Parasitology

cambridge.org/par

Research Article

Cite this article: Graepp-Fontoura I *et al* (2020). Epidemiological aspects and spatial patterns of human visceral leishmaniasis in Brazil. *Parasitology* **147**, 1665–1677. https://doi.org/10.1017/S0031182020001754

Received: 1 July 2020
Revised: 8 September 2020
Accepted: 13 September 2020
First published online: 21 September 2020

Key words:
Brazil; human visceral leishmaniasis; leishmaniasis; spatial analysis

Author for correspondence:
Iolanda Graepp-Fontoura,
E-mail: iolandagraepp@hotmail.com

Epidemiological aspects and spatial patterns of human visceral leishmaniasis in Brazil

Iolanda Graepp-Fontoura[1,2], David Soeiro Barbosa[3], Luiz Fernando Costa Nascimento[4,9], Volmar Morais Fontoura[5], Adriana Gomes Nogueira Ferreira[2,6], Francisca Aline Arrais Sampaio Santos[2], Benedito Salazar Sousa[7], Floriacy Stabnow Santos[2,6], Marcelino Santos-Neto[2,6], Leonardo Hunaldo dos Santos[2,6] and Ana Lúcia Abreu-Silva[1,8]

[1]Graduate Program in Health Sciences, Universidade Federal do Maranhão, Avenue of Portuguese 1966, 65080-805, Bacanga, São Luís, Maranhão, Brazil; [2]Department of Nursing, Universidade Federal do Maranhão, Avenue da Universidade, Dom Afonso Felipe Gregory, 65.915-240, Imperatriz, Maranhão, Brazil; [3]Department of Parasitology, Institute of Biological Sciences, Universidade Federal de Minas Gerais, Avenue Presidente Antônio Carlos 6627, 31275-035, Belo Horizonte, Minas Gerais, Brazil; [4]Postgraduate Program on Mechanical Engineering, Department of Energy, Universidade Estadual de São Paulo, Avenue Ariberto Pereira da Cunha, 333, 12516-410, Guaratinguetá, São Paulo, Brazil; [5]Department of Nursing, Universidade Estadual do Tocantins, Pedro Ludovico, 535, Boa Vista, 77960-000, Augustinópolis, Tocantins, Brazil; [6]Master Course in Health and Technology (PPGST-UFMA), Avenue da Universidade, Dom Afonso Felipe Gregory, 65.915-240, Imperatriz (MA), Brazil; [7]Instituto de Ensino Superior do Maranhão – IESMA/UNISULMA, São Pedro, 11, Jardim Cristo Rei, 65907-070, Imperatriz, Maranhão, Brazil; [8]Department of Pathology, Universidade Estadual do Maranhão, Cross Paulo VI, 65080-805, Cidade Universitária, São Luís, Maranhão, Brazil and [9]Department of Environmental Sciences, Universidade de Taubaté, Dr. José Luiz Cembranelli, 5000, Taubaté, São Paulo, 12081-010, Itaim District, Brazil

Abstract

Human visceral leishmaniasis (HVL) cases are important public health problems due to their zoonotic aspect, with high rates of morbidity and mortality in Brazil. The aim of this this study was to identify spatial patterns in both rates of HVL cases in Brazilian states during the period from 2006 to 2015. This is an ecological study, using geoprocessing tools to create choropleth maps, based on secondary data from open access platforms, to identify priority areas for control actions of the disease. Data were collected in 2017 and analysed according to the global and local Moran's *I*, using TerraView 4.2.2 software. Similar clusters were observed in neighbouring municipalities in thematic maps of HVL, suggesting spatial similarity in the distribution of the disease in humans mainly in the North and Northeast Regions, which concentrate the states with the highest rates of HVL. Heterogeneous spatial patterns were observed in the distribution of HVL, which show municipalities that need higher priority in the intensification of disease surveillance and control strategies.

Introduction

Leishmaniasis occupies the ninth position in the world ranking among the priority infectious diseases (World Health Organization., 2015; Machado *et al*., 2016; Carvalho *et al*., 2018). Visceral leishmaniasis (VL) is present in more than 80 countries (Mehrjou *et al*., 2016), nevertheless 90% of these cases are concentrated in 10 of them (Brazil, Bangladesh, Ethiopia, China, Kenya, Nepal, India, Sudan, Somalia and South Sudan) (World Health Organisation, 2009; Arruda *et al*., 2019). In the Americas, it is present in 12 countries, and 95% of the cases are reported in Brazil (Mehrjou *et al*., 2016).

In the 1990s, the highest index of Brazilian notifications was around 90% in the Northeast Region. The unplanned expansion of the peripheries in small and large cities, associated with the lack ok of adequate infrastructure (Albuquerque *et al*., 2014; Silva and Abud, 2016), and the presence of dog, the main reservoir of *Leishmania infantum* (Mehrjou *et al*., 2016), favoured environments conducive to the proliferation and adaptation of the vector, as well as the consequent expansion of the disease to other regions, as Midwest and Southeast. Thus, the percentage in the Northeast Region decreased to 77% (Brasil, 2014, 2015).

In Brazil the disease is more prevalence in Maranhão, Ceará, Bahia, Piauí, Tocantins, Pará, Minas Gerais, Mato Grosso do Sul and São Paulo State (Brasil, 2015). The cases are often related to poor quality of life and child malnutrition (Duarte-Cunha *et al*., 2012).

Epidemiological and socioeconomic situations and ecological processes can reduce the impact of control programmes (Otranto and Dantas-Torres, 2013). The Secretariat of Health Surveillance of Ministry of Health coordinates the VL control and surveillance activities in Brazil (Mehrjou *et al*., 2016). However, the control strategies currently applied were not successful in decreasing the incidence of the disease to acceptable levels (Costa *et al*., 2013), exposing the vulnerabilities of such measures (Araújo *et al*., 2013; Arruda *et al*., 2019).

Using spatial analysis tools and those from Geographic Information System (GIS) allows the creation of thematic maps that assist in the checking and offer a better understanding of the spatial patterns of data distribution, making it possible to detect risk areas and associated factors, as well as indicate the regions with greater need to intensify and/or prioritize control measures, in addition to implementing control strategies, both for the disease and the limited financial resources (Arruda *et al.*, 2019).

A model of geographic distribution has been used in the human visceral leishmaniasis (HVL) (Barbosa and Werneck, 2011; Karagiannis-Voules *et al.*, 2013; Barbosa *et al.*, 2014; Fontoura *et al.*, 2016) and is widely used to analyse the spatial distributions of other studies, as dengue (Rodrigues *et al.*, 2016), Zika virus (de Oliveira *et al.*, 2017), tuberculosis (Santos Neto *et al.*, 2017), diarrhoea (Fontoura *et al.*, 2018*a*), among others.

Although spatial analyses have already been used in other Brazilian research studies, this study was necessary to identify spatial patterns during the period of last 10-years in order to determine areas that must be prioritized regarding planning disease surveillance and control actions in the country, mainly taking into account the HVL rates in the Brazilian states.

Materials and methods

Study area

Brazil is located in South America, and its area comprises 8.5 million km^2. Its population was estimated in 211 million residents in 2020. It is divided into five regions, i.e. Northeast, North, Midwest, Southeast and South, with 27 federated states (1 Federal District and 26 States) and 5570 cities (IBGE, 2020).

Study design and population

We carried out an ecological spatial analysis based on secondary data and time series related to HVL cases in Brazilian cities between 2006 and 2015. We analysed the epidemiological characteristics, spatial patterns with time trends of the HVL distribution, as well as the identification of risk areas.

Data sources

Populational data collected in 2017 originated from the 2010 Demographic Brazilian Census (IBGE, 2017*a*) carried out by the Brazilian Institute of Geography and Statistics (IBGE, 2017*b*). HVL data were obtained from Information System of Disease Notification (SINAN, acronym in Portuguese) from 2006 (Brasil, 2017*a*) and between 2007 and 2015 (Brasil, 2017*b*), which includes standardized forms that are completed by the physicians in charge of notification. The disease notification form provides demographic data (gender, skin colour/ethnicity, age range, years of study, data regarding region and states), and clinical information (HIV coinfection, evolution, entrance type, diagnosis examinations, confirmatory criteria). These data are available in the website of Computing Department of the Brazilian Unified Health System (DATASUS, acronym in Portuguese) and they are of public domain, therefore they can be accessed for free. We included all data available between 2006 and 2015 regarding HVL in Brazil.

The selection of indicators was based on the distribution of HVL cases reported and their association with risk factors for its occurrence. The analysis was based on indicators that determine the HVL (Araújo *et al.*, 2013; Arruda *et al.*, 2019). The HVL epidemiological characteristics were compared with gender, skin colour/ethnicity, age range, evolution, type of entrance, diagnosis examinations, years of study grouped in a biennial form and data regarding region and states.

Statistical analysis

We described the available variables of the studied population: gender, skin colour/ethnicity, age range, disease evolution, entrance type, HIV coinfection, parasitological diagnosis, immunofluorescent diagnosis, confirmatory criterion, region, and states. The descriptive statistics included absolute number, 95% confidence interval (95% CI) for categorical variables, and average annual rate (AAR), standard deviation (S.D.) and 95% CI for continuous variables.

Gross rate and AAR were calculated by dividing the HVL number in each year through the direct method using the 2010 Brazilian population, multiplied by 100 000 residents.

Prais–Winsten linear regressions were used between 2006 and 2015, a statistical procedure for the analysis of prevalence trend regression and autocorrelation in time series (Falavina *et al.*, 2019). It was used for annual increment rates and respective confidence intervals (95%). Based on these parameters, they were classified as increasing (positive rate), stable (regression coefficient not significant between its value and zero, $P > 0.05$) or decreasing (negative rate) (Brilhante *et al.*, 2017; Costa *et al.*, 2019).

Finally, we analysed the spatial patterns of HVL distribution in Brazil using the home cities ($n = 5570$; 2010 territorial division). The geographic units were analysed per tool of the GIS, which are useful in the geographic distribution assessment, as well as in the spatial dependence of the HVL rates.

The development of thematic maps occurred based on gross rates (number of HVL/population living in Brazil in 2010 × 100 000 residents) (Martins-Melo *et al.*, 2014*b*). The gross rates of HVL were grouped in every 2 years (2006–2007; 2008–2009; 2010–2011; 2012–2013; 2014–2015) and in the total period (2006–2015).

After the descriptive analysis of data, we estimated global and local Moran's *I* indices (Local Indicators of Spatial Association – LISA), which estimate the spatial correlation and local self-correlation by helping to identify sub-regions with the occurrence of spatial self-correlation. We used a first-order neighbourhood criterion to concretize calculations, in which the cities defined as neighbours were those in the borders (Barbosa and Werneck, 2011; Fontoura *et al.*, 2016). Moran's *I* global index is defined between −1 and 1, in a way that values close to 0 suggest absence of spatial correlation or randomness and next to 1, positive spatial dependence with more similarity between the adjacent cities (grouping). Negative spatial dependence is pointed as −1, which indicates dissimilarity (dispersion) and negative spatial self-correlation (Martins-Melo *et al.*, 2014*a*; INPE, 2015).

Data available between 2006 and 2015 were analysed in order to observe a potential overlap between HVL (Fontoura *et al.*, 2016). It was defined in quantiles (form in which the classes are divided, each one receives the same number of occurrences), because this is the best configuration to represent data using the intervals: 0,0 for absence of cases; >0,1 to 5,0, very low; >5,0 to 10,0, low; >10,0 to 20,0, medium; >20,0, high (this format was used to classify the gross rate per 100 000 residents). Choropleth maps were developed to better visualize the attribute variation (Barbosa and Werneck, 2011; INPE, 2015).

The generation of LISA map showed clusters of HVL and CVL cases, suggesting places with higher and lower need of interventions, in which 0 indicated non-significant ($P > 0.05$) that showed inexistence of self-correlation; 1 had low self-correlation, with a 95% confidence level ($P = 0.05$); 2, medium self-correlation and 99% confidence ($P = 0.01$); and 3 indicated existence of high self-correlation and 99.9% ($P = 0.001$) (Barbosa *et al.*, 2014; Carvalho and Nascimento, 2014; Fontoura *et al.*, 2016).

Data for Moran's *I* Map construction were generated indicating a significance level in the interface (>95% confidence) and suggested places with priority of intervention (INPE, 2015), considering as criteria: zero for non-significant (absence of data); quadrant 1, Q1 – high–high, high priority (positive values, positive means); quadrant 2, Q2 – low–low, low priority (negative values, negative means); quadrant 3, Q3 – high–low (high variable values and low of neighbours) and quadrant 4, Q4 – low–high (low variable values and high of neighbours), which are considered of medium priority (negative spatial association) (Barbosa and Werneck, 2011; Fontoura *et al*., 2016). Random oscillations were minimized, considering that several consecutive years were analysed according to each variable.

For the spatial analysis, cartographic data presentation, calculation of spatial and local self-correlation indicators and construction of thematic maps, we used the TerraView 4.2.2 software (Instituto Nacional de Pesquisas Espaciais, INPE, São José dos Campos, SP, Brazil – INPE, 2013). The descriptive analysis of the data, as well as the Prais–Winsten regression tests, with 5% significance, was performed using the IBM SPSS 24 programme (IBM SPSS Statistics, 2016).

Results

During the study period, 37 411 cases of VL were reported between 2006 and 2015, representing AAR of 1.95 case/100 000 inhabitants (S.D. ±0.14; 95% CI 2.05–1.88). The Prais–Winsten regression showed that the incidence rate of the total number of cases remained stable −4.9/100 000 inhabitants ($P = 0.12$).

Male gender (23 510; 63%; AAR of 2.51/100 000 inhabitants) and mixed-race (72%) corresponded to the predominant characteristics of HVL. The highest incidence was found among indigenous people (AAR of 4.28/100 000 inhabitants). The highest proportion was in the age group of children between 1 and 4 years old (27.73%), but with a higher incidence in children under 1 year old (AAR 2.42/100 000 inhabitants). We found 2408 deaths reported (AAR of 0.13/100 000 inhabitants), 26 857 (AAR of 1.39/100 000 inhabitants) were considered cured, 33 916 were new cases (AAR of 1.77/100 000 inhabitants), and 1534 (AAR of 0.08/100 000 inhabitants) presented recurrences.

Among the diagnostic tests performed, 13 260 cases (AAR of 0.68/100 000 inhabitants) were confirmed by parasitological examination, and 15 641 by the indirect immunofluorescence test (AAR of 0.80/100 000 inhabitants). The LVH/HIV co-infection was present in 2229 people (AAR of 0.13/100 000 inhabitants) (Table 1).

Regarding sex over the years, both AAR of total and of male and female sex were similar, with a slight decrease between 2012 and 2013, then increasing again (Table 2). Rates related to colour skin or race and to indigenous race had significant increase between 2010 and 2011, with a slight decrease between 2012 and 2013, then increasing again. Concerning the age, rates continued similarly, with an increase between the years 2008 and 2011, and then they decreased. Mortality and cure rates remained almost the same, with a slight growth in 2015. The rates of new cases increased significantly between 2010 and 2011, with an important decrease in the period between 2012 and 2013, increasing again between 2014 and 2015, unlike recurrences that were remained the same between 2006 and 2011, with an increase between 2012 and 2013, getting higher between 2014 and 2015. The diagnosis rates confirmed by parasitological method presented with significant regression over the years, unlike the rates of positive diagnoses confirmed by the indirect immunofluorescence test that significantly increased over the years until 2010 and 2011, with an important decrease between 2012 and 2013 and an increase between 2014 and 2015. The HVL/HIV coinfection rates gradually increased over the years, especially after 2010.

The Prais–Winsten regression showed that the incidence rate of the total number of cases remained stable −4.9/100 000 inhabitants ($P = 0.12$), in the period from 2006 to 2015, without significant changes over the years, conferring a stable trend, without statistical significance ($P > 0.05$). However, in some variables, the incidence rates presented an increasing trend with positive values among indigenous peoples 61.44/100 000 inhabitants (3.75–151.19; $P = 0.04$), in the age groups between 40 and 59 years 6.41/100 000 in inhabitants (1.81–11.22; $P = 0.01$), 60–64 years old 0.93/100 000 inhabitants (0.37–1.48; P 0.00), 65–69 years old 1.86/100 000 inhabitants (0.74–2.99; $P = 0.01$), 70–79 years old 5.68/100 000 inhabitants (3.37–8.04; $P < 0.001$), >80 years old 5.44/100 000 inhabitants (−0.23 to 11.43; P 0.05), relapses 1.16/100 000 inhabitants (0.60 to 1.72; P 0.01) and co-infected HVL/HIV patients HIV 3.99/100 000 inhabitants (2.28 to 5.73; P 0.00). In other variables, it was possible to observe a decrease ($P < 0.05$), with negative values, such as female gender −7.1/100 000 inhabitants (−12.2 to −1.7; $P = 0.02$), individuals with white colour/ethnicity −9.0/100 000 inhabitants (−10.00 to −7.99; $P < 0.001$), Asian descendants −17.59/100 000 inhabitants (−32.45 to 0.55; $P = 0.05$), aged between 5 and 9 years −5.59/100 000 inhabitants (−8.67 to −2.41; $P = 0.00$), cure −7.10/100 000 inhabitants (−12.58 to −1.28; $P = 0.03$ inhabitants parasitological tests positive −7.74/100 000 inhabitants (−9.76 to −5.68; $P < 0.001$) and negative −0.69/100 000 inhabitants (−1.24 to −0.14; $P = 0.03$). The other variables remained stable ($P > 0.05$) (Table 3).

The highest proportion of cases of HVL was in the Northeast (19 908; 53%), but the highest incidence was in the North Region (AAR of 7.35/100 000 inhabitants). Among the states with the highest rates of HVL, Ceará was the prevalent, with 5654 (15%) of the reported cases, but the highest rate was in the state of Tocantins (AAR of 24.18/100 000 inhabitants) (Table 4).

In relation to the regions and states of Brazil, the annual increase in incidence rates of VL in the period from 2006 to 2015 remained stable, without significant changes, over the years, in most variables, conferring a stable trend, without statistical significance ($P > 0.05$). Except for the variables that showed a decreasing trend ($P < 0.05$), with negative values, as in the North −67.79/100 000 inhabitants (−82.56 to −40.52; $P = 0.00$), in the states of Pará −47.03/100 000 inhabitants (−60.92 to −28.22; $P = 0.00$) and São Paulo −6.24/100 000 inhabitants (−9.30 to −3.08; $P = 0.00$), as well as the variables with increasing trend, with positive values ($P < 0.05$), such as the states of Goiás 8.89/100 000 inhabitants (0.79–17.65; $P = 0.03$), Paraíba 17.76/1 000 000 inhabitants (5.44–31.52; $P = 0.01$; $P = 0.76$ Paraná 0.69/100 000 inhabitants (0.14–1.25; $P = 0.02$) and Roraima 44.54/100 000 inhabitants (−7.62 to 126.15; $P = 0.00$) (Table 5).

The highest rates presented, according to the classification from the highest to the lowest, referring to the total number of notified cases, were from the North (AAR of 7.35/100 000 inhabitants), Northeast (AAR of 6.20/100 000 inhabitants), Midwest (AAR of 3.79/100 000 inhabitants), Southeast (AAR of 1.50/100 000 inhabitants) and South (AAR of 0.04/100 000 inhabitants). The highest proportion of cases (64%; mean: 53; median: 63; S.D. ±5) and the highest rate of HVL over the years were from Northeast Region, between the years 2014 and 2015 (AAR of 10.83/100 000 inhabitants; mean: 6.94; 95% CI 5.40–8.47). The North Region had the second highest incidence over the years, in the period between 2008 and 2009 (AAR of 8.95/100 000 inhabitants).

In order of classification, the states that had the highest HVL rates, between 2006 and 2015, were Tocantins (AAR of 24.18/100 000 inhabitants), Mato Grosso do Sul (AAR of 8.94/100 000 inhabitants), Maranhão (AAR of 7.99/100 000 inhabitants), Piauí (AAR of 7.45/100 000 inhabitants), Ceará (AAR of 6.47/100 000 inhabitants) and Pará (AAR of 4.48/100 000 inhabitants).

The thematic maps showed the presence of municipalities and/or clusters statistically significant ($P < 0.05$), with high HVL rates, in the Northeast, North, Midwest and Southeast Regions (Fig. 1A). A higher concentration of LVH rates forming clusters was found in the Northeast Region, covering the nine

Table 1. Epidemiological characteristics of HVL in Brazil, from 2006 to 2015

Characteristic	*n*	%	95% CI	AAR	95% CI	±s.d.
Sex						
Male	23 510	62.84	62.17–63.83	2.57	2.42–2.61	0.15
Female	13 901	37.16	36.32–37.68	1.35	1.34–1.52	0.14
Total	37 411	100.00	–	1.95	1.88–2.05	0.14
Skin colour/ethnicity						
White/Caucasian	6032	17.00	16.48–17.52	0.49	0.58–0.74	0.13
Black/Afro-descendant	2991	9.00	8.69–17.31	2.12	1.95–2.17	0.18
Yellow/Asian descendant	290	0.78	0.78–1.12	1.20	1.15–1.63	0.39
Mixed	24 479	72.00	71.17–72.83	3.26	2.82–3.33	0.25
Indigenous	280	0.75	0.56–1.14	4.28	2.80–5.05	1.01
Age group, years						
<1	3516	9.40	8.63–9.47	2.42	2.05–4.26	0.98
1–4	10 373	27.73	27.37–28.63	2.35	1.56–3.05	0.39
5–9	3861	10.32	9.63–10.37	0.69	0.63–0.86	0.11
10–14	1875	5.01	4.77–5.23	0.32	0.24–0.39	0.05
15–19	1874	5.01	4.75–5.25	0.23	0.19–0.39	0.08
20–39	8012	21.42	20.52–21.48	0.90	0.51–0.95	0.19
40–59	5500	14.70	14.58–15.42	1.06	0.68–1.39	0.17
60–64	762	2.04	1.85–2.15	0.21	0.13–0.27	0.03
65–69	580	1.55	1.46–2.14	0.31	0.15–0.34	0.08
70–79	739	1.98	1.84–2.16	0.81	0.32–0.91	0.23
>80	300	0.80	0.78–1.12	0.41	0.29–0.42	0.10
Deaths	2408	8.23	6.18–9.82	0.14	0.12–0.14	0.01
Cure	26 857	91.77	85.96–98.04	1.29	1.32–1.50	0.15
New case	33 916	95.67	89.16–102.84	1.77	1.70–1.85	0.12
Recurrence	1534	4.33	2.56–5.44	0.10	0.07–0.12	0.02
Positive parasitological	13 260	78.24	73.82–82.18	0.58	0.53–0.76	0.11
Negative parasitological	3688	21.76	19.75–24.25	0.18	0.18–0.21	0.02
IF positive	15 641	85.86	81.27–90.73	0.66	0.65–0.89	0.12
IF negative	2575	14.14	12.08–15.92	0.14	0.12–0.15	0.02
HIV coinfection	2229	5.96	4.02–7.98	0.17	0.08–0.19	0.05

95% CI, 95% confidence interval; AAR, average annual rate per 100 000 inhabitants; s.d., standard deviation; IF, indirect immunofluorescence.
Ignored or unspecified values were not considered.

northeastern states. In the North Region, there was a concentration of clusters throughout the state of Tocantins and the southeast of the state of Pará. In the Midwest Region, the rate clusters encompassed practically the entire state of Mato Grosso do Sul and the central and southern part of the state of Mato Grosso. The global Moran's I was 0.46 ($P < 0.01$), indicating similarity between neighbouring municipalities.

Discussion

This study provides an in-depth view of the HVL in Brazil, characterizing spatial and temporal patterns of its occurrence, in the period. Spatial clusters of HVL were presented in this study. Despite the slight decrease in the number of cases reported nationally in recent years, HVL has expanded geographically to other regions. This information is worrying and follow different pattern, related to regions, as sex, age group and skin colour, exposing a problem for the public health (Nascimento *et al.*, 2011; Martins-Melo *et al.*, 2014*a*; Brasil, 2015; Druzian *et al.*, 2015; Herrador *et al.*, 2015; Lane, 2016).

HVL is expanding geographically in Brazil. The epidemiological profile of this disease has been modified in developing countries (Herrador *et al.*, 2015), due to its expansion from rural to urban areas (Nascimento *et al.*, 2011; Albuquerque *et al.*, 2014; Brasil, 2015; Druzian *et al.*, 2015).

The higher prevalence found in male individuals may be related to socioeconomic, behavioural and environmental factors (Martins-Melo *et al.*, 2014*b*). The literature indicates that the disease affects both sexes, but men are described as the most susceptible (Lane, 2016). Occurrence was higher in the age group between 1 and 4 years old, with higher incidence between those who were under 1 year, possibly because children are more susceptible to morbidity and mortality, probably due to the greater contact with animals, the cycle of home/peridomestic

https://doi.org/10.1017/S0031182020001754 Published online by Cambridge University Press

Table 2. Epidemiological characteristics over the years of HVL in Brazil, from 2006 to 2015

	2006–2007 (*n*)	%	Rate[a]	2008–2009 (*n*)	%	Rate[a]	2010–2011 (*n*)	%	Rate[a]	2012–2013 (*n*)	%	Rate[a]	2014–2015 (*n*)	%	Rate[a]
Sex															
Male	4.568	61	2.49	4.967	63	2.66	4.819	62	2.56	4.306	64	2.29	4.850	65	2.57
Female	2.920	39	1.54	2.915	37	1.51	2.985	38	1.52	2.430	36	1.24	2.651	35	1.35
Total[b]	7.488	20	2.01	7.882	21	2.07	7.804	21	2.03	6.736	18	1.75	7.501	20	1.95
Skin colour/ethnicity															
White/Caucasian	1.489	22	0.82	1.394	19	0.77	1.203	17	0.66	1.046	17	0.57	900	13	0.49
Black/Afro-descendant	597	9	2.06	600	8	2.07	636	9	2.19	543	9	1.87	615	9	2.12
Yellow/Asian descendant	75	1	1.80	53	1	1.27	74	1	1.78	38	1	0.91	50	1	1.20
Mixed	4.483	67	2.72	5.034	72	3.06	5.091	72	3.09	4.508	73	2.74	5.363	76	3.26
White/Caucasian	37	1	2.26	51	1	3.12	67	1	4.10	55	1	3.36	70	1	4.28
Indigenous	37	0	4.52	51	1	6.24	67	1	8.19	55	1	6.72	70	1	8.56
Age group, years															
<1	720	10	3.63	780	10	4.20	684	9	4.05	671	10	3.97	661	9	3.91
1–4	2.413	32	2.94	2.315	28	2.97	2.158	27	3.24	1.683	25	2.53	1.804	24	2.71
5–9	922	12	0.88	912	12	0.90	756	10	0.83	610	9	0.67	661	9	0.73
10–14	403	5	0.38	421	5	0.42	395	5	0.38	322	5	0.31	334	4	0.32
15–19	404	5	0.37	402	5	0.39	399	5	0.39	313	5	0.30	356	5	0.35
20–39	1473	20	0.55	1568	19	0.57	1718	22	0.61	1517	23	0.54	1736	23	0.61
40–59	818	11	0.61	1069	14	0.74	1179	15	0.78	1082	16	0.72	1352	18	0.90
60–64	111	1	0.12	141	2	0.14	169	2	0.15	162	2	0.15	179	2	0.16
65–69	92	1	0.16	88	1	0.14	130	2	0.19	121	2	0.18	149	2	0.22
70–79	93	1	0.29	135	2	0.39	155	1	0.41	161	2	0.42	195	3	0.51
>80	38	1	0.28	44	1	0.27	56	1	0.32	89	1	0.50	73	1	0.41
Death	470	7	0.12	455	8	0.12	499	8	0.13	448	9	0.12	536	10	0.14
Cure	5825	93	1.53	5517	92	1.45	5841	92	1.53	4743	91	1.24	4931	90	1.29
New case	6851	96	1.80	6935	96	1.82	7244	96	1.90	6132	95	1.61	6754	95	1.77
Recurrence	261	4	0.07	252	4	0.07	280	4	0.07	354	5	0.09	387	5	0.10
Positive parasitological[b]	3195	80	0.84	2984	80	0.78	2612	77	0.68	2244	76	0.59	2225	77	0.58
Negative parasitological[b]	789	20	0.21	752	20	0.20	774	23	0.20	698	24	0.18	675	23	0.18
IF positive[b]	3122	88	0.82	3511	86	0.92	3676	86	0.96	2807	86	0.74	2525	82	0.66

(*Continued*)

Table 2. (*Continued.*)

	2006–2007 (*n*)	%	Rate[a]	2008–2009 (*n*)	%	Rate[a]	2010–2011 (*n*)	%	Rate[a]	2012–2013 (*n*)	%	Rate[a]	2014–2015 (*n*)	%	Rate[a]
IF negative[b]	428	12	0.11	549	14	0.14	597	14	0.16	453	14	0.12	548	18	0.14
HIV coinfection[ab]	112	5	0.03	385	17	0.10	493	22	0.13	609	28	0.16	630	28	0.14

IF, indirect immunofluorescence.
Ignored or unspecified values were not considered.
[a]Average biennial rate per 100 000 inhabitants; †percentage values compared horizontally and total vertically.
[b]Calculated percentage between positive and negative in parasitological examination and positive and negative indirect immunofluorescence test.

transmission and by vectors, as well as nutritional and immune deficiencies (Martins-Melo *et al.*, 2014*a*; Guimarães *et al.*, 2015).

The HVL prevalence was higher between those with mixed-race – and most of the Brazilian population considers themselves as with mixed-race. The higher incidence was found between the indigenous people. Indigenous populations are more susceptible to HVL, probably due because of the gold mining activities, the increased immigration from endemic areas and the visits to family members taking dogs contaminated by *Leishmania* or contaminated in the place visited (Guimarães *et al.*, 2015; Silva and Abud, 2016).

The method for diagnosing HVL used with the greatest number of positive cases was the indirect immunofluorescence test. This test is more effective than the parasitological test, since it is based on the antibody response (World Health Organization., 2010; Dupnik *et al.*, 2011;Souza *et al.*, 2012; Cota *et al.*, 2013, 2014; Albuquerque *et al.*, 2014; Druzian *et al.*, 2015; Távora *et al.*, 2015).

According to DATASUS, out of the HVL patients, 93% were considered cured and 7% died, with prevalent numbers in the Northeast Region (49.74%) and in the state of Minas Gerais (18.87%). HVL is a potentially lethal disease if not treated and diagnosed early (Martins-Melo *et al.*, 2014*a*).

Concerning the type of entry, 96% were new cases and 4% were recurrence. The mortality rates are often higher in immunocompromised individuals and in recurrences (Gomes *et al.*, 2012; Fontoura *et al.*, 2018*b*).

Using geoprocessing techniques, we analysed the distribution of the occurrence of HVL, and the detection of statistically significant spatial clusters. The HVL distribution is heterogeneous, but, with the different techniques for spatial analysis, it is possible to identify areas with greater and lower needs for interventions, where control measures, when targeted, become more effective (Martins-Melo *et al.*, 2014*a*; Silva and Abud, 2016).

The national AAR of HVL was 1.95 per 100 000 inhabitants. When analysing the spatial distribution of HVL rates, we found that HVL was recorded in all Brazilian regions – with clusters prevalent in the Northeast Region. However, the highest rate was in the North Region (rate 7.04/100 000 inhabitants), specifically in the state of Tocantins (rate 21.65/100 000 inhabitants). The HVL notified cases have increased and expanded to other areas in the state of Tocantins (Fontoura *et al.*, 2016). Irregular land occupation causes environmental imbalance.

A study carried out in Tocantins State evaluated the correlation of the HVL incidence rate with environmental and climate variables. These rates increase as night temperature increases, as well as air humidity and precipitation (Reis *et al.*, 2019). Temperature increase is associated with phlebotomine density increase, contributing to the occurrence of higher contact between vector and host and favouring the disease spread (Galati *et al.*, 2015), as well as its activity (Rivas *et al.*, 2014). Consequently, there is higher parasitic load in the vector due to the increase in the number of times blood repast occurs (Serafim *et al.*, 2018) and Straw mosquito infectivity.

The city of Araguaia, in the North of the state, has one of the highest rates of HVL (Silva, 2016). In addition to intense urban expansion, deforestation without proper planning and inadequate infrastructure shows climate and environmental factors favourable to the vector development (Reis *et al.*, 2019). Besides climate and environmental factors, others have been associated with subjects, including socioeconomic status, low immunity, and nutritional condition (Toledo *et al.*, 2017).

The VL is a disease associated with poverty that also perpetuates it (Lane, 2016). The high number of cases in the Northeast Region reflects the socio-environmental conditions that favour the spread of HVL (Martins-Melo *et al.*, 2014*b*; Silva *et al.*, 2015).

https://doi.org/10.1017/S0031182020001754 Published online by Cambridge University Press

Table 3. Regression analysis with annual percentage of incidence rates of characteristics of HVL in Brazil, from 2006 to 2015

	Annual incidence rates												
Variables	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Annual rate of change % ($IC_{95\%}$)	*P**	Situation
Sex													
Male	2.61	2.37	2.66	2.66	2.43	2.69	2.20	2.37	2.57	2.58	−2.1 (−10.3 to 7.0)	0.58	Stable
Female	1.69	1.40	1.56	1.45	1.44	1.60	1.21	1.26	1.33	1.37	−7.1 (−12.2 to −1.7)	0.02	Descending
Total	2.14	1.87	2.09	2.04	1.92	2.13	1.69	1.80	1.93	1.95	−4.9 (−11.0 to 1.6)	0.12	Stable
Skin colour/ethnicity													
White/Caucasian	0.87	0.76	0.82	0.71	0.63	0.69	0.58	0.57	0.52	0.47	−9.0 (−10.00 to −7.99)	*<0.001*	Descending
Black/Afro-descendant	2.30	1.81	1.96	2.17	2.14	2.25	1.76	1.98	2.25	1.99	−0.23 (−10.17 to 10.82)	*0.97*	Stable
Yellow/Asian descendant	1.78	1.82	1.49	1.06	1.82	1.73	1.20	0.62	1.39	1.01	−17.59 (−32.45 to 0.55)	*0.05*	Descending
Mixed	2.75	2.70	3.07	3.05	2.87	3.32	2.60	2.88	3.17	3.35	9.40 (−4.19 to 24.91)	*0.15*	Stable
Indigenous	1.96	2.57	3.06	3.18	4.65	3.55	2.45	4.28	3.18	5.38	61.44 (3.75 to 151.19)	*0.04*	Growing
Age group, years													
<1	3.96	3.30	4.66	3.74	3.85	4.25	3.37	4.57	3.84	3.99	5.20 (−8.88 to 21.45)	*0.43*	Stable
1–4	3.10	2.78	3.15	2.79	3.09	3.38	2.33	2.72	2.71	2.70	−9.64 (−21.73 to 4.33)	*0.13*	Stable
5–9	0.90	0.86	0.91	0.89	0.76	0.91	0.63	0.72	0.77	0.68	−5.59 (−8.67 to −2.41)	*0.00*	Descending
10–14	0.35	0.42	0.42	0.42	0.38	0.38	0.30	0.32	0.34	0.31	−2.28 (−4.94 to 0.46)	*0.06*	Stable
15–19	0.37	0.37	0.37	0.42	0.36	0.42	0.34	0.27	0.33	0.36	−1.37 (−4.06 to 1.39)	*0.22*	Stable
20–39	0.56	0.54	0.56	0.58	0.59	0.63	0.53	0.54	0.59	0.64	1.39 (−0.83 to 3.66)	*0.23*	Stable
40–59	0.65	0.57	0.69	0.80	0.73	0.84	0.74	0.70	0.90	0.90	6.41 (1.81 to 11.22)	*0.01*	Growing
60–64	0.13	0.12	0.14	0.14	0.16	0.14	0.16	0.13	0.18	0.15	0.93 (0.37 to 1.48)	*0.00*	Growing
65–69	0.16	0.17	0.13	0.16	0.16	0.22	0.17	0.18	0.20	0.23	1.86 (0.74 to 2.99)	*0.01*	Growing
70–79	0.30	0.29	0.38	0.39	0.34	0.48	0.43	0.41	0.50	0.52	5.68 (3.37 to 8.04)	*<0.001*	Growing
>80	0.29	0.26	0.29	0.26	0.29	0.34	0.62	0.38	0.43	0.39	5.44 (−0.23 to 11.43)	*0.05*	Growing
Deaths	0.15	0.10	0.12	0.12	0.12	0.14	0.11	0.12	0.13	0.15	0.46 (−0.09 to 1.02)	*0.26*	Stable
Cure	1.69	1.36	1.48	1.41	1.43	1.64	1.23	1.26	1.29	1.30	−7.10 (−12.58 to −1.28)	*0.03*	Descending
New case	1.91	1.68	1.77	1.86	1.80	2.00	1.55	1.67	1.76	1.78	−2.50 (−9.26 to 4.76)	*0.41*	Stable
Recurrence	0.09	0.04	0.06	0.08	0.07	0.08	0.10	0.09	0.09	0.11	1.16 (0.60 to 1.72)	*0.01*	Growing
Positive parasitological	0.92	0.76	0.81	0.75	0.68	0.69	0.59	0.58	0.62	0.54	−7.74 (−9.76 to −5.68)	*<0.001*	Descending
Negative parasitological	0.21	0.20	0.18	0.21	0.19	0.21	0.16	0.21	0.17	0.18	−0.69 (−1.24 to −0.14)	*0.03*	Descending
IF positive	0.78	0.86	0.94	0.90	0.89	1.04	0.77	0.70	0.65	0.68	−4.50 (−12.58 to 4.33)	*0.25*	Stable
IF negative	0.12	0.11	0.14	0.15	0.17	0.15	0.11	0.13	0.15	0.14	0.46 (−1.19 to 2.14)	*0.54*	Stable
HIV coinfection	0.00	0.06	0.09	0.11	0.12	0.14	0.17	0.15	0.16	0.17	3.99 (2.28 to 5.73)	*0.00*	Growing

*Prais–Winsten regression ($P < 0.05$).

Table 4. Epidemiological characteristics of HVL in Brazilian regions and states, from 2006 to 2015

	2006–2007 (*n*)	%	Rate[a]	2008–2009 (*n*)	%	Rate[a]	2010–2011 (*n*)	%	Rate[a]	2012–2013 (*n*)	%	Rate[a]	2014–2015 (*n*)	%	Rate[a]	Total	%	AAR
Region																		
North	1563	21	8.72	1642	21	8.95	1605	21	8.31	1209	18	6.26	961	13	2.81	6980	19	7.35
Northeast	3828	51	6.16	3854	48	6.06	3913	49	6.10	3549	53	5.53	4764	64	10.83	19 908	53	6.20
Southeast	1463	20	1.54	1689	21	1.75	1570	19	1.62	1222	17	1.26	1266	17	4.60	7210	19	1.50
South	8	0	0.02	13	1	0.04	13	1	0.04	9	1	0.03	12	0	0.04	55	0	0.04
Midwest	625	8	3.91	684	9	4.16	705	9	4.13	748	11	4.38	498	7	5.28	3260	9	3.79
States																		
Alagoas	83	1	1.33	59	1	0.95	70	1	1.12	61	1	0.98	95	1	4.57	368	1	1.15
Amazonas	3	0	0.04	6	0	0.09	1	0	0.01	2	0	0.03	1	0	0.01	13	0	0.04
Amapá	2	0	0.15	1	0	0.07	0	0	0.00	1	0	0.07	0	0	0.00	4	0	0.07
Bahia	636	8	2.27	573	7	2.04	806	11	2.88	644	10	2.30	937	13	9.90	3596	10	2.49
Ceará	1187	17	7.02	1237	16	7.32	1152	14	6.81	890	13	5.26	1188	16	11.76	5654	15	6,47
Distrito Federal	32	0	0.62	32	0	0.62	19	0	0.37	29	0	0.56	26	0	0.35	138	0	0,67
Espírito Santo	1	0	0.01	10	0	0.14	10	0	0.14	5	0	0.07	14	0	0.13	40	0	0.15
Goiás	66	1	0.55	74	1	0.62	84	1	0.70	76	1	0.63	113	2	0.62	413	1	0.68
Maranhão	907	12	6.90	1029	13	7.83	933	11	7.10	1050	16	7.99	1213	16	17.45	5132	14	7.99
Minas Gerais	834	11	2.13	1147	14	2.93	1111	14	2.83	756	11	1.93	889	12	9.17	4737	13	2.45
Mato Grosso do Sul	475	6	9.70	450	6	9.19	490	7	10.00	554	8	11.31	312	4	4.50	2281	6	8.94
Mato Grosso	53	1	0.87	128	2	2.11	112	1	1.85	89	1	1.47	47	1	0.68	429	1	1.33
Pará	878	12	5.79	719	9	4.74	708	9	4.67	546	8	3.60	540	7	3.29	3391	9	4.48
Paraíba	62	1	0.82	62	1	0.82	73	1	0.97	81	1	1.08	107	1	1.55	385	1	1.01
Pernambuco	179	2	1.02	160	2	0.91	158	2	0.90	142	2	0.81	347	5	1.81	986	3	1.14
Piauí	505	7	8.10	466	6	7.47	367	5	5.88	403	6	6.46	551	7	5.40	2292	6	7.45
Paraná	3	0	0.01	4	0	0.02	7	0	0.03	5	0	0.02	7	0	0.09	26	0	0.03
Rio de Janeiro	12	0	0.04	4	0	0.01	7	0	0.02	14	0	0.04	12	0	0.24	49	0	0.03
Rio Grande do Norte	146	2	2.30	189	3	2.98	204	3	3.22	175	2	2.76	193	3	11.81	907	2	2.85
Rondônia	4	0	0.13	1	0	0.03	0	0	0.00	6	0	0.19	1	0	0.03	12	0	0.07
Roraima	7	0	0.78	8	0	0.89	30	0	3.33	30	0	3.33	39	1	2.17	114	0	3.17
Rio Grande do Sul	2	0	0.01	9	0	0.04	4	0	0.02	2	0	0.01	5	0	0.04	22	0	0.02
Santa Catarina	1	0	0.01	1	0	0.01	2	0	0.02	3	0	0.02	0	0	0.00	7	0	0.01
Sergipe	123	2	2.97	79	1	1.91	150	2	3.63	103	1	2.49	133	2	4.01	588	2	2.83
São Paulo	533	7	0.65	528	7	0.64	442	6	0.54	447	8	0.54	351	5	0.43	2301	6	0.55
Tocantins	668	9	24.14	907	11	32.78	865	11	31.26	624	9	22.55	380	5	6.45	3444	9	24.18

AAR, average annual rate per 100 000 inhabitants.
Ignored or unspecified values were not considered.
[a]Average biennial rate per 100 000 inhabitants.

Table 5. Regression analysis with annual percentage of incidence rates of HVL in Brazil regions and states

Variables	Annual incidence rates 2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Taxa de variação anual % ($IC_{95\%}$)	*P**	Situação
Region													
North	8.63	8.80	9.43	8.47	7.25	9.37	6.59	5.92	4.53	5.41	−67.79 (−82.56 to −40.52)	0.00	Descending
Northeast	6.85	5.47	5.99	6.14	5.79	6.40	4.84	6.22	7.60	7.24	25.31 (−26.28 to 113.01)	0.34	Stable
Southeast	1.61	1.46	1.76	1.74	1.66	1.57	1.36	1.15	1.20	1.41	−9.01 (−20.31 to 3.90)	0.14	Stable
South	0.03	0.02	0.02	0.06	0.05	0.03	0.04	0.02	0.04	0.04	0.23 (−0.87 to 1.34)	0.78	Stable
Midwest	4.10	3.73	4.48	3.84	3.83	4.42	4.79	3.97	3.10	2.73	−22.91 (−52.07 to 23.99)	0.23	Stable
States													
Alagoas	1.63	1.03	0.87	1.03	1.12	1.12	1.15	0.80	1.38	1.67	3.99 (−15.71 to 28.29)	0.68	Stable
Amazonas	0.03	0.06	0.09	0.09	0.00	0.03	0.06	0.00	0.03	0.00	−1.37 (−2.99 to 0.28)	0.10	Stable
Amapá	0.15	0.15	0.15	0.00	0.00	0.00	0.00	0.15	0.00	0.00	−3.39 (−7.57 to 0.97)	0.13	Stable
Bahia	2.78	1.76	1.47	2.62	2.91	2.84	2.22	2.38	3.74	2.95	31.52 (−7.15 to 86.29)	0.10	Stable
Ceará	7.52	6.52	6.58	8.06	6.39	7.24	4.85	5.68	7.31	6.74	−18.72 (−52.97 to 40.48)	0.40	Stable
Distrito Federal	0.70	0.54	0.78	0.47	0.27	0.47	0.47	0.66	0.47	0.54	−3.17 (−11.85 to 6.37)	0.44	Stable
Espírito Santo	0.03	0.00	0.09	0.20	0.06	0.23	0.03	0.11	0.09	0.31	3.51 (−0.96 to 8.19)	0.09	Stable
Goiás	0.63	0.47	0.60	0.63	0.78	0.62	0.57	0.70	0.95	0.93	8.89 (0.79 to 17.65)	0.03	Growing
Maranhão	7.60	6.19	8.78	6.87	6.84	7.35	5.20	10.77	8.68	9.76	81.97 (−16.52 to 296.64)	0.11	Stable
Minas Gerais	1.99	2.27	2.79	3.06	3.00	2.67	2.09	1.77	2.01	2.53	6.17 (−32.52 to 67.03)	0.76	Stable
Mato Grosso do Sul	9.88	9.51	10.33	8.04	8.86	11.15	12.66	9.96	7.23	5.51	−54.50 (−91.75 to 150.96)	0.31	Stable
Mato Grosso	0.69	1.05	1.94	2.27	1.85	1.85	1.75	1.19	0.63	0.92	0.23 (−42.00 to 73.22)	0.99	Stable
Pará	6.65	4.93	5.26	4.22	4.26	5.08	3.67	3.54	3.18	3.94	−47.03 (−60.92 to −28.22)	0.00	Descending
Paraíba	0.98	0.66	1.09	0.56	0.80	1.14	1.14	1.01	1.59	1.25	17.76 (5.44 to 31.52)	0.01	Growing
Pernambuco	1.15	0.89	0.95	0.86	0.81	0.99	0.82	0.80	1.93	2.01	22.74 (−10.92 to 69.12)	0.17	Stable
Piauí	7.98	8.21	9.04	5.90	5.03	6.73	6.13	6.80	9.14	8.53	69.00 (−69.0 to 268.64)	0.90	Stable
Paraná	0.03	0.00	0.02	0.02	0.01	0.06	0.01	0.04	0.02	0.05	0.69 (0.14 to 1.25)	0.02	Growing
Rio de Janeiro	0.06	0.02	0.00	0.03	0.01	0.03	0.03	0.06	0.03	0.04	0.46 (−0.64 to 1.58)	0.40	Stable
Rio Grande do Norte	2.37	2.24	2.94	3.03	2.68	3.76	3.00	2.53	3.19	2.90	15.61 (−9.84 to 48.25)	0.20	Stable
Rondônia	0.00	0.26	0.00	0.06	0.00	0.00	0.13	0.26	0.06	0.00	0.23 (−0.32 to 0.79)	0.94	Stable
Roraima	1.11	0.44	0.44	1.33	3.55	3.11	2.22	4.44	4.00	4.66	44.54 (−7.62 to 126.15)	0.00	Growing
Rio Grande do Sul	0.02	0.00	0.00	0.08	0.02	0.02	0.00	0.02	0.04	0.01	0.23 (−1.42 to 1.91)	0.93	Stable
Santa Catarina	0.00	0.02	0.02	0.00	0.00	0.03	0.03	0.02	0.00	0.00	0.02 (−1.08 to 1.13)	0.97	Stable

(*Continued*)

Table 5. (*Continued.*)

Variables	Annual incidence rates										Taxa de variação anual % ($IC_{95\%}$)	*P**	Situação
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015			
Sergipe	2.47	3.48	1.84	1.98	4.01	3.24	2.56	2.42	3.24	3.19	12.20 (−25.87 to 69.82)	0.52	Stable
São Paulo	0.66	0.63	0.73	0.55	0.52	0.55	0.60	0.48	0.44	0.41	−6.24 (−9.30 to −3.08)	0.00	Descending
Tocantins	17.64	30.65	33.25	32.31	26.09	36.43	24.94	20.17	12.79	14.67	−74.88 (−95.21 to 31.83)	0.28	Stable

*Prais–Winsten regression ($P < 0.05$).

According to the Moran maps of HVL, the Northeast Region, part of the North Region and part of the Midwest Region are among the regions with the greatest need for intervention (in red, which corresponds to high-high). The LISA map indicated the statistically significant clusters ($P = 0.001$). Thus, it is possible to observe the importance of TerraView software for spatial analysis studies, showing regions with greater and lower intervention needs (Campi and Nascimento, 2014).

Poor living conditions in the community favour the proliferation of diseases (Diro *et al.*, 2014; Castelo Branco *et al.*, 2016). It is necessary to develop the correction of precarious infrastructure questions and inadequate packaging waste, and to improve HDI indicators (Brasil, 2014; Ursine *et al.*, 2016). The lack of basic sanitation and the breeding of animals around the home favour human and canine infections by attracting *Lutzomyia longipalpis* (Lane, 2016).

From the moment one invests to improve the poor living conditions of a population, the spread of disease must be minimized. The number of HVL cases increases in regions with conditions conducive to the development of sandflies, especially in the peridomicile (Nascimento *et al.*, 2011; Albuquerque *et al.*, 2014; Brasil, 2015; Druzian *et al.*, 2015). In a place where rigorous control measures were adopted, with the reorganization of the home, construction of suitable places for animal shelters away from the residence, improvement of the sanitary facilities, proper packaging waste, pruning of trees, it was possible to drastically reduce the number of sandflies around 90% (Machado *et al.*, 2016). Ignorance in relation to VL control measures, both for the population and health professionals, added to the lack of infrastructure for early diagnosis and treatment in health services, has contributed to the expansion of VL in Brazil (Lane, 2016).

The HVL has changed its epidemiological profile and increased its morbidity and mortality. This fact requires urgent attention from epidemiological surveillance agencies, aiming at preventive and interventional measures, such as combating the vector and breeding sites, mainly with investments from the agencies responsible for correcting deficiencies in infrastructure of basic sanitation (adequate waste disposal and sewage), especially in communities with poor living conditions (Ursine *et al.*, 2016). The HVL has been spread to other areas, but it has also maintained the old outbreaks, indicating the inefficiency of current control measures.

There are still many obstacles to control HVL, with enormous challenges (Araújo *et al.*, 2012; Menon *et al.*, 2016; Silva and Abud, 2016). All patients with characteristic signs and symptoms of HVL in endemic areas should be investigated, aiming at early diagnosis and treatment (Alexandrino-de-Oliveira *et al.*, 2010; Martins-Melo *et al.*, 2014*b*; Brasil, 2015), in addition to making compulsory notification (World Health Organization., 2010; Brasil, 2014; Albuquerque *et al.*, 2014), so that databases of institutions such as the World Health Organization and the Pan American Health Organization were fed (Araújo *et al.*, 2012; Das *et al.*, 2014; Albuquerque *et al.*, 2014). However, despite the adoption of preventive measures, intending to interrupt the transmission cycle, such as early treatment of positive human cases, chemical control of vectors, and elimination of infected domestic reservoirs, there has been an increase in the HVL impulse in national public health (Machado *et al.*, 2016). The adaptive characteristics of the *L. longipalpis* vector hinder the epidemiological control (Van Griensven *et al.*, 2014; Castelo Branco *et al.*, 2016).

Secondary data are subject to limitations due to possible inconsistencies in information and/or underreporting, despite significant progress in the quality and the coverage of information in recent years (Martins-Melo *et al.*, 2014*b*; Cardim *et al.*, 2015). In addition to underreporting, there are ignored or blank items, which should have been filled out or reported correctly, limiting the robustness of the data. As the canine data are incomplete

https://doi.org/10.1017/S0031182020001754 Published online by Cambridge University Press

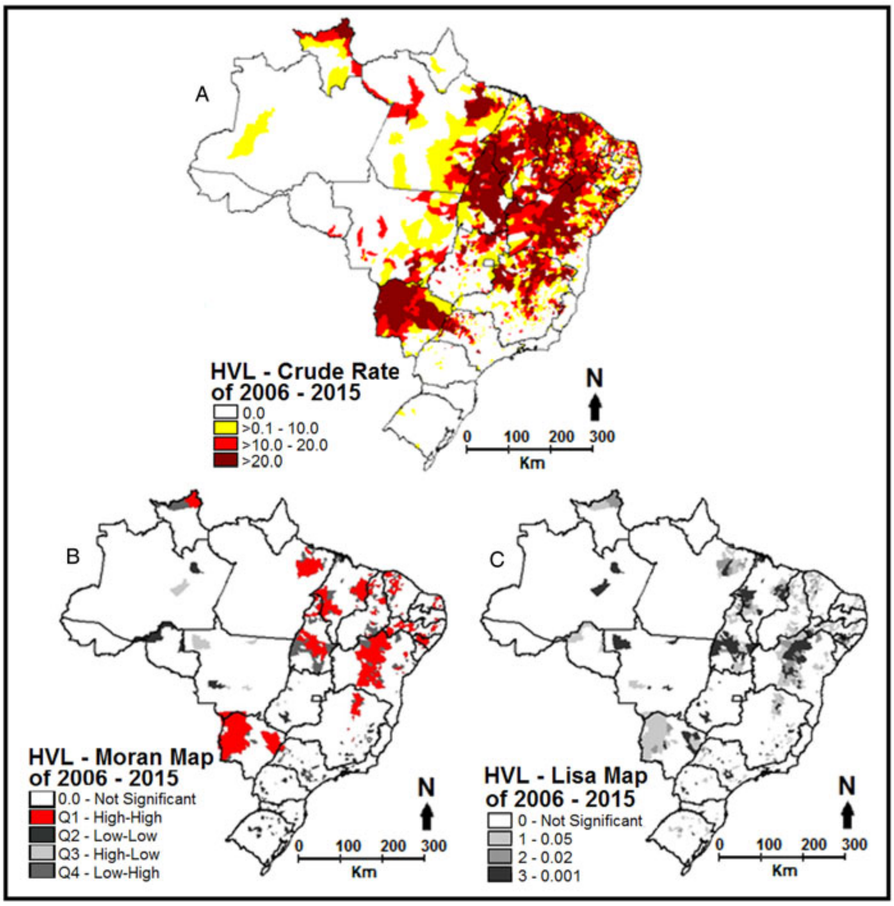

Fig. 1. HVL data by municipalities of residence in Brazil, between the years 2006 to 2015. (A) Crude rate distribution per 100 000 inhabitants; (B) Moran map; (C) LISA map.

for many municipalities, with little information about areas research, universe of dogs and type of survey (sample or census), the occurrence values can be biased and/or inconclusive.

Conclusion

Our study offered the detection and analysis of clusters of HVL rates and the occurrence, as well as pointed out the sites with greater and lower need for intervention. Based on the Prais–Winsten estimation, we found a stabilization of HVL in the average annual rates per 100 000 inhabitants. Mortality rates have remained stable in the last 5 years, and there has been a slight drop in the average annual rates of new cases in the last 9 years, suggesting that, in some way, interventional actions have an effect on reducing or maintaining cases of VL in different epidemiological contexts, despite the many obstacles to the control of this disease. It is expected that these findings will be useful for planning disease surveillance and control actions in the country.

Financial support. This work was supported by the Foundation for Research and Scientific and Technological Development of Maranhão – FAPEMA (PAEDT, concession number 02290/15; UNIVERSAL, concession number 01015/17). Dr Ana Lucia Abreu-Silva is a research productivity fellow of National Scientific and Technological Development Council (Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq) grant number 309885/2017-5.

Conflict of interest. The authors declare no conflict of interest.

Ethical standards. This study was approved by the ethics committee of the *Universidade Federal do Maranhão* (UFMA), under protocol: 1.073.550 and CAAE: 41557314.5.0000.5087.

References

Albuquerque LCPD, Mendonça IR, Cardoso PN, Baldaçara LR, Borges MRMM, da Borges JC and da Pranchevicius MCS (2014) HIV/AIDS-related visceral leishmaniasis: a clinical and epidemiological description of visceral leishmaniasis in northern Brazil. *Revista da Sociedade Brasileira de Medicina Tropical* **47**, 38–46.

Alexandrino-de-Oliveira P, Santos-Oliveira JR, Dorval MEC, das Da-Costa FCB, Pereira GROL, da Cunha RV, Paniago AMM and Da-Cruz AM (2010) HIV/AIDS-associated visceral leishmaniasis in patients from an endemic area in Central-west Brazil. *Memórias do Instituto Oswaldo Cruz* **105**, 692–697.

Araújo VEM, Morais MHF, Reis IA, Rabello A and Carneiro M (2012) Early clinical manifestations associated with death from visceral leishmaniasis. *PLoS Neglected Tropical Diseases* **6**, e1511.

Araújo VEM, Pinheiro LC, de Almeida MCM, de Menezes FC, Morais MHF, Reis IA, Assunção RM and Carneiro M (2013) Relative risk of visceral leishmaniasis in Brazil: a spatial analysis in urban area. *PLoS Neglected Tropical Diseases* **7**, e2540.

Arruda RMF, Cardoso DT, Teixeira-Neto RG, Barbosa DS, Ferraz RK, Morais MHF, Belo VS and da Silva ES (2019) Space-time analysis of the incidence of human visceral leishmaniasis (VL) and prevalence of canine VL in a municipality of southeastern Brazil: identification of priority areas for surveillance and control. *Acta Tropica* **197**, 105052.

Barbosa DS and Werneck GL (2011) Spatial distribution and definition of priority areas for surveillance of visceral leishmaniasis in São Luís, Maranhão, Brazil, 1999–2007. *FIOCRUZ – Fundação Oswaldo Cruz Escola Nacional de Saúde Pública Sergio Arouca Programa de Pós-graduação Epidemiologia em Saúde Pública*, **1**, 30–61.

Barbosa DS, Belo VS, Rangel MES and Werneck GL (2014) Spatial analysis for identification of priority areas for surveillance and control in a visceral leishmaniasis endemic area in Brazil. *Acta Tropica* **131**, 56–62.

Brasil MS (2014) *Manual de vigilância e controle da leishmaniose visceral*, 1a. ed. Brasil: Brasília-Distrito FederalMinistério da Saúde, S. de V. em S. D. de V. and Transmissíveis. Ministério da Saúde, Brasília-Distrito Federal.

Brasil MS (2015) *Manual de recomendações para diagnóstico, tratamento e acompanhamento de pacientes com a coinfecção Leishmania-HIV*, 1a. ed. Brasil: Ministério da Saúde, S. de V. em S. D. de V. and Transmissíveis. Ministério da Saúde, Brasília-Distrito Federal.

Brasil MS (2017*a*) Sistemas de Informação de Agravos de Notificação (SINAN). Leishmaniose visceral: Casos confirmados de 2001 a 2006.

Brasil MS (2017*b*) Sistemas de Informação de Agravos de Notificação (SINAN), leishmaniose visceral: Casos confirmados de 2007 a 2015. Brasil. Ministério da Saúde (MS).

Brilhante AF, Melchior LAK, Nunes VLB, de Cardoso CO and Galati EAB (2017) Epidemiological aspects of American cutaneous leishmaniasis (ACL) in an endemic area of forest extractivist culture in western Brazilian Amazonia. *Revista do Instituto de Medicina Tropical de São Paulo* **59**, 159–166.

Campi SFS and Nascimento LFC (2014) Spatial distribution of C-sections within the state of São Paulo. *Revista da Associação Médica Brasileira* **60**, 419–423.

Cardim MFM, Vieira CP and Chiaravalloti-Neto F (2015) Spatial and spatio-temporal occurrence of human visceral leishmaniasis in Adamantina, State of São Paulo, Brazil. *Revista da Sociedade Brasileira de Medicina Tropical* **48**, 716–723.

Carvalho RM and Nascimento LF (2014). Space-time description of dengue outbreaks in Cruzeiro, Sao Paulo, in 2006 and 2011. *Revista da Associação Médica Brasileira* (1992) **60**, 565–570.

Carvalho FLN, Riboldi EDO, Bello GL, Ramos RR, Barcellos RB, Gehlen M, Halon ML, Romão PRT, Dallegrave E and Rossetti MLR (2018) Canine visceral leishmaniasis diagnosis: a comparative performance of serological and molecular tests in symptomatic and asymptomatic dogs. *Epidemiology and Infection* **146**, 571–576.

Castelo Branco PV, Soares R-EP, de Jesus LCL, Moreira VR, Alves HJ, de Castro Belfort MR, Silva VLM and Ferreira Pereira SR (2016) The antileishmanial drug miltefosine (Impavido®) causes oxidation of DNA bases, apoptosis, and necrosis in mammalian cells. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* **806**, 34–39.

Costa DL, Rocha RL, Carvalho RMA, Lima-Neto AS, Harhay MO, Costa CHN, Barral-Neto M and Barral AP (2013) Serum cytokines associated with severity and complications of kala-azar. *Pathogens and Global Health* **107**, 78–87.

Costa JS, Dos Santos-Júnior FM, Moreira RS and Góes MADO (2019) Tendência temporal da sífilis congênita em Sergipe, Brasil, 2006–2017. *Revista de Saúde Coletiva da UEFS* **9**, 8.

Cota GF, de Sousa MR, de Freitas Nogueira BM, Gomes LI, Oliveira E, Assis TSM, de Mendonça ALP, Pinto BF, Saliba JW and Rabello A (2013) Comparison of parasitological, serological, and molecular tests for visceral leishmaniasis in HIV-infected patients: a cross-sectional delayed-type study. *The American Journal of Tropical Medicine and Hygiene* **89**, 570–577.

Cota GF, de Sousa MR, de Mendonça ALP, Patrocinio A, Assunção LS, de Faria SR and Rabello A (2014) Leishmania-HIV co-infection: clinical presentation and outcomes in an urban area in Brazil. *PLoS Neglected Tropical Diseases* **8**, e2816.

Das S, Halder A, Rabidas VN, Mandal A and Das P (2014) Specific non-invasive detection of *Leishmania donovani* in desquamated buccal cell swab samples from human visceral Leishmaniasis-HIV coinfected patients. *Journal of Clinical Microbiology* **52**, 1238–1241.

Diro E, Lynen L, Mohammed R, Boelaert M, Hailu A and van Griensven J (2014) High parasitological failure rate of visceral leishmaniasis to sodium stibogluconate among HIV co-infected adults in Ethiopia. *PLoS Neglected Tropical Diseases* **8**, e2875.

Druzian AF, de Souza AS, de Campos DN, Croda J, Higa MG, Dorval MEC, Pompilio MA, de Oliveira PA and Paniago AMM (2015) Risk factors for death from visceral leishmaniasis in an urban area of Brazil. *PLoS neglected tropical diseases* **9**, e0003982.

Duarte-Cunha M, Souza-Santos R, Matos HJ and Oliveira ML (2012) Epidemiological aspects of leprosy: a spatial approach. *Cadernos de Saude Publica* **28**, 1143–1155.

Dupnik KM, Nascimento EL, Rodrigues-neto JF, Keesen T, Duarte I and Jeronimo SMB (2011) New challenges in the epidemiology and treatment of visceral leishmaniasis in periurban areas. *Drug Development Research* **72**, 451–462.

Falavina LP, Lentsck MH and de Mathias TAF (2019) Tendência e distribuição espacial de doenças infecciosas em gestantes no estado do Paraná-Brasil. *Revista Latino-Americana de Enfermagem* **27**, 1–10. doi: 10.1590/1518-8345.2838.3160

Fontoura IG, Fontoura VM and Nascimento LFC (2016) Análise espacial da ocorrência de leishmaniose visceral no estado do Tocantins, Brasil. *Ambiente e Agua – An Interdisciplinary Journal of Applied Science* **11**, 1088.

Fontoura VM, Graepp-Fontoura I, Santos FS, Santos Neto M, de Tavares HSA, Bezerra MOL, de Feitosa MO, Neves AF, de Morais JCM and Nascimento LFC (2018*a*) Socio-environmental factors and diarrheal diseases in under five-year old children in the state of Tocantins, Brazil. *PLoS ONE* **13**, e0196702.

Fontoura IG, Barbosa DS, de Andrade Paes AM, Santos FS, Neto MS, Fontoura VM, Lopes Costa JM and Abreu Silva AL (2018*b*) Epidemiological, clinical and laboratory aspects of human visceral leishmaniasis (HVL) associated with human immunodeficiency virus (HIV) coinfection: a systematic review – CORRIGENDUM. *Parasitology* **145**, 1819–1819.

Galati EAB, de Camara TNL, Natal D and Chiaravalloti-neto F (2015) Mudanças climáticas e saúde urbana. *Revista Universidade de São Paulo – USP* **107**, 79–90.

Gomes MLS, Romero GAS and Werneck GL (2012) Coinfecção leishmaniose visceral e Aids no Brasil, 2001 a 2010. Dissertação (Mestrado) – Escola Nacional de Saúde Pública Sergio Arouca 105.

Guimarães AGF, Alves GBM, de Pessoa AM and da Junior NJS (2015) Spatial analysis of visceral leishmaniasis in the municipality of Rondonópolis, in the Brazilian State of Mato Grosso, from 2003 to 2012: human, canine and vector distribution in areas of disease transmission. *Revista da Sociedade Brasileira de Medicina Tropical* **48**, 291–300.

Herrador Z, Gherasim A, Jimenez BC, Granados M, San Martín JV and Aparicio P (2015) Epidemiological changes in leishmaniasis in Spain according to hospitalization-based records, 1997–2011: raising awareness towards leishmaniasis in non-HIV patients. *PLoS Neglected Tropical Diseases* **9**, e0003594.

IBGE (2017*a*) Instituto Brasileiro de Geografia e Estatística. Divisão regional do Brasil em regiões geográficas imediatas e regiões geográficas intermediárias. Brasil, Ministério da Saúde.

IBGE (2017*b*) Instituto Brasileiro de Geografia e Estatística. Banco de tabelas - SIDRA. Instituto Brasileiro de Geografia e Estatística.

IBGE (2020) Instituto Brasileiro de Geografia e Estatística. Sistema IBGE de Recuperação Automática - SIDRA. Brasil, Ministério da Saúde.

INPE, Instituto de Pesquisas Espaciais and (2015) AULA 8 – Operações de Análise Espacial. In *Inpe*. São José dos Campos-São Paulo, pp. 1–53. http://www.dpi.inpe.br/DPI/ .

Karagiannis-Voules D-A, Scholte RGC, Guimarães LH, Utzinger J and Vounatsou P (2013) Bayesian geostatistical modeling of leishmaniasis incidence in Brazil. *PLoS Neglected Tropical Diseases* **7**, e2213.

Lane VFM (2016) Análise Epidemiológica Da Leishmaniose Visceral Humana No Brasil: Contribuição Às Politicas De Controle. Tese (Doutorado) – Universidade de Brasilia 158.

Machado CJS, Silva EG and Vilani RM (2016) O uso de um instrumento de política de saúde pública controverso: a eutanásia de cães contaminados por leishmaniose no Brasil. *Saúde e Sociedade* **25**, 247–258.

Martins-Melo FR, Lima MDS, Ramos AN, Alencar CH and Heukelbach J (2014*a*) Mortality and case fatality due to visceral leishmaniasis in Brazil: a nationwide analysis of epidemiology, trends and spatial patterns. *PLoS ONE* **9**, e93770.

Martins-Melo FR, da Lima MS, Alencar CH, Ramos AN and Heukelbach J (2014*b*) Epidemiological patterns of mortality due to visceral leishmaniasis and HIV/AIDS co-infection in Brazil, 2000–2011. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **108**, 338–347.

Mehrjou A, Hosseini R and Nadjar Araabi B (2016) Improved Bayesian information criterion for mixture model selection. *Pattern Recognition Letters* **69**, 22–27.

Menon SS, Rossi R, Nshimyumukiza L and Zinszer K (2016) Decentralized control of human visceral leishmaniasis in endemic urban areas of Brazil: a literature review. *Tropical Medicine and Health* **44**, 9.

Nascimento ET, Moura MLN, Queiroz JW, Barroso AW, Araujo AF, Rego EF, Wilson ME, Pearson RD and Jeronimo SM (2011) The emergence of concurrent HIV-1/AIDS and visceral leishmaniasis in Northeast Brazil. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **105**, 298–300.

Oliveira WK, de França GVA, Carmo EH, Duncan BB, de Souza Kuchenbecker R and Schmidt MI (2017) Infection-related microcephaly after the 2015 and 2016 Zika virus outbreaks in Brazil: a surveillance-based analysis. *The Lancet* **23**, 861–870. doi: 10.1016/S0140-6736(17)31368-5

Otranto D and Dantas-Torres F (2013) The prevention of canine leishmaniasis and its impact on public health. *Trends in Parasitology* **29**, 339–345.
Reis LL, da Balieiro AAS, Fonseca FR and Gonçalves MJF (2019) Leishmaniose visceral e sua relação com fatores climáticos e ambientais no Estado do Tocantins, Brasil, 2007 a 2014. *Cadernos de Saúde Pública* **35**, 1–14.
Rivas GB, de Souza NA, Peixoto AA and Bruno RV (2014) Effects of temperature and photoperiod on daily activity rhythms of *Lutzomyia longipalpis* (Diptera: Psychodidae). *Parasites & Vectors* **7**, 278.
Rodrigues NCP, Lino VTS, Daumas RP, de Andrade MKN, O'Dwyer G, Monteiro DLM, Gerardi A, Fernandes GHBV, Ramos JAS, Ferreira CEG and da Leite IC (2016) Temporal and spatial evolution of dengue incidence in Brazil, 2001–2012. *PLoS ONE* **11**, e0165945.
Santos Neto M, Da Silva FBG, Sodré MB, Yamamura M, Santos FS, de Costa ACPJ, de Serra MAAO, de Gordon ASA, Pascoal LM, Bezerra JM, dos Santos LH, de Andrade HLP, Fontoura IG, Pieri FM and Arcêncio RA (2017) Deaths by tuberculosis in a priority city for disease control in the Brazilian Northeast: sociodemographic-operational characteristics and vulnerable territories. *International Archives of Medicine* **10**, 1–12.
Serafim TD, Coutinho-Abreu IV, Oliveira F, Meneses C, Kamhawi S and Valenzuela JG (2018) Sequential blood meals promote Leishmania replication and reverse metacyclogenesis augmenting vector infectivity. *Nature Microbiology* **3**, 548–555.
Silva RA (2016) Urbanização pela Migração em Araguaína – TO. *Caminhos de Geografia* **17**, 1–15.
Silva CEDF and Abud AKDS (2016) Anaerobic biodigestion of sugarcane vinasse under mesophilic conditions using manure as inoculum. *Ambiente e Agua – An Interdisciplinary Journal of Applied Science* **11**, 763.
Silva TAM, Gomes LI, Oliveira E, Coura-Vital W, de Silva LA, Pais FS-M, Ker HG, Reis AB, Rabello A and Carneiro M (2015) Genetic homogeneity among *Leishmania* (*Leishmania*) *infantum* isolates from dog and human samples in Belo Horizonte Metropolitan Area (BHMA), Minas Gerais, Brazil. *Parasites & Vectors* **8**, 226.
Souza GF, Biscione F, Greco DB and Rabello A (2012) Slow clinical improvement after treatment initiation in Leishmania/HIV coinfected patients. *Revista da Sociedade Brasileira de Medicina Tropical* **45**, 147–150.
Távora LGF, Nogueira MB and Gomes ST (2015) Visceral Leishmaniasis/HIV co-infection in northeast Brazil: evaluation of outcome. *The Brazilian journal of infectious diseases : an official publication of the Brazilian Society of Infectious Diseases* **19**, 651–656.
Toledo CRS, de Almeida AS, de Chaves SAM, Sabroza PC, Toledo LM and Caldas JP (2017) Vulnerability to the transmission of human visceral leishmaniasis in a Brazilian urban area. *Revista de Saúde Pública* **51**, 1–11.
Ursine RL, Dias JVL, Morais HA and Pires HHR (2016) Human and canine visceral leishmaniasis in an emerging focus in Araçuaí, Minas Gerais: spatial distribution and socio-environmental factors. *Memórias do Instituto Oswaldo Cruz* **111**, 505–511.
Van Griensven J, Diro E, Lopez-Velez R, Ritmeijer K, Boelaert M, Zijlstra EE, Hailu A and Lynen L (2014) A screen-and-treat strategy targeting visceral leishmaniasis in HIV-infected individuals in endemic East African countries: the way forward? *PLoS Neglected Tropical Diseases* **8**, e3011.
World Health Organisation (2009) International Symposium on advances in visceral leishmaniasis therapy – Statement on the outcome of the meeting, Madrid, 18–19 June. International Symposium on advances in visceral leishmaniasis therapy – Statement on the outcome of the meeting, Madrid, 18–19 June 4–8.
World Health Organization (2010) Control of the leishmaniases: report of a meeting of the WHO Expert Committee on the Control of Leishmaniases. Geneva, Switzerland.
World Health Organization (2015) Visceral leishmaniasis: control strategies and epidemiological situation update in East Africa. Geneva, Switzerland.

https://doi.org/10.1017/S0031182020001754 Published online by Cambridge University Press