Epidemiology of human visceral leishmaniasis in Pernambuco-Brazil: a descriptive study, 2015 to 2020

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Research Article

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Abstract

Introduction: Leishmaniasis is a systemic pathology caused by a parasite of the genres *Leishmania* which Dogs are the main disease reservoir. The main parasite form of transmission in Brazil is through *Lutzomyia longipalpis* female bite. **Objective:** The objective of this work is to assess the epidemiological profile of the VL in Pernambuco from 2015 to 2020. **Method:** It is observational, descriptive, cross-sectional, and retrospective from secondary dates about LV rates in Pernambuco. Data were collected from DATASUS, SINAN, and IBGE all Brazilian official systems. **Results:** Pernambuco located in the Northeast region of Brazil presented high rates of Leishmaniasis which is a disease with a very intense infection with more distribution in the backwoods of the state. The notification index of the state in the studied period was 175, 118, 185, 200, 181, and 113 respectively for each year. In 2016 there was a reduction of 32% in cases in relation to 2015. There was an increase in 2017 of 56.8%, and in 2018 there was an increase of 8,1%. In 2019 there was a decrease of 9,5% and in 2020 there was the smallest number of cases, a decrease of 37.6%. The mortality average of VL in the state of Pernambuco between 2015 and 2020 was 8.1%. The co-infection of LV with HIV revealed an increase during the years.

**Conclusion:** It was identified that there may be conflict regarding canine euthanasia. In addition, the incidence of Co-infected patients with Visceral Leishmaniasis and HIV is a worrying factor. Also, basic sanitation is the main measure to reduce several neglected diseases, and for that reason the development of social actions to raise awareness against the disease in all aspects is essential.

Introduction

Visceral leishmaniasis (VL) is an anthropozoonosis caused by a protozoan of the genus *Leishmania* spp. It is a neglected tropical disease with pathological development systemic and chronic that can be fatal if it is left untreated briefly. In Brazil, VL transmission occurs vectorially by infected sandflies of the genus *Lutzomyia* in an urban area, which has the promastigote evolutionary form. Dogs or wild animals are the main reservoir of the amastigote evolutionary form of the protozoan [9]. In Brazil, the etiologic agent more prevalent is the species *L. chagasi*, which looks like *L. infantum* and *L. donovani* which are found in the Mediterranean and Asia [18].

The VL can be asymptomatic or with symptoms as the disease reaches the organ and tissues related to the immune system as it hits cells of the phagocytic mononuclear system, because of this factors that decrease the immunity aggravate the clinical symptoms which may lead to death when an association with other pathology [18]. The clinical signs are manifested according to infection degree and the host immunity, such as onychogryphosis, splenomegaly, lymph adenomegaly, dermatitis, and keratoconjunctivitis may occur in different stages of the disease. Diagnosis of VL is performed through patient clinical analysis together with confirmatory serological and parasitological tests. Early diagnosis and treatment of human cases, serological investigation, infected dog elimination, and insecticide employment against sandflies are important criteria for VL control [6].

VL is endemic in several tropical countries in east Africa, Southeast Asia, and Brazil. Since, 2016, worldwide its incidence has reduced by more than 30%. However, the World Health Organization (WHO) proposed the
global elimination of the neglected disease until 2030. Victims affected by Brazil are people living in rural and peri-urban areas, leading to the highest country in the rate of individual infections in Latin America [6] [11]. Annually in Brazil, an average of 3500 new cases are reported nationwide with an overall incidence rate of about 2.0 cases/100,000 inhabitants [10].

The impact of human activity on the environment and population migrations to urban areas mark the epidemiological profile of VL in northeastern Brazil. Since the first report of this disease, it was observed that the spread of VL was punctual in the rural areas in the Northeast, along the time there was an advance for other regions and urban areas. The urbanization process can be attributed to government programs installed for socio-economic development, which favored an economic movement and expansion of urban territory, but in a disorderly way.

In the American continent, there are about 40 sandfly species involved in the *Leishmania spp.* transmission. The main sandflies vector of VL is *Lutzomyia longipalpis*, which is highly adaptable to urban regions, dispersing for about 200 meters in urban areas and 700 meters in rural areas. The mosquito has nocturnal habits, and only females are hematophagous living about 20 days. Their eggs are laid under organic matter and in humid places. An important prophylactic measure is vector reduction, which can be made by using insecticides, and canvas on windows and doors of homes and kennels. To increase vector control, basic sanitation is needed in urban areas, since in the state of Pernambuco the situation of the sewage network is precarious, with little coverage, offering risk to public health [12].

In addition, other factors, such as housing conditions and lack of basic and environmental sanitation increase exposure risk to vector sandflies and consequently, increases the chances of acquiring the infection [3][9]. The objective of this work is to assess the epidemiological profile of the VL in Pernambuco, a state Northeast of Brazil from 2015 to 2020.

**Method**

This is an observational, descriptive, cross-sectional, and retrospective study about secondary dates involving LV disease in the state of Pernambuco – Brazil in the period from 2015 to 2020. The state of Pernambuco is localized in the Northeast region of Brazil, there being 184 municipalities and the island of Fernando de Noronha. The capital of the state of Pernambuco in Recife. The state has an estimated population of approximately 9.6 million inhabitants, occupying an area of 37.86427 mi², representing a demographic density of 34.6 in hab./mi². The nominal monthly household income per capita is US$ 163.30. The synthesis of social indicators, the Gini index is 0.536 [8] and this Brazilian macro-region is marked by social inequalities.

The state of Pernambuco is organized into 12 regions, and it is grouped into four macro-regions based on its geographic features. These are: 1) Metropolitan macro-region; 2) Agreste macro-region; 3) Sertão macro-region and 4) River São Francisco Valley and Araripe macro-region. The macro-region division has been considered for analysis of the dates.

**Availability of data and materials**
The epidemiological analysis was carried out through data collection using a Brazilian system for disease-specific notification (SINAN) and official reports from the Brazilian authorities’ website (DATASUS), where the national surveillance database is hosted. All data collected are in the public domain. The data were collected from information available on the websites TABNET/DATASUS (https://datasus.saude.gov.br/) of the Brazil Ministry of Health. In the Portal, the data were obtained following the steps: The ministry > Access to information > TANBET > Epidemiology and Morbidity > Notifiable Diseases and Conditions - 2007 onwards (SINAN) > Visceral Leishmaniasis (http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sinannet/cnv/leishvbr.def).

Data were trialed according to the variables such as the number of infected per year, gender, age, confirmatory criteria, education level, and coinfection with Human Immunodeficiency Virus, and it was searched according to the year of notification in DATASUS. Demographic and socioeconomic information were included based on a demographic census from the Brazilian Institute of Geography and Statistics (IBGE). The data contained in IBGE is also open to the public domain (https://www.ibge.gov.br/). Data were tabulated by using Excel Microsoft Office 2016 producing graphics and realizing statistical analysis.

Results And Discussion

VL is a pathology considered endemic in the American continent. 97% of the cases reported in 2020 happened in Brazil, and the other cases were reported in Argentina, Bolivia, Colombia, Paraguay, Venezuela, and Uruguay [9]. In Brazil, the region with the highest VL incidence is the Northeast, with about 61% (1767) of incidence in comparison with another region in Brazil as shown in figure1.

In 2016 the incidence in the Northeast was 53% (1490) and 49% (1824) in 2017, in the following years, 2018 and 2019 incidence were 57% (1735;1241 respectively), also year 2020 the incidence was 59% (959) of cases in Northeast. The highest incidence per 100,000 inhabitants was in 2017 which there was in the northeast 3.2/with 1000.000 inhabitants, the North region 4.3/100,000 inhabitants, the Midwest region reported 1.1 cases per hundred thousand, the Southeast 1/100.000 inhabitants, and the South region with 0.1 /100.000 inhabitants.

There was a fall in cases notified in 2020. Cases per hundred thousand in the Northeast were 1.7, North reported 1.6 cases per hundred thousand, Midwest there were 0.5/100.000 inhabitants and Southeast 0.3/100.000 inhabitants. In the region south no cases were reported in 2020 [2]. The Northern and Northeastern regions presented the highest levels of income per 100,000 inhabitants, as the regions present an ascending and uncontrolled urban development accompanied by precarious housing and sanity conditions. These parts of the country, suffer from a lack of effective preventive measures. In addition, climate, and regional vegetation further the population growth of Lutzomyia, as well as more mosquitoes in these regions than in others, thus the most intense infection occurs in these regions. In some cases, the variations in the environment provide niches to the sandflies in a region with lower humidity, lower rainfall, and higher temperature as is the climate present in Brazilian North [14].

Figure 1 shows the case evolution of the LV notification according to the macro-region of Brazil. Brazilian Northeast is a leader in the notification, second is Sullenenest followed by North and Midwest. South region has the lowest incidence. In 2017 and 2018 the Northeast shows that there was a high notification, and it
has a drop in cases in 2020, which can be related to underreporting due to the overload in health sectors caused by the Covid-19 pandemic. Lack of priority is common in neglected diseases and can be led to the reduction of epidemiological control measures and notifications, which poses a risk to public health, as the disease is spreading without the necessary care to control it [2].

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Data indicated in Figure 2 show the evolution of the VL incidence coefficient per 100,000 inhabitants in the state of Pernambuco located in the Brazilian Northeast, between the years 2015 and 2020. The VL incidence in Pernambuco in 2015 was 1.3 per 100,000 inhabitants higher than in 2016 when there was 0.8 per 100,000 inhabitants. In the year 2017, the incidence was 1 per 100,000 inhabitants. Also, in 2018 there were 1.2 per 100,000 inhabitants, while in 2019 were 1.1 per 100,000 inhabitants and in 2020 were 0.7 per 100,000 inhabitants [4].

Pernambuco has a notification index of 175, 118, 185, 200, 181, and 113 respectively for each year. In 2016 there was a reduction of 32% in cases in relation to 2015 and the three subsequent years. There was a significant increase, in the year of 2017 there was an increase of 56.8% concerning the year 2016, and in 2018 there was an increase of 8.1% in relation to the previous year. In 2019 there was a decrease of 9.5% in relation to the year 2018. And in 2020 there was the smallest number of cases, a decrease of 37.6%. [2].

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Figure 3 represents data on notifications of VL between 2015 and 2020 divided by Pernambuco macro-regions. It was observed that River São Francisco Valley and Araripe macro-region in 2015 had the highest rate compared to other regions. The same profile of LV case incidence in this region was observed in 2016 and 2017. River São Francisco Valley and Araripe macro-region is a region with outstanding agriculture and livestock, which is in the city of Petrolina, the largest fruit production center of the state. Thus, the environment propitiates a favorable ambient for mosquito reproduction and propagation, increasing the rate of infected dogs, humans, and other wild animals [19]. That may be the reason, the disease spreads quickly through the River São Francisco Valley and Araripe macro-region [2].

An increase of case notifications in the Metropolitan macro-region in 2018 may be observed in Figure 3, showing an advance of the disease in an urban area. In 2019 occurred an outbreak of the disease in the Metropolitan Region, which was reduced in 2020. One of the reasons why this region has elevated values is because of high population density, due to sanitation problems, and the history of regular floods also other problems [2]. As it is shown in the study made by Buarque et al. (2021) the VL there are more cases in the Agreste macro-region and River São Francisco Valley and Araripe macro-region, but it was observed that because of growing urbanization in the Metropolitan macro-region the VL is increasing [17].

Agreste macro-Region presented the lowest rate of VL-infected people between 2015 to 2016, showing an increase in the following two years and a reduction in 2019 and 2020, as can see in figure 3. The Sertão macro-region presented a similar profile of LV confirmed cases as compared with Agreste macro-Region.
The cases of the LV for the Sertão macro-region showed a relatively controlled oscillation because this region is marked by drought, sparse vegetation, and an area where livestock predominates. The Sertão macro-region does not present a favorable environment for mosquitoes to infect a greater number of the host than other regions of the state because of the dry weather, high thermal amplitude, and little vegetation which reduces the moist places propitious to mosquitoes breeding [2][18].

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From 2017 to 2019 there was a reduction in cases in the River São Francisco Valley and Araripe Macro Region and an increase in the Metropolitan Macro Region, proving that the immigration of the population from rural to urban endemic areas favors the expansion of the disease throughout the state.

The mortality average of VL in the state of Pernambuco between 2015 and 2020 was 8.1%. The co-infection of the LV with HIV revealed an increase during the years (Figure 4). 2020 showed the highest percentage of incidence of co-infection, about 11.5 % of patients with Leishmaniasis and HIV at the same time [2]. As shown in Figure 4, the mortality of co-infected patients has been rising since 2017, a worrying fact and there must be greater control to avoid co-infected patients, and by that the mortality can be reduced [3]. An interaction occurs between HIV and *leishmania* in the host cellular that aggravates the clinical development and increases the lethality rate three times higher than an infection only with VL [16] The coinfection worsens the patient’s clinical condition, and it is a serious health challenge to public health [14].

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To obtain an LV epidemiological profile, table 1 summarizes the distribution of the variables investigated according to the case notification per year. Regarding sex, it was observed higher prevalence of men LV infected. The data reveals an average of 67.2% of male incidence between the years 2015 to 2020. The susceptibility of males has been observed in other studies and it is supposed that higher levels of testosterone are associated with the increase of VL in males [14]. But as it is demonstrated by Buarque et al. (2021) the cause of prevalence in males is unknown and the prevalence could be related to greater traffic of males in the region where the vector is. Another factor is that males do not take care of health and hygiene and do not go to doctor's appointments frequently [17].

As can be shown in Table 1, according to age, it was observed high LV incidence cases in children under 10 years old and adults with age between 20 and 59. The higher incidence in children can be explained by the factor that they have more contact with dogs, which increases the probability of an infected dog passing the disease to a child and their immune system is not mature which favors a lot of neglected diseases [17]. As shown in the study by Lima *et al.* (2018) in children, VL has been associated with malnutrition and poverty and as a method of intervention it is for supplementation of micronutrients then these measures will lead to a healthier childhood, and this could lead to protection against opportunistic pathogens [14], improve the immunity system also can be used in adulthood against various opportunists’ pathologies.

Regarding the LV method of diagnostic laboratory, the method is the first choice to confirm the infection. The clinical analysis is especially important in an endemic region once the correct diagnostic provides more
chance of cure if they follow the suitable treatment. The index of patients that abandoned the treatments is extremely low, there were two patients in 2016 and one in 2020. The percentage of patients that dies due to VL is about 12.5% on average between the years 2015 to 2020.

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Figure 5 shows the percentage of incidence of VL in the schooling profile of VL-infected patients in the state of Pernambuco between 2015 and 2020. According to information from DATASUS, every year there is a higher omission about schooling an average of 40.3% of the total reported cases. In all years, it was observed an increase in the number of the case of patients with early childhood education, followed by elementary, high school, illiterate, and bachelor education. Because of the lack of information, this proportion may not report the reality concerning the education of sick people. This profile can be explained by the fact VL mainly affects people with little education, where an illiterate is eight times more likely to be infected by VL. It is worth mentioning that there is a high incidence in children under 5 years old who are not yet literate. Due to the incidence of omission, the present study is not conclusive to evaluate the real profile of the diseased [15].

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Currently, in Brazil is adopted the strategy of the National Visceral Leishmaniasis Surveillance and Control Program (PNVCLV) that citing euthanasia as a measure to control the pathology in canine reservoirs, as the main standard to prevent the transmission of the disease to a human. Despite being used, this measure must follow the current law and it presents many challenges such as lack of resources and infrastructure, and ethical and emotional issues, which raises the question of how effective this practice is. Alternative methods are sought to avoid canine infection such as vaccination and the use of collars with deltamethrin. These measures should be studied and implemented, mainly in regions with a high incidence as prophylactic measures to prevent the spread of the disease and consequently, control the disease [7]. The spread of the disease is caused by the changes in the agrarian structure of Brazil, mosquito adaptation, malnutrition, and lack of basic sanitation are considered factors that favor urbanization and geographic expansion of VL. In Pernambuco, this factor is quite remarkable due to the socioeconomic situation of the state [15].

The COVID-19 pandemic affected surveillance and control actions across Brazil in actions such as field searches to identify mosquito outbreaks and early diagnosis in dogs and humans, and detailed analysis of endemic cities, among other actions. Until 2019 the disease was endemic with a higher incidence even if there is a strategy to control neglected diseases, the state does not have a significant reduction in cases, which proves that it must increase the vector control measures, identification, and treatment of patients and preventive measures. After the COVID-19 pandemic, the number fell, which can be related to underreporting. Therefore, plans must be made to contain the disease, especially in endemic regions, with treatment for humans, the use of collars in dogs, and vaccines as a preventive method [3].

**Conclusion**
For being a disease that is hard to control due to the complexity caused by infection diversity, parasitic cycle
between humans, dogs, and mosquitoes, weather diversity, and region division, it is recommended that the
public health departments improve control and prevention measures, especially in endemic regions. Basic
sanitation is the main measure to reduce several neglected diseases, thus, it should be a priority for cities.
This study identified that there may be conflict regarding canine euthanasia, although is only possible if
euthanasia is made in infected dogs. The incidence of Co-infected patients with Visceral Leishmaniasis and
HIV is a worrying factor, since the year 2020 there was a significant increase, so measures must be presented
to avoid co-infection since these patients have a higher risk of death. The development of social actions to
raise awareness against the disease in all aspects is essential.

Declarations

Ethical approval and consent to participate: Not applicable as the study does not involve humans or
animals.

Consent for publication: Not applicable

Availability of data and materials: Microsoft excel ® was used to tabulate data which were obtained by
combining some variables available. All data are published on the Ministry of Health website. Available in
<http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sinannet/cnv/leishvpe.def>

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Authors’ contributions: L.S.M., S.M.P., and J.S.G. participation in the design of this work, review, and
validation; L.S.M., J.S.G, and B.V.M.S.C conceptualization, manuscript review, and editing. All authors have
read and agreed to the published version of the manuscript.

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Table 1 is available in the Supplementary Files section

Figures
Figure 1

Evolution of the number of patients with Visceral Leishmaniasis in Brazil divided by macro-region between 2015 and 2020, according to DATASUS.
Figure 2

Incidence of patients with VL per 100,000 inhabitants in Pernambuco state between the years 2015 and 2020, according to DATASUS.

Figure 3

Distribution of the number confirmed cases of VL in macro-regions of the Pernambuco between 2015 to 2020, according to dates obtained from DATASUS.
Figure 4

Percentage mortality rate from patients infected with HIV and VL between 2015 to 2020. Data obtained from DATASUS.

Figure 5

Percentage of VL cases according to schooling between the years 2015 and 2020 in the Pernambuco state. Data obtained from DATASUS.
Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TableEpidemiologyofhumanvisceralleishmaniasisinPernambucoBraziladescriptivestudy2015to2020.pdf