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Canine Visceral Leishmaniasis in Rio Grande do Norte State, Northeastern Brazil - Spatial Analysis

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ABSTRACT

***Background*:** Human visceral leishmaniasis (HVL) is a potentially fatal disease with a worldwide distribution, being endemic in 12 countries in the Americas. The main reservoir in the urban environment is the dog, whose cases precede the disease in humans. For the control of HVL, the Ministry of Health of Brazil recommends efficiency in the notification of human cases, control of sandflies, elimination of reservoirs and health education, in addition to the interruption in the transmission of the disease by the intensification of surveillance and control of priority areas based on identification by spatial analysis. The objective of the study was to investigate the spatial distribution of canine visceral leishmaniasis (CVL) in the state of Rio Grande do Norte, Brazil, determining areas of risk by identifying spatial clusters, with a view to monitoring and implementing preventive actions.

***Materials, Methods & Results*:** Secondary data from sample and/or routine serological surveys for serological diagnosis of LVC in the period from 2011 to 2018 were used. The inclusion of animals in the routine diagnosis per municipality resulted from demands of veterinarians, veterinary clinics, dog tutors, zoonoses control centers and environmental surveillance. The spatial statistical analysis was performed with SatScan software version 9.6 for the detection of spatial clusters, based on using the statistical scan method. Of the total of 231,123 dogs tested in the period, 24,642 (10.6%) were seroreactive for CVL. During the study, the municipalities with the highest number of cases were Natal and Mossoró, with 9,671 and 4,514 cases, respectively. During the years 2011 to 2018, 38 significant clusters ($P < 0.05$) were identified that included one or more municipalities.

***Discussion*:** The state of Rio Grande do Norte has an urban environment susceptible to the occurrence of CVL, with climate and topography that favor the proliferation of the vector and housing in precarious socio-sanitary conditions. The high number of CVL cases in Natal can be explained by the fact that the city is considered endemic for CVL, characterized as an area of intense transmission of the disease, according to the Ministry of Health. In addition, public infrastructure in some locations is deficient and living conditions are unfavorable, so that there is a need to invest in effective protection measures for vector control, as well as a focus on health education, whose HVL control measures in the municipality need to be readjusted. The high rate of cases and the constant presence of clusters in the municipality of Açu can be explained by the increasing degradation of the Caatinga biome, evidenced by the removal of firewood for use in the ceramist pole, whose activity is concentrated on a large scale in the use of raw material and energy, through the production of charcoal, for agricultural and livestock fronts, putting species of fauna and flora at risk. It is also noteworthy that this fact contributes to the destruction of wild ecotopes, resulting in the search for the vector for other sources of human and animal food, allowing an increase in the number of cases of the disease. It's concluded that canine visceral leishmaniasis is distributed in a large part of the state of Rio Grande do Norte. The underreporting and/or deficiency in the disclosure of data by some municipalities represents a challenge in complying with the actions of the Visceral Leishmaniasis Surveillance and Control Program, and attention should be paid to the monitoring and inspection of the execution actions of municipal managers, as well as how to train professionals who are part of the service.

Keywords: georeferencing, public health, zoonoses, leishmaniasis, epidemiology.

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INTRODUCTION

The Pan American and World Health Organizations consider human visceral leishmaniasis (HVL) a cosmopolitan and potentially fatal disease. It is endemic in 12 countries in the Americas, and almost 96% of cases occur in Brazil [21]. The circulation of the disease is facilitated by deforestation, urbanization, intense migratory flow [18,20], lack of basic sanitation and destruction of wild ecotopes [24].

Canine leishmaniasis is risk factor for HVL [23], which is more prevalent and precedes the disease in humans, with the dog as the main reservoir in urban areas, and other reservoirs are foxes, marsupials [19] and rodents [14]. The most important vector in Brazilian territory is the sand fly *Lutzomyia longipalpis* [18]. HVL was essentially rural, but expanded into urban areas [18]. In Northeastern Brazil, the concentration of cases is urban with 91%, 76.1% and 71.3% in the states of Rio Grande do Norte [30], Sergipe [25] and Piauí [31], respectively. Considered endemic for HVL, Rio Grande do Norte had, between 1990-2014, an annual incidence of 4.6 cases/100,000 inhabitants and a case fatality rate of 6.4% [1].

For the control of HVL, the Ministry of Health of Brazil recommends efficiency in the notification of human cases, control of sandflies, elimination of reservoirs and health education [18], in addition to the interruption in the transmission of the disease by the intensification of surveillance and control of priority areas based on identification by spatial analysis [8]. The objective of this study was to investigate the spatial distribution of CVL in that state, identifying highly prevalent spatial clusters, with focus to monitoring and implementing preventive actions.

MATERIALS AND METHODS

Study area and data collection

The state of Rio Grande do Norte is located in the Northeast region of Brazil, and covers an area of 52,809,602 km², with 167 municipalities and an estimated population of 3,534,165 inhabitants and a Human Development Index of 0.684 [12], ranking 16th position in the country. It is geographically divided into 4 mesoregions: Central Potiguar, West Potiguar, Agreste Potiguar and East Potiguar (Figure 1).

Secondary data were obtained from the Subcoordination of Epidemiological Surveillance, Arboviruses and Leishmaniasis Sector, State Department of Public Health (SESAP), Natal, Rio Grande do Norte. These data come from routine serological diagnosis of CVL in the period from 2011 to 2018. The inclusion of animals in the routine diagnosis per municipality resulted from demands of veterinarians, veterinary clinics, dog tutors, zoonoses control centers and environmental surveillance.

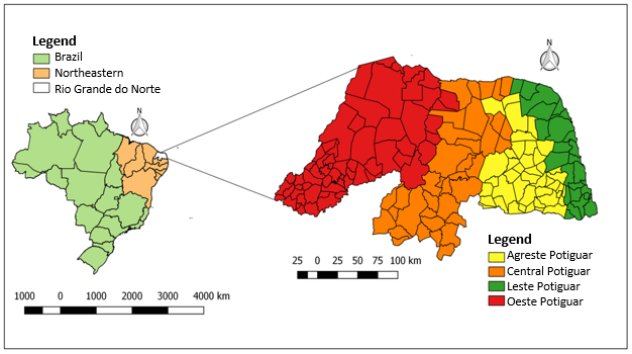

Figure 1. Map of Brazil highlighting the geographic divisions of the Rio Grande do Norte state, Northeastern of Brazil.

Serological diagnosis of CVL

Serum samples from the animals were screened using the DPP test® (Canine Visceral Leishmaniasis rapid test)[1] performed at the Secretary of Health of each municipality, and the positive sera were sent to the Central Public Health Laboratory (LACEN) in Rio Grande do Norte for the confirmatory diagnostic test (ELISA), as recommended by the Ministry of Health [18].

Spatial analysis

For spatial mapping, data from the period 2011 to 2018 of positive dogs for CVL were used, and the maps were made with the software QGis 2.18.0[2], adopting the Datum SIRGAS 2000, a geodetic reference system for the Americas, and the cartographic meshes of the state of Rio Grande do Norte extracted from the website of the Instituto Brasileiro de Geografia e Estatística (IBGE). Thematic maps of the sum of CVL cases between 2011 to 2018 of all municipalities in the state were prepared; the distribution of cases (positive/negative/no notification); and significant clusters.

To identify the clusters, the geographic coordinates of the municipalities in the state were used, obtained from QGIS, georeferenced through the centroid, the most central location of each municipality. Spatial statistical analysis was performed using the SatScan software version 9.6 [13], to detect spatial clusters in the state, based on the scan statistical technique, defined by an irregular geographic window that moves through the area of interest, that is, it is a sweep statistic whose circle is capable of including different sets of neighboring areas. If the centroid (most central part) of an area is contained in the window, this area is deemed included in the circle, being treated as a potential cluster [17]. The comparison of the proportions of positive dogs among years was made using the chi-square test, and the significance level adopted in the analysis was 5%.

RESULTS

Of the total of 231,123 dogs tested, 24,642 (10.6%) were seroreactive for CVL. The municipalities that presented the highest numbers of cases were Natal and Mossoró, with 9,671 and 4,514 cases, respectively. The municipalities with the highest number of CVL cases per year are shown in Table 1. A significant difference was observed in the frequencies of cases among the years ($P < 0.001$).

It was verified that, during the study period (2011-2018), the disease in dogs was found to be widespread in a large part of the Potiguar territory: 38.32% (64/167) of the municipalities had more than 21 cases; 20.4% (34/167) resulted in 7 to 21 cases; 13.8% (23/167) had up to 6 cases, however, 5.4% (9/167) had no positive animals (Figure 2)

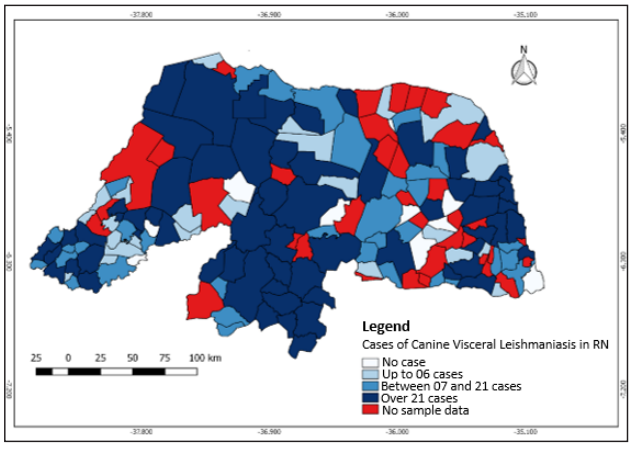

Figure 2. Map highlighting the number of canine visceral leishmaniasis (CVL) cases in Rio Grande do Norte state, Northeastern of Brazil, during the period of 2011 to 2018.

Only 8.9% (15/167) of the municipalities presented data throughout the study period (2011-2018). Of these, 40% were located in the East Potiguar mesoregion: municipalities of Extremoz, Macaíba, Natal, Parnamirim, São Gonçalo do Amarante and São José de Mipibu; 26.7% in Oeste Potiguar: Caraúbas, Ipanguaçu, Portalegre and Upanema; 20% in Agreste Potiguar: João Câmara, Santo Antônio and Santa Cruz; and 13.3% were located in Central Potiguar, with emphasis on the municipalities of Caicó and Jardim de Piranhas. Thirty-seven municipalities (22.1%) did not present data for LVC (Figure 3), such as Apodi and Felipe Guerra, located in the West Potiguar, bordering the municipalities of Alto Santo, Potiretama and Tabuleiro do Norte, located in the state of Ceará, as well as the municipality of Serra Negra do Norte, Central Potiguar, which borders the municipalities of São Bento, Paulista and São José de Espinharas, located in the state of Paraíba.

In 2011 and 2012, in several municipalities in the West Potiguar mesoregion there were no records of cases, however, in subsequent years there were cases of the disease in dogs in the municipalities of Pau dos Ferros and Patu, with more than 200 cases (2017-2018). Other municipalities in this region that presented high and constant numbers of cases were Mossoró and Açu. In the Central Potiguar, the municipality of Caicó stood out, whose number of cases in the 8 years of the study remained constant, in addition to the growing increase in the number of cases in the municipalities close to the border with Paraíba state (Figure 3).

The use of the statistical scanning tool allowed the detection of 38 significant ($P < 0.05$) spatial clusters of CVL cases in several municipalities in the state (Table 2 and Figure 4). In 2011, 3 clusters were identified, all including a single municipality in each cluster and the primary cluster comprised the municipality of Natal, with a relative risk (RR) of 2.26 and $P < 0.001$; in 2012 there were 5 clusters and the primary cluster, with a radius of 67.23 km and RR of 2.65 ($P < 0.001$) included the municipalities of Governador Dix-Sept Rosado, Mossoró, Upanema, Caraúbas, Açu and Janduis; in 2013, 5 clusters were also detected, whose primary cluster was located in Parelhas, with RR 3.56 ($P < 0.001$); In 2014, 2 clusters were found, and the primary cluster was Extremoz, with RR

2.57 ($P < 0.001$); in 2015 there were 5 clusters, with the primary cluster located in Açu (RR 2.44; $P < 0.001$); in 2016, 3 clusters, and the primary cluster had a radius of 160.94 km and included 34 municipalities (RR 1.70; $P < 0.001$); in 2017, 5 clusters were identified, and the primary cluster was the municipality of Assu (RR 3.60; $P < 0.001$); and in 2018, 10 clusters were registered, with the municipality of Extremoz being the primary cluster (RR 3.93; $P < 0.001$).

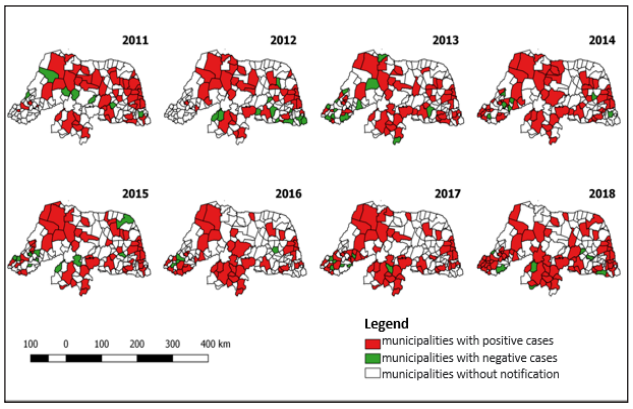

Figure 3. Distribution of canine visceral leishmaniasis (CVL) cases in Rio Grande do Norte state, Northeastern of Brazil, according the year of the survey during the period of 2011 to 2018.

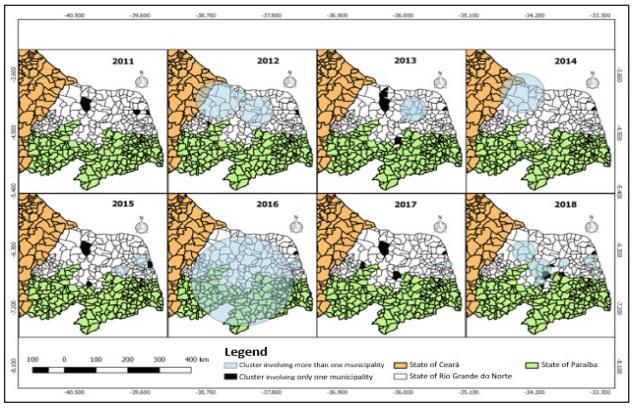

Figure 4. Significant clusters of canine visceral leishmaniasis (CVL) cases in Rio Grande do Norte state, Northeastern of Brazil, according the year of the survey during the period of 2011 to 2018..

Table 1. Number of dogs tested and reactive to canine visceral leishmaniasis in Rio Grande do Norte state, Northeastern of Brazil, during the period of 2011 to 2018.

Year	Number of tested dogs	Number of reactive dogs	Frequency of reactive dogs (%)	Counties with higher number of cases)
2011	29,881	3,199	10.7	Natal (1,178), Mossoró (887)
2012	22,095	2,472	11.1	Mossoró (1,041), Natal (668)
2013	27,754	2,256	8.1	Natal (1,258), Mossoró (340)
2014	30,219	4,982	16.4	Natal (1,981), Mossoró (1,125)
2015	32,060	3,218	10.03	Natal (1,629), Mossoró (451)
2016	28,841	2,192	7.6	Natal (870), Caicó (353)
2017	35,291	3,884	11	Natal (1,684), Mossoró (403)
2018	24,982	2,439	9.7	Natal (403), Pau dos Ferros (233)
Total	231,123	24,642	10.6	

Table 2. Statistically significant clusters of canine visceral leishmaniasis cases in Rio Grande do Norte state, Northeastern of Brazil, during the period of 2011 to 2018.

Year	Radius (km)	No. of counties into the cluster	No. of cases into the cluster		RR[b]	P-value
			Observed	Expected		
2011	0[a]	1	1,178	655.62	2.26	< 0.001
	0	1	150	71.41	2.15	< 0.001
	0	1	26	11.78	2.22	0.015
2012	67.23[a]	6	1,150	611.65	2.65	< 0.001
	54.45	6	210	98.45	2.24	< 0.001
	19.87	2	21	4.92	4.29	< 0.001
	0	1	668	570.59	1.23	< 0.001
	0	1	3	0.34	8.95	0.015
2013	0[a]	1	54	15.44	3.56	< 0.001
	0	1	31	6.26	5.01	< 0.001
	0	1	87	37.39	2.38	< 0.001
	41.99	4	38	14.06	2.73	< 0.001
	0	1	48	28.86	1.68	0.037
2014	0[a]	1	372	151.67	2.57	< 0.001
	70.48	9	1,425	1,106.89	1.40	< 0.001
2015	0[a]	1	123	51.59	2.44	< 0.001
	19.84	2	31	10.24	3.05	< 0.001
	0	1	108	64.54	1.70	< 0.001
	0	1	4	0.80	9.97	< 0.001
	21.66	3	282	223.23	1.29	< 0.001
2016	160.94[a]	34	710	482.54	1.70	< 0.001
	0	1	72	18.32	4.03	< 0.001
	17.89	2	114	65.51	1.78	< 0.001
2017	0[a]	1	324	95.86	3.60	< 0.001
	0	1	96	23.44	4.17	< 0.001
	12.89	2	173	90.36	1.96	< 0.001
	0	1	16	2.97	5.40	< 0.001
	0	1	217	156.83	1.41	< 0.001
2018	0[a]	1	163	43.64	3.93	< 0.001
	17	2	290	179.74	1.70	< 0.001
	36.11	3	140	67.85	2.13	< 0.001
	35.42	6	89	40.81	2.23	< 0.001
	16.70	4	59	24.41	2.45	< 0.001
	0	1	19	5.37	3.56	< 0.001
	0	1	4	0.39	10.26	< 0.001
	17.78	2	21	7.91	2.67	0.012
	0	1	3	0.29	10.25	0.024
	0	1	22	9.76	2.26	0.042

[a]Primary cluster; [b]Relative risk.

DISCUSSION

The state of Rio Grande do Norte has an urban environment susceptible to the occurrence of CVL, with climate and topography that favor the proliferation of the vector and housing in precarious socio-sanitary conditions [1]. The high number of CVL cases in Natal can be explained by the fact that the city is considered endemic for CVL, characterized as an area of intense transmission of the disease, according to the Ministry of Health. In addition, public infrastructure in some locations is deficient and living conditions are unfavorable, so that there is a need to invest in effective protection measures for vector control, as well as a focus on health education, whose HVL control measures in the municipality need to be readjusted [32].

The municipality of Mossoró, the second largest economic center in the state, had a high number of cases in the period, which may be related to the precarious socioeconomic conditions of some neighborhoods, poor living conditions and low level of information about CVL [6]. In 2018, no LVC data were recorded in the municipality, and such information may be related to complete closure of the Zoonosis Control Center (CCZ), making combat actions difficult and consequently favoring the increase in the number of cases of leishmaniasis and other zoonoses [4] Historically, the occurrence of HVL in the state of Rio Grande do Norte was centered in the Metropolitan (Eastern Potiguar) and Agreste regions. However, in recent years there has been a clear expansion of the human and canine disease to several regions of the state, mainly in the East and West Potiguar mesoregions, with the municipalities of Mossoró as the second municipality with concentrations of the number of cases [27], reinforcing the growing expansion of the disease in several regions of the state.

The absence of data on the occurrence of CVL in some municipalities may be associated with the failure to carry out serological surveys or even with the non-disclosure by the municipalities to official service. That is, it is likely that there were underreporting during the analyzed period. The lack of data in several locations in the state indicates the existence of difficulties in implementing the guidelines of the Visceral Leishmaniasis Surveillance and Control Program by the municipalities, and among the factors that contribute to this deficit in operationalization are the very high cost, lack of financial and human resources, in addition to the little involvement of other sectors, directly influencing the lack of commitment on the part of municipal managers [33]. It is worth noting, in this context, that Brazil is currently facing difficulties in the human visceral leishmaniasis control, and the dialogue between Health and Law is important as a strategy to avoid the expansion and/or maintenance of the disease, highlighting the need to discuss the euthanasia of symptomatic and seropositive dogs, due to the resistance of the tutors in handing them over, showing a high affective value [29].

The high number of cases of CVL in the Central and West Potiguar mesoregions can be explained by the location that the municipalities of Caicó and Pau dos Ferros occupy, as they are located in border regions, whose urban network is fragmented and consists of small towns, with about 90% of the municipalities (with a population of less than 10,000 inhabitants), in addition to acting as integrated cities and/or with possibilities of integration to the dynamics of urbanization, offering various specialized services (areas of education and health), as well as act as a 'job basin' for the region [9], whose disordered urbanization constitutes a risk factor for the emergence of new cases of CVL [7,34]. The high rate of cases and the constant presence of clusters in the municipality of Açu can be explained by the increasing degradation of the Caatinga biome, evidenced by the removal of firewood for use in the ceramist pole, whose activity is concentrated on a large scale in the use of raw material. and energy, through the production of charcoal, for agricultural and livestock fronts, putting species of fauna and flora at risk [22]. It is also noteworthy that this fact contributes to the destruction of wild ecotopes, resulting in the search for the vector for other sources of human and animal food, allowing an increase in the number of cases of the disease [24].

In view of the identification of clusters in the municipalities Baraúnas and Governador Dix-Sept Rosado, located close to the border of the state of Ceará, more precisely to the municipalities that make up the Jaguaribe mesoregion, monitoring in this location is essential, given that the state of Ceará has one of the highest rates of HVL cases in the Northeastern region of Brazil [15]. Although the municipalities of this mesoregion (21 municipalities) during the years 2011-2014 had low frequency of cases (1.7%) of HVL

[34] it is worth noting the frequency of canine cases in the municipality of Jaguaribe, being 86.6% (168/194) in the rural area and 13.4% (26/194) in the urban area [28]. In the years 2015 to 2018, the state of Rio Grande do Norte presented CVL frequency of 9.68% (11,733 positives out of 121,174 dogs tested), a percentage higher than that found in the state of Ceará in the same period, in which of the 491,857 dogs tested 33,102 (6.73%) were positive [26].

The use of spatial distribution tools for disease monitoring in the state of Rio Grande do Norte has been scarce, despite the importance of the georeferencing instrument to help monitor endemic diseases. The detection of clusters in this study made it possible to identify areas at risk for CVL, emphasizing the importance of monitoring, highlighting locations that had high rates of the disease.

A limitation of the present study was the impossibility of carrying out a space-time analysis for the period 2011-2018, given that there was no information on case notification in several municipalities in the entire period of the historical series. However, the results obtained are important, as they allowed the epidemiological characterization of the infection in the state and point to the need to carry out studies on reservoirs and vectors to identify factors related to the occurrence of cases and to know the dispersive behavior of the vector in the territory [10,15], as the control of CVL is still deficient among surveillance services and public health programs [11]. The importance of government support is highlighted regarding the insufficient or poorly managed amount of human and financial resources, to carry out the actions recommended by the Ministry of Health, so that it is through these actions that the emergence of new cases of CVL can be reduced and prevent new cases of HVL [5].

It is essential to carry out permanent actions in health education with the population and health professionals, in view of the need for information about the disease, as many studies report the lack of knowledge, in addition to studies that can estimate the level of knowledge of the population in the state of Rio Grande do Norte about CVL, given that there are no reports in the literature that attest to such information, emphasizing that knowledge about CVL enhances the active and permanent contribution of the population in controlling the disease [2], as the population that has a low level of knowledge about leishmaniasis is subject to some risk factor, which may contribute to the maintenance of the disease cycle [16].

CONCLUSIONS

Canine visceral leishmaniasis is distributed in a large part of the state of Rio Grande do Norte. The underreporting and/or deficiency in the dissemination of data by some municipalities represents a challenge in complying with the actions of the Visceral Leishmaniasis Surveillance and Control Program, and attention should be paid to the monitoring and inspection of execution actions by municipal managers, as well as how to train the professionals who are part of the service. It is expected that the present study can contribute by promoting strategies for the control of CVL in the state of Rio Grande do Norte, through the identification of risk areas and monitoring of these locations so that there is a reduction of new canine cases.

MANUFACTURERS

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***Declaration of interest*.** The authors inform that there are no conflicts of interest. Authors are solely responsible for the content of the article.

REFERENCES

1 **Barbosa I.L. 2013.** Epidemiology of Visceral Leishmaniasis in the state of Rio Grande do Norte, Brazil. *Journal of Epidemiology and Infection Control*. 3(1): 17-21. DOI: 10.17058/reci.v3i1.3148.

2 **Borges B.K.A., Silva J.Á., Haddad J.P.A., Moreira E.C., Magalhães D.F., Ribeiro L.M.L. & Fiúza V.O.P. 2008.** Assessment of the population's level of knowledge and preventive attitudes about visceral leishmaniasis in Belo Horizonte, Minas Gerais, Brazil. *Cadernos de Saúde Pública*. 24(4): 777-784. DOI: 10.1590/S0102-311X2008000400007.

3 **Cavalcante I.J.M. & Vale M.R. 2014.** Epidemiological aspects of visceral leishmaniasis (kala-azar) in Ceará from 2007 to 2011. *Revista Brasileira de Epidemiologia*. 17(4): 911-924. DOI: 10.1590/1809-4503201400040010.

4 **Conselho Regional de Medicina Veterinária (CRMV-RN). 2019.** CRMV-RN faz reunião com Secretaria de Saúde sobre reabertura do CCZ de Mossoró. Available at: <http://www.crmvrn.gov.br/2020/02/12/crmv-rn-faz-reuniao-com-secretaria-de-saude-sobre-reabertura-do-ccz-de-mossoro/>.

5 **Costa G.R.T., Cruz L.M., Francisco A.K.P.R., Coelho T.O., Cunha Neto A.F. & Santos I.B. 2016.** Atuação da Vigilância Ambiental em saúde no controle da Leishmaniose visceral em condomínio horizontal na Região Administrativa Jardim Botânico, Distrito Federal. *Comunicação em Ciências da Saúde*. 27(2): 167-172.

6 **Costa K.F.L., Amóra S.S.A., Couto C.F.A., Souza C.S.F., Silva L.F., D'Escoffer L.N., Sousa M.L.R. & Kazimoto T.A. 2014.** Awareness of visceral leishmaniasis and its relationship to dog infection in endemic riverine areas of Northeastern Brazil. *Revista da Sociedade Brasileira de Medicina Tropical*. 47(5): 607-612. DOI: 10.1590/0037-8682-0167-2014.

7 **Coura-Vital W., Marques M.J., Veloso V.M., Roatt B.M., Aguiar-Soares R.D.O., Reis L.E.S., Braga S.L., Morais M.H.F., Reis A.B. & Carneiro M. 2011.** Prevalence and factors associated with *Leishmania infantum* infections of dogs from an urban area of Brazil as identified by molecular methods. *PLoS Neglected Tropical Diseases*. 5(8): e1291. DOI: 10.1371/journal.pntd.0001291.

8 **D'andrea L.A.Z. & Guimarães R.L. 2018.** A importância da análise de distribuição espacial da leishmaniose visceral humana e canina para as ações de vigilância em saúde. *Hygeia-Revista Brasileira de Geografia Médica e da Saúde*. 14(28): 121-138. DOI: 10.14393/Hygeia142810.

9 **Dantas J.R.Q. & Clementino M.L.M. 2014.** Desenvolvimento e urbanização: a rede urbana potiguar sob a ótica dos 'REGICS'. *Revista Geotemas*. 4(1): 71-82.

10 **Figueredo W.T.X., Maciel M., Araújo S.R. & Assis D.S.M. 2019.** Uso do geoprocessamento na avaliação da leishmaniose visceral canina em Currais Novos/RN e sua relação com a leishmaniose humana. *Ciência Animal*. 29(2): 56-64.

11 **Foganholi J.N. & Zappa V. 2011.** Importância da Leishmaniose na Saúde Pública. *Revista Científica Eletrônica de Medicina Veterinária*. 9(17): 1-45.

12 **Instituto Brasileiro de Geografia e Estatística (IBGE). 2020.** Rio Grande do Norte. Available at: <https://cidades.ibge.gov.br/brasil/rn/panorama>.

13 **Kulldorff M. & Nagarwalla N. 1995.** Spatial disease clusters: detection and inference. *Statistics in Medicine*. 14(8): 799-810. DOI: 10.1002/sim.4780140809.

14 **Lima B.S., Dantas-Torres F., Carvalho M.R., Marinho-Júnior J.F., Almeida E.L., Brito M.E., Gomes F. & Brandão-Filho S.P. 2013.** Small mammals as hosts of *Leishmania* spp. in a highly endemic area for zoonotic leishmaniasis in North-Eastern Brazil. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 107(9): 592-597. DOI: 10.1093/trstmh /trt062.

15 **Lucena R.V. & Medeiros J.S. 2018.** Caracterização epidemiológica da leishmaniose visceral humana no nordeste brasileiro entre 2010 e 2017. *Journal of Biology & Pharmacy and Agricultural Management*. 14(4): 285-298.

16 **Menezes J.A., Luz T.C.B, Sousa F.F., Verne R.N., Lima F.P. & Margonari C. 2016.** Peridomiciliary risk factors and knowledge concerning visceral leishmaniasis in the population of formiga, Minas Gerais, Brazil. *Revista Brasileira de Epidemiologia*. 19(2): 362-374. DOI: 10.1590/1980-5497201600020013.

17 **Ministério da Saúde. 2007.** *Introdução à Estatística Espacial para a Saúde Pública*. Brasília: Ministério da Saúde, 120p. Available at: <https://ares.unasus.gov.br/acervo/handle/ARES/1199?mode=full>.

18 **Ministério da Saúde. 2014.** *Manual de Vigilância e Controle da Leishmaniose Visceral*. Brasília: Ministério da Saúde, 120p. Available at: <https://bvsms.saude.gov.br/bvs/publicacoes/manual_vigilancia_controle_leishmaniose_visceral_1edicao.pdf >.

19 **Ministério da Saúde. Secretaria de Vigilância em Saúde. 2019.** *Guia de Vigilância em Saúde*. Brasília: Ministério da Saúde, 741p. Available at: <http://bvsms.saude.gov.br/>.

20 **Monteiro E.M., Silva J.C.F., Costa R.T., Costa D.C., Barata R.A., Paula E.V., Machado-Coelho G.L.L., Rocha M.F., Fortes-Dias C.L. & Dias E.S. 2005.** Visceral Leishmaniasis: study of sandflies and canine infection in Montes Claros, Minas Gerais. *Revista da Sociedade Brasileira de Medicina Tropical*. 38(2): 147-152. DOI: 10.1590/S0037-86822005000200004.

21 **Pan American Health Organization (PAHO). 2019.** Leishmaniasis: Epidemiological Report in the Americas. v.7. Washington: PAHO/WHO, 8p. Available at: <https://iris.paho.org/bitstream/handle/10665.2/50505/2019-cde-leish-informe-epi-das-americas.pdf?ua=1>.

22 **Prudêncio M.A. & Cândido D.K. 2019.** Degradação da vegetação nativa do município de Assú/RN: indicadores e ações mitigadoras. *Sociedade e Território*. 21(1-2): 144-156.

23 **Rocha M.A.N., Matos-Rocha T.J., Ribeiro C.M.B. & Abreu S.R.O. 2018.** Epidemiological aspects of human and canine visceral leishmaniasis in state of Alagoas, Northeast, Brazil. *Brazilian Journal of Biology*. 78(4): 609-614. DOI: 10.1590/1519-6984.166622.

24 **Sales D.P., Chaves D.P., Martins N.S. & Silva M.I.S. 2017.** Aspectos epidemiológicos da Leishmaniose Visceral Canina e Humana no estado do Maranhão, Brasil (2009-2012). *Revista Brasileira de Ciência Veterinária*. 24 (3): 144-150. DOI: 10.4322/rbcv.2017.028

25 **Santos M.A., Rodrigues S.L.C., Nascimento A.L.F., Rodrigues J.S. & Góes M.A.O. 2018.** Visceral Leishmaniasis: clinical-epidemiological characteristics of cases and deaths in the state of Sergipe. *Journal of Epidemiology and Infection Control*. 8(4): 1-14. DOI: 10.17058/reci.v8i4.11591.

26 **Secretaria de Estado da Saúde do Ceará. 2018.** Boletim Epidemiológico - Leishmaniose Visceral. Available at: <https://www.saude.ce.gov.br/wp-content/uploads/sites/9/2018/06/boletim_leishimaniose_24_10_2018.pdf>.

27 **Secretaria de Estado da Saúde Pública do Rio Grande do Norte. 2009.** Plano de contenção do avanço da leishmaniose visceral no Rio Grande do Norte. Available at: <https://portalcovid19.saude.rn.gov.br/>.

28 **Silva A.P., Santos F.E., Silva F.G., Cavalcante Y.C.S., André W.P.P. & Silva K.Q. 2018.** Prevalência da leishmaniose visceral canina no município de Jaguaribe, Ceará. *Ciência Animal*. 28(4): 1-4.

29 **Silva S.T.P., Marques L.D.F.V., Lamounier K.C.C., Castro J.M. & Borja-Cabrera G.P. 2017.** Leishmaniose visceral humana: reflexões éticas e jurídicas acerca do controle do reservatório canino no Brasil. *Revista de Bioética y Derecho*. 39: 135-151.

30 **Silva T.A.M., Coura-Vital W., Barbosa D.S., Oiko C.S.F., Morais M.H.F., Tourinho B.D., Melo D.P.O., Reis I.A. & Carneiro M. 2017.** Spatial and temporal trends of visceral leishmaniasis by mesoregion in the southeastern state of Brazil, 2002-2013. *PLoS Neglected Tropical Diseases*. 11(10): e0005950. DOI: 10.1371/journal.pntd.0005950.

31 **Sousa R.L.T., Nunes M.I. & Freire S.M. 2019.** Perfil epidemiológico de pacientes com Leishmaniose Visceral notificados em hospital de referência em Teresina-PI. *Revista Interdisciplinar de Estudos em Saúde*. 8(1): 126-135. DOI: 10.33362/ries.v8i1.1475.

32 **Teixeira K.K., Nascimento K.G., Santana R.L., Souza A.M.G., Souza T.A. & Barbosa I.R. 2019.** Padrões espaciais da ocorrência de Leishmaniose Visceral Humana na cidade de Natal-RN: a influência das áreas de risco social. *Revista Brasileira de Geografia Médica e da Saúde*. 15(32): 121-133. DOI: 10.14393/Hygeia153249966.

33 **von Zuben A.P.B. & Donalísio M.R. 2016.** Difficulties in implementing the guidelines of the Brazilian Visceral Leishmaniasis Control Program in large cities. *Cadernos de Saúde Pública*. 32(6): e00087415. DOI: 10.1590/0102-311X00087415.

34 **Werneck G.L. 2011.** Trinta anos de urbanização da leishmaniose visceral no Brasil. Available at: <http://sbmt.org.br/portal/noticias-113>.