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Review

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Factors associated with human visceral leishmaniasis cases during urban epidemics in Brazil: a systematic review

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Abstract

Visceral leishmaniasis (VL) is endemic in 70 countries and has been reported in 12 countries of Latin America, with over 90% of the cases reported in Brazil, where epidemics have occurred since 1980. The objective of this review is to describe the factors associated with the occurrence of VL epidemics in humans in urban areas. A systematic review was conducted according to the PRISMA-P guidelines. The databases PubMed (by Medline), Cochrane Library, Embase, Amed, LILACS and grey literature [Google Scholar and handsearch of the database of the Information System for Notifiable Diseases (SINAN) of Brazil's Unified Health System] were used. The protocol was registered under PROSPERO (CRD42019128998). Climatic, environmental factors and indicators of urban social structure were described as influencing the outbreaks in the North and Northeast regions. Gender and age characteristics were related to a greater chance of developing VL in the Central-West, Northeast and Southeast regions. Vector indicators showed a positive correlation with the incidence of VL in studies in the Northeast region. In the Southeast and Northeast regions, studies revealed the presence of dogs with positive correlation with VL. Knowledge gaps remain regarding the contribution to the increase in the risk factors described in ecological approaches, as no analysis was performed at the individual level, and it is still necessary to discuss the influence of other associated elements in epidemic episodes in the spread of VL.

Introduction

Visceral leishmaniasis (VL) is a neglected tropical disease that accounts for 200 000–400 000 new cases each year worldwide, and is endemic in 70 countries on the five continents (Alvar *et al.*, 2012; WHO, 2018). Currently, VL is present in 12 countries of the Americas, with 96% of the cases being reported in Brazil (4200–6300 cases per year), an incidence rate of 2/100 000 inhabitants and a case fatality rate of around 7% (Romero and Boelaert, 2010; Menon *et al.*, 2016). In the Americas, the aetiologic agent is the protozoan *Leishmania (Leishmania) infantum*, which is usually transmitted by the bite of the sandfly *Lutzomyia longipalpis* (Romero and Boelaert, 2010), although there is already a study that has identified other species as transmitters of *leishmania* (Rêgo *et al.*, 2020). Dogs represent the main urban reservoir (Romero and Boelaert, 2010).

In Brazil, the first urban epidemic was reported in Teresina (Piauí state) between 1981 and 1985, when the disease, initially limited to rural areas, expanded to peripheral areas of the city (Costa *et al.*, 1990). Since then, the disease has been expanding from cities in the Northeast to other regions of the country (Badaro *et al.*, 1986; Costa *et al.*, 1990; Evans *et al.*, 1992; Jerônimo *et al.*, 2004; Moreno *et al.*, 2005; de Oliveira *et al.*, 2008; Falqueto *et al.*, 2009).

The literature reports occurrences of VL epidemics in different countries worldwide (Imamura *et al.*, 2016). However, there is no literature record of systematic reviews and meta-analysis regarding factors associated with occurrences of VL epidemics. In this respect, our study sets out to elucidate the knowledge gaps regarding the factors associated with VL occurrence in different urban contexts during epidemic processes. This systematic review aims to describe the factors associated with the occurrence of VL epidemics in humans in urban areas.

Materials and methods

This study was conducted using the guideline *Preferred Reporting Items for Systematic Review and Meta-Analysis* (Moher *et al.*, 2015). We registered the protocol before its execution in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42019128998.

Selection criteria

In this review, we included epidemiological ecological, case series, cross-sectional and case-control studies that described associations among individual characteristics (demographic variables), socioeconomic and environmental variables (climates, household characteristics and social, urban and population structures), presence of vectors and animals (dogs and other animals) and the occurrence of any outcome related to VL. This outcome could be the infection by *L. infantum*, the clinical disease or the notification of cases to the health services.

Eligibility criteria

We included studies that investigated factors associated with VL infection and clinical disease confirmed and notified in situations of epidemics in Brazil. No restrictions were applied regarding language for the inclusion of the studies.

Research and selection of studies

The search was carried out in the electronic databases PubMed (by Medline), Cochrane Library, Embase, Amed, LILACS and grey literature [Google Scholar and handsearch of the database of the Information System for Notifiable Diseases (SINAN), Department of Informatics of the Brazilian Unified Health System (DATASUS)]. Papers cited in the selected studies were included as grey literature. Pre-defined descriptors were used for each database to increase the sensitivity of the search. The search strategy was defined following prior consultation of the uniterms leishmaniasis, association and occurrence. This consultation was carried out in MeSH (PubMed by Medline) and adapted for other databases. For LILACS, we used the Health Sciences Descriptors (DeCS), and for Embase, we used Emtree.

The references retrieved in the search strategies were exported to an Endnote® X7 file and the duplicates were removed. The studies were independently selected by two researchers who used a form previously tested in five selected articles to identify any adjustments needed before their application in the remaining studies. Any disagreements were resolved by consensus.

Studies were included according to our criteria for each section following the order of evaluation in three phases: 1st: titles; 2nd: abstracts and 3rd: main text.

An epidemic was defined as the occurrence of a health-related event that exceeds normal expectations, with a number of cases higher than expected in a specific area and time, in the presence of an epidemiological link (Braga and Werneck, 2008).

Studies analysing factors associated with VL that did not specify whether they were carried out at the time of an epidemic and were investigated using the database of the Information System for Notifiable Diseases (SINAN), Department of Informatics of the Brazilian Unified Health System (DATASUS). For each study, we searched for the number of confirmed cases in the places and years in which the study was carried out, including an interval of 3 years before and after, to verify the number of cases of the disease. Therefore, if an above-expected increase in the number of cases that would characterize an epidemic was detected, even if the article did not describe the occurrence of an epidemic, it was included in the present review.

Analysis and presentation of results

The results of the synthesis of the articles were presented qualitatively and quantitatively with the factors related to the occurrence of VL pointing out the specificities and regional differences of the occurrence of the disease considering the context of the study (Table 1). The characteristics of the included studies were described considering each group of factors by region studied.

Results

Description of included studies

The search strategies retrieved 3143 titles, out of which 23 studies met the eligibility criteria and were included in this systematic review (Fig. 1). Studies have shown the factors present in the context of epidemics between the years 1980 and 2014 in Brazil. In the 1980s, two epidemics were analysed, and in the 1990s epidemics were described between 1990 and 1998. In the first decade of the 2000s, the studies analysed included epidemics that occurred in all years, except in 2001 and 2002. As of 2010, studies described epidemics in 2010, 2011 and 2014. The first urban epidemic occurred in 1980 in the state of Piauí, and the most recent epidemic process included in this review occurred in 2014 in the state of Ceará.

Of the 23 selected studies, nine (39%) were ecological studies, nine (39%) were cross-sectional studies, two (9%) were case series studies and three (13%) were case-control studies. Regarding the coverage areas, 15 (65%) studies were carried out in the Northeast region of Brazil, three (13%) in the Central-West, three (13%) in the North and two (9%) in the Southeast (Table 1 and Supplementary material 1).

Four studies (17%) evaluated factors associated with asymptomatic *L. infantum* infection, and the others analysed factors associated with the VL clinical disease.

From 1980 to 2000, VL epidemics were described and analysed in five Brazilian states, four in the Northeast and one in the Central-West. An increase in the epidemic record was observed in the first decade of the 2000s, with expansion to the North and Southeast regions, and records in seven states. Between 2010 and 2019, the studies in this review presented epidemic records in three states in the North and Northeast regions (Fig. 2).

The factors related to VL in urban epidemics are shown in Table 2, Fig. 3 and Supplementary material 1 by author and occurrence of visceral leishmaniasis by region of Brazil.

Climate and environmental factors

Six studies pointed out climatic and environmental factors related to VL in the context of an epidemic in the Northeast region. Living in areas covered by green vegetation (Werneck and Maguire, 2002), and increased vegetation have been associated with a high incidence of human VL (Werneck *et al.*, 2007). VL was also correlated with locations with the presence of green areas (Cerbino-Neto *et al.*, 2009). Bavia *et al.* (2005) demonstrated that low values of the normalized difference vegetation index (NDVI) in municipalities at high risk for VL were related to the high number of positive cases of the disease.

Precipitation showed a positive correlation with the incidence rate of VL (dos Reis *et al.*, 2019), and also with the incidence of VL in the previous year (Lima *et al.*, 2017). There was an association between the number of cases of VL and precipitation (Viana *et al.*, 2011).

The average temperature was negatively correlated with the incidence rate of VL (de Freitas *et al.*, 2013; Oliveira *et al.*, 2014). Similarly, daytime temperature also showed a negative correlation with VL (dos Reis *et al.*, 2019). However, night-time temperature showed a positive correlation with the incidence rate of VL (dos Reis *et al.*, 2019).

The relative humidity of the air showed divergent behaviour patterns in the studies of the North and Northeast regions. It

Table 1. Studies carried out in periods of epidemics in Brazil, according to the location of the study, year of execution and period of epidemics, from 1980 to 2019

Study (author/year)	Region	Study design	Location of the study municipalities and state	Year(s) of execution of the study	Year(s) of epidemics record
Costa *et al.* (1990)[a]	Northeast	Ecological	Municipalities of Piauí	1971–1986	1980–1986
Lima *et al.* (2017)[a]	Northeast	Cross-sectional	Natal, Rio Grande do Norte	1990–2014	Peak between 1990 and 1994
Jerônimo *et al.* (2004)[a]	Northeast	Cross-sectional	Natal, Rio Grande do Norte	1994–2000	1991
Cerbino-Neto *et al.* (2009)[a]	Northeast	Ecological	Teresina, Piauí	1991–2000	Peak between 1992 and 1995 and in 1998
Werneck *et al.* (2002)[a]	Northeast	Cross-sectional	Teresina, Piauí	1993–1996	1993–1996
Werneck and Maguire (2002)[a]	Northeast	Ecological	Teresina, Piauí	1995–1996	1993–1996
Costa *et al.* (2005)[a]	Northeast	Case control	Teresina, Piauí	1995–1996	1993–1996
Werneck *et al.* (2007)[a]	Northeast	Ecological	Teresina, Piauí	1993–1996	1993–1996
Ximenes *et al.* (2007)[a]	Northeast	Ecological	Municipalities from Rio Grande do Norte	1995–2005	Peak in 1995 and 2000
Araújo *et al.* (2018)[a]	Northeast	Cross-sectional	State of Ceará	1986–2017	Peak in 1995, 2000, 2006, 2011 and 2014
Bavia *et al.* (2005)[a]	Northeast	Ecological	Municipalities of Bahia	1990–1998	1997
de Oliveira *et al.* (2008)[a]	Central West	Cross-sectional	Três Lagoas, Mato Grosso do Sul	2002	Epidemic since 2000
de Almeida *et al.* (2011)[b]	Northeast	Ecological	Teresina, Piauí	2001–2006	Peak in 2003
Borges *et al.* (2008)[b]	Southeast	Case control	Belo Horizonte, Minas Gerais	2006	Peak from 2004 to 2006
Borges *et al.* (2009)[b]	Southeast	Case control	Belo Horizonte, Minas Gerais	2004	Peak from 2004 to 2006
Viana *et al.* (2011)[b]	Northeast	Cross-sectional	São Luis, Maranhão	2002–2010	Peak from 2004 to 2006
Brazuna *et al.* (2012)[b]	Central West	Case series	Campo Grande, Mato Grosso do Sul	2002–2009	Peak from 2004
Oliveira *et al.* (2014)[b]	North	Cross-sectional	Araguaína, Tocantins	2007–2012	Peak in 2007 and 2008
Carranza-Tamayo *et al.* (2016)[b]	Central West	Cross-sectional	Brasília, Distrito Federal	2007–2008	Peak in 2007 and 2008
dos Reis *et al.* (2019)	North	Ecological	Municipalities of Tocantins	2007–2014	Peak in 2007–2011
de Toledo *et al.* (2017)[a]	North	Ecological	Araguaína, Tocantins	2007–2012	Peak in 2008 and 2011
Rocha *et al.* (2018)[b]	Northeast	Ecological	Teresina, Piauí	2007–2016	Peak in 2008 and 2014
de Freitas *et al.* (2013)[b]	Northeast	Case series	Fortaleza, Ceará	2006–2016	Peak in 2009, 2010 and 2011

[a]Studies carried out during periods of an epidemic as described in the paper.
[b]Studies identified in the periods of epidemic according to the analysis of the data from the DATASUS.

presented a negative correlation with the incidence rate of VL (de Freitas *et al.*, 2013) and a positive correlation between the incidence rate of VL minimum and maximum humidity (dos Reis *et al.*, 2019).

The effects of altitude were analysed in the municipalities of the state of Tocantins and the results showed a negative correlation between the municipalities with higher altitudes and the incidence rate of VL (dos Reis *et al.*, 2019).

Factors related to social, urban and population structure

Studies conducted in the North and Northeast states showed a positive correlation between indicators of social and urban structure and the incidence of VL (de Toledo *et al.*, 2017; Rocha *et al.*, 2018). Rocha *et al.* (2018) pointed out statistically significant clusters between the incidence of the disease and the indicators of vulnerability of social structure, household structure, urban infrastructure and composite index of vulnerability. Cerbino-Neto *et al.* (2009) demonstrated that the incidence of VL was positively correlated with population growth.

Socioeconomic factors

Studies related to socioeconomic factors were carried out in states in the Northeast region. The factors that were associated with the incidence of VL in the context of epidemics were: living in a slum (Werneck and Maguire, 2002), percentage of literacy in the neighbourhood and homes without sanitation (Lima *et al.*, 2017). The average percentage of households with at least one indoor bathroom connected to the sewage network was associated with the average annual incidence rate of VL (Cerbino-Neto *et al.*, 2009).

As for the risk of developing VL, living in a house with more than four members doubled the risk of VL, and living in a house with an inadequate sewage network (without a bathroom) showed a high risk of VL (Costa *et al.*, 2005). People living in households without regular garbage collection were more likely to develop VL (Costa *et al.*, 2005).

The average number of residents per household (Lima *et al.*, 2017), households with no garbage collection (Cerbino-Neto *et al.*, 2009) and areas with a lower percentage of households with garbage collection (de Almeida *et al.*, 2011; Lima *et al.*, 2017) were positively correlated with the incidence of VL.

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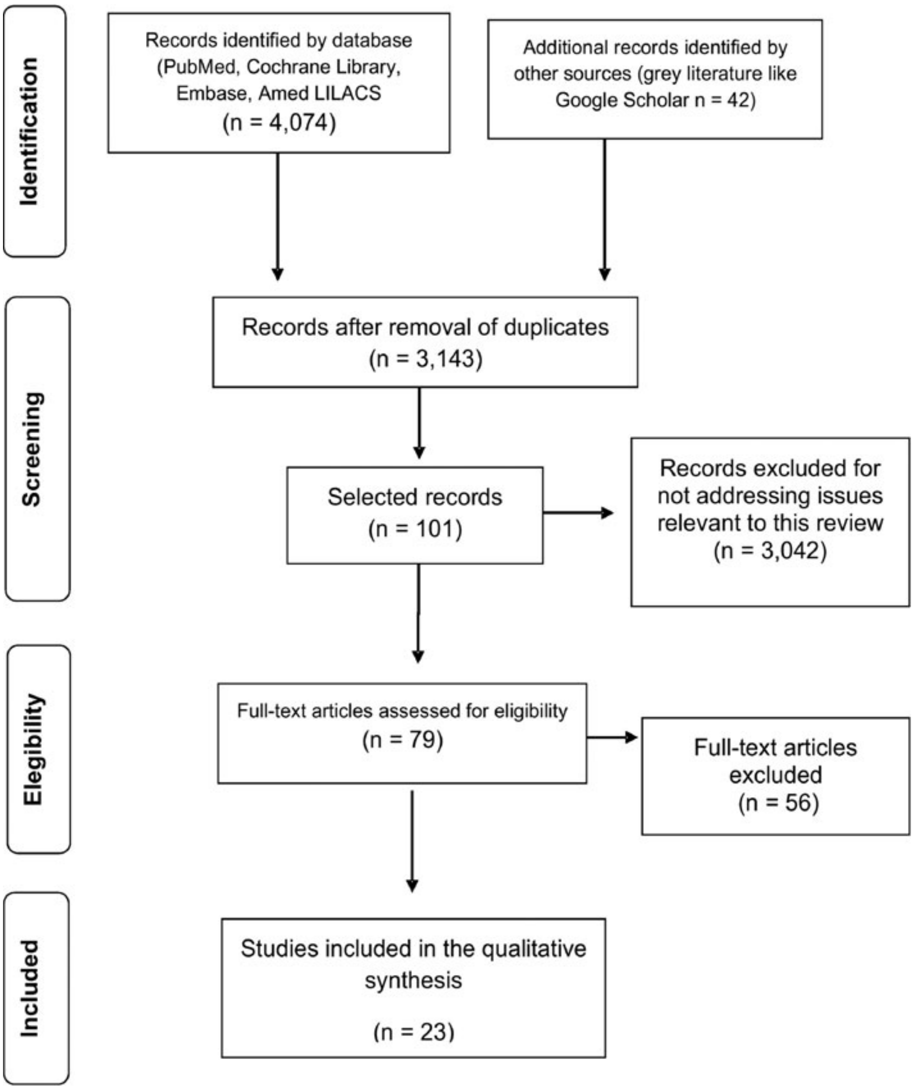

Fig. 1. Systematic review on factors associated with urban epidemics of human VL in Brazil.

The lowest *per capita* income and the lowest human development index showed a positive correlation with the average number of cases of VL (Araújo *et al.*, 2018). The annual incidence rates of VL correlated with the average income and illiteracy (Cerbino-Neto *et al.*, 2009).

The average percentage of households with running water was negatively correlated with the incidence rate of VL (Cerbino-Neto *et al.*, 2009). There was a spatial correlation between VL rates and the lowest average income of heads of households and illiteracy and a lower percentage of households with garbage collection (de Almeida *et al.*, 2011).

However, in the Northeast, de Oliveira *et al.* (2008) found no relationship among accumulation of waste in the home, literacy of the head of household and infection by *Leishmania*.

Individual factors

A greater number of cases of VL in men were reported when compared to women (Brazuna *et al.*, 2012) and men were more likely to contract the disease than women (Borges *et al.*, 2008). VL was also associated with males and age groups (Lima *et al.*, 2017). In the Northeast, de Oliveira *et al.* (2008) found no relationship between gender and infection by *Leishmania*.

The positivity in the skin test for *Leishmania* increased with age in the study by Werneck *et al.* (2002). Costa *et al.* (2005) pointed out that greater chances of developing VL were found in children aged 5–10 years, and children aged 1–4 years were 14 times more likely to develop the disease than those older than 10 years. The study by Borges *et al.* (2008) showed an increased risk of contracting VL in children under 10 years old. Carranza-Tamayo *et al.* (2016) demonstrated that VL infection in humans was associated with an age greater than 7 years. Oliveira *et al.* (2014) described that there was a higher prevalence of the disease in children under 15 years old than in the age group from 1 to 5 years. However, in the Northeast, de Oliveira *et al.* (2008) found no relationship between age and infection by *Leishmania*.

Factors related to vectors

Ximenes *et al.* (2007) found an association of vector species and distribution of diseases with demographic and physiognomic characteristics, disordered growth in the metropolitan region, living conditions and environmental degradation of the East Coast of the state of Rio Grande do Norte. The number of sandflies was associated with VL in the study by Bavia *et al.* (2005). Studies have demonstrated a correlation between the incidence of VL and vector infestation and relative abundance of *L. longipalpis* (Lima *et al.*, 2017), as well as a correlation between households investigated and infested by *L. longipalpis* (Costa *et al.*, 1990). The number of sandflies was associated with VL (Bavia *et al.*, 2005).

Presence of dogs

Studies carried out in the states of the Northeast and Southeast regions showed divergent patterns for the presence of dogs and VL. Dog owners were more likely to contract VL when compared

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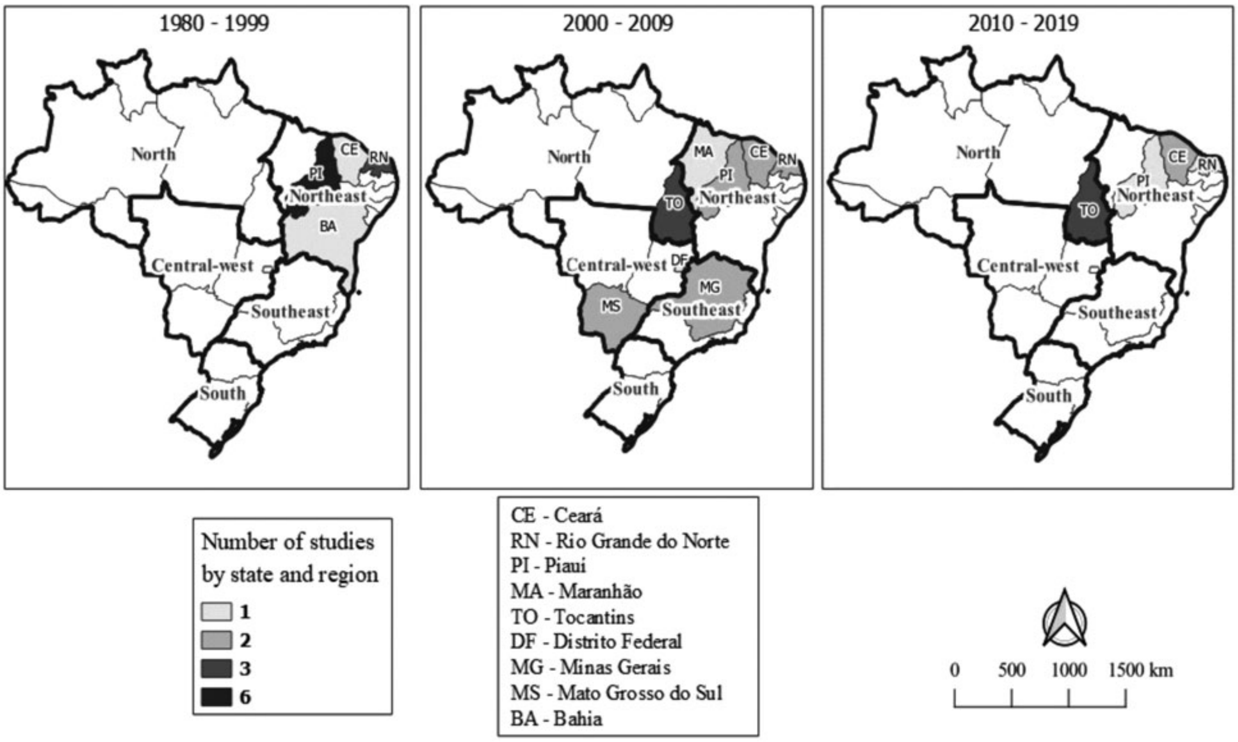

Fig. 2. Distribution of studies on VL epidemics in Brazil from 1980 to 2019, by state.

to individuals who did not have them, and an increased chance of contracting VL was observed for individuals with two dogs and for people who kept their dogs indoors during the day (Borges *et al*., 2009). The canine population negatively influenced the number of cases of VL and the percentage of positive dogs showed a correlation and positive influence on the incidence rate of VL (de Freitas *et al*., 2013). In a multilevel model study, Werneck *et al*. (2007) described an association between the prevalence of canine seropositivity and the incidence of the disease in humans. Jerônimo *et al*. (2004) found no association between LV and dog ownership.

Presence of other animals

The relationship between the presence of other animals and VL has been described in the Southeast and Central-West regions. The increase in the number of cases of VL was associated with the presence of ducks, rodents and chickens (Borges *et al*., 2009). The presence of opossums in the vicinity reduced the chances of falling ill with VL (Borges *et al*., 2009). In another study, the presence of opossums around the homes increased the chances of human infection (Carranza-Tamayo *et al*., 2016). However, in the Northeast region Jerônimo *et al*. (2004) did not find an association between LV and the possession of other animals.

Discussion

Urban VL has occurred in Brazil since 1980, but little is known about the dynamics of *L. infantum* transmission in urban centres or the variables that determine the distribution of the disease in these places in the context of an epidemic. As this is a relatively rare event, the context of epidemics provided us with more robust results in quantitative terms in analytical approaches in this review.

Factors related to the occurrence of VL in the context of epidemics were compared among regions and described on an individual and aggregate scale. In this scenario, the Northeast region stands out with the largest number of variables studied and related to the occurrence of the disease.

As for the individual factors analysed in this review, men were more likely to contract the disease or infection, which was also observed in studies carried out in the endemic period (de Delgado *et al*., 1998; Oliveira *et al*., 2006; Gouvêa *et al*., 2007; da Silva *et al*., 2016; Menezes *et al*., 2016). Other studies on VL and male sex suggest explanations for these results: hormonal or immunological problems can affect the progress of the infection (Sharma *et al*., 1990); men could be more exposed to vector bites (Costa *et al*., 1990) and men are more frequently involved in domestic chores or outdoor leisure activities during the period of greatest vector activity (Gouvêa *et al*., 2007).

Considering age as a factor related to VL, in studies carried out in the context of an epidemic, the results showed that children are more susceptible to both infection and illness. When analysing the difference between skin and serological tests in Teresina, the study showed that prevalence estimates based on the leishmanin skin test increased with age and that those based on serological tests showed a non-significant variation with age (Werneck *et al*., 2002). Still in Teresina in an endemic period, a study showed an association between a positive reaction to the Montenegro skin test and age (Gouvêa *et al*., 2007). The meta-analysis study by Belo *et al*. (2013) of VL in the Americas showed that children are more likely to develop the clinical disease and less likely to become infected. However, as it is known that children are less likely to have asymptomatic infection, the Montenegro test indicates infections that have occurred throughout an individual's life (Nascimento *et al*., 1993). However, the study by Silva *et al*. (2006) in Porteirinha, Minas Gerais, which must also be considered, demonstrated that serological tests for VL can also continue to be positive after the treatment of the disease, not indicating a bad prognosis or a poor therapeutic response.

The studies by Cunha *et al*. (1995); Desjeux (2001) and Albuquerque *et al*. (2009) showed that the occurrence of VL in

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Table 2. Categorization of studies on factors associated with the occurrence of VL in the context of epidemics, according to the geographical area and type of factor

Study (author/year)	Brazilian region	Climatic and environmental	Social, urban, household and populational structure	Socioeconomic	Individual	Vector	Presence of dogs	Presence of other animals
Costa *et al.* (1990)	Northeast							
Werneck *et al.* (2002)	Northeast							
Werneck and Maguire (2002)	Northeast							
Jerônimo *et al.* (2004)	Northeast							
Bavia *et al.* (2005)	Northeast							
Costa *et al.* (2005)	Northeast							
Werneck *et al.* (2007)	Northeast							
Ximenes *et al.* (2007)	Northeast							
Borges *et al.* (2008)	Southeast							
de Oliveira *et al.* (2008)	Central West							
Borges *et al.* (2009)	Southeast							
Cerbino-Neto *et al.* (2009)	Northeast							
de Almeida *et al.* (2011)	Northeast							
Viana *et al.* (2011)	Northeast							
Brazuna *et al.* (2012)	Central West							
de Freitas *et al.* (2013)	Northeast							
Oliveira *et al.* (2014)	North							
Carranza-Tamayo *et al.* (2016)	Central West							
de Toledo *et al.* (2017)	North							
Lima *et al.* (2017)	Northeast							
Araújo *et al.* (2018)	Northeast							
Rocha *et al.* (2018)	Northeast							
dos Reis *et al.* (2019)	North							

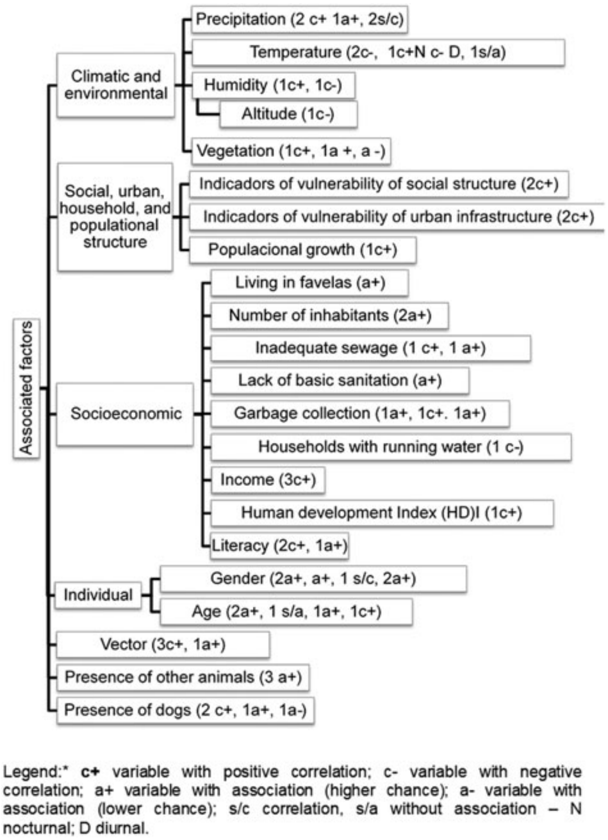

Fig. 3. Factors related to human VL described in the studies included in this systematic review.

the North and Northeast regions was related to socioeconomic and migratory factors. However, the results of this review indicate the occurrence of climatic and environmental factors, socioeconomic factors, vulnerability indicators of the social structure and urban infrastructure, individual characteristics, factors related to the vector, presence of dogs and other animals present during the context of the epidemic in the Northeast region of Brazil. These results corroborate with the observation of Sherlock (1996) in Bahia and other regions of the country in which poverty, malnutrition and high density of phlebotomines were associated with the presence of domestic animals, sanitary conditions and low socioeconomic level in the areas of transmission of VL. Among the factors present in the context of epidemics in Brazil, climatic and environmental factors deserve to be highlighted as the spread of VL may be related to these conditions normally found in poorer areas, with less urban infrastructure and with little sanitation.

Some points in the temperature and precipitation variables identified in this review should be considered as related to the increase in the number of cases of VL in the context of epidemics. Among the points, we highlight the influences of these climatic variables in the epidemiological cycle of VL, due to their influence on the activity of sandflies (Rivas *et al.*, 2014; Lima *et al.*, 2017; Sevá *et al.*, 2017) which can influence the spread of the disease.

The influence of vegetation on VL cases can also be related to the different forms of urbanization and infrastructure of the studied places (or areas) and to the demographic and environmental characteristics, and also to the presence of the vector. As demonstrated in Teresina, the periods with high rates of the disease in the peripheral neighbourhoods were coincident with the expansion of the city area and population growth; and that green areas are positively associated with the occurrence of VL (Werneck and Maguire, 2002; Cerbino-Neto *et al.*, 2009). These results were corroborated with the evidence from Feliciangeli *et al.* (2006) in which the proximity of houses to the forest is a probable risk factor for *Leishmania* infection. In the state of Bahia, the spatial comparison of human disease cases between NDVI and vegetation maps suggests that the highest incidence of VL is concentrated in areas with lower NDVI values, with the caatinga as the predominant vegetation (Bavia *et al.*, 2005).

Other climatic and environmental factors, such as altitude and relative humidity, were discussed in only one of the studies included in this review, which limits the analysis of these variables. Studies that address these variables in other contexts and locations are still needed.

Studies have demonstrated socioeconomic factors related to VL in different locations (Werneck *et al.*, 2002, Costa *et al.*, 2005) through different mechanisms. The included studies pointed out the high incidence of VL associated with the worst living conditions of the populations and the lowest urban structure corroborating with the study by Araújo *et al.* (2018). Such factors are also responsible for the expansion of the disease in endemic regions (da Silva *et al.*, 2008). The poor living conditions of the population contribute to the strengthening of the VL epidemiological chain (Ponte *et al.*, 2011).

Studies carried out in epidemic periods point to a relationship between infestation and vector abundance and disease, which is also observed in the occurrence of VL in endemic periods. Ponte *et al.* (2011) showed that the presence of sandflies in the home was among the variables associated with infection in the municipality of Raposa (state of Maranhão). The fact that *L. longipalpis* is capable of adapting to different habitats (de Oliveira and Araújo *et al.*, 2003; Barata *et al.*, 2005) with evidence of the presence of sandflies in intra- and peri-domiciliary areas (Resende *et al.*, 2006) may explain the relationship with the disease.

Cases of positive dogs have been linked to VL in humans in epidemic periods in the study by de Freitas *et al.* (2013) in Fortaleza (Ceará), from 2006 to 2012. Similar observations were reported in Belo Horizonte (Minas Gerais) (Oliveira *et al.*, 2001; de Araújo *et al.*, 2013; Bruhn *et al.*, 2018) and in Feira de Santana (Bahia) (Carneiro *et al.*, 2004) in endemic periods. In addition to the dog being considered the most important reservoir of infection in urban environments (Braga *et al.*, 1986), the proximity between homes and shelters for domestic animals may be responsible for the presence of insects inside the home, together with their capacity for endophilia (Missawa and Dias, 2007).

For the presence of other animals, although there is no clear evidence about risk factors, and they are not reservoirs for *Leishmania* (Otranto *et al.*, 2010), the studies in this review showed a relationship between VL and the presence of other animals. The presence of other animals in the household may be related to the favourable environment for the breeding of phlebotomine by the production of organic waste produced by these animals (Carvalho *et al.*, 2000).

This study has some limitations that should be mentioned. In the sample of studies selected and analysed, there was no longitudinal study addressing the factors associated with VL, despite the importance of these studies to increase the strength of the scientific evidence of the results. Moreover, it was not possible to perform a meta-analysis due to the weaknesses of the measurements used and the differences in them performed in each study.

The studies included in this review took place in the states of the Northeast, North, Southeast and Central-West regions. The higher concentration and the absence of studies in certain regions reflect the distribution of the disease in Brazil. Studies that better clarify the risk factors are needed for intervention and planning of disease control policies in different regions of the country and to help design effective strategies to control the spread of VL in urban areas.

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Despite the identification and description of the factors related to epidemics in Brazil presented here, more robust studies are needed to investigate the different behaviour patterns of the factors in different regions and within the same region. These studies will guide strategies to control VL transmission in epidemic contexts.

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Author contributions. CSSC, DSB and MC conceptualized the study design. CSSC and NSG independently selected the studies. CSSC, VCO and DTC contributed to analysing the studies. CSSC, DSB, NSG and MC drafted the manuscript. All authors read and approved the final version of the manuscript.

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Conflict of interest. None to declare.

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