

Factors associated with the expansion of leishmaniasis in urban areas: a systematic and bibliometric review (1959–2021)

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Abstract

This work describes a systematic and bibliometric review of the factors that contribute to the expansion of leishmaniasis in urban areas. Three scientific databases were used: *Scientific Electronic Library (SciELO)*, *Scopus* and *Web of Science*, encompassing all original and review articles between 1959 and 2021. Three descriptors were used: “leishmaniasis” AND “urban” AND “rural.” Planning, execution, summarization, and selection processes were performed using *StArt (State of the Art through Systematic Review)* software. We obtained a total of 304 articles, 60 of which concerned canine leishmaniasis. The factors associated with the expansion of leishmaniasis in urban areas are interrelated, including socioenvironmental and economic complexity, the type of leishmaniasis, the reservoirs, vectors, deforestation, disorderly occupation of space, poor sanitary conditions, and human migration trends. A lack of diagnosis and underreporting of cases in some regions may reflect the increase of cases seen in urban areas. A majority ($n = 121$) of studies were conducted in Brazil, followed by Iran ($n = 43$). In relation to publications; in general, output has increased over the years, particularly in 2021. The majority of published studies were in the area of epidemiology ($n = 158$).

Keywords

Cutaneous leishmaniasis, dogs, migration, visceral leishmaniasis

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Introduction

Leishmaniasis are common anthroponoses in tropical and subtropical regions of the world and are caused by protozoa of at least 20 species of the genus *Leishmania*.¹ The parasite is transmitted to hosts through infected phlebotomine vectors and has diverse clinical manifestations, varying according to the *Leishmania* species involved.²

The transmission cycle of leishmaniasis occurs through a reservoir-parasitic interaction.³ Reservoirs are vertebrate animals that harbor the parasite in the wild, which become infected upon biting by vectors, thus favoring the propagation of the cycle.⁴ About 70 animal species, including humans, were reported as natural hosts of *Leishmania* parasites,⁵ however, dogs are reported as the main reservoirs in urban areas.^{4,6,7}

There are three main forms of the disease: visceral or kala-azar, cutaneous and mucocutaneous.¹ Visceral leishmaniasis is the most severe form and is almost

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always fatal if not treated. Most cases occur in Brazil, East Africa and Southeast Asia. In 2017, more than 95% of new cases occurred in Bangladesh, Brazil, China, Ethiopia, India, Kenya, Nepal, Somalia, South Sudan, and Sudan. The most common form of the disease is cutaneous, which is manifested mainly by ulcers on exposed parts of the body. In 2017, more than 95% of new cases of cutaneous leishmaniasis occurred in Afghanistan, Algeria, Brazil, Colombia, Iran, Iraq and the Syrian Arab Republic. The third main form of the disease (mucocutaneous), leads to partial or total destruction of the mucous membranes of the nose, mouth and throat.⁵

Leishmaniasis is one of those diseases classified as neglected, in which diseases characterized by infectious or parasitic causes are included and are considered endemic in low-income populations. Addressing this group of diseases requires collaborative and intersectoral health system efforts and a multidisciplinary approach that considers the environmental complexities where humans and animals coexist.⁸

According to Souza,⁹ leishmaniasis has been a health concern both because of its geographic expansion and because of the trend toward urbanization. According to Bevilacqua et al.¹⁰ the urbanization of diseases usually characterized as rural endemics, such as leishmaniasis, which has always been characterized as a typically rural disease, stems both from the precarious conditions in the peripheries of cities and the articulation of these areas with the rural environment. According to Waitz et al.¹¹ any environmental change that alters the structure of the landscape inhabited by hosts and vectors can modify diseases that occur in humans, either positively or negatively. Along with climate change, man-made actions in the landscape are occurring simultaneously with population growth, potentially altering the availability of habitats for hosts and vectors.¹¹

Faced with this scenario, it becomes necessary to understand the factors that have been changing the ecological space of the disease and consequently expanding its endemic areas. To elucidate this, some questions are raised: What factors contribute to the expansion of leishmaniasis in urban areas? How do anthropic actions interfere with this process? Do migratory movements influence it? Is the disorderly occupation of geographical space a conditioning factor? Is poverty and poor sanitation a reality in regions with registered cases? Are there reservoirs of the disease still little studied?

Based on this assumption, this paper presents a systematic review of studies published between 1959 and 2021, with the objective of understanding the factors that contribute to the expansion of leishmaniasis in urban areas. We also sought to profile the origins of scientific studies, by means of bibliometric indicators. We hope that this work will serve as a resource for future research and reveal research gaps in the subject.

Methods

Initially, a systematic review was performed in three international online databases: *Scientific Electronic Library (SciELO)*, *Scopus* and *Web of Science*, including all original and review articles between 1959 (year of first publication) and December 2021. For this purpose, three descriptors were used in English, combined with Boolean operators: “leishmaniasis” AND “urban” AND “rural” in abstract, title and keywords.

The planning, execution and summarization of this survey, including the filtering and selection of publications, were performed in the StArt (*State of the Art through Systematic Review*) software version 3.4, as shown in Table 1:

For duplicate articles (execution stage), only one was kept for analysis. In some cases, it was necessary to read the articles in their entirety in order to clearly distinguish the importance of the data in the contribution of this work and thus apply the inclusion and exclusion criteria (Table 2).

The publications found in the databases included in this research were also analyzed in order to perform the bibliometric analysis, where it was possible to draw the profile of scientific productions, check their trends and thematic areas over the years 1959 to December 2021.^{12,13} All articles were systematically organized, grouped by region, year of publication and study categories.

Results

The results of this survey were systematized through four main steps. In the initial stage of identification, 571 publications were found, and from their analysis, some were eliminated, according to criteria established in Table 2. Thus, we obtained a total of 304 articles related to the theme, as described in Figure 1.

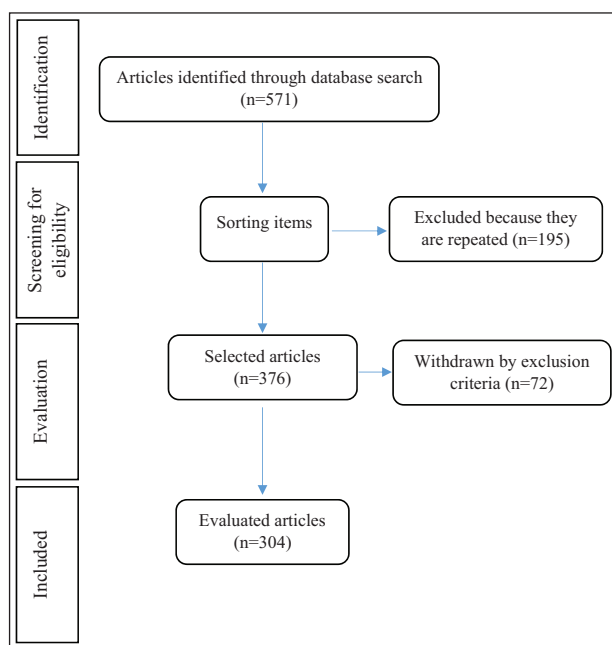
We analyzed the factors related to the dissemination of leishmaniasis and found a number of studies aimed at the reservoir animals of the disease. In total, we found 69 studies specifically conducted in animals, all mammals. Dogs were particularly relevant in research conducted, with a total of 60 studies, followed by cats ($n=2$), bats ($n=2$), rodents ($n=4$) and horse (1). A recent study investigated the presence of DNA and anti-*Leishmania* spp. antibodies in the serum of 112 healthy horses. These animals can be considered environmental bioindicators of the presence of *Leishmania* spp. in Brazil.¹⁴ In order to understand the epidemiology of canine leishmaniasis, many studies were dedicated to serological investigation, where they found the presence of *Leishmania* antibodies in the analyzed samples.¹⁵⁻²¹ Other studies showed the participation of dogs in the process of urbanization^{22,23} and resurgence of leishmaniasis,²² as well as suggesting that the disease is expanding in urban areas, with an exponential increase of positivity within dogs.²⁴

Table 1. Stages of the systematic review in the StArt software.

| Stages | Description |
|---------------|--|
| Planning | - Filling in the research protocol: objective, guiding question, databases investigated, exclusion and inclusion criteria, and the key words in English that represent factors associated with the expansion of leishmaniasis (<i>deforestation, migration, poverty, and sanitation</i>). |
| Execution | - Extraction of articles from databases (in BibTeX format) and insertion into the software (identified by title, authors and year of publication). - The publications were classified in a score from zero to 100, where 100 represented the highest occurrence of keywords in the articles, and zero, the lowest. - The articles were classified in reading priority (low, high or very high). - Evaluation using the selection tool, with articles classified as: accepted, rejected or duplicated. |
| Summarization | - Data visualization, organization by year of publication and transfer to Microsoft Excel program. |

Table 2. Criteria adopted for the inclusion and exclusion of articles.

| Inclusion criteria | Exclusion criteria |
|--|---|
| Articles published in English, Portuguese and Spanish. | Articles related to therapeutic alternatives for the treatment and prevention of leishmaniasis. |
| Articles dealing with leishmaniasis in a specific way. | Studies focusing on insecticides for the control of leishmaniasis transmission vectors. |

**Figure 1.** Selection steps in article identification.

In addition, according to López et al.²⁵ besides the characteristics and behaviors of dogs, their relationship with environmental conditions and disorderly occupations are relevant to the high prevalence of leishmaniasis. In fact, a study conducted in Argentina observed that poverty is a social determinant of risk, resulting in increased probability of contact between humans and infected animals.²⁵

Vector insects that transmit *Leishmania* species, because they are important in entomological surveillance studies, have also been the focus of investigations.^{19,26}

Moreover, the geographical distribution of infected phlebotomine vectors has been analyzed in some studies.^{19,27,28} This makes it possible to detect the areas in which they are concentrated, providing important information for health surveillance actions.

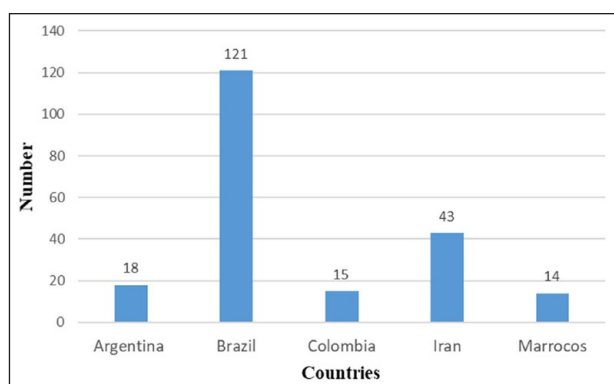
Studies note that factors related to the expansion of leishmaniasis involve the presence of several animal species, both vectors and reservoirs. However, the issue cannot be addressed in isolation, as it involves multifactorial complexity, which according to Conti et al.²⁹ are interrelated variables. Similarly, a review on urban parasitology in Brazil verified the main factors associated with disease expansion, listing three main causes: the large population of urban canine reservoirs, the presence of vectors and human migration.⁷

Among other variables, it is possible to highlight the importance of socioeconomic issues, observed by Gutierrez et al.,³⁰ Lima et al.,³¹ and El Omari et al.³² Furthermore, an epidemiological study conducted with residents of urban areas found a strong association of the disease with socioeconomic conditions, highlighting that the poorest are more exposed to risk.³³ The study by Gutierrez et al.³⁰ even associated the occurrence of leishmaniasis with environmental determinants, a factor also observed by other studies.^{16,34}

Socio-environmental analysis in a city of more than 37,000 inhabitants revealed that the large number of animals, organic material from trees and deficiencies in environmental sanitation possibly contribute to the continuation of the transmission cycle.³⁵ The absence of toilets and sanitation was also highlighted by Ribeiro et al.³⁶ as an epidemiological indicator in urban areas. Similar findings on poor sanitation were pointed out in other studies.^{37,38}

Table 3. Grouping of publications according to study categories.

| Study class | Description | Number of studies |
|--|---|-------------------|
| Methodological comparison | Comparison of methods for vector sampling, comparison of serological detection methods. | 2 |
| Geographical distribution, epidemiology and socio-environmental analysis | Identification of areas of infection, ecological approaches, land use, environmental risks, sanitation conditions of endemic areas. | 21 |
| Geographical distribution, epidemiology and entomology | Spatio-temporal analysis of the presence of insects in sites with recorded cases of leishmaniasis. Identification of vector species. | 38 |
| Entomology | Capture, identification of vector species in endemic areas, analysis of the presence of parasites in insects. | 47 |
| Interviews | Implementation of questionnaires with the population and veterinarians. | 7 |
| Epidemiology | Case studies, clinical aspects, histopathology, prevalence analysis and seroprevalence in humans, dogs, cats, horses, bats and rodents. | 158 |
| Immunology | Eosinophil analysis in blood samples from infected patients. | 2 |
| Reports, bulletins, reviews | Characterization of obstacles faced in disease control, prevention, urbanization, disease status, ecoepidemiology. | 28 |
| Taxonomy | Identification of <i>Leishmania</i> spp. species. | 1 |
| Total | | 304 |

**Figure 2.** Country of origin of published studies on leishmaniasis.

Vilela et al.³⁴ points out that deforestation can facilitate the spread of leishmaniasis. This aspect was also observed in the study by Ramos et al.³⁹ which highlights the main causes of this phenomenon, including the construction of hydroelectric plants, roads and railroads, selective logging, agriculture, cattle raising, and especially the establishment of new settlements.

According to Ghatee et al.,⁴⁰ environmental variables such as land cover, including in urban areas, climate and temperature factors, influence the distribution of leishmaniasis. However, this same study pointed out the proximity of the investigated area to nomadic travel routes, which represented the most important factor in the distribution of the disease.⁴⁰

The influence of migration patterns has also been discussed by other authors.^{7,29,34,41} A study by Mott et al.⁴² on the development of urban parasitologies, including

leishmaniasis, explores this, addressing the relationship between human migration, endemic areas, the ordering of urbanization and the presence of vectors.

Therefore, reaffirming the above, the factors associated with the expansion of leishmaniasis are interrelated, involving social, environmental, economic, ecological and public health complexity. Above all, it is necessary to know the social and geographic scenario where the disease is established in order to develop intervention actions aimed at promoting the health of the population in the main endemic regions.

In this sense, from the 304 articles of the systematic review, for bibliometric analysis purposes, it was possible to verify the geographical location of the published studies, which allowed us to identify and quantify the countries where research on leishmaniasis was carried out. We highlighted those countries with more than 10 studies, and we noted that Brazil represents the origin of most published research, as shown in Figure 2.

After the analysis of origin, articles were organized by study areas, where they were separated by categories and identified by nine different classes, as shown in Table 3.

In relation to the analysis of research output over the years, in general, we have noticed a growth, especially in 2021, as seen in Figure 3.

Discussion

The participation of dogs in the disseminations of leishmaniasis in urban areas is a consolidated theme and is discussed in many studies.⁴³⁻⁴⁹ According to Menn et al.,⁵⁰ canine leishmaniasis is an emerging disease in many parts of the world due to the increasing number of dogs being transported by their owners to different regions, including

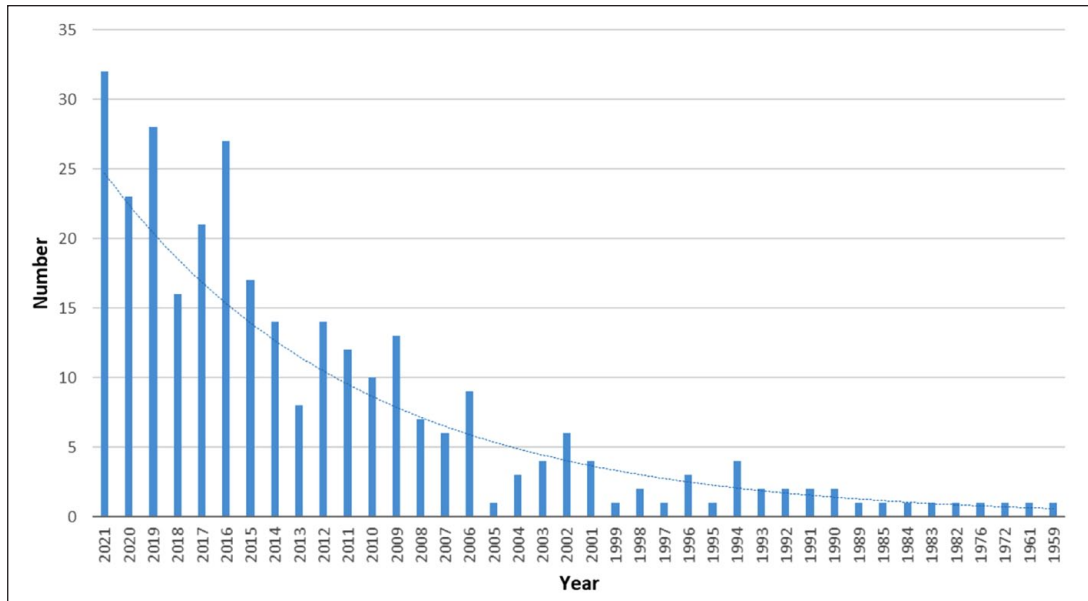


Figure 3. Scientific output from 1959 onward.

non-endemic areas. Also, Deane's study⁵¹ on visceral leishmaniasis conducted in Brazil claims that outbreaks among dogs apparently precede human epidemics, reinforcing the importance of the dog in leishmaniasis transmission.

According to Gontijo and Melo,⁵² there is difficulty in diagnosing canine leishmaniasis, as many tests do not have 100% reliability and specificity. Associated with the broad spectrum of clinical signs, the diagnosis is a challenge for the veterinarian. According to this study, in canine leishmaniasis there are cases of animals that remain asymptomatic for long periods of time and there are also animals that go through oligosymptomatic stages, even those that present with severe illness.⁵²

The contribution of other animals as possible reservoirs of the disease, such as cats, rodents and bats, although noted, is little studied. It's important to highlight the participation of bats in the process of dissemination of leishmaniasis, as there is evidence of *Leishmania* infections in blood samples of these mammals, as observed by Gómez-Hernández et al.⁵³ which is of epidemiological importance due to the absence of cases in the region studied. Although the importance of bats as a reservoir is considered uncertain,⁵³ it is relevant to note that some vector species can live in places also inhabited by bats, for example, in caves, crevices, houses and abandoned buildings, where in these environments bats can be a food source to insects and vice versa. In addition, another factor to be discussed is the high dispersion capacity and longevity of bats, which if infected, can have an important impact on the spread of *Leishmania* parasites.⁵⁴

Regarding vectors, Ramos et al.³⁹ states that some species of phlebotomines tend to synanthropize, due an

increase in food availability and places for rest and oviposition. In settled regions, the presence of domestic and savage animals provides a food source for vectors, thus favoring their adaptation to new environments. Such vector adaptation was also observed by De Melo Ximenes et al.⁵⁵ who verified the distribution of insects in peridomestic areas in northeastern Brazil.

A study of cutaneous leishmaniasis by Oliveira et al.⁵⁶ reports that the presence of potential transmitter phlebotomines of *Leishmania* and their adaptation to human homes is worrying, as it puts thousands of people at risk. The author also noted that the disease was previously considered rural, but in recent years has presented at the urban-rural interface, emerging as an important public health problem.⁵⁶ According to Werneck et al.⁵⁷ this fact is associated with the characteristics of urban areas, where social networks, population density and housing relationships with the natural environment are more varied and complex compared to rural settings.

Although there is favorable evidence for the geographic and epidemiological transitions of leishmaniasis to urban areas, other authors show opposing results. A study of visceral leishmaniasis urbanization in Morocco observed that in spite of the disease is established in urban areas, the geographic distribution of cases has been predominantly in rural areas.⁵⁸ This was also observed in a study conducted in Iran regarding visceral leishmaniasis, where the author noted a higher risk of infection in rural areas.⁵⁹ Confirming this, Almeida et al.³⁷ noted that dogs in rural areas had an approximately twofold higher risk of infection than those in urban environments.

Considering these studies, it is necessary to reflect on disparities of diagnosis and underreporting in various

regions. According to Gontijo and Melo⁵² although leishmaniasis is a notifiable disease, available data are based on passive case detection. The number of people exposed to infection or asymptomatic is in some areas much greater than the number of cases detected.

It is important to highlight that the local environment and risk factors can vary from one region to another, highlighting that the way of life of animals is one of the determinants for acquiring infection.⁶⁰ Besides this, others factors may present particularities in various regions, such as poor maintenance of houses, low socioeconomic conditions, the presence of trees and others vegetation, including in urban areas.¹⁶

Regarding vegetation, areas containing *Adhatoda schimperiana* and *Acacia* spp. are associated with cutaneous leishmaniasis, as they can be important species for the shelter of vectors during the day,⁶¹ and a source of nutrition to these insects.⁶²

Many environmental influences are involved in the dynamics of fauna in anthropized areas. The disordered human occupation of space, the use of landscapes,⁶³ precarious housing, poor sanitation conditions,⁶⁴ climate change, environmental degradation,⁶⁵ deforestation,⁶⁶ reduced investments in health and education, discontinuity of health control actions, and migration of large population to urban centers⁵² are all determinants that shape the epidemiology of parasitic diseases such as leishmaniasis.

Of particular note is the migration of socioeconomic phenomena, such as the search for new employment opportunities in urban environments.⁴² Costa et al.⁶⁷ suggested that migration movements have triggered the visceral leishmaniasis epidemic in Piauí, Brazil where it was observed that the geographic distribution of the epidemic process occurred concomitantly with a long drought, accompanied by widespread migration of people and domestic animals from endemic regions.

The contribution of migration, as well as other factors already mentioned, are characteristics that provide a favorable environment for the transmission of infectious and parasitic diseases in developing countries⁶⁴ such as Brazil, a tropical country with a hot and humid climate.⁶⁸ In addition, Brazil is among those countries with more than 95% of new cases of visceral and cutaneous leishmaniasis registered by WHO in 2017.⁶⁹ This fact possibly justifies the high quantity of studies conducted in the area of leishmaniasis in Brazil, as shown in the results of this research.

Iran was the second country in terms of numbers of studies, and is one of the seven countries listed by the WHO with new cases of cutaneous leishmaniasis registered in 2017.⁶⁹ Alongside other countries of the Middle East and North Africa (Algeria, Libya, Morocco, Syria, Egypt and Yemen), Iran has high rates of neglected tropical diseases,⁷⁰ which arouses the interest of scientists to dedicate themselves to research in this area.

Regarding the study categories, it is clear that epidemiological research is necessary to describe, analyze and understand epidemic processes in quantitative form. In addition, it allows the investigation of factors related to the identification of etiological agents, vectors and reservoirs, so that extent of the problem is known, thus allowing the proposition of effective control measures.⁷¹ However, isolated numbers can be limiting to the researcher who seeks to infer more comprehensive explanations of health events, and who seeks to overcome a potential reductionist or fragmented understanding, characteristic of risk analysis.⁶⁶

Therefore, relevant studies in epidemiological areas are necessary to afford a wider understanding, coupled with interdisciplinary approaches, as well as amassing knowledge about social, anthropological and cultural determinants.⁷²

The quantification of scientific output on leishmaniasis has shown, in general terms, a growth over the years. Such increase in knowledge can contribute to the planning of control measures, as the incidence of visceral leishmaniasis has decreased substantially since 2012 in some regions. In 2015, the incidence of new cases decreased about 67% in Bangladesh, 61% in India and 46% in Nepal.⁷³ In Nepal, medications with anti-leishmanial activity, diagnostic tests with easy handling, and effective vector control methods were primary drivers in reducing the incidence to a historically low level.⁷⁴

In the Americas, a total of 940,396 new cases of cutaneous and mucocutaneous leishmaniasis were reported by 17 of the 18 endemic countries in the period of 2001–2017.⁷⁵ The 17 years historical series showed that in 2015 was registered the lowest number of new cases (46,074); however, as of 2016 there was an increase.⁷⁵ This fact may be related with enhanced reporting of leishmaniasis in 2016. However, in the years 2019 and 2021, there was a growing scientific contribution in the area of leishmaniasis, with emphasis on the publications in the year 2021, which contributes to the improvement of actions, management and control of the disease.

Strengths of this research include the use of systematic review in three databases, associated with a bibliometric analysis. In addition, no restrictions were made regarding the year of the publication, thus including the totality of evidence in the databases. A limitation of this study is the absence of meta-analysis, although this was not the object of the study.

Conclusion

In this systematic review, 304 studies were analyzed, in which it was possible to explore how factors associated with the expansion of leishmaniasis in urban areas are interrelated. Particularities of each region should be analyzed as a whole, considering the socio-environment and economic complexity, the type of leishmaniasis, reservoirs, vectors, deforestation, the disordered occupation of space,

sanitary conditions and human migratory tendencies. A lack of diagnosis and underreporting of cases in some regions may contribute to the findings of this research.

The participation of mammalian species such as dogs in the dissemination of the disease in urban areas is well consolidated, however more studies should be undertaken exploring other species as potential reservoirs as horses and bats.

The analysis of scientific output showed that most studies on the subject were conducted in Brazil, followed by Iran, which represent endemic areas of leishmaniasis. The number of publications, in general, has grown over the years, particularly 2021. Most of the studies were directed to the epidemiological area, and many were also dedicated to investigations in the entomology area and space-temporal distribution.

Contributors

MSB, conceptualized this article, drafted and composed the introduction, results, discussion, conclusion, and references, sections; LBN, participated in the editing and contributed to the methodology and results section; LDSR; contributed to the methodology and references section; VCZ participated in the discussion and contributed to the final reading of the manuscript; GAE, contributed to the methodology and provided mentorship and guidance; PAA, provided mentorship and contributed to the critical review of the content and final proof of the version to be published.

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Patient consent for publication

Not applicable.

Informed consent

The manuscript does not contain any individual person's data in any form.

Significance for public health

Leishmaniasis is one of those diseases classified as neglected. The disease has been a health public concern both because of its geographic expansion and because of the trend toward urbanization. Addressing this group of diseases requires collaborative and

intersectoral health system efforts and a multidisciplinary approach that considers the environmental complexities. Studies note that factors related to the expansion of leishmaniasis are interrelated, involving social, economic, ecological and public health complexity. It is necessary to know the social and geographic scenario where the disease is established in order to develop intervention actions aimed at promoting the health of the population in the main endemic regions.

Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

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