

FORTY YEARS OF VISCERAL LEISHMANIASIS IN THE STATE OF PIAUÍ: A REVIEW

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SUMMARY

Visceral leishmaniasis (VL) has been known to occur in the state of Piauí since 1934. The typically rural disease began to appear in urban areas over time, being concentrated mainly in Teresina, the capital of Piauí. Teresina was also affected by the first urban epidemic of VL in Brazil. Over 1,000 cases of the disease were reported during urbanization (1981-1986). Human population growth and migration led to land occupation on the outskirts of Teresina. These factors have contributed to vector proliferation, increasing the incidence of VL. At present, the incidence of human and canine disease is quite high and uncontrolled in Piauí. It seems that some measures, such as the elimination of seropositive dogs, failed to significantly reduce the number of new VL cases in Teresina. Despite previously conducted studies, little is known about VL epidemiology in urban areas. The aim of this review is to reveal the situation of VL in Teresina during the last 40 years, focusing on the major factors that may contribute to the high incidence and persistence of VL infection.

KEYWORDS: Visceral leishmaniasis; Human; Dog; Epidemiology.

INTRODUCTION

Visceral leishmaniasis (VL) is a major vector-borne disease found in many countries worldwide, occurring in Asia, Europe, the Middle East, Africa and the Americas⁷⁸. At present, VL is internationally considered one of the six highest priority endemic diseases^{17,79}.

In Brazil, VL is caused by *Leishmania (Leishmania) chagasi*. The disease is more prevalent in the Northeastern part of the country⁹. In Piauí, it has been known to occur since 1934. From 1971 to 1979, VL appeared as an endemic disease and the majority of reported cases originated in Teresina. Most cases from inland Piauí originated in the semiarid region. An epidemic sweeping a vast area of the territory has been observed since 1980, concentrated primarily in the urban area of the capital. In that area, over 1000 cases were reported from 1981 to 1986. The epidemic coincided with growth of the population, which rose from 370,000 to 460,000 inhabitants. Most people came from the new districts, migrant settlements in the south and northeast of the city. These people later moved to the northern area where early settlements had been established²⁰.

In 1981, after the discovery of the epidemic, the Piauí Superintendence of Public Health Campaigns (SUCAM) began an active search for human VL cases in all public and private hospitals in the State. Attempts to control the disease began with indoor spraying throughout Teresina. In the state of Piauí, only one round of spraying was performed in other

selected cities. In 1982, the Superintendence initiated a biannual indoor and outdoor entomological survey of sandflies in all the districts of Teresina. A canine survey was also started, using Immunofluorescence Assay (IFA) for serologic testing of all domestic dogs in the city. Systematic elimination of stray dogs or those seropositive for *L. (L.) chagasi* also began that year.

From 1992 to 1995 the incidence of human VL in Teresina was analyzed. A VL epidemic included more than 1140 cases among a population of 650,000 inhabitants. A worse VL epidemic struck in 1993, followed by an epidemic with lower incidence rates which lasted until 1998, when a new growing trend occurred. In the 1990s, mapping the incidence of VL according to neighborhood showed a heterogeneous distribution of disease incidence in Teresina. The frequency of occurrence was higher in the suburbs, which represented the latest area of expansion in the city¹⁹.

The aim of this review is to reveal the VL situation in Teresina, Piauí during the last 40 years, focusing on the major aspects that may contribute to the high incidence and persistence of infection.

VECTOR BEHAVIOR

In Teresina, the highest percentage of insects infected with *Leishmania* sp was found four months after the period of heaviest rainfall, suggesting that environmental factors may foretell not only the abundance

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of sandflies, but also their level of natural infection⁶⁸. It was also observed that the natural infection of *Lutzomyia longipalpis* originated both from infected dogs and wild reservoirs living in neighboring woods³⁷.

Lu. longipalpis is very adaptable to the peridomestic environment. The highest concentration of sandflies occurs between 18h (6 p.m.) and 22h (10 p.m.) peridomestically and between 20h (8 p.m.) and 2h (2 a.m.) intradomestically. It is more common peridomestically than intradomestically^{11,52,61}. The highest frequency rates are observed mainly in the rainy season^{55,61}.

Lu. longipalpis feeds on a wide variety of vertebrate, domestic and wild animals in many regions in Brazil^{11,53,58}. Among other animals, chickens live in close contact with man and are attractive food sources for sandflies in Teresina. In this city, it is common practice to raise chickens^{27,28,32,59}. Therefore, the connection between the domestic and sylvatic cycle of disease transmission may be facilitated by these farm birds. Thus, in some regions, domestic fowl should be seen as a risk factor in the presence of *Leishmania* vectors and hosts in human dwellings²⁸.

In Brazil, several mammals have been found to be infected by *Leishmania* (*L.*) *chagasi*, canids like the fox (*Cerdocyon thous*), the maned wolf (*Chrysocyon brachyurus*), hoary zorro (*Lycalopex vetulus*) and bush dog (*Sphoebus venaticus*), and other mammals such as the marsupial *Didelphis albiventris* and *D. marsupialis*, but only the fox (*Cerdocyon thous*), considered a natural reservoir of visceral leishmaniasis, appears to be important as a link in the enzootic cycle for maintenance of the disease^{26,31,63,65,66}.

Foxes (*Cerdocyon thous*) naturally infected by *L. chagasi* have been observed in dense residual forests, remnants of palm grove forests, near orchards and peridomestically on the outskirts of Teresina. These animals have presented high titers of antibodies protecting against the saliva of *Lu. longipalpis*, suggesting contact between the fox and the VL vector. Serum samples from humans and dogs living in the same area showed less reactivity against vector saliva when compared to fox saliva. These findings suggest that a natural focus of *L. chagasi* transmission exists, regardless of transmission between dogs and humans³. It appears that transmission of VL infection to humans may partly originate from a sylvatic cycle and not depend solely on the presence of infected dogs⁷⁶.

Furthermore, this can be explained by the destruction of natural fox habitats with the occupation of new areas and subsequent reorganization of the food chain. Foxes have frequently been noticed on the outskirts of the city, turning over garbage cans and scavenging for food. A case-control study conducted in these areas showed that about 2% of the population reported seeing one or more foxes in the vicinity of their homes. The risk of being infected with VL was about five times higher among subjects who reported the presence of these animals peridomestically⁷⁴.

Stray dogs from peripheral areas may also come into direct contact with wild animal reservoirs and become infected, subsequently transmitting the disease to other dogs and humans⁴¹.

EPIDEMIOLOGY OF VISCERAL LEISHMANIASIS

At first, VL was mainly a rural disease in Brazil. However, it has recently spread to medium and large urban areas. Some factors may partly

explain why VL was restricted to rural areas until the 1970s and then became endemic and epidemic in major cities in Northeastern Brazil. These factors are primarily related to environmental changes such as uncontrolled deforestation, migration and urbanization^{20,38,51}.

In the city of Teresina, the population increased more than 400% from 1960 to 1990, mainly due to migration from rural areas. In 1990, migrants accounted for more than 50% of the city population⁶⁰. From 1999 to 2008, the population grew more than 100%⁴⁶. Migration took human and canine populations to the outskirts of the city. These migrant populations originated from rural areas where the disease is endemic⁸. Population growth and migration established land settlements on the boundaries of Teresina, near forests and grasslands. In addition, poor sanitation contributed to the accumulation of organic matter and vector breeding that attracted sandflies to urban areas⁴¹.

Chaotic urbanization resulted in precarious living conditions and environmental destruction. This process has influenced disease emergence in urban areas, since the vector *Lu. longipalpis* adapts easily to the peridomestic conditions in impoverished areas, exploring the accumulation of organic matter generated by livestock and poor sanitation^{1,9,73}.

Social and environmental factors were associated with the incidence of human VL in urban areas of Teresina. Remote areas of the city had the highest incidence of disease. An interaction also exists between population growth and vegetation index. Areas with enormous population growth and abundant vegetation showed the highest incidence of disease¹⁹.

Visceral leishmaniasis occurs mainly in tropical areas, such as the state of Piauí. Teresina, the capital of the state, where the disease is endemic, occupies an area of 1,756 km² at the confluence of the Parnaíba and Poti Rivers⁴⁰. It is 72 m above sea level and lies 339 km inland at latitude 05 ° 05' south and longitude 42 ° 48' west. The climate is tropical with an average temperature of 27 °C and total annual rainfall of 1300 mm. The predominant vegetation found in the city consists of grass, shrubs and sparse mango and palm trees. Peri-urban areas are covered by tropical forest and farmland^{13,75}. It is hot any day of the year. Temperatures vary little when the coldest months are compared to the warmest ones, sometimes surpassing 40 °C. The lowest temperature is rarely below 20 °C. Rain has considerable influence on city temperature. The coldest months (December-April) are also the rainiest. It rains about 287 mm mostly in April, which is a relatively heavy rainfall. Similarly, the driest months (June-September) have the highest temperatures. August is the driest month with a very low rainfall (about 13 mm). The hydrographic network that covers Teresina is the Parnaíba River, serving as a natural demarcation for the state of Piauí and the Poti River Basin. The western part of this basin has a greater surface and is inserted in an area of ecological tension. The eastern part of the basin surrounding the headwaters of the tributaries from the left margin with a consequent drainage pattern is inserted in the caatinga. The caatinga dominates the semiarid region of southern and eastern Piauí³⁹.

At present, there are five districts in Teresina subject to more intense VL control. These districts have an average of three to five human cases of the disease and are spread among the Northern, Southern and Eastern/Southeastern zones³⁶. Sewage treatment is still seriously deficient and

extreme poverty prevails in these neighborhoods. Of these 169,771 households in Teresina, only 22,108 (13.06%) have sewage treatment or rainwater⁴⁰. In northern Teresina there is a complex system of lagoons, enveloped in slums with little infrastructure. In this area, there is moderate and intense VL transmission, as classified by the Ministry of Health³⁶.

The high concentration of poverty throughout the large cities of the country determines the existence of 1) a formal city, focused on public investments; and 2) an informal city, lacking in equal benefits. Growth in urban lawlessness accentuates the socioeconomic and environmental differences. Insecurity and lawlessness contribute to the formation of urban spaces without urban attributes⁴².

Areas with poor socioeconomic conditions, such as Teresina, have been associated with an abundance of vectors in urban areas and incidence of canine and human VL^{22,75}. People living in homes with inadequate sewage systems and irregular garbage collection showed a significantly higher risk (four and six times higher, respectively) of developing VL²². Furthermore, canine infection and the incidence of human VL were amplified in these areas⁷⁵. Improvements in house construction and basic urban services could be effective strategies to control the spread of VL in urban areas²².

The association between the leishmanin (Montenegro) skin tests and socioeconomic/environmental conditions in the urban area of Teresina revealed that test positivity was more prevalent among individuals who owned dogs for three years or more, as well as among males and older subjects. Test positivity was lower in more educated individuals living in households with three or less people⁴¹. People living with more than four family members with no basic sanitation had twice the risk of developing VL²².

A change in the circumstances of the disease is found, induced by vector adaptation to a new reality, and it has already become a widely known fact. Deforestation decreased the availability of animals serving as food sources for the sandfly vector in rural environments. Dogs and humans became more attainable alternatives¹⁶. This may explain the invasion of the vector *Lu. longipalpis* in urban areas, increasing the transmission capacity of *L. chagasi*.

Although urbanization of VL has been in progress for over 25 years in Brazil, little is known about the determinants of urban transmission. In urban areas, social networks, population density, housing and the relationship with the natural environment are more varied and complex when compared to rural environments⁷⁷. Furthermore, environmental and climate changes coexist. Investments in health and education have been reduced, thus interrupting VL control and causing the vector to adapt to an environment modified by man. Studies relating to the vector (genetic variants) are lacking. There are also new immunosuppressive factors, such as HIV infection. Disease control is difficult in large urban areas, where malnutrition, housing and sanitation problems are present³⁸.

From 1999 to 2009, 2,498 cases of human VL were confirmed in Piauí. Of these, 1,369 cases were reported in Teresina. The prevalence of disease in the state was 7.70 cases/100,000 inhabitants during this period. In Teresina, the prevalence of VL was 16.34 cases/100,000 inhabitants. From 1999 to 2002, the incidence of VL in Piauí ranged from 4.13 to 6.5 cases/100,000 inhabitants and increased to 14.46 cases/100,000 inhabitants in 2003. Although the incidence of VL decreased to 13.27 cases/100,000 inhabitants in 2004, it still remained high. Between 2005 and 2007, there was a further decrease in the number of new cases. The number increased to 11.22 cases/100,000 inhabitants in 2008 and decreased again in 2009 (8.97 cases/100,000 inhabitants). In Teresina, during the same period (1999-2009), the incidence of human VL was also higher than during the period between 2003 and 2004 (Table 1)⁶⁴.

Data showed that VL is a cyclical disease, with outbreaks repeated approximately every 10 years. There were epidemic peaks in the years 1983/84 and 1993/94. Ten years later, the greatest number of new VL cases was concentrated in 2003/2004, when the period from 1999 to 2009 was studied.

The periodicity of this disease has been explained by the accumulation of susceptible individuals and the frequently cyclical occurrence of natural disasters, such as drought (more frequent) and flooding (as occurred in 2004). These situations determine migration and cause a deterioration in the socioeconomic conditions of the affected populations. At present, the incidence of VL in Piauí is quite high (8.93 cases/100,000 inhabitants) and uncontrolled. The Ministry of Health considers the disease under control

Table 1

Incidence of human visceral leishmaniasis/100,000 inhabitants in Piauí State and Teresina and incidence of canine visceral leishmaniasis/100,000 dogs in Teresina between the period 1999 to 2009

No. cases of VL	Period (1999 - 2009)										
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
No. of cases of HVL in PI	113	176	141	188	423	395	357	280	294	350	281
Incidence/100,000 inhab.	4.13	6.4	4.9	6.5	14.46	13.27	11.87	9.22	9.7	11.22	8.93
No. of cases of HVL in THE	101	127	94	132	234	189	137	107	78	98	72
Incidence/100,000 inhab.	14.6	17.75	12.9	17.84	31.14	24.37	17.37	13.34	10.00	12.34	8.97
No. of cases of CVL in THE	758	1,703	2,930	1,558	1,304	640	540	2,130	2,504	3,573	3,332
Incidence/1,000 dogs	8.43	18.31	30.92	16.19	13.35	6.35	5.26	20.43	24.66	34.62	31.94

VL = visceral leishmaniasis; inhab. = inhabitants; HVL = human visceral leishmaniasis; CVL = canine visceral leishmaniasis; THE = Teresina.

Fonte: Secretaria Estadual de Saúde do Piauí, 2009. Gerência de Zoonozes de Teresina-PI, Brazil, 2009.

if the coefficient does not exceed five cases per 100,000 inhabitants. Teresina is the most affected city in Piauí and that is where efforts to control VL should be intensified.

The dog is the main urban reservoir for the disease, and 20,969 VL-positive canine cases were confirmed from 1999 to 2009³⁵. In general, there is no association between human infection and the number of infected dogs, when compared to human cases. When the number of new cases of Canine Visceral Leishmaniasis (CVL) is low, the incidence of human cases is high and vice versa (Fig. 1, Table 1), suggesting that there is no correlation between the incidence of canine and human VL infection.

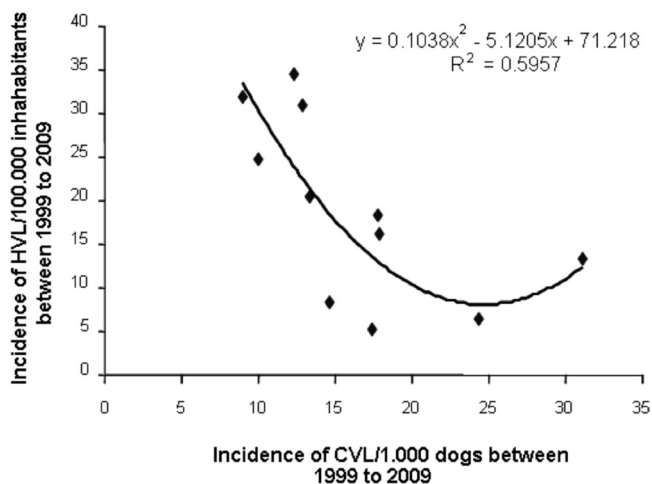


Fig. 1 - Correlation between the incidence of human and canine visceral leishmaniasis between the period 1999 to 2009 in Teresina, Piauí.

Some authors suggest that the elimination of dogs testing seropositive for VL to control the disease did not seriously interfere in the incidence of human cases in Teresina⁷. The situation in three endemic regions of Espírito Santo State were compared, where it was also observed that the elimination of VL-positive dogs did not result in any significant difference in human serologic conversion²⁹. In Araçatuba, however, a systematic elimination of VL-positive dogs tended to decrease the incidence of human VL cases⁵⁴. In Teresina, *L. chagasi* was easily transmitted from dog to dog and from dog to sandfly, suggesting that the infected dog is the main source of human VL. The role of the dog in the infectious disease life cycle is complex and not fully elucidated⁷³.

The prevalence of CVL was 19.27 cases/1,000 dogs from 1999 to 2009. In 2008 and 2009, the incidence of the disease was higher than in previous years (Table 1). The prevalence and incidence rates were very high, despite the elimination of seropositive dogs in the city³⁵. Some factors may explain these rates: a) infected dogs persisted in areas of intense and moderate transmissibility, due to failure to detect infection by serologic testing, thus delaying the removal of seropositive dogs, b) presence of other animal species surrounding the domestic environment, acting as a food source and attracting sandflies, c) replacement of dogs^{6,8,12,25}. In addition, little more than 30% of the canine serologic survey related to the conducted programs. Therefore, the incidence of CVL may be much higher than that observed in data from Table 1³⁴.

HIV AND VISCERAL LEISHMANIASIS CO-INFECTION

Cases of visceral leishmaniasis in patients infected with human immunodeficiency virus (HIV) have been reported in many regions of the world where the geographical distribution of both infections overlap. To date, co-infection with leishmaniasis and HIV has reached 35 countries⁷⁸. There is a significant number of individuals with concomitant HIV and *Leishmania* infection in countries in Southern Europe. In those countries, more than 70% of adult VL cases are associated with HIV/AIDS and 9% of all AIDS patients suffer from newly acquired VL or a disease reactivated from past infection. Overlap between the geographical areas with risk of both infections has recently been accentuated by the urbanization of leishmaniasis and ruralization of HIV/AIDS⁴.

Various studies have demonstrated the epidemiological significance of this simultaneous spread. Patients with HIV/AIDS who live in endemic areas for leishmaniasis have a higher risk of catching the disease. Co-infection with HIV and *Leishmania* also accelerates the clinical course of HIV infection. As a result, leishmaniasis has gained importance as an opportunistic infection among HIV-infected patients who live or have lived in endemic areas for parasites^{4,15}. In Teresina, this fact is no different. An epidemiological and clinical study of HIV/AIDS patients admitted to the Natan Portella Institute of Tropical Diseases (which places emphasis on opportunistic infections) found that 8.2% of recorded cases had contracted VL. All patients originated from endemic areas of VL in Piauí and Maranhão⁶⁹.

The risk of developing VL in endemic areas is about 100 to 1000 times higher in individuals infected with HIV. HIV infection also impairs treatment response and increases the likelihood of recurrence. Both diseases cause cumulative immunosuppression on affected individuals^{44,57}.

Co-infected individuals also play a major role in the epidemiology of the VL life cycle, concerning the potential transmission of *Leishmania* to the sandfly vector. Recent studies conducted in Teresina demonstrated that patients with VL and HIV co-infection seem to be more important reservoirs than people with symptomatic VL. Xenodiagnosis was used to compare reservoir host competence among symptomatic patients with VL and HIV; HIV-negative patients with asymptomatic VL; and HIV-negative patients with symptomatic VL. Patients co-infected with HIV and VL were highly competent as reservoirs and may be sources of infection for other people and animals⁵⁰. This trend indicates that juxtaposition of VL and HIV/AIDS in areas of risk can lead to a rising number of VL cases in young adults. This changes the profile of VL in Brazil and contributes to further urbanization of the disease³⁸.

CLINICAL AND PATHOLOGICAL ASPECTS OF VISCERAL LEISHMANIASIS

Visceral leishmaniasis is a disease with a broad spectrum of clinical manifestations, categorized into three types: 1) asymptomatic form, characterized by positive serology for *Leishmania* without any clinical manifestation; 2) oligosymptomatic form, characterized by positive serology and presence of signs and/or mild symptoms such as fever, mild hepatomegaly and/or splenomegaly; 3) classic form or full-blown disease, characterized by massive hepatosplenomegaly, fever, pancytopenia, hypergammaglobulinemia and severe impairment of one's general health condition¹⁰. Manifestations can progress to: diarrhea, nausea, vomiting,

abdominal pain, nonproductive coughing and progressive weight loss, and indicating advanced stages of the disease: headaches, malnutrition, lower limb edema, anasarca, bleeding, jaundice and ascites. Death occurs in untreated symptomatic patients^{15,17,38,45,56}. In patients infected with HIV, the clinical features may reveal unusual manifestations due to parasite locations in organs that are rarely affected in the course of leishmaniasis in HIV-negative persons, e.g. the esophagus, stomach, rectum, lung, adrenal gland, myocardium, and even the central nervous system³. Disseminated cutaneous lesions have also been observed in intravenous drug users^{14,18}.

Classic VL affects people of all age groups. In endemic areas, 80% of reported cases occur in children under 10 years^{48,67}. The clinical manifestations most frequently associated with death of infected patients include anasarca, lower limb edema, dyspnea, epistaxis, gum bleeding, petechiae, hematuria, melena, jaundice and abnormal lung auscultation. Low hematocrit, hemoglobin and serum albumin, increased total bilirubin; HIV-positive serology on myelogram were shown to be risk factors⁴⁵.

The pathological feature of human VL is similar in different endemic areas. In response to parasitism, hypertrophy and hyperplasia of the mononuclear phagocytic system occurs. Liver lesions of VL are grouped into three patterns. In the typical or classic liver pattern, there is liver enlargement. On light microscopy, numerous amastigotes are observed in Kupffer cells. Focal lymphocytic infiltrate and parasite phagocytosis are observed in the lobules and portal tracts. Immunohistochemistry reveals a large amount of particulate antigenic material in Kupffer cells, intralobular macrophages, portal tract and free antigenic material in the space of Disse. In the nodular liver pattern, generally observed in oligosymptomatic cases and patients with a typical post-treatment pattern, there is Kupffer cell hypertrophy and hyperplasia and formation of mononuclear cell aggregates (macrophages, plasma cells and lymphocytes, mainly CD4+) with a small number of phagocytized amastigotes. In the fibrogenic liver pattern, mild portal and intralobular mononuclear infiltrate, multiple foci of intralobular fibrosis and Kupffer cell hypertrophy and hyperplasia are observed but amastigotes are rarely found. In the spleen, there is marked splenomegaly resulting from the reactivity of the mononuclear phagocytic system and splenic sinusoidal congestion. Hypertrophy and hyperplasia of the mononuclear phagocytic system with many macrophages heavily parasitized by amastigotes are seen through microscopic analysis. A significant decrease in lymphocytes from lymphoid follicles, reduction in T lymphocytes and plasma cell infiltration and macrophages densely parasitized by amastigotes are observed. Eventually, there are foci of amyloidosis in the white pulp or sinusoids. The bone marrow presents hypocellularity of the granulocytic series and blocked maturation of neutrophilic granulocyte lineage. Anemia results from impairment of bone marrow production, splenic sequestration and immune-mediated hemolysis. A decrease in bone marrow maturation and peripheral immune destruction lead to low platelet count. Lymph nodes fail to reveal expressive adenopathy but exhibit reactivity of the germinal center, sinusoidal hypertrophy and hyperplasia, intracellular parasitism of macrophages and plasmacytosis. Follicle volume increases, mainly by reactivity of germinal centers. In severe cases, there is paracortical lymphocyte depletion. The lungs show interstitial pneumonia characterized by thickening of alveolar septa composed of macrophages, lymphocytes, plasma cells and interstitial cells with lipid inclusions. Mononuclear cell infiltration shows no preference for any specific area of the parenchyma. Congestion of septal

capillaries and mild edema also occur. Focal areas of thin septal fibrosis are found in 50% of autopsy cases. Leishmanial etiology of interstitial pneumonitis has also been supported by finding antigenic material in the macrophage cytoplasm and lying free in the interstitial septa. The presence of amastigotes is rare. When visible in specimens, they are located in the macrophage cytoplasm or lie free in the alveoli lumen³⁰.

The clinical and pathological manifestations of CVL are important elements for identifying animals that pose a higher risk of disease transmission. These aspects differ from animal to animal, organ to organ and animals with and without manifestation of the disease⁶². It is known that CVL causes a wide spectrum of nonspecific clinical signs that may be confused with other infectious diseases, complicating the diagnosis^{2,33}. The major clinical manifestations found in symptomatic dogs from endemic areas of Teresina are alopecia, onychogryposis, skin lesions, conjunctivitis, lymphadenopathy and weight loss^{5,49,72}. Based on those results, the presence of one or two clinical signs are not sufficient to arouse suspicion of the disease. VL infection is suspected when the animal presents three clinical signs. Five or more signs can be strongly considered suggestive of VL. Early identification of VL-infected dogs in endemic areas can be facilitated by using this criterion⁷².

VL primarily affects organs of the mononuclear phagocytic system, e.g. the spleen, liver, lymph nodes, bone marrow and skin, causing gross and microscopic lesions. It can also affect other organs such as the kidneys, lungs and heart^{5,23,24,70,72}. Changes in these organs have recently been studied in symptomatic and asymptomatic dogs in Teresina.

The examination of spleen obtained from 36 dogs showed that clinical manifestation of VL progressed with the severity of parasite load in the organ. Histopathological analysis revealed changes characterized by infiltration of neutrophils, granuloma, follicle hyperplasia and T cell depletion. These changes were more intense as clinical manifestation progressed. Follicle depletion was more intense in animals with few clinical signs. Follicle hyperplasia was significantly higher in the canine group that had five clinical signs compared to a group with one and two clinical signs (unpublished data).

In lymph nodes obtained from 25 dogs, the number of parasites was significantly higher in animals showing clinical signs (N = 12) compared to animals with no clinical signs of VL (N = 13). Intense cell hyperplasia of the medullary sinus was also more common in symptomatic dogs than in those asymptomatic. In the liver, focally or diffusely distributed fatty metamorphosis was observed, ranging from minimum to severe in intensity, located in zone 1 of the liver lobule or around the terminal hepatic vein. The portal tract area was widened with inflammatory infiltration consisting of macrophages, lymphocytes, plasma cells and polymorphonuclear cells. In the sinusoids, the presence of polymorphonuclear cells was more evident in some cases and moderately severe in asymptomatic animals. Hyperplasia of Kupffer cells was more common in asymptomatic animals. Intralobular granuloma was more frequent in symptomatic animals (unpublished data).

Analysis of renal changes in 55 dogs naturally infected with *Leishmania (Leishmania) chagasi* indicated a glomerular lesion characterized as minimal, diffuse mesangial proliferative glomerulonephritis, diffuse membranoproliferative, focal segmental glomerulosclerosis, crescentic and chronic glomerulonephritis. Interstitial nephritis was adjacent to

the glomerular lesions. Increased levels of serum protein, creatinine and cholesterol were only observed in cases with concomitant interstitial nephritis and glomerulonephritis. Amastigotes were not found in the kidneys, but parasite antigens were present in all infected animals²⁴.

Cardiac and pulmonary changes related to the presence of *Leishmania* and *Leishmania* antigens were studied in 22 dogs, 15 with clinical manifestations of VL and seven without symptoms. Cytological examination of heart and lung imprints revealed the presence of amastigotes in two symptomatic dogs. Heart imprints were found in an asymptomatic animal. The evidence suggests that cardiac and pulmonary changes do not reflect the degree of disease progression, since the infection is chronic. Professionals are thus educated about cardiac and pulmonary involvement in the disease course of dogs with and without clinical manifestations⁵.

Analysis of skin from 23 VL-infected dogs was performed to identify clinical and pathological parameters that represented immediate risk of parasite transmission to the vector. Findings revealed that six of the nine symptomatic animals were infected by the sandfly, while none of the five asymptomatic dogs was infected by the vector. *Leishmania* amastigotes were present in the skin of all symptomatic dogs, but not in asymptomatic dogs. Parasite load was higher in the ears, ungual region and lower abdomen. In clinically compromised dogs, *Leishmania* amastigotes were few or absent, the inflammatory infiltrate was mainly composed of lymphocytes and macrophages. Lymphocytes, macrophages, and a larger number of polymorphonuclear neutrophils (PMNs) also constituted the infiltrate when many parasites were present⁷².

DIAGNOSIS, PREVENTION AND CONTROL MEASURES

In Teresina-PI, the Management of Zoonoses is responsible for the diagnosis and control of CVL. It carries out a canine serologic survey. IFA and enzyme immunoassay (ELISA) tests are currently recommended by the Ministry of Health (2006). Titles with a cutoff value of more than 1:40 are considered seropositive for IFA¹⁷.

The diagnosis of human VL is performed by the Nathan Portella Institute for Tropical Diseases. For disease control, the Municipal Health Foundation (FMS) of Teresina-PI is employed. In addition to IFA and ELISA (serology tests), parasitological examinations are also performed. For IFA, the result is considered positive when the sample exhibits a title of 1:80. For titles of 1:40, a request for a new sample is recommended within 30 days.

For VL control, entomological surveillance was developed to capture the sandfly using CDC (Centers for Disease Control) light traps. In neighborhoods of intense, moderate and sporadic transmission two rounds of cypermethrin-containing spray (Cynoff) are done per year (first and second semester) to combat the sandfly vector. The goal of spraying is often not achieved because of an insufficient number of sprayers, a lack of insecticide, staff with justified or unjustified absence from work, relocation of personnel and a vigorous rabies campaign in the countryside³⁵, hindering the effectiveness of spraying as a vector control measure.

A study that evaluated the effectiveness of vector control and elimination of infected dogs to reduce the incidence of *L. chagasi* infection compared spraying of homes and outbuildings; spraying of homes and dog culling; spraying of homes and outbuildings combined

with dog culling; and sole spraying of homes. Dog culling was shown to decrease the incidence of *L. chagasi* infection by 80%, when compared to spraying of homes. The removal of infected dogs may reduce the sources of infection for the vector, limiting the capacity of these vectors to transmit the parasite to humans. Spraying of outbuildings, in addition to spraying of homes without dog culling (or dog disposal), was not significantly associated with decreased seroconversion²¹. This was an intriguing result because spraying of outbuildings and dog culling were expected to reduce the incidence of infection.

Preventive measures are directed at human and canine populations as well as the vector. The MH recommends that humans use mosquito bed nets, place fine mesh screens on doors and windows and apply insect repellents. People should avoid exposure in settings where vectors are usually found, especially from dusk to dawn, when these insects are most active¹⁷. These measures, however, are never or almost never adopted by the population of Teresina.

Environmental sanitation should be carried out to prevent vector proliferation²². In Teresina, this practice is rarely followed. Stray dogs are captured by GEZOON. However, there are many difficulties in implementing this service, e.g difficulty in finding addresses, limited access to addresses by car, vehicle problems, change of addresses, closed houses and an insufficient number of ropers/lassoers. The MH also recommends the use of canvas in individual and collective kennels, as well as insect repellent collars with 4% deltamethrin. These measures are rarely or never adopted¹⁷.

Due to these epidemiological characteristics and a limited knowledge of various elements that may form the chain of VL transmission, disease control is still far from effective. Strategies focus on the early diagnosis and treatment of human cases to reduce sandfly population.

FINAL CONSIDERATIONS

Human and canine visceral leishmaniasis has high prevalence and incidence rates in Teresina. Every year new cases of the disease appear, forcing us to rethink control measures. Inadequate sanitation in more than 80% of the city, especially in areas most affected by VL (the suburbs), contributes greatly to this situation. It seems that intense and moderate transmissibility occurs in the peripheral areas of the city, where a large number of low income people live without adequate sanitation.

Further studies should be conducted to better assess the VL control program and determine whether another mode of action against the canine population associated with environmental measures may be more effective at controlling the disease in Piauí. Other reservoirs seem to act in the course of the disease in Teresina, such as the wild fox and human. Despite huge efforts and epidemiological studies concerning VL, little is known about disease epidemiology in urban areas.

RESUMO

Quarenta anos de leishmaniose visceral no Estado do Piauí: revisão

A leishmaniose visceral (LV) é conhecida no Piauí desde 1934. Ao longo dos anos a doença, que era tipicamente rural, passou a ocorrer

também em zonas urbanas, concentrando-se, principalmente em Teresina. Durante o processo de urbanização, Teresina experimentou a primeira epidemia urbana da leishmaniose visceral no Brasil, com mais de 1.000 casos notificados entre o período de 1981 a 1986. O crescimento populacional juntamente com o processo migratório promoveu ocupação de terras na periferia de Teresina que contribuíram para a proliferação dos vetores e aumento da incidência da doença humana e canina no Estado. Atualmente a incidência da doença humana e canina em Teresina é bastante elevada e fora de controle. Algumas medidas, como a eliminação de cães sorologicamente positivos no município, parecem não contribuir de modo relevante para a diminuição do número de casos novos de LV. Apesar dos estudos relacionados aos aspectos epidemiológicos da doença, ainda pouco se conhece sobre o real papel de cães no ciclo da LV. Objetivou-se com esta revisão divulgar a situação da LV em Teresina-PI, nos últimos 40 anos, enfocando os principais aspectos que contribuem para a alta incidência e persistência da infecção.

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