on the epidemiology of VL, due to the development of all clinical manifestations²⁴.

The cases with low level of education make up the majority of those affected, showing that the high prevalence of VL in this group may be associated with less health education and less potential for epidemiological control. However, the degree of education for more than half of the total cases considered was ignored or was not applied in this study, followed by incomplete primary education. The prevalence of individuals with low schooling can be justified, in part, by the fact that the majority of notified cases of affected by VL correspond to children under 10 years of age, who either do not attend the school environment or have not finished. A result similar to this was obtained by a study carried out in Sobral, from 2001 to 2010²⁵.





Regarding symptoms, the present study identified that the clinical manifestations of VL did not differ from those reported in the literature. Fever, splenomegaly and hepatomegaly were present in most cases of kala-azar, respectively^{26,27,1,18}. As for the diagnostic tests, the findings corroborate with studies in the literature, in which they stated that the parasitological diagnosis was obtained in most cases^{1,26.}

There was a high number of new cases of the disease. In some areas, many residents had low socioeconomic levels, with extremely poor housing. In addition, living with domestic animals is quite high, resulting in the accumulation of organic matter. Allied to this, the system of garbage collection and basic sanitation in several regions of the city is precarious. All of these factors, together, provide extremely favorable conditions for the occurrence of disease transmission²⁸.

Similar to what is reported in the literature, the treatment of cases was performed with a pentavalent antimonial treatment (glucantine), this is the classic treatment for leishmaniasis in Brazil. The cure rate is high, at least 95%. The antimony treatment failed in only 1.7% of patients in a study carried out in Teresina. Amphotericin B was used as a secondary therapy²⁹. It is also recommended that treatment be carried out in a hospital environment, due to toxicity and various adverse reactions caused by medications30. The pentavalent antimonial treatment has the advantage that it can be administered on an outpatient basis, which reduces the risks related to hospitalization. Amphotericin B, on the other hand, is the only option for the treatment of pregnant women and patients who have contraindications, who manifest toxicity or refractoriness related to the use of pentavalent antimonial treatments. The duration of treatment should be based on clinical evolution, considering the speed of response and the presence of comorbidities³¹.

The ignored/blank data occur because the 'evolution' field remains active in the system even after disposal. The importance of filling out all fields in the notification form is emphasized here, since studies for interventions for this disease depend on complete and reliable information obtained from

these documents. Therefore, it is essential that this information/data available is of a good quality and reliably portrays the health situation in the state. We must master access to information, looking for ways to be able to use it at any time³².

Thus, a positive point obtained in this study was the lethality coefficient being below the state and national average, given the disparity in the incidence of the disease; taking into account that there was no death from VL. The cure tends decrease and the lethality tends to increase, when VL affects children under one year old and elderly people over 60 years²².

The final classification of leishmaniasis cases showed a statistically significant association with the parasitological diagnosis, the type of confirmation criterion, the autochthonous cases and the relationship between the disease and work, contrary to the results of other studies. In the state of Maranhão, municipality of Raposa, a significant association was found regarding the type of housing (thatched roof and dirt floor), family income, zone, race, the destination of outdoor garbage, the presence of dumps nearby the residences, the presence of sandflies and outdoor bathing of the homes with the occurrence of VL³³. In a case-control study conducted among residents and migrants from different regions of Ethiopia and a metaanalysis on studies of risk factors associated with VL in humans in the Americas, risk factors for VL were demonstrated having a social trait, essentially linked to poverty and a low educational level, which lead to a greater vulnerability of the population³⁴.

In the present study, most of the registered cases were in the urban area of the municipality. The region of Montes Claros, MG had a similar result in its study, with about 71% of the notified cases coming from the urban area, and only 18% from the rural area17. The main factors responsible for the growing number of cases in the urban area are: I) the migratory process; II) precariousness in basic sanitation; III) low socioeconomic status; IV) rampant deforestation for the construction of settlements, roads and factories; V) growth of agriculture, among others, destroying and invading the habitat of sand flies, which is a vector of Leishmaniasis35. The majority of cases of VL



in the present study in relation to occupation were of agricultural workers or students. Leishmaniasis can be considered as a work-related disease since the occupational circumstances of exposure to the transmitting mosquito can be considered as risk factors²⁸.

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Spatial analysis indicated the highest prevalence of cases in the central region of the municipality. A study carried out in Petrolina emphasizes that the disease expansion process that has been occurring in several Brazilian regions, with human and canine cases being registered in fully urbanized areas or in the urbanization phase. Due to this fact, the use of results obtained through spatial analysis of the VL allow us to conclude that the disease is in the urbanization phase, still being associated with areas of transition between rural and urban. However, there is no apparent association between human and canine disease⁹.

As for geographic distribution, a study carried out in the state of Tocantins, where the highest rates are found in the north and northwest of the state, on the border with the states of Pará and Maranhão, there are municipalities with high rates in the central region 7. From the analysis of the spatial distribution of the VL in the state of Rio Grande do Norte, two distribution patterns were pointed out: the first, located in the north area of the city, characterized as an area of intense transmission, and a second pattern, located mainly in the area west, considered the main zone of expansion of the disease, with annual registration of new cases in a dispersed form³⁶.

The absence of empirical data in the municipality of Aldeias Altas, regarding geographic aspects, relief, distribution of sandflies and dogs, breeding of other animals and data on the prevalence of canine VL, is a factor that makes it more difficult to explain the number of cases of VL in the municipality; as there are no published studies covering these points, it is impossible to correlate such facts with other regions.

Therefore, the use of spatial analysis is a tool that contributes to the understanding of the dynamics of the distribution of the risks of becoming ill and dying from visceral leishmaniasis. The collection and display of information in the geographic space and its application in the Health area is essential due to its power to expand the evidence and support the understanding of the dynamics of this disease and support important health surveillance actions³⁶.

CONCLUSION

It is concluded that leishmaniasis was characterized as affecting notified residents in Aldeias Altas, females, aged between one and nine years, brown skin and who lived in the urban area. Among the clinical manifestations, the most frequent were fevers, weakness, paleness. The spatial analysis of the urban area indicated the prevalence of cases in residents in the central area and towards the east, while in the rural area it was possible to observe that the majority of cases were concentrated in the villages in the north of the city of Aldeias Altas.

It is noteworthy that tracing the

epidemiological clinical profile and the use of georeferencing in the health field has proved to be an important tool in the surveillance, prevention and control of health problems. Through these tools, it was possible to visualize the distribution of the disease, thus, identifying the population and the most vulnerable areas in the municipality, in this sense, enabling health surveillance and education to be more effective. In addition, it helps both in the planning process and in decision making, aiming at the prevention and control of VL.

In view of the above, it is important to note





that VL is still a challenge to public health in the restrictions resulting from the use of the country, so surveillance, health education and basic sanitation must go hand in hand, thus providing an improvement in the quality of life of individuals.

It is understood that the explanation of the results of this study must take into account SINAN data. These data, despite having their value defined, are prone to underreporting, in addition to occasional errors due to problems of integrity and consistency, which turn into problems of quantity and quality of information.

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> Received in october 2019. Accepted in april 2020.

