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PROTOZOOLOGY - REVIEW

Environmental and socioeconomic risk factors associated with visceral and cutaneous leishmaniasis: a systematic review

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Abstract

We performed a systematic review of the literature published since 1900 about leishmaniasis a neglected vector-borne disease, focused on environmental and social risk factors for visceral (VL) and cutaneous leishmaniasis (CL) to better understand their impact on the incidence of disease. The search terms were "leishmaniasis" AND "risk factors" using Google Scholar, PudMed, and Scielo. We reviewed 177 articles, 95 studies for VL, 75 for CL, and 7 on both forms. We identified 14 categories of risk factors which were divided into three groups: socioeconomic (7), environmental (5), and climate (2) variables. Socioeconomic factors were also associated with disease incidence in vulnerable human populations of arid and tropical developing regions. Environmental and climate factors showed significant associations with the incidence of VL and CL in all the studies that considered them. Proximity to natural vegetation remnants increased disease risk in both the New and Old World while the climate conditions favorable for disease transmission differed among regions. We propose a common conceptual framework for both clinical forms that highlights networks of interaction among risk factors. In both clinical forms, the interplay of these factors played a major role in disease incidence. Although there are similarities in environmental and socioeconomic conditions that mediate the transmission cycle of tropical, arid, and Mediterranean regions, the behavior of vector and reservoirs in each region is different. Special attention should be given to the possibility of vector adaptation to urban environments in developing countries where populations with low socioeconomic status are particularly vulnerable to the disease.

Keywords Leishmaniasis · Risk factors · Socioeconomic · Landscape · Climate

Introduction

Leishmaniasis is a vector-borne disease caused by a protozoan of the genus *Leishmania*, which comprises 20 species pathogenic to humans (Akhoundi et al. 2016). *Leishmania* is endemic in 97 countries; more than 350 million people are at risk for the disease, and approximately 50,000 to 90,000 cases of VL and 0.7 to 1.2 million cases of CL occur each year. A tentative estimate of mortality based on sparse data using hospital-based fatalities reported 20,000 to 30,000 deaths of leishmaniasis per year in the world (Alvar et al. 2012; World Health Organization 2017). Over 90% of global cases of most fatal leishmaniasis infections are from VL and occur in Brazil, Ethiopia, Sudan, South Sudan, India, and Bangladesh (World Health Organization 2010; Pigott et al. 2014a). In addition, the 84% of global CL incidence in 2016 were reported in Afghanistan, Algeria, Brazil, Colombia, Iraq, Pakistan, Peru, the Syrian Arab Republic, Tunisia, and Yemen (World Health Organization 2018).

The disease has two main clinical forms in humans, visceral (VL) and cutaneous leishmaniasis (CL). In the Old World, VL is caused by parasites of the *Leishmania donovani* species and *L. infantum* in the New World. The cutaneous form, CL, is caused by five species of *Leishmania: L. major*, *L. tropica*, *L.*

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aethiopica, *L. donovani*, and in some cases *L. infantum* in the Old World and by multiple phylogenetically distinct *Leishmania* species in the New World (World Health Organization 2010). The clinical manifestations that will develop depend on the *Leishmania* species and host immunological response. Visceral leishmaniasis could present splenomegaly, hepatomegaly, or affect lymphoid tissues. Depending on the form, cutaneous leishmaniasis could present cutaneous nodules, non-ulcerative nodules, or naso-buccal mucosal tissue destruction (Pace 2014).

A total of 93 species of sand flies are probable vectors of *Leishmania* but information on species-specific infection rates is scarce because it is difficult to find infected sand flies in the wild (World Health Organization 2010; Akhoundi et al. 2016). There are two types of *Leishmania* vectors: generalists, which support the growth of more than one species; and specialists, that support only one species of *Leishmania* (World Health Organization 2010). In the Old World, *Phlebotomus* is the principal genus of vectors for the parasite responsible for both VL and CL forms. In the New World, *Lutzomyia longipalpis* is the main vector of *L. infantum*, responsible for VL, while multiple sand fly vectors transmit the various *Leishmania* species responsible for CL (Bates et al. 2015). In the absence of known vectors, however, many sand fly species have been considered as potential *Leishmania* vectors albeit without corroboratory evidence (Akhoundi et al. 2016).

The complex transmission cycle of leishmaniasis also includes several species of mammals other than humans which can be hosts and/or reservoirs of *Leishmania* spp. (Roque and Jansen 2014). Any mammal infected with the parasite can act as a host and may or may not be important in transmission (Roque and Jansen 2014) while reservoirs are only those mammal species highly competent for *Leishmania* spp., responsible for maintaining the parasite in nature (Ashford 1996; Haydon et al. 2002; Roque and Jansen 2014). One important reservoir is the domestic dog (*Canis familiaris*), which is the main reservoir of *L. infantum* in urban areas and is largely responsible for VL around the world and for CL in the Old World. Humans are the reservoir of *Leishmania donovani* responsible for anthroponotic VL transmission in East Africa, Bangladesh, Nepal, Bhutan, and India; and also of *L. tropica* responsible for anthroponotic CL in South-East Asia (World Health Organization 2010). In the New World, other specific reservoirs related to the parasite responsible for CL have not been identified (Reyes and Arrivillaga 2009) and in peri-urban areas close to the forest, other wild mammals are involved in the transmission cycle, especially small mammals such as rodents and marsupials (Roque and Jansen 2014).

The cycle of *Leishmania* spp. depends on a successful transmission between the vector and the host/reservoir. *Leishmania* have two developmental stages: amastigotes inside the macrophages of the mammals and promastigotes in the digestive track of the sand fly (World Health Organization 2010). Sand fly females acquire macrophage infected with amastigotes of *Leishmania* when they feed on blood of a mammal infected. After, the blood meal, amastigotes transform into promastigotes and mature and divide within 3 days of ingestion in the midgut. Then, promastigotes migrate to the proboscis of the sand fly and are ready to be regurgitated into the skin of the vertebrate in the next blood meal (Dawit et al. 2013; Pace 2014; Alemayehu and Alemayehu 2017).

The presence of vector species and potential mammalian reservoirs is favored by some environmental and climatic conditions, such as warm climates and the presence of forest (Desjeux 2001). Such favorable conditions allow sand fly development, providing shelter and protection for both the vector and the reservoir. In fact, both clinical forms of leishmaniasis were initially found only in natural, undisturbed environments (Grimaldi and Tesh 1993). Over the past few decades, however, human migration has led to the creation of settlements close to natural ecosystems, where the cycle of leishmaniasis was already established, increasing human exposure to infected sand flies (Desjeux 2001; Dujardin 2006). These developments have changed the ecology of vectors since the parasite adapted its cycle to peri-domestic sand fly species and reservoir animals (e.g., dogs).

Leishmaniasis transmission occurrence became particularly favorable in developing countries. One potentially important factor underlying this trend is the large human populations of low socioeconomic status living in recently expanded peri-urban areas close to forest or dense vegetation. Peri-urban settlements in these countries are often characterized by poor housing and sanitary conditions that facilitate human contact with vectors, increasing the abundance of potential reservoirs near houses and possibly reducing the efficiency of control programs (Dantas-Torres and Brandão-Filho 2006). Underreporting, deficiency in vector control, and the lack of treatment options in these regions has turned leishmaniasis into one of the most neglected tropical diseases (Desjeux 2001). In addition, shifts in temperature and precipitation in these developing regions could lead to further changes in vector-borne disease incidence as climate conditions for the sand flies and reservoirs are altered (Moo Llanes 2016).

Previous reviews on the risk factors related to the transmission of the disease focused on visceral leishmaniasis in Asia (Bern et al. 2010; Singh and Singh 2019), Africa (Assefa 2018), and in the Americas (Belo et al. 2013). Additionally, the last reviews describing both clinical forms and their risk factors around the world took place over 10 years ago and did not provide a description of the network of risk factors for each clinical form (Desjeux 2001, 2004; Shaw 2007). As result, how interactions between environmental and socioeconomic factors influence leishmaniasis risk is not well understood. The aims of the present study are to (1) review literature on environmental and social factors associated with leishmaniasis in humans and (2) determine the influence of social, environment and climate factors on disease incidence in order to make a conceptual model about the dynamic of leishmaniasis transmission. We hope that this approach to data synthesis will help to better understand and highlight the interplay of the network of risk factors that influence the incidence of both clinical forms and to guide control efforts.

Methods

We searched the literature for relevant publications between 1900 and September 2019 using Web of Science ("all fields"), Google Scholar ("with all of the words"), PubMed ("all fields"), and Scielo ("all indexes"). Search terms included both "leishmaniasis" AND "risk factors" together. We examined the titles and abstracts of all articles identified in the searches and the full texts if necessary in order to identify risk factors included in the studies. We did not analyze articles that focused on (1) canine leishmaniasis exclusively; (2) treatment or clinical factors; (3) asymptomatic leishmaniasis (because we cannot identify the factors that influence the occurrence of leishmaniasis); (4) genetics of the disease or its vectors; and (5) leishmaniasis associations with other disease or clinical descriptions. Additional articles were located through citations from the selected articles or from suggestions from disease experts.

All potential articles were screened for risk variables considered in this review. These variables were then split into three categories: socioeconomic and demographic factors, landscape and environment factors, and climatic factors. We identified 14 variables that were most frequently included in the studies: 7 socioeconomic and demographic factors, 5 landscape and environmental factors, and 2 climatic factors (Table 1).

We considered all the regions affected by leishmaniasis around the world to see similarities in disease dynamics for both clinical forms and highlight the differences between Mediterranean regions and tropical and arid regions, where the transmission cycle is similar but the behavior of vector and reservoirs differs.

Results

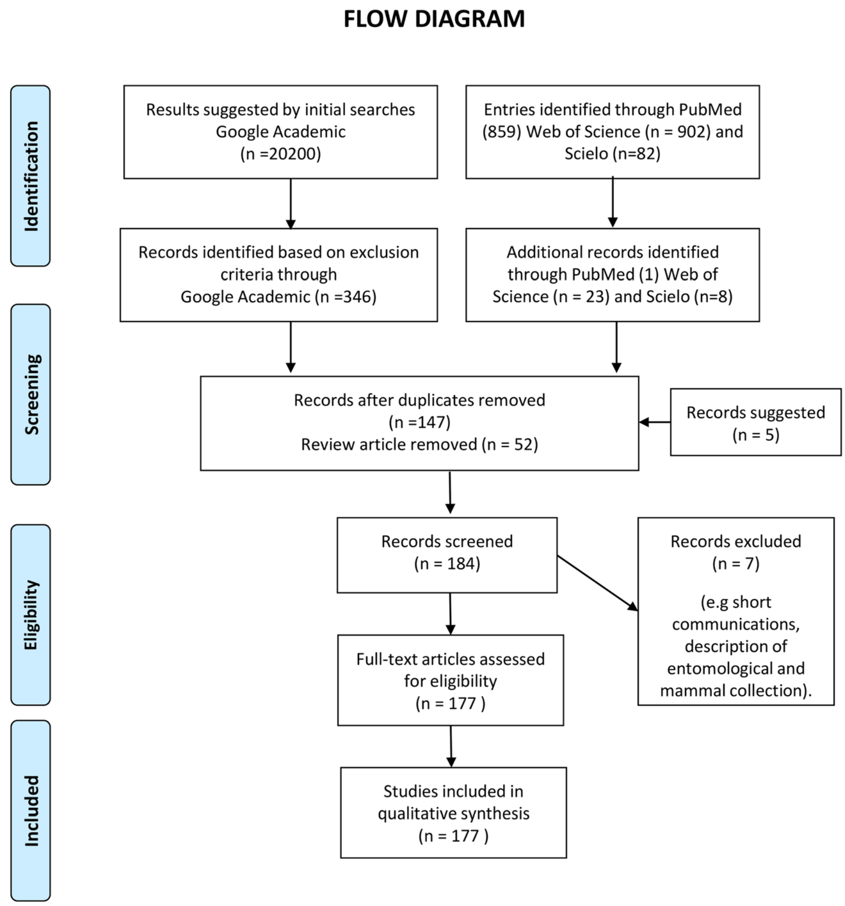
Selection of publications and general description

Our search resulted in 184 potentially relevant articles, of which 177 met our inclusion criteria. Among these 177 articles, 75 focused on cutaneous leishmaniasis (CL), 95 on visceral leishmaniasis (VL), and 7 on both clinical forms (Fig. 1). A total of 52 articles were studies conducted in Brazil, 18 were conducted in Iran, and 15 in Ethiopia, with the remainder distributed across other countries (Fig. 2).

Table 1 List of risk factor variables for leishmaniasis identified in the studies included in the review

Category	Risk variables	Influences
Social and demographic	Socioeconomic status	Influence of quality of life (type of house). Houses built with straw and mud, provide shelter to sand flies.
	Water supply/sewage system/garbage collection	Trash, sewage water, and wells create environmental conditions suitable for sand fly breeding sites.
	Characteristics of population (age, gender, education level, migrant)	Children and elderly people are more vulnerable. Agricultural workers are usually males. Migration increases the number of informal settlements. Low education level can influence the lack of adequate preventive measures.
	Presence of domestic or wild animals	Potential reservoirs or blood meal source.
	Behavior	Sleeping outside without protection against sand flies and working in vegetated areas increase exposure to sand flies.
	Health factors	Immunosuppressed people with other illness or poor nutrition may be vulnerable. Contact with other leishmaniasis cases (anthroponotic tranmission).
	Population density	Household size increase attractiveness to sand flies.
Landscape and environmental variables	Vegetation	Vegetation provides shelter to vector and reservoirs.
	Presence of waterbodies	Humid conditions foster sand fly breeding.
	Altitude/slope/soil type	Physical conditions favorable for breeding sites of vectors.
	Urban/rural landscape	Leishmaniasis cycle presence near rural and urban areas, depending on the parasite species, increases the risk.
	Construction	Anthropogenic disturbance in forested areas increase human-vector contact.
Climatic	Temperature/precipitation	Conditions may be favorable to sand fly development.

Fig. 1. Flow diagram of literature search process



For each clinical form, we examined the relationship between the number of times risk variables were included in studies and their significance (Fig. 3). Landscape variables were implicated with incidence of VL in 48% of the studies and in 62% for CL. Climatic variables were associated with VL in 25% of the studies and in 30% for CL. Socioeconomic and demographic variables were most commonly considered for VL and CL in 67% and 63% respectively (Fig. 4).

To summarize the information of the risk factors considered in our review, we extracted metrics of variable significance directly from the original articles. In addition, for the studies (20% of 177) that provided data for odds ratios (OR), the ratio of disease odds given exposure status, or relative risk (RR), the probability of developing leishmaniasis in an exposed group compared with non-exposed group, we used the OR/RR values. For the studies which provide land cover (10%), data were collected using *in situ* observations or satellite images coupled with geographic information systems (GIS). Metrics of vegetation cover near leishmaniasis cases (36%) included the Normalized Difference Vegetation Index (NDVI), classification of the type and extent of vegetation cover within a given radius of the household, and the distance from the household to vegetation. Detailed information for all studies is included in online resource (Table S1).

Socioeconomic variables

Socioeconomic and demographic factors (Table 1) were significant in 41% of VL and 49% of CL of the cases in the studies (Fig. 3).

Visceral leishmaniasis

Household characteristics that reflect precarious living conditions were analyzed in 44 studies, with 52% finding significant results. For instance, in Posadas, Argentina, the majority of people with VL lived in poor quality houses with sand floors, wooden walls, totally or partially open roofs, and without window screens (López et al. 2016). For anthroponotic VL in Bihar, India mud-plastered walls resulted in a twofold risk increase (OR = 2.40) compared with cement-plastered ones (Ranjan et al. 2005) and in Fulbaria, Bangladesh the prevalence of cases was 59% in houses made of mud floor and tin wall (Bhowmick and Khanum 2017).

Indicators of low educational status were also significant VL risk factors for 39% of the 31 studies that considered this factor. In Belo Horizonte, Minas Gerais, Brazil, a study found a higher risk of VL for illiterate people (RR = 2.87) and for households with less than 4 years of education (RR = 1.82) (de

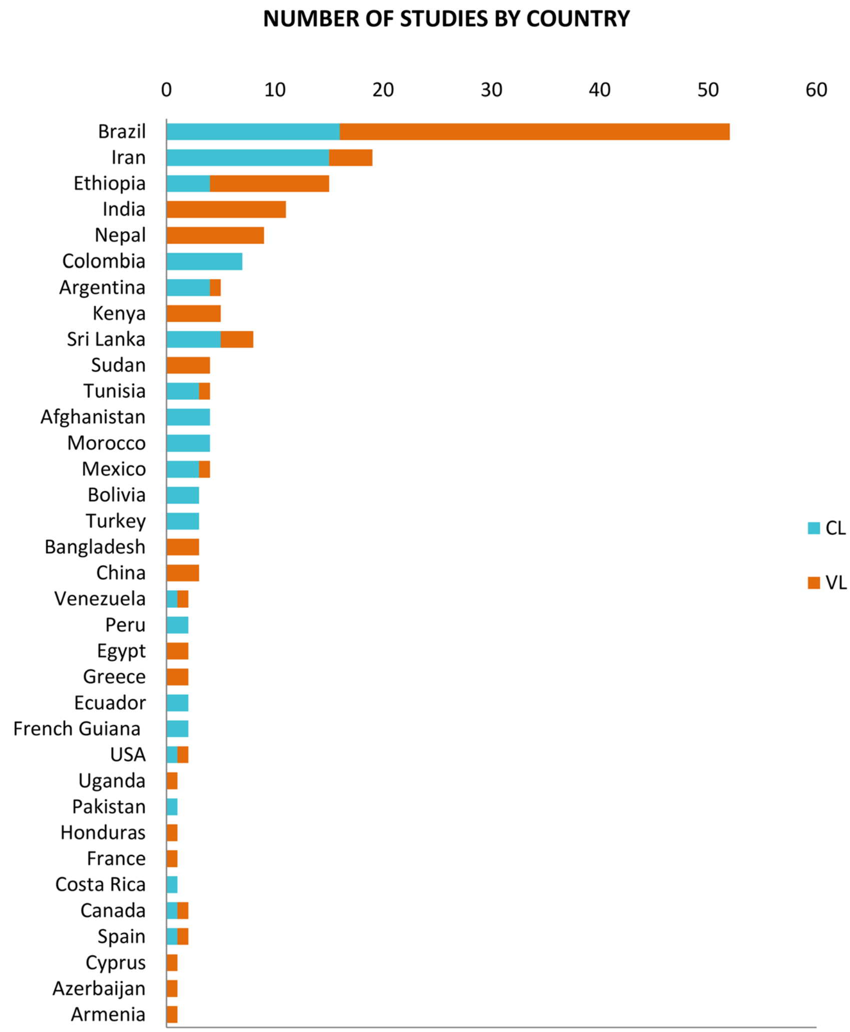


Fig. 2 Geographic distribution of number of studies on leishmaniasis risk factors examined in this review. (*VL* visceral, *CL* cutaneous)

Araújo et al. 2013). For the study in Bihar, India, with anthroponotic VL risk for illiterate people was higher (OR = 1.66) than for literate people (Ranjan et al. 2005).

Lack of access to sewage services, water supply, and garbage collection also presented a significant risk for 33% of the 51 studies that included these factors. In two studies in Brazil, high incidence of VL was associated with lack of these basic sanitary services (Moreno et al. 2005; de Almeida et al. 2011). In these same localities, people with low income were also concentrated in high-risk areas in peripheral neighborhoods for VL (Werneck et al. 2007; de Araújo et al. 2013). A rapid recent increase in population density was also a characteristic of areas of high VL incidence (Cerbino Neto et al. 2009). However, low income in itself was only significant in 34% of 35 studies.

The dog as the main reservoir of *Leishmania infantum* in urban areas is associated with high risks of infection for VL in 67% of 15 studies. For instance, in two studies in Belo Horizonte (RR = 19.11, OR = 2.17) (Borges et al. 2009; de Araújo et al. 2013), and in Posadas where the presence of at least one infected dog was associated with the risk of VL infection (OR = 120.30) and reported in 100% (n = 24) of VL cases analyzed (López et al. 2016).

The presence of other peri-domestic animals was a significant VL risk factor in 47% of 30 studies. In Belo Horizonte, Brazil, the presence of chickens and ducks led to a twofold increase in risk of VL (OR = 2.10) (Moreno et al. 2005). In the same city, another study found a risk increment for people who kept ducks, chickens, and other birds (OR = 4.18, 1.57, 1.47 respectively) (Borges et al. 2009). Presence of rodents (OR = 1.81) in Brazil (Borges et al. 2009) and goats (OR = 6.50) in Tigray, Ethiopia (Yared et al. 2014) also incremented the risk of VL.

Although not strictly socioeconomic conditions, certain activities such as sleeping outside the house, either on the ground (OR = 4.53), under vegetation (OR = 2.77), or near dogs (OR = 4.30) increased the risk ratio of VL in Tigray, Ethiopia (Argaw et al. 2013). Time spent outdoors was also a risk factor for VL in Posadas, Argentina (OR = 4.50) (López et al. 2016) and in Belo Horizonte, Brazil (OR = 1.90) (Moreno et al. 2005). The proximity to the household of a VL patient increase the risk in countries with anthroponotic

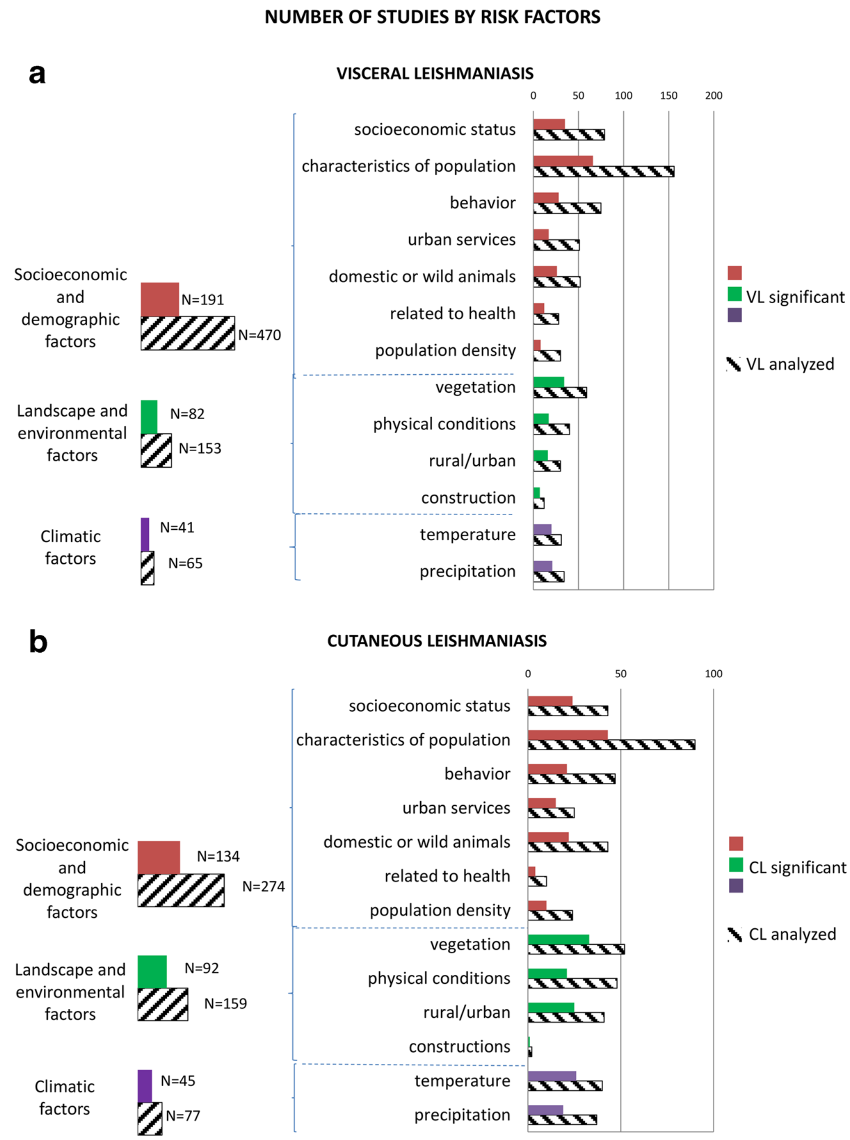


Fig. 3 Number of times that each of the three category of risk variables listed in Table 1 were considered in the 176 studies and number reporting significant values. For **a** visceral (VL) and **b** cutaneous (CL) leishmaniasis studies. Left panels show results aggregated for each category. Right panels show subdivisions for each category based on Table 1

transmission as India (OR = 76, RR = 11.89) (Barnett et al. 2005; Perry et al. 2013), Bangladesh (OR = 25.40) (Bern et al. 2005), and Nepal (OR = 3.49) (Mandal et al. 2019). History of another disease in the previous year (OR = 2.76) had a significant impact on the occurrence of VL in Bihar, India (Ranjan et al. 2005). Malnutrition was another risk factor related to health associated with an increase of VL incidence in Jacobina, Bahia, Brazil (Badaró 1988).

Cutaneous leishmaniasis

Among CL studies, household characteristics were significant for 50% of 28 studies. In Salta, Argentina, windows that cannot be locked represented a high risk for CL transmission (OR = 2.93) (Sosa-Estani et al. 2001). Households built with non-durable wall materials had increasing risk of acquiring CL (OR = 2.36) in Alagoas State, Brazil (de Araújo and de Alencar Ximenes 2009; de Oliveira et al. 2012). In Matara, Sri Lanka, unplastered walls were associated with higher CL risk (Kariyawasam et al. 2015), and in Tigray Ethiopia, the presence of cracks or holes in the walls led to a fourfold risk increase (OR = 4.04) for VL (Bsrat et al. 2015). Household characteristics were also risk factors for anthroponotic CL in Kabul, Afghanistan where brick wall type led to a twofold risk (OR = 2.33) (Reithinger et al. 2010) and poor interior housing conditions (OR = 1.99) in Kerman, Iran (Bamorovat et al. 2018).

Low economic level and related factors are important risk factors for CL (67% of 15 studies). Poverty had a significant association with infection risk in Isfahan, Iran, (OR = 2.03) (Nilforoushzadeh et al. 2014) and in Matara, Sri Lanka (OR = 28.66) (Kariyawasam et al. 2015). Furthermore, the absence of a gas stove in Alagoas (OR = 2.41), in houses of people with low-income status in Brazil (de Araújo and de Alencar Ximenes 2009), were also associated with populations affected with CL.

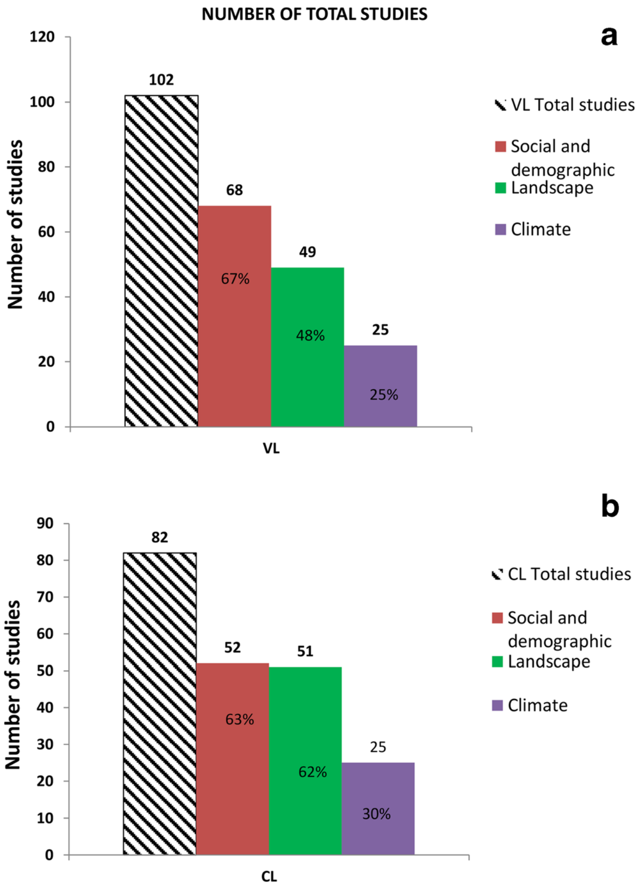


Fig. 4 Number of total studies analyzed. For **a** visceral (VL) and **b** cutaneous leishmaniasis (CL). Hatched bars show total number of studies. Colored bars show the number of studies that found factors in each category significant. Note that some studies examined several factors

As for VL, the presence of peri-domestic animals was important for the transmission of CL (38% of 16 studies), whether they were inside (OR = 2.93) (de Araújo and de Alencar Ximenes 2009) or outside the house (OR = 2.38) (Sosa-Estani et al. 2001; Nilforoushzadeh et al. 2014).

Activities such as sleeping at the workplace (rural work OR = 4.14) and sleeping outdoor at night (OR = 6.29) were associated with higher incidence in Salta, Argentina, (Sosa-Estani et al. 2001). The absence of protection measures against sand flies bites (OR = 6.13) during the time spent outdoors represented a higher risk for CL transmission in Matara, Sri Lanka (OR = 24.60) (Kariyawasam et al. 2015). Agricultural work (OR = 7.75) and leisure activities inside the forest (OR = 9.23) were associated with the incidence of CL in Alagoas State, Brazil (de Araújo and de Alencar Ximenes 2009).

Environmental and landscape factors

These factors are a range of descriptors of the area in which leishmaniasis occurred (Table 1). Land cover data, vegetation cover near leishmaniasis cases and the distance from the household to vegetation. Also were considered physical variables such as soil type and elevation in a number of studies. These environmental and landscape factors were significant in 54% of VL and 58% of CL of the cases (Fig. 3).

Visceral leishmaniasis

For VL, distance to vegetation was a significant risk factor for 54% of the 26 studies that included this variable. In Bihar, India, the presence of bamboo near the house resulted in a twofold risk increment (OR = 2.30) relative to areas with creepers, herbs, and bushes (Ranjan et al. 2005) and in Dharan, Nepal were proximity to a forest island increase the risk of VL with anthroponotic transmission (Khanal et al. 2010). Similarly, in Teresina, Brazil, the predominant vegetation in the city was shrubs, palm trees, and sparse mango trees. However, Teresina is surrounded by Brazilian Cerrado (Savannah) and pastureland and the high incidence rates were found in the peripheral neighborhoods close to both vegetation types (Werneck et al. 2002).

Vegetation cover type was significant in 60% of the ten studies that considered it, particularly when vegetation was interspersed with urban development in peri-urban areas. In the Gangetic plain of NE India, the presence of woodland (< 10% tree cover) was associated with high anthroponotic VL risk due to the proximity to peri-urban area (Bhunia et al. 2010b). On the other hand, in the Mediterranean city of Fuenlabrada, Spain, a spatial analysis located a cluster of high incidence of leishmaniasis (VL and CL) close to the forest of Bosquesur Park, an urban ecological corridor (Gomez-Barroso et al. 2015). In the Provence-Alpes-Cotes d'Azur, France, a cluster of VL was located in Nice in scattered dwellings close to the Mediterranean mixed forest. These examples demonstrate that this effect is not restricted to leishmaniasis of tropical areas (Faucher et al. 2012).

Fourteen studies considered NDVI index as a predictor of incidence and 10 found significant associations. High NDVI values were associated with incidence of VL in Teresina and Campo Grande with a vegetation typical of Brazilian Cerrado (Cerbino Neto et al. 2009; de Oliveira et al. 2012). However, incidence was higher in areas of low NDVI in Distrito Sanitário de Barra, Bahia, Brazil, where Caatinga (Brazilian Thorny scrub) seasonal loss of leaves in this habitat is associated with low NDVI (Bavia et al. 2005). In India, low NDVI values were also significant for anthroponotic VL incidence because most of the cases occurred in areas with low density of vegetation where live the vector *Phlebotomus argentipes* (Bhunia et al. 2010b, 2012).

Others variables related to land use and geography include the presence of waterbodies near dwellings and the location of study sites in relation to urban or rural areas. The presence of waterbodies close to the dwellings was a risk factor for VL in

6 out of 16 studies. High susceptibility areas of VL were close to the rivers in Kalaybar and Ahar, Iran (Rajabi et al. 2014) and in Sri Lanka, water reservoirs represented also a risk of VL incidence (Weerakoon et al. 2018). In addition, increased risk of anthroponotic VL was greater closer to ponds in Dulari, Dharan, Nepal (OR = 3.70) (Schenkel et al. 2006), rivers and waterbodies in the Gangetic plain, especially in non-perennial river banks in India (Bhunia et al. 2010b, 2011).

The majority of studies of VL risk factors were conducted in urban areas. However, 17 studies specifically consider urban cover as a risk factor with 59% studies finding a significant relationship between urban cover and VL risk. High incidence of VL was centered in peripheral neighborhoods in Teresina, Brazil (Werneck et al. 2002) and in Kyrenia, Cyprus (Ruh et al. 2017). Continuous urban area in Marseille, France (Faucher et al. 2012) and Green urban areas in Attica, Greece (Iliopoulou et al. 2018) presented also a high incidence of VL. In addition, built-up areas in northwest India represented a high anthroponotic VL risk (Bhunia et al. 2010b). However, other studies found high VL risk in rural areas (four of seven studies), for example, cultivated and irrigated land in Thessaly, Greece (Giannakopoulos et al. 2016); and in northwestern Iran (Rajabi et al. 2016b). In addition, construction projects such as highways and pipelines were also associated with an increase in VL incidence in Brazil (58% of 12 studies) (Antonialli et al. 2007; Cardim et al. 2013, 2016).

Eight studies considered the effects of soil type on VL and four of these found significant associations. Soil characteristics are hypothesized to reflect moisture conditions suitable for breeding sites; soil types associated with high VL incidence areas include fluvisols in the Gangetic plain in India (anthroponotic transmission), alluvial soil characteristic of the rivers areas as the Ganges river (Bhunia et al. 2010b), and vertisols (OR = 24.32), lixisols, cambisols, and luvisols characteristic of tropical grasslands and savannas in Ethiopia (Tsegaw et al. 2013; Kirstein et al. 2018).

Altitude of the study area has also been associated with VL incidence with 7 of 12 studies finding this variable a significant risk factor. For instance, 95% of VL cases in Ethiopia were located in areas lower than 1872 m asl in a range between 1000 and 3000 m asl (Tsegaw et al. 2013). In Gedaref, Sudan, high risk areas were found in areas lower than 550 m asl (range 400–1000 m asl) (Elnaiem et al. 2003b) and in Thessaly, Greece in areas lower than 200 m asl (range 27–1083 m asl) (Giannakopoulos et al. 2016).

Cutaneous leishmaniasis

Environmental and landscape variables were also high risk factors for CL transmission. Vegetation close to the dwellings was a significant risk factor for 63% of 19 studies. Areas with a predominance of pastures and secondary vegetation close to households in Seropédica, Rio de Janeiro were favorable for CL occurrence (de Oliveira et al. 2016). In Alagoas State, Brazil, originally covered by Caatinga and Atlantic coastal forest, the presence of forest less than 200 m from households resulted in a fourfold greater risk (OR = 4.70) relative to areas farther from the forest (de Araújo and de Alencar Ximenes 2009). Areas characterized by residual forests and riparian forests resulting from reforestation in Campinas, São Paulo State, Brazil, accounted for 82% of the cases east of the city and 50% of the cases in the southeast occurred in sites less than 200 m from forest (Nasser et al. 2009).

Vegetation cover was also a significant risk factor for 92% of 13 studies which analyzed it for CL. In the district of Matara in Southern Sri Lanka, a spatial analysis found that clusters of CL were more prevalent in proximity to native xeric shrublands (Kariyawasam et al. 2015). CL transmission was also observed in the Colombian Andean region, an area characterized by a mosaic of savanna, rainforest, and woodlands. Among all categories of land cover analyzed in this study, rainforest cover was positively associated with CL incidence (Pérez-Flórez et al. 2016). Other studies conducted in a department located in the same Andean region of Colombia found that areas of high incidence had a 20% higher cover of wooded and shrubs relative to disease free areas (Valderrama-Ardila et al. 2010; Ocampo et al. 2012).

NDVI values had significant associations with CL in 55% of nine studies. In Itapira, Brazil, high NDVI values represented 50% of CL risk areas (Aparicio and Bitencourt 2004) and also CL incidence was associated with NDVI values in Adana, Turkey (Artun and Kavur 2017). In Iran, high NDVI values were significant for CL cases (Ramezankhani et al. 2017b; Shiravand et al. 2018) and with prevalence of anthroponotic CL (Golpayegani et al. 2018).

Other landscape characteristics, such as the extent agricultural area, were associated with CL for 71% of 17 studies. The study areas previously mentioned associated with vegetation were rural areas in the case of Seropédica (de Oliveira et al. 2016) and cultivated and livestock areas in the Colombian Andean region (Pérez-Flórez et al. 2016). Likewise, in Caratinga, Minas Gerais, Brazil, 77% of CL cases were located in rural areas (Machado-Coelho et al. 1999), and in Tsaeda-emba, Tigray, Ethiopia farm land within 300 m radius from the households (OR = 1.86) increased CL risk (Bsrat et al. 2015). In western Afghanistan, irrigated cultivated lands (OR = 14.34) were the land cover more significantly associated with anthroponotic CL (Fakhar et al. 2017).

Six of 12 studies analyzed distance of households to waterbodies. Population centers affected with CL were characterized by the presence of riverbeds and embankments in Isfahan, Iran (Nilforoushzadeh et al. 2014; Rajabi et al. 2016a) and presence of ponds or waterways in Loreto, Santiago del Estero province in northern Argentina (Yadon et al. 2003). In western Afghanistan, Harirud river ($p < 0.01$) was a risk factor of CL with anthroponotic transmission (Fakhar et al. 2017).

Only four studies of five studies found significant associations of CL with soil type. In Seropedica, Rio de Janeiro, planosol characterized favorable areas of CL (de Oliveira et al. 2016), inceptisol soil type were significant for CL incidence in Ilam and Dehloran, Iran (Mokhtari et al. 2016; Nikonahad et al. 2017). For anthroponotic CL, haplocalcids with torriorthents and torrifluvents soil types had highest association (OR = 13.08) in western Afghanistan (Fakhar et al. 2017).

Altitude and elevation data (slope) were also found to be significant in 11 out of 31 CL studies. In Seropédica (range 0–520 m asl), favorable areas of CL incidence were characterized by low altitude in areas ranging from 0 to 40 m asl and slope of 0–2.5° (de Oliveira et al. 2016). Human contact risk zones (between the vector and human) in Itapira, São Paulo State, Brazil (1–1200 m asl) were at altitudes lower than 750 m asl (Aparicio and Bitencourt 2004). In contrast, altitudes between 1400 and 2700 m asl (OR = 2.32) and slopes higher than 4.6° (OR = 4.36) were most favorable for CL incidence in Ethiopia (range 1000–3000 m asl) (Seid et al. 2014).

Climate variables

Climate variables were analyzed in studies that considered other environmental variables (i.e., vegetation, soil type, altitude). These variables were significant in 63% of VL and 58% of CL of the cases in the studies (Fig. 3). The most commonly studied climate variables for both clinical forms were temperature and rainfall. The approach of most studies was to examine the range of temperatures and rainfall that were favorable to disease incidence. Other studies used Environmental Niche Models to examine the association between climate variables and disease occurrence.

Visceral leishmaniasis

Temperature was significant for 60% of 25 studies, rainfall for 60% of 25 studies, and relative humidity for 67% of 9 studies. Incidence areas in the Gangetic plain, India (anthroponotic transmission) had a temperature range between 25° and 27 °C and precipitation between 100 and 160 mm with relative humidity between 66 and 75% (Bhunia et al. 2010b). In China, temperature range between 21° and 28 °C and relative humidity less than 80% had significant association with VL in Kashi prefecture (Li and Zheng 2019); and also rainfall below 91.9 mm (Zheng et al. 2018). In the Mediterranean region of Thessaly, Greece, maximum temperature (32 ± 1 °C) accounted for 6% of the variance in an ecological niche model (ENM) for *Leishmania* infection (Giannakopoulos et al. 2016). In Africa, Ethiopia, a semiarid country, annual average temperatures between 20° and 37 °C (OR = 5.16) and annual rainfall below 766 mm were also predictors of VL (Tsegaw et al. 2013). In Geradaf, Sudan, rainfall below 939 mm was the best predictor of VL incidence (Elnaiem et al. 2003b). In South America, Brazil, the incidence of VL increased in Tocantis with a mean night temperature range between 19° and 23 °C, humidity range between 8.42 and 16.72 g/kg, and annual rainfall between 1154.4 and 1710.2 mm (dos Reis et al. 2019). In São Paulo State, a rainfall range between 270 and 540 mm contributed the incidence of VL (da Paixão Sevá et al. 2017); other study in the same State found also positive association of VL cases with rainfall 1407 ± 123 mm but rainy days of 112 ± 18 were negative associated with VL cases (Oliveira et al. 2018),

Cutaneous leishmaniasis

Climate variables were also significant risk factors for CL studies; temperature was significant for 67% of 30 studies, rainfall for 40% of 30 studies, and relative humidity for 7 studies. In South America, a peak of incidence of CL was found in Chaparral, Colombia with a mean temperature of 20.6 ± 1.4 °C (Valderrama-Ardila et al. 2010), and a ~16 ± 5.7 °C with all areas of incidence in the Andean region of Colombia (Pérez-Flórez et al. 2016). In addition, the same study in this Andean region found CL incidence was higher in areas where annual rainfall was 1841 ± 660.3 mm. In a geostatistical model of leishmaniasis incidence in Brazil, a 207–530 mm range of precipitation in the warmest quarter was an important risk factor for CL (Karagiannis-Voules et al. 2013).

In North Africa, a temperature of 9.4° to 22.1 °C contributed 20.7% of the variation in an Ecological Niche Model of the vector in Tunisia. Furthermore, in this country, the vector occurred in the driest quarter of the year with rainfall below to 37 mm (Chalghaf et al. 2016) and the relative humidity between 30 and 45% increase the CL incidence (Talmoudi et al. 2017). In addition, in Ethiopia, a temperature range between 17.2° and 23.8 °C was associated with CL occurrence (OR = 25.70) and annual rainfall between 903.4 and 1715.8 mm increased the risk of CL (OR = 2.67) (Seid et al. 2014).

In Isfahan, Iran, hot spot areas of CL presented annual temperature range between 15° and 19 °C, annual rainfall 5–20 mm, and relative humidity range between 27 and 36% (Ramezankhani et al. 2017b, 2018). In the same country, climate variables associated with the increase of CL incidence in Fars were rainy days 31 ± 13 and relative humidity of 47 ± 17% (Ali-Akbarpour et al. 2012); and in Khuzestan were temperatures of 34 ± 10 °C, rainy days from 30 to 65 days, and relative humidity of 10–78% (Azimi et al. 2017). However, in central region of Afghanistan, outdoor temperature of 2.16 °C was associated with increase of anthroponotic CL risk (Adegboye et al. 2019).

Discussion

Our analyses demonstrate that the incidence of leishmaniasis is influenced by a variety of environmental, landscape, and socioeconomic factors. In the first half of the twentieth century, the major risk factors for leishmaniasis were proximity to forest areas and distance from population centers (Southgate 1964; Moškovskij and Duhanina 1971; Ashford et al. 1973; Forattini et al. 1976). In the early 1990s, studies demonstrated that deforestation and development of rural settlements near forests increased VL and CL incidence (Montoya et al. 1990; Mott et al. 1990; Grimaldi and Tesh 1993), suggesting that the parasite life cycle can persist under altered ecological conditions by adopting peri-domestic sand flies as vectors and domestic animals as reservoirs. At present, people living in urban or peri-urban areas are at the greatest risk of infection (Machado-Coelho et al. 1999; Pigott et al. 2014a; Rocha et al. 2018). These populations have a high probability of contact with sand flies coupled with socioeconomic characteristics that make them particularly vulnerable to leishmaniasis.

We found a greater number of studies of VL relative to CL, consistent with previous reviews (Perilla-González et al. 2014). VL is lethal without treatment and is more common in urban environments and as a result, has received more attention. However, CL was also present in periurban environments (Steffens 2010; Gomez-Barroso et al. 2015; de Oliveira et al. 2016) and without treatment could be associated with other health problems.

Below, we present a conceptual model to illustrate the interplay between risk factors analyzed in the studies included in this review and how such interactions can be used to understand the leishmaniasis transmission cycle (Fig. 5). The studies reviewed here not only identify several important factors related to leishmaniasis risk but also highlight how socioeconomic (Fig. 5a), landscape (Fig. 5b), and climatic factors (Fig. 5c) influence disease transmission.

Socioeconomic factors

In the Old World, Mediterranean, tropical, and arid regions have a long history of human intervention that has placed human populations close to the transmission foci. In contrast, environmental modifications in tropical areas of the New World are more recent and the percentage of the landscape that remains unmodified is still considerable in proportion to the modified area.

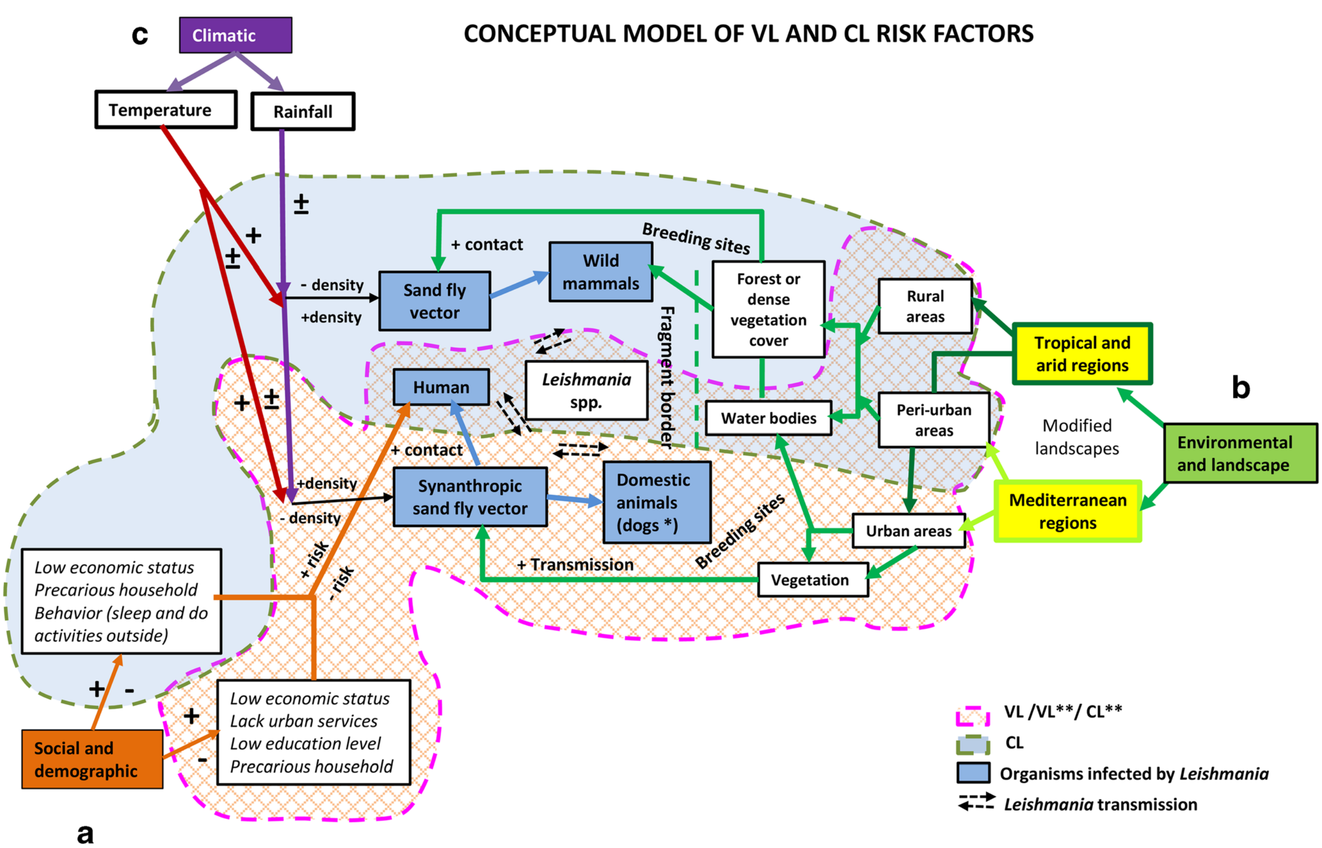


Fig. 5 Interaction of risk factors which influence the incidence of visceral (VL) and cutaneous leishmaniasis (CL). Arrows show factors that influence transmission: **a** orange = socioeconomic factors; **b** green = environmental factors; **c** climatic factors: brown = temperature; purple = rainfall. (±) Represent intermediate values of temperature and rainfall. (*) Dogs are susceptible to some species responsible of VL especially in the New World. Segmented green line represents vegetation border between landscape components. (**) Anthroponotic leishmaniasis

Our analysis demonstrates that urbanization is linked with VL in the New World and with both clinical forms in the Old World. These observations are consistent with Pigott et al. (2014a), who found that urban land cover is associated with an increment of VL risk worldwide and for CL in the Old World. To become urbanized, leishmaniasis depends on the main vector species associated with transmission of the parasite. In the Old World where *Phlebotomus* spp. with synanthropic and anthropophilic behavior is the main vector, the transmission of VL and CL occurs in the peri-domestic environment in tropical rural areas while in Mediterranean regions, it occurs in urban areas and other peripheral urban settlements (Ready 2013). Similarly, in the tropical New World, *Lutzomyia longipalpis* is the main vector of *Leishmania infantum* responsible of VL. This vector species can survive in urban areas, even in the absence of surrounding forests (Lainson and Rangel 2005) and *L. infantum* has the dog as main reservoir, a species that is quite susceptible to infection. However, vector species of CL in the New World tropics usually remain in peripheral areas close to forest. In fact, the reservoirs for the parasites of CL are generally wild rodents that surround peri-urban areas (da Silva and Cunha 2007; Chavy et al. 2019).

Socioeconomic factors such as education level and poverty are frequently associated with malnutrition, poor housing, and lack of sanitary services (Navin et al. 1985; Adhikari et al. 2010b; Rijal et al. 2010; Maia et al. 2013, 2016; Abaker et al. 2017; Loiseau et al. 2019). These conditions can foster the occurrence of continued incidence of the disease (Ranjan et al. 2005; de Araújo and de Alencar Ximenes 2009; Adhikari et al. 2010a; Hasker et al. 2012; Bulstra et al. 2018). For example, precarious living conditions increase leishmaniasis risk because some types of household construction materials offer optimal conditions for sand fly development (Armijos et al. 1997; Reithinger et al. 2010; Singh et al. 2010; Ponte et al. 2011; Bamorovat et al. 2018). Phlebotomine adults find suitable resting and breeding sites in places where cracks or holes in the walls or damp floors are available (Bern et al. 2000; Ryan et al. 2006; Schenkel et al. 2006; Uranw et al. 2013). Lack of sanitation services can also attract wild or domestics reservoirs (Machado-Coelho et al. 1999; Arroub et al. 2012; Prestes-Carneiro et al. 2019) or be a potential breeding site for sand flies (Costa et al. 2005; Moreno et al. 2005).

All of these factors could increase the risk of leishmaniasis and also allow the development of the disease in infected individuals, especially if medical services are inadequate (Alvar et al. 2006; Perilla-González et al. 2014; Pigott et al. 2014a; Rodrigues et al. 2019) and households lack water supply (de Almeida et al. 2011; Lopez et al. 2018; Godana et al. 2019), increasing the prevalence in areas with these characteristics (Boelaert et al. 2009). Moreover, in areas where leishmaniasis overlaps with AIDS or other diseases, the risk of leishmaniasis infection increases considerably (Desjeux 2001; Melchior et al. 2017; Lima et al. 2018). Such overlap is a risk factor in urban areas of the Mediterranean region of Europe where the re-emergence of VL and CL has been caused by an increase in the number of immunosuppressed people rather than lack of sanitation and health services (Steffens 2010).

A high number of individuals per dwelling could also reflect low socioeconomic status (Shah 2005; Alves et al. 2016). Rising population densities in peripheral neighborhoods could attract more sand flies because human CO_2 emissions attract the flies (Chaniotis 1983; Campbell-Lendrum et al. 1999; Chavy et al. 2019). Migration from rural to urban areas (Alcais et al. 1997; Monteiro et al. 2009; Lemma et al. 2015; Abdulla et al. 2018) and the exponential population growth in peri-urban areas have increased the number of dwellings lacking sanitation services (Madalosso et al. 2012; Toledo et al. 2017; Hernández et al. 2019).

In addition, characteristics of population as age and gender were also associated as leishmaniasis risk factors. Adult males were the most exposed at sand flies bites due their occupational activities (Abaker et al. 2017; Nazari et al. 2017; Eid et al. 2018). Work in agriculture, hunting, or timber collection inside the forest especially at the end of the afternoon exposes individuals to sand fly bites, increasing the incidence of the disease (Jones et al. 1987; Espejo et al. 1989; Weigle et al. 1993; Azene et al. 2017; Bellali et al. 2017; Guerra et al. 2019). Sand flies are active at twilight and night; less so at dawn when the decrease of temperature drives them to their natural hiding places (Forattini et al. 1976). Sleeping outdoors or without protection against sand flies bites increments disease risk (Davies et al. 1997; Barnett et al. 2005; Bashaye et al. 2009; Nackers et al. 2015; Kumar et al. 2017). These conditions are generally more common in rural areas or areas close to forest (Almeida and Werneck 2014; Iddawela et al. 2018).

Likewise, disease risk increase with the presence of mammals that can act as potential reservoirs of the parasite. Wild, synanthropic, or domestic animals could be part of the cycle (Beier et al. 1986; Oliveira et al. 2006; Khanal et al. 2010; Cardoso et al. 2015; De Araujo et al. 2016). The presence of dogs in households is considered a high risk factor for the incidence of VL especially in the New World (Votýpka et al. 2012). Dogs are very susceptible to infection, develop the disease, and act as a source of further infection of *Leishmania infantum* one of the main agents responsible of VL in the New World, and both VL and CL in the Old World (Faris et al. 1988; Dantas-Torres et al. 2012; Bsrat et al. 2015, 2018). Although cattle can increase the risk (Ullah et al. 2016; Bhowmick and Khanum 2017; Ghatee et al. 2018), they may also decrease leishmaniasis (Bern et al. 2010) by serving as the principal source of sand fly blood meal and diverting bites to humans (Bern et al. 2005; Kolaczinski et al. 2008).

More research to establish control measures is needed to understand the influence of poverty on leishmaniasis occurrence (Bern et al. 2010; Rodríguez-Morales et al. 2010; El Alem et al. 2018). In the absence of control measures, other factors such as high educational level, good nutrition, and high wealth level cannot by themselves reduce the risk of infection. Furthermore, without the presence of the vector at high densities, new settlements in periurban areas are not always at high risk for leishmaniasis (Alves et al. 2016; Gijón-Robles et al. 2018).

Environmental and landscape factors

Conversion of natural forest to other land uses in the last decades has led to habitat fragmentation and altered landscape composition (Wade et al. 2003). The spread of the vector and disease at macro scales is associated with migration and expansion of human population into natural areas, creation of roadways, energy networks, new farm lands, and poorly planned urban development (Cardim et al. 2013; Afonso et al. 2017; Gutierrez et al. 2017; Oliveira et al. 2018). These changes in the landscape increase contact of human populations with the edges of vegetation areas which shelter sand fly vectors (Patz et al. 2004). New settlements near forests act as foci of leishmaniasis enabling the domestication of the cycle. At the same time, expansion of agricultural crops provides a new food source for natural reservoirs of leishmaniasis such as rodents (Zorrilla et al. 2005; Dawit et al. 2013; Ranasinghe et al. 2013; Carrada Figueroa Gdel et al. 2014; de Oliveira et al. 2016; Gebremichael Tedla et al. 2018).

In human-modified landscapes, fragments of vegetation close to dwellings play an important role in the transmission cycle. Vegetation areas provide the environmental conditions for sand fly breeding sites and development while at the same time act as shelters of wild reservoirs (Negera et al. 2008; Ocampo et al. 2012; de Almeida et al. 2014; de Santana Martins 2015; Temponi et al. 2018; Melo et al. 2018). Populations of many phlebotomine species increase from secondary forest to mature forests (Rutledge and Gupta 2002; Gil et al. 2010; Kariyawasam et al. 2015) except for the species that have adapted to urban environments and do not need dense vegetation to survive such as *Lutzomyia longipalpis* (Salomón et al. 2015) and *Phlebotomus argentipes* (Bhunia et al. 2010a, 2012).

High values of NDVI or vegetation near incidence areas found in several studies suggest proximity to natural habitats connects human dwellings with the vector breeding sites (Aparicio and Bitencourt 2004; Cerbino Neto et al. 2009; Gomez-Barroso et al. 2015; Menezes et al. 2016; Artun and Kavur 2017). The presence of vegetation or forest areas near houses increase the number of sand flies in peri-domestic areas and the probability of being infected (Miranda et al. 1998; Andrade-Narvaez et al. 2003; Dias et al. 2007). Indeed, studies that analyzed the abundance of the vector at different distances from the forest to households of infected people found the number of cases decreased with distance (Werneck et al. 2002; Feliciangeli et al. 2006). The flight range of sand flies is around 200 m, with *P. argentipes* and *P. orientalis* having flight ranges of ca. 500 m and those of *L. longipalpis* and *P. caucasicus* 1000 m or more (Rutledge and Gupta 2002). However, vegetation is a risk factor in tropical forest areas and Mediterranean forest, but not in arid areas where vegetation is not dense and the burrows of mammals, caves, crevice, termite hills, and walls with cracks may serve as breeding sites of sand flies (Holakouie-Naieni et al. 2017; Lotukoi 2017; Ramezankhani et al. 2017a; Alebie et al. 2019; Dulacha et al. 2019).

The presence of waterbodies is also related to vector abundance and its distribution (Yadon et al. 2003; Schenkel et al. 2006; Nilforoushzadeh et al. 2014; de Oliveira et al. 2016; Rajabi et al. 2016b), possibly because waterbodies provide the air moisture necessary for sand fly breeding (Bhunia et al. 2011). The effects of soil type on disease incidence may also reflect moisture conditions. Studies showed that soil types characterized by water retention as fluvisols, the typical soil of river areas, soils with some organic material as inceptisol, planosol which maintain moisture, torrifluvents, humid haplocalcid soils with torriorthents, and clayey soils which also retain water were associated with high disease incidence, possibly by facilitating larval development of sand flies (Elnaiem et al. 2003a; Sharma and Singh 2008).

Because proximity to forests and waterbodies have been associated with disease incidence, control measures in recent years have focused on forest clearing and wetland drainage near incidence areas (Wood et al. 2014). However, we do not advocate that deforestation and wetland draining is the solution for decreasing the risk of leishmaniasis. More studies are necessary to clarify how exposure to the disease agent would change the structure, composition, or function of landscape changes (Myers et al. 2013), seeking environmentally friendly alternatives of disease control.

In our review, we could not identify a range of altitudes significant for leishmaniasis incidence. Clearly, altitude is related with other environmental features that influence vector distribution (Quintana et al. 2012; Ferro et al. 2015; Prudhomme et al. 2015; Mokhtari et al. 2016; Moradi-Asl et al. 2017; Al-Warid et al. 2019). Likewise, topographic characteristics such as slope show a significant impact on the presence and abundance of vectors. However, it is unclear whether these effects simply reflect the indirect effects of temperature shifts with elevation or soil moisture with topography highlighting the need for more studies that can clarify the importance of these factors in the genesis and transmission of the disease.

Climatic factors

Climatic conditions are generally important risk factors for vector-borne diseases (Cardenas et al. 2006). Their effects on leishmaniasis vary according to geographic area and depend on the clinical form and vector species. Studies in Mediterranean, tropical, and arid regions suggest that sand flies thrive between 19° and 30 °C (Kassem et al. 2012; de Souza et al. 2015; Giannakopoulos et al. 2016; Pérez-Flórez et al. 2016; Amro et al. 2017; Abdullah et al. 2017; Artun and Kavur 2018; Moradiasl et al. 2018; Galgamuwa et al. 2018) with a relative humidity above 30% (Gao and Cao 2019), and bite at temperatures between 20° and 30 °C (Rutledge and Gupta 2002). Temperatures over 30 °C and without enough relative humidity negatively affect sand fly population density (Karagiannis-Voules et al. 2013; Moo Llanes 2016). However, in central Afghanistan, a cold outdoor temperature range between 2° and 6 °C increases the incidence of anthroponotic CL, because *Phlebotomus sergenti* the main vector of *L. tropica* is anthropophilic and individuals are mostly indoors where there is a temperature range between 21° and 26 °C (Adegboye et al. 2019).

Rainfall was also associated with leishmaniasis transmission and vector abundance. High rainfall and relative humidity (Elnaiem et al. 2003b; Pérez-Flórez et al. 2016) increase primary productivity (Salomón et al. 2004; Ben-Ahmed et al. 2009; Souza et al. 2012) of forest vegetation which provides food and burrows for reservoirs (Chalghaf et al. 2016), providing an ideal environment for sand flies (Andrade-Narvaez et al. 2003; Quintana et al. 2012; Adegboye and Adegboye 2017). The vectors of *Leishmania* involved in each of the two clinical forms have a different rainfall range around the world. Based on the literature reviewed, we cannot specify a range of precipitation as we did with temperature. However, some modeling analysis report a high precipitation index is an important environmental factor for cutaneous leishmaniasis incidence in the tropics (Chaves and Pascual 2006; Ali-Akbarpour et al. 2012) because the vectors related to this clinical form are associated with the presence of dense vegetation. However, according to some studies, high precipitation is not favorable for visceral leishmaniasis in the tropics (Thompson et al. 2002; Viana et al. 2011; Karagiannis-Voules et al. 2013; Pigott et al. 2014b), but other studies positively correlated rainfall indices with VL (da Paixão Sevá et al. 2017; Oliveira et al. 2018; dos Reis et al. 2019). Taking into account that VL in tropical regions occurs in highly urbanized areas, we can hypothesize that moderate levels of precipitation can foster incidence areas by maintaining humidity in the environment, and sand fly vectors are able to thrive in climatic variations in this regions. Nevertheless, without the protection of vegetation, heavy precipitation could decimate sand fly populations.

There are some limitations for this systematic review. In order to do a comprehensive descriptive review, we did not restrict our inclusion criteria according to the study design (e.g., cohort studies, case-control studies, spatial analysis, ecological niche modelling), and all the studies which analyze risk factors of VL and CL were included. Some studies did not describe the range values of environmental variables significant. Some studies in regions where anthroponotic and zoonotic leishmaniasis coexists did not specify the type of transmission, so we considered only the clinical form. However, the summary of information assessed provides a data-based assessment of the degree to which recent changes in land use, the size and distribution of human populations, and a changing climate have influenced the occurrence of transmission dynamics for the disease.

Conclusion

Our review describes the complexity of transmission and incidence of a disease that presents two main clinical forms and can exist at a broad range of environmental and climatic conditions. We also highlight how complex interaction between risk factors can exacerbate or moderate the incidence of leishmaniasis.

High disease incidence is associated with several environmental, climatic, and socioeconomic conditions. Transmission patterns are similar in all regions, requiring human contact with vegetation areas that harbor reservoir vectors and mammals under warm climatic conditions. Differences among clinical forms and regions depend on the species of vectors involved in each type of leishmaniasis and if these are able to easily adapt to urban environments (e.g., VL in the tropics, arid and Mediterranean regions) or depend on less disturbed environments (e.g., CL in the Neotropics). More research that analyze the interactions of risks factors and how they vary across vector, reservoir species, and environmental conditions in countries where the disease is endemic, is needed. Thus, developing effective control measures will be possible and also require a better understanding of the likely impacts of future climatic conditions on the transmission cycle.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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