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Review

Asymptomatic *Leishmania* infection in humans: A systematic review

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ABSTRACT

Background: Leishmaniasis is a highly prevalent neglected tropical disease. It mainly presents as two forms: cutaneous and visceral leishmaniasis, the latter being the most severe form. However, asymptomatic cases of *Leishmania* infection result in an increase in the underreporting and transmission of the protozoan
Objectives: In this study, articles on the incidence of asymptomatic *Leishmania* infection were systematically reviewed.
Methods: The publications identified in the Medline/PubMed and Science Direct databases included 4568 articles. Inclusion, exclusion, and eligibility criterion analysis resulted in 83 articles being retained. These studies were mostly performed in Brazil (n = 26) and India (n = 15).
Results: Several detection techniques have been used for diagnosis. Among the species found were *L. infantum* and *L. donovani*, which result in visceral leishmaniasis, and *L. amazonensis*, *L. braziliensis*, and *L. panamensis*. The incidence rates varied between the analyzed locations, largely due to sampling and the presence or absence of endemism in the regions. The largest populations analyzed were in two studies performed in India and Nepal. One of these studies evaluated 32,529 people and the incidence rate was 8.3% (n = 2702), while the other study evaluated 21,267 people and the incidence rate was 1.76% (n = 375). Only 14.28% of the studies investigated leishmaniasis in blood donors. Preexisting diseases have also been reported.
Conclusion: The findings of this systematic review present the incidence of cases of asymptomatic *Leishmania* infection worldwide, in addition to detailing the studies and offering information for researchers and health authorities to seek alternatives to reduce the number of leishmaniasis cases.

Contents

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Introduction

Leishmaniasis is a parasitic disease caused by more than 20 different *Leishmania* species. It belongs to what are referred to as neglected tropical diseases (NTDs), infecting 700,000–1 million people annually, especially in underdeveloped countries [1]. The disease is transmitted through the bite of sandflies and affects several animal species, including humans, who are a natural reservoir for these protozoa [2]. In addition to vector transmission, other transmission routes include congenital transmission [3], blood transfusion [4], organ transplantation [5], and accidental laboratory exposure [6].

When infecting humans, the disease manifests itself as two main forms: visceral leishmaniasis (VL), or kala-azar, caused by the species *Leishmania* (*Leishmania*) *donovani* in the Old World and *Leishmania* (*Leishmania*) *infantum* in the New World and also in the vast majority of endemic countries of the Old World, including developed countries characterized by irregular episodes of fever, weight loss, enlarged spleen and liver, and anemia [7], which is fatal in more than 95% of untreated cases [8]; and cutaneous leishmaniasis (CL), which is the most common form, caused by several species belonging to the *Viannia* and *Leishmania* subgenera, causing ulcers and scarring of the skin, in addition to disability [9].

Some infections result in asymptomatic cases and are clinically unnoticeable. Asymptomatic *Leishmania* infection is common in endemic areas and may be more common than symptomatic cases [10]. However, asymptomatic carriers can transmit the infection [11]. Considering the capacity of humans to be a reservoir of *Leishmania*, the objective here is to carry out a systematic review of asymptomatic cases in the world to document the frequency and distribution of these cases and reinforce the importance of monitoring asymptomatic individuals in endemic regions.

Methods

Search strategy

A systematic review of asymptomatic *Leishmania* infection in humans was carried out in the Medline/PubMed and Science Direct (Elsevier) databases with the descriptors “Asymptomatic leishmaniasis”. The search was conducted from August to September of 2020. This review was conducted according to the Cochrane Handbook for Systematic Reviews of Interventions [12] described in Fig. 1.

Inclusion criteria

For the selection of articles, studies had to be on asymptomatic *Leishmania* infection in humans, published in English and in peer-reviewed scientific journals. In the first phase of the search, duplicates were manually removed. The remaining titles and abstracts were then examined to remove any articles that were unrelated to the inclusion criteria.

Exclusion criteria

Articles published in a language other than English, bibliographic reviews, articles without access to the full text, studies of molecular markers, pharmacology, diagnostic and treatment techniques, *in vitro* and *ex vivo* studies, book chapters, comments, and letters to the editor were excluded.

Obtaining and analyzing data

At this stage, the studies included in the systematic review were analyzed to ensure the complete collection of data to be included in Table 1. The analyzed data included the study location, type of detection technique, *Leishmania* species found, total population analyzed, number of positive samples, pre-existing diseases, and age group.

Results

Literature revision

The search resulted in 4568 studies: 834 from Medline/PubMed and 3734 from Science Direct. Only 157 articles remained after removing duplicates among the platforms and applying the exclusion criteria. After the eligibility analysis, 84 articles were retained (Fig. 1).

Studies with asymptomatic Leishmania infection

The reviewed studies reported the global incidence of asymptomatic infection, with the majority of studies conducted in Brazil (n = 27), including the states of Mato Grosso do Sul, São Paulo, Maranhão, Rio de Janeiro, Piauí , Rio Grande do Norte, and Minas Gerais. Other studies were carried out in India (n = 15), Spain (n = 9), Ethiopia (n = 7), Iran (n = 5), Italy (n = 4), Turkey (n = 3), Nepal (n = 2), Israel (n = 2), Croatia, Sri Lanka, Thailand, Austria, France, Tunisia, Morocco, Sudan, the United States, and Argentina (n = 1 each) (Table 1).

Diagnostic techniques and Leishmania species

The detection techniques used to diagnose the disease were different between the studies. Included parasitological (culture and microscopy), serological tests, enzyme-linked immunosorbent assay (ELISA), fast agglutination screening test (FAST), soluble leishmania antigen (SLA), immunochromathographic test (ICT); immunochromatographic test (rK39), immunofluorescence antibody

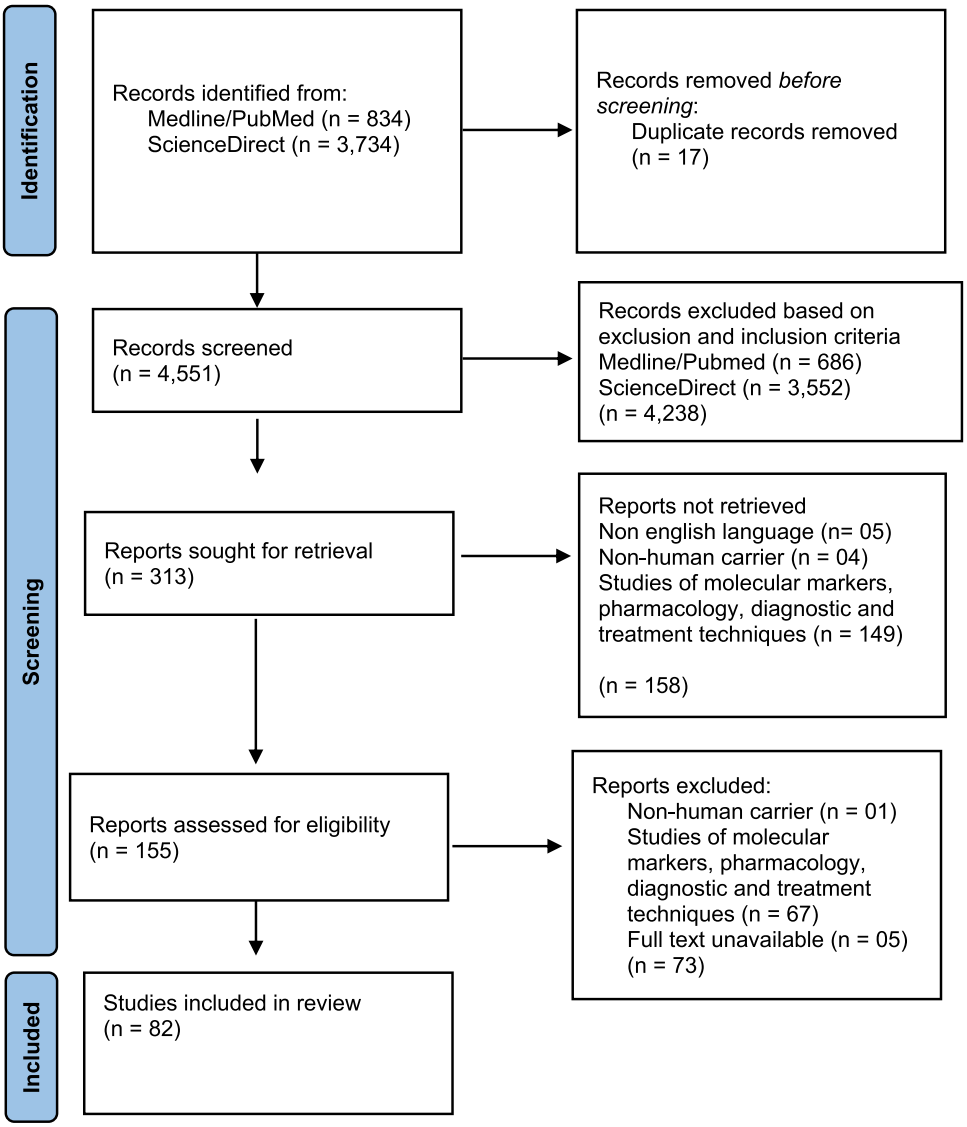

Fig. 1. Flow diagram of selection of articles used for the systematic review.

test (IFAT), western blot (WB), direct agglutination test (DAT), latex agglutination test (KAtex), montenegro skin test (MST), and fucose mannose ligand (FML); molecular test, polymerase chain reaction (PCR), real-time PCR (qPCR) and single nucleotide polymorphism (SNP); cellular test Leishmanin skin test (LST), delayed-type hypersensitivity (DTH), microcapillary culture method (MCM), interferon gama release assay (IGRA); Among the species analyzed were the *L. infantum* and *L. donovani* etiological agents of VL, and *L. amazonensis*, *L. braziliensis*, and *L. panamensis* responsible for CL (Table 1).

Number of people tested and incidence, pre-existing diseases, and age groups

The studies with the highest number of people tested were carried out in India and Nepal, one of which involved 32,529 people and reported an incidence of 8.3% (n = 2702), and the other involved 21,267 people and reported an incidence of 1.76% (n = 375). The study with the smallest number of tested individuals (n = 20) was carried out in Spain, with 100% asymptomatic cases. The locations with the highest positivity were the Balearic Islands (Spain), Pará (Brazil), and Minas Gerais (Brazil), with positivity rates of 100%, 73.2%, and 71.3%, respectively. Only 14.28% of the studies investigated leishmaniasis in blood donors (Table 1).

The vast majority of authors did not report the presence of pre-existing diseases in the participants, but studies carried out in Minas Gerais and Mato Grosso do Sul (Brazil) analyzed liver transplant donor and recipient populations as well as patients with chronic kidney failure. Other analyses carried out in countries such as Thailand, Spain, Iran, Morocco, and Ethiopia determined pre-existing diseases such as HIV, malaria, multiple myeloma, and candidates for kidney transplantation (Table 1).

The age group of the studied population ranged from zero to 94 years of age, and some authors did not describe data regarding the age selected for the study (Table 1).

Discussion

The nature of the articles selected for the systematic review shows that there were only a limited number of studies involving asymptomatic infection in humans, compared to articles involving animals or studies not related to the pathology. Although only 19 countries were the targets of asymptomatic case studies, leishmaniasis is a major public health problem and has a wide geographic distribution, with more than 1 billion people living in endemic areas

Table 1
Characteristics of the studies of cases of asymptomatic *Leishmania* infection and their groups of detection techniques and Leishmania species.

Study location	Detection technique	*Leishmania* species	Total population number (n)	Number of positive (% of asymptomatic)	Preexisting disease	Age groups	Source
Argentina (Salta)	MST	*L. panamensis*, *L. amazonensis*	7336	134 (1.8%)	N/I	30–59 years	Sosa-Estani 2000[13]
Austria	ELISA	*Leishmania* sp.	1048	47 (4.5%)	N/I	18 and 60 years	Poeppl 2013[14]
Brazil (Bahia)	ELISA	*Leishmania* sp.	86	20 (23.2%)	N/I	Average 8.1 years	Badaro 1986[15]
Brazil (Bahia)	ELISA, MST	*L. infantum*	135	44 (32.59%)	N/I	N/I	D'Oliveira 1997[16]
Brazil (Bahia)	ELISA	*Leishmania* sp.	700	38 (5.4%)	N/I	Average 42 years	Fukutani 2014[17]
Brazil (Ceará, Piauí and Minas Gerais)	ELISA, WB, PCR	*L. infantum*	608	37 (6%)	N/I	18–30 years	Ferreira-Silva 2018[18]
Brazil (Federal District)	MST, rK39	*L. amazonensis*, *L. infantum*	700	233 (33.28%)	N/I	2–14 years	Carranza-Tamayo 2016[19]
Brazil (Fortaleza)	ELISA	*L. infantum*	431	57 (13.2%)	N/I	N/I	Monteiro 2016[20]
Brazil (Maranhão)	DTH, ELISA	*Leishmania* sp.	638 and 572	56%/41% and 58%/98%	N/I	0–5 years	Caldas 2002[21]
Brazil (Maranhão)	ELISA	*Leishmania* sp.	905	144 (18.3%)	N/I	0–5 years	Gama 2004[22]
Brazil (Maranhão)	ELISA	*L. braziliensis*, *L. infantum*	1100	91 (8.2%)	N/I	N/I	Mendes 2007[23]
Brazil (Maranhão)	MST, ELISA	*L. infantum*	361	35 (9.7%)	N/I	< 16 years	Moura 2012[24]
Brazil (Mato Grosso do Sul)	IFAT, ELISA	*Leishmania* sp.	220	80 (36.3%)	N/I	4 ≤ - ≥ 60 years	De Oliveira 2008[25]
Brazil (Mato Grosso do Sul)	IFAT	*L. major*	430	67 (15.6%)	N/I	18–68 years	França 2013[26]
Brazil (Mato Grosso do Sul)	IFAT, rK39	*Leishmania* sp.	50	16 (32%)	chronic renal failure	20–77 years	França 2020[27]
Brazil (Minas Gerais)	IFAT, ELISA, rk39, PCR	*L. infantum*	226	102 (45.1%)	N/I	13–38 years	Moreno 2006[28]
Brazil (Minas Gerais)	PCR, ELISA, rK39	*L. donovani*, *L. infatum*, *L. amazonensis*	136	97 (71.3%)	N/I	14–51 years	Moreno 2009[29]
Brazil (Minas Gerais)	IFAT, rK39, rK26, MST	*L. amazonensis*	246	156 (63.4%)	N/I	N/I	Silva 2011[30]
Brazil (Minas Gerais)	PCR	*Leishmania* sp.	67	5 (7.5%)	Liver transplant*	5–70 years	Clemente 2014[31]
Brazil (Minas Gerais)	SLA, rK39	*L. infantum*	935	304 (32.5%)	N/I	3 months - 10 years	Marques 2017[32]
Brazil (Minas Gerais)	rK39	*L. infantum*	1875	6 (0.32%)	N/I	2 months - 7 years	Da Rocha 2018[33]
Brazil (Minas Gerais)	rK39, ELISA, qPCR	*L. infantum*	179	81 (45.2%)	N/I	1–10 years	Da Cunha 2020[34]
Brazil (Pará)	DTH, IFAT	*Leishmania* sp.	231	169 (73.2%)	N/I	1–89 years	Silveira 2010[35]
Brazil (Piauí)	PCR	*L. infantum*	108	8 (7.4%)	N/I	4–28 years	Costa 2002[36]
Brazil (Rio de Janeiro)	MST	*L. braziliensis*	28	11 (39.28%)	N/I	Average 37 years	Bittar 2007[37]
Brazil (Rio Grande do Norte)	FML ELISA, PCR	*L. donovani*	21	14 (66.66%)	N/I	N/I	Otero 2000[38]
Brazil (Rio Grande do Norte)	ELISA	*L. infantum*	345	85 (24.6%)	N/I	N/I	De Lima 2012[39]
Brazil (Rio Grande do Sul)	MST	*L. amazonensis*	151	60 (39.7%)	N/I	N/I	Fagundes 2007[40]
Brazil (São Paulo)	rK39	*L. infantum*	250	29 (11.6%)	N/I	> 31,5 years	Barão 2007[41]
Croatia	ELISA	*L. infantum*	2035	231 (11.4%)	N/I	6 months - 88 years	Šiško-Kraljević 2013[42]
Ethiopia	FAST	*L. donovani*	1390	45 (3.2%)	N/I	0 - > 60 years	Hailu 2002[43]
Ethiopia	DAT, rK39, PCR, KAtex	*L. donovani*	534	36 (6.7%)	HIV	18 - ≥ 48 years	Griensven 2019[44]
Ethiopia	LST, DAT	*L. donovani*	650 and 1040	59 (9.08%) and 9 (0.87%)	N/I	> 2 years	Tadese 2019[45]
Ethiopia (Amhara)	rK39, DAT, DTH	*L. donovani*	605	61 (10%)	Malaria and HIV	5 < - 15 years	Gadisa 2012[46]
Ethiopia (Amhara)	rK39, DAT	*L. major*	565	56 (9.9%)	N/I	4–15 years	Custodio 2012[47]
Ethiopia (Armachiho)	rk39	*L. donovani*	185	14 (7.5%)	N/I	20–30 years	Ayehu 2018[48]
Ethiopia (Omo)	MST, DAT, rK39	*Leishmania* sp.	1682	30 (1.8%)	N/I	> 18 months	Bekele 2018[49]
France (Monaco)	WB	*L. infantum*	565	76 (13.4%)	N/I	N/I	Le Fichoux 1999[50]
India (Bihar)	Microscopy	*L. donovani*	450	6 (1.3%)	N/I	N/I	Sosa 2000
India (Bihar)	rK39, ELISA	*L. infantum*	150	50 (33.3%)	N/I	N/I	Singh 2002[51]
India (Bihar)	rK39, PCR	*L. donovani*	997	21 (2.1%)	N/I	17–25 years	Das 2011[52]
India (Bihar)	rK39, DAT	*Leishmania* sp.	870	287 (32.98%)	N/I	5 - > 15 years	Gidwani 2011[53]
India (Bihar)	rK39, DAT, PCR	*L. donovani*	355	50 (14%)	N/I	0 - ≥ 60 years	Topno 2010[54]
India (Bihar)	qPCR	*Leishmania* sp.	210	40 (19.04%)	N/I	6–55 years	Sudarshan 2014[55]
India (Bihar)	rK39	*L. donovani*	5144	116 (2.2%)	N/I	1 - ≥ 46 years	Das 2016[56]
India (Bihar)	DAT, rK39, qPCR	*L. donovani*	5794	120 (2.07%)	N/I	≥ 6 years	Das 2020[57]
India (Malda)	rK39	*Leishmania* sp.	2890	79 (2.7%)	N/I	N/I	Saha 2017[58]

(*continued on next page*)

Table 1 (*continued*)

Study location	Detection technique	*Leishmania* species	Total population number (n)	Number of positive (% of asymptomatic)	Preexisting disease	Age groups	Source
India (Muzaffarpur)	qPCR, DAT, rK39	*L. donovani*	1469	511 (34.7%)	N/I	≥ 18 years	Sudarshan 2014[59]
India and Nepal	DAT	*L. donovani*	21,267	375 (1.76%)	N/I	N/I	Ostyn 2011[60]
India and Nepal	DAT	*L. donovani*	7538	510 (6.7%)	N/I	> 2 years	Picado 2014[61]
India (West Bengal)	qPCR, rK39, ELISA	*L. donovani*	246	27 (10.9%)	N/I	≤ 18 - ≥ 45 years	Kaushal 2017[62]
Iran	PCR-ELISA	*Leishmania* sp.	388	95 (24.5%)	N/I	1–35 years	Alborzi 2008[63]
Iran (Ardabil)	DAT, PCR	*L. infantum*	600	23 (3.8%)	N/I	20–61 years	Asfaram 2017[64]
Iran (Fars)	DAT, PCR	*L. infantum*	426	68 (15.96%)	N/I	5–10 years	Fakhar 2008[65]
Iran (Fars)	ELISA, PCR	*L. infantum*	617	17 (2.7%)	N/I	5–8 years	Gigloo 2018[66]
Iran (Fars)	ELISA, PCR	*L. infantum*	251	19 (7.5%)	HIV	14–83 years	Rezaei 2018[67]
Israel	ELISA	*L. donovani*	2580	67 (2.59%)	N/I	18–45 years	Adini 2003[68]
Israel (Kafr Yarka)	ELISA	*L. donovani*	648	67 (10%)	N/I	N/I	Adini 1994
Italy (Bologna)	WB, PCR	*L. infantum*	119	19 (15.9%)	renal transplant candidates	20–94 years	Comai 2020[69]
Italy (Ferrara)	qPCR	*Leishmania* sp.	150	22 (14.6%)	CIRDs	31–72 years	Maritati 2018[70]
Italy (Sicily)	ELISA	*L. infantum*	500	0 (0%)	N/I	N/I	Colomba 2005[71]
Italy (Valsamoggia)	WB, qPCR	*L. infantum*	240	30 (12.5%)	N/I	22–70 years	Ortalli 2020[72]
Morocco	PCR, IFAT	*L. infantum*	200	10 (5%)	HIV	22–68 years	Echchakery 2018[73]
Nepal	PCR	*L. donovani*	418	40 (9.6%)	N/I	2 - > 46 years	Ostyn 2015[74]
Nepal (Dharan)	DAT	*L. donovani*	507	5 (0.9%)	N/I	18–45 years	Timilsina 2016[75]
Spain	IFAT	*L. donovani*	179	6 (3.3%)	HIV	29–33 years	Ena 2014[76]
Spain	IFAT	*L. infantum*	625	30 (4.8%)	N/I	11–81 years	Elmahallawy 2015[77]
Spain	rK39, PCR, qPCR	*L. infantum*	50	29 (58%)	HIV, Myeloma	> 18 years	Molina 2020[78]
Spain (Balearic Islands)	ELISA, PCR, WB	*L. infantum*	122	36 (29.5%)	N/I	N/I	Riera 2004[79]
Spain (Balearic Islands)	WB	*L. infantum*	1437	44 (3.1%)	N/I	N/I	Riera 2008[80]
Spain (Balearic Islands)	WB, qPCR	*L. infantum*	20	20 (100%)	N/I	40–60 years	Jimenez-Marco 2018[81]
Spain (Madrid)	PCR	*L. infantum*	330	47 (14.24%)	N/I	N/I	Ibarra-Meneses 2016[82]
Spain (Murcia)	ELISA, PCR	*L. infantum*	657 and 618	13 (2%) and 49 (8%)	N/I	18–65 years	P é rez-Cutillas 2015[83]
Spain (Province of Grenada)	IFAT, qPCR, PCR-ELISA	*L. infantum*	1260	129 (10.2%)	N/I	18–65 years	Aliaga 2019[84]
Sri Lanka (Anuradhapura)	rK39, MST	*L. donovani*	955	31 (3.2%)	N/I	1 - > 65 years	Ranasinghe 2013[85]
Sudan (Gedaref)	DAT, PCR	*L. donovani*	95	31 (32%)	N/I	≤ 40 and ≥ 40 years	Mohamed 2019[86]
Thailand (Trang)	DAT	*Leishmania* sp.	724	180 (24.9%)	HIV/AIDS	> 18 years	Manomat 2017[87]
Tunisia	WB	*Leishmania* sp.	94	38 (40.4%)	N/I	8 months - 75 years	Saghrouni 2012[88]
Turkey	WB, IFAT, ELISA	*L. infantum*	82	5 (6%)	N/I	1–72 years	Sakru 2007[89]
Turkey (Istanbul)	IFAT	*L. infantum*	188	12 (6.4%)	N/I	19–64 years	Ates 2012[90]
Turkey (Istambul)	PCR, MCM, ELISA, IFAT, ICT	*L. infantum*	343	21 (6.1%)	N/I	18–65 years	Ates 2013[91]
United States (Washington)	ELISA, PCR, IGRA rK39	*L. infantum*	200	39 (19.5%)	N/I	24–60 years	Mody 2019[92]

N/I, Uninformed; DAT, Direct Agglutination test; DTH, Delayed-Type Hypersensitivity; ELISA, Enzyme Immunoabsorbent Assay; ELISA and chromatographic test of antibodies against rK26; ELISA and chromatographic test of antibodies against rK39; FAST, Fast Agglutination Screening Test; FML, Fucose Mannose Ligand; IFAT, Antibody Immunofluorescence Test; IGRA, Interferon Gama Release Assay; ICT, immunochromathographic test; MCM, microcapillary culture method; MST, Montenegro Skin Test; PCR, Polymerase Chain Reaction; qPCR, real time PCR; rK39, Immunochromatographic test rK39; SLA, ELISA based on Soluble *Leishmania* Antigens; SNP, Single nucleotide polymorphism; WB, Western blot; *Liver transplant donor.

and at risk of contracting the parasite, which is the second most prevalent pathogen of parasitic diseases [1]. The selected studies demonstrated that the occurrence of asymptomatic infection by *Leishmania* is common in endemic regions, especially in developing countries such as Brazil and India.

Asymptomatic infection refers to an individual who has had a confirmed diagnosis of Leishmaniasis, without showing signs or symptoms of the disease, common in endemic regions. Sandflies are the main vectors of *Leishmania* and their evolution with mammals are well documented in the literature. Its transmission can follow an anthroponotic or zoonotic cycle. Domestic dogs are the main reservoirs of *L. infantum*, although other mammals are reservoirs of the parasite. A cohort study in Brazil demonstrated, through PCR tests, infection for asymptomatic leishmaniasis in up to 80% of the analyzed dogs. Despite the amount of clinical research, the nature of asymptomatic infection remains poorly understood [10,93–95].

A variety of diagnostic techniques were used across the different study areas. Most studies used combined immunological methods, while others plot molecular and parasitological tests. Immunological assays, although appropriate for regions with a high infection rate, cannot distinguish whether it is an active infection. Molecular methods, on the other hand, have high sensitivity and specificity, but do not indicate whether the infection is active. Parasitological techniques are time consuming, require trained personnel to visualize the parasite and, in asymptomatic cases, parasite identification is limited. It is difficult to diagnose asymptomatic cases due to the low parasite load and low levels of antibodies. The combination of methods raises the threshold for detecting asymptomatic infections in endemic regions [96].

In Brazil, the leishmaniasis control program involves rapid diagnosis and treatment of human cases [97]. Many asymptomatic infection detection techniques are used for the symptomatic form and have already allowed cross-reactions to be avoided. Owing to the low parasite load, combining tests improves performance and provides greater diagnostic certainty. Once asymptomatic infection in humans is identified, its monitoring is essential for the adoption of adequate therapy upon the onset of the first symptoms.

Four *Leishmania* species that cause CL (*L. braziliensis, L. amazonensis, L. major*, and *L. panamensis*) and two species that cause CL (*L. infantum* and *L. donovani*) were identified. *L. braziliensis* has a high prevalence in South America and is associated with mucosal forms. In contrast, *L. amazonensis* is responsible for disseminated forms [98].

The main risk factors for leishmaniasis are climate and environmental changes, socioeconomic conditions, malnutrition, and population mobility [99]. These are common factors in developing countries such as Brazil and India, which are the main countries with a high incidence of CL. In the case of asymptomatic infection by *Leishmania*, because it is “silent,” its incidence is underestimated, although epidemiological surveillance of asymptomatic infection allows for subsidization of prevention measures. The determinants of asymptomatic conditions have not yet been elucidated, but factors such as a high albumin concentration, high levels of vitamin A, high birth weight, and high consumption of red meat can favor asymptomatic infection [100].

In the research on asymptomatic infection by *Leishmania*, the presence of comorbidities such as HIV, malaria, multiple myeloma, and chronic renal failure was also described. In the case of infectious diseases, further studies are needed to verify whether the treatment of these diseases could inhibit the activity of *Leishmania*.

Some patients with immunosuppressive diseases such as HIV/AIDS undergoing antiretroviral treatment have asymptomatic *Leishmania* infection even with an increase in the parasite load, which enhances the infectivity of the vector and consequently transmission of the parasite [52,78]. The condition of individuals with asymptomatic *Leishmania* infection in HIV patients needs further studies to elucidate the immune status that allows this condition.

Asymptomatic *Leishmania* infection has been reported in organ donors [27,31,69] and in blood donors [17,101], thus reinforcing the need for screening in donors in countries that have not yet adopted such screening, especially if they come from endemic areas. To avoid discarding a large number of blood bags from suitable donors with only asymptomatic *Leishmania* infection, leuko-depletion can be adopted, which, in addition to preventing transfusion transmission, improves the quality of blood products [64].

Most of the studies evaluated covered a wide age range, showing that asymptomatic cases can occur from children to the elderly, thus proving that age is not a determining factor for asymptomatic infection. The investigation of asymptomatic *Leishmania* infection is considered a priority to eliminate and reduce the transmissibility of the disease, since transmission remains in these hosts. More studies should be carried out in an attempt to investigate the percentage of individuals who can progress to clinical disease.

The determining factors (such as genetic background, nutritional aspects, and co-infections) for the asymptomatic condition caused by *Leishmania* have not yet been elucidated. Asymptomatic cases are a source of infection and contribute to the endemicity of the disease. Therefore, the detection of asymptomatic infection is important so that treatment can be started in a timely manner if the infection evolves into the symptomatic form, as this increases the chance of a therapeutic response. Studies performed in several endemic countries have highlighted the need to screen blood banks and organ donors, as this allows horizontal transmission through blood and organ donation to be avoided.

Conclusions

Our review demonstrates the worldwide incidence of asymptomatic *Leishmania* infection cases, describing the relevance of the search for alternatives in order to increase the detection rate and reduce the number of cases.

Ethics approval

Not applicable.

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Author contributions

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Data Availability

The authors declare that data supporting the findings of this study are available in the article in the References topic.

Conflict of interest

The authors declare they have no competing interests.

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