

Visceral leishmaniasis in Brazil: trends and challenges

Leishmaniose visceral no Brasil: evolução e desafios

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Abstract

The urbanization of visceral leishmaniasis in Brazil has been related to environmental changes, migration, interaction and spread of sylvatic reservoirs and infected dogs to areas with no transmission, and adaptation of the vector Lutzomyia longipalpis to the peridomestic environment. From 1980 to 2005, Brazil recorded 59,129 cases of visceral leishmaniasis, 82.5% of which in the Northeast region. Visceral leishmaniasis gradually spread to other regions of the country: in 1998 these other regions reported 15% of all cases, but by 2005 this proportion had increased to 44%. From 1998 to 2005, indigenous cases were reported in 1,904 different municipalities of the country (34.2%). Reservoir and vector control pose major challenges for disease control, since there is a need for better knowledge of vector behavior in urban areas, and control activities involve high operational costs. In recent years the Brazilian Ministry of Health has supported research on the laboratory diagnosis of infection and disease in humans and dogs, treatment of patients, evaluation of the effectiveness of control strategies, and development of new technologies that could contribute to the surveillance and control of visceral leishmaniasis in the country.

Disease Reservoirs; Vector Control; Visceral Leishmaniasis; Urbanization; Epidemiological Surveillance

Visceral leishmaniasis is a zoonosis characterized by chronic evolution and systemic involvement, which if untreated results in death in 90% of cases. It is caused by different species of genus *Leishmania*, and in the Americas *L. (L.) chagasi* is the etiological agent of the disease. Visceral leishmaniasis is transmitted by a vector belonging to the family Psychodidae and genus *Lutzomyia*, and in Brazil the principal vector is *Lu. longipalpis*. In 1998, *Lu. cruzi* was identified as the vector in Corumbá, Mato Grosso do Sul, and evidence of transmission of visceral leishmaniasis by this species was recently described in the municipality (county) of Jaciara, Mato Grosso ^{1,2,3,4,5,6}.

The potential sylvatic reservoirs are fox (*Lycalopex vetulus* and *Cerdocyon thous*) and opossum (*Didelphis albiventris*). Dogs (*Canis familiaris*) are domestic reservoirs of *L. (L.) chagasi* and are identified as the vector's principal source of infection ^{7,8,9,10,11,12}.

Visceral leishmaniasis is endemic in 65 countries, with 500 thousand new cases reported annually, 90% of which are concentrated in India, Nepal, Sudan, Bangladesh, and Brazil ⁵ (with the latter accounting for approximately 90% of cases in the Americas).

The first report of a case of visceral leishmaniasis in Brazil was in 1913, in a patient from Boa Esperança, Mato Grosso ¹³. Afterwards, it was not until 1934 that more cases of the disease were reported, based on post-mortem viscerotomy in 41 patients from the Northeast who had been

suspected of yellow fever¹⁴. Until the early 1950s, only 379 cases of visceral leishmaniasis had been reported, distributed in 13 States, and it was believed that visceral leishmaniasis transmission was exclusively rural or sylvatic^{15,16,17}.

However, in the 1950s, a study in Sobral, Ceará State, showed that of the 177 patients that were examined, 96% had been infected in rural areas such as foothills, hollows, and grottos. Meanwhile 4% (7) of the patients had been infected in the urban area of Sobral, as confirmed by cases of canine infection in a survey¹⁸. Since the 1970s, urbanization of the disease has intensified, especially on the urban peripheries and in the so-called transition zones of medium and large cities¹⁵.

It is believed that urbanization of visceral leishmaniasis results from anthropogenic environmental alterations and the rapid and intense migration of rural populations to urban peripheries that lack adequate housing and sanitation infrastructure, with the concurrent interaction and mobilization of sylvatic reservoirs and dogs infected with *L. (L.) chagasi* to areas without visceral leishmaniasis transmission^{19,20}. Furthermore, it has been observed that *Lu. longipalpis*, responsible for transmission of the disease, has adapted easily to the peridomicile, facilitated by factors still not completely understood, but possibly related to those mentioned above, along with the maintenance of conditions favoring the vector's breeding in this setting and the species' development of capacity to cohabit anthropic environments^{21,22}.

Over the last 30 years, transmission of visceral leishmaniasis has been described in medium and large cities in various Brazilian municipalities, and in particular since the 1980s, cases and outbreaks of human visceral leishmaniasis have been reported, with indigenous transmission within city limits in São Luís (Maranhão), Teresina (Piauí), Natal (Rio Grande do Norte), Aracajú (Sergipe), Fortaleza (Ceará), Rio de Janeiro, Corumbá (Mato Grosso do Sul), and Montes Claros and Sabará (Minas Gerais). In the early 1990s, more municipalities reported outbreaks of visceral leishmaniasis in urban areas, as in Belo Horizonte (Minas Gerais), Feira de Santana (Bahia), Várzea Grande (Mato Grosso), Araçatuba (São Paulo), Aquidauana (Mato Grosso do Sul), and others, and since 2000 new urban epidemics have been reported in the municipalities of Palmas (Tocantins), Três Lagoas and Campo Grande (Mato Grosso do Sul), Caxias, Timon, Codó, and Imperatriz (Maranhão), Bauru (São Paulo), Paracatu (Minas Gerais), Cametá (Paraná), and others^{12,19,23,24}.

With the urbanization of visceral leishmaniasis, from 1980 to 2005 Brazil recorded 59,129

new cases of the disease, with an annual mean of 2,274 new cases. Of all the cases, 82.5% (48,783) occurred in the Northeast region. Visceral leishmaniasis gradually spread to the Central-West, North, and Southeast, increasing from 15% of the cases in 1998 to 44% in 2005. Currently, 20 (74%) of the States of Brazil are recording indigenous cases.

From 1998 to 2005, indigenous cases of the disease were recorded in 1,904 (34.2%) different Brazilian municipalities (counties). Table 1 shows that the number of municipalities with cases of visceral leishmaniasis varies from year to year, as do the means and ranges of cases, suggesting intensification of the disease in some municipalities, as well as the transmission of human visceral leishmaniasis in new municipalities.

Table 2 shows a decrease in the number of municipalities without transmission of visceral leishmaniasis and an increase in new areas with transmission of the disease in the country, but approximately 82% of the municipalities with reported cases are classified as having sporadic transmission (mean of fewer than 2.4 cases in the last 5 years). During the periods analyzed, there was a mean/period of 150 municipalities with intense transmission of visceral leishmaniasis (mean of ≥ 4.4 cases in the last 5 years) and 141 with moderate transmission (mean cases in the last 5 years: ≥ 2.4 and < 4.4), indicating that the cases of visceral leishmaniasis are concentrated in some 5% of Brazilian municipalities (Figure 1).

Despite the increase in cases recorded in the last 12 years, a recent study linking different data sources in the Unified National Health System (SUS) and using the capture-recapture method allowed estimating the cases and underreporting of visceral leishmaniasis in Brazil as a whole and in some specific municipalities. The National Database on Reportable Diseases (SINAN) show 42% underreporting of cases when compared to the visceral leishmaniasis records in the Hospital Information System (SIH) and 45.5% when compared to the Mortality Information System (SIM). Furthermore, this underreporting varied between municipalities, given the different organizational formats in the municipal and hospital surveillance systems²⁵.

The mean incidence of visceral leishmaniasis in the last 12 years was 2 cases/100,000 inhabitants and the case-fatality rate was 5.5%, emphasizing an increase of 117% in 2005 (6.9%) when compared to the case-fatality rate in 1994 (3.2%). The distribution of visceral leishmaniasis in Brazil is cyclical, with an increase in cases at average intervals of some five years, but this trend varies between the different municipalities and States.

Table 1

Distribution of municipalities (counties) by occurrence of visceral leishmaniasis cases and year of reporting. Brazil, 1998-2005.

Year *	Municipalities with cases (N = 5,561)	Mean ± SD **	2nd quartile	Median ***	3rd quartile	Range
1998	521	3.8 ± 9.3	1	2	3	1-113
1999	688	5.3 ± 13.5	1	2	4	1-186
2000	867	5.5 ± 13.3	1	2	5	1-203
2001	839	4.3 ± 9.5	1	2	4	1-121
2002	690	4.5 ± 13.3	1	2	3	1-192
2003	572	5.4 ± 17.9	1	2	3	1-291
2004	728	4.6 ± 12.6	1	2	3	1-177
2005	747	5.0 ± 12.6	1	2	3	1-154

Source: Health Surveillance Secretariat, Ministry of Health.

* Year of occurrence of cases of visceral leishmaniasis;

** Mean number of cases by year and municipality;

*** Median number of cases by year and municipality.

Table 2

Distribution of municipalities with and without reported cases of visceral leishmaniasis, by year of occurrence and stratification of transmission areas. Brazil, 1998-2005.

Period *	Municipalities (N = 5,561)						Transmission			
	With cases		Without cases		Sporadic **		Moderate ***		Intense #	
	n	%	n	%	n	%	n	%	n	%
1998-2002	1,595	28.7	3,966	71.3	1,281	23.0	152	2.7	162	2.9
1999-2003	1,653	29.7	3,908	70.3	1,356	24.4	144	2.6	153	2.8
2000-2004	1,642	29.5	3,919	70.5	1,380	24.8	125	2.2	137	2.5
2001-2005	1,650	29.7	3,911	70.1	1,366	24.6	143	2.6	151	2.7

Source: Health Surveillance Secretariat, Ministry of Health.

* Five-year period;

** Municipalities with a mean of ≤ 2.4 cases of visceral leishmaniasis in the five-year period;

*** Municipalities with a mean of > 2.4 and < 4.4 cases of visceral leishmaniasis in the five-year period;

Municipalities with a mean of ≥ 4.4 cases of visceral leishmaniasis in the five-year period.

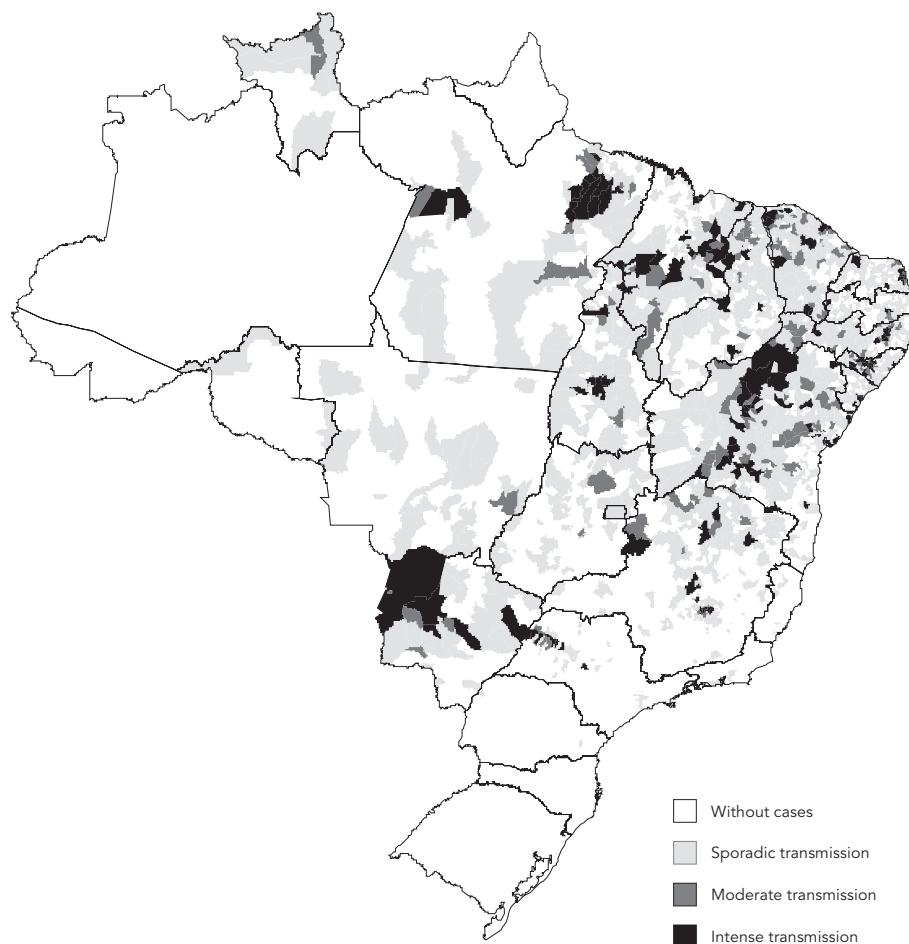
According to available data in the SINAN, from 2001 to 2005 the disease was distributed in the various age brackets, but occurred most frequently in children up to 10 years (56.7%), with 43.4% of cases in children under five years. Males are proportionally more affected (60.4%). In Brazil, visceral leishmaniasis shows a varied epidemiological profile due to climatic, physiogeographic, biological, and social characteristics that vary according to region and that interact to produce the disease. An example is the statistically significant differences in the age pro-

file of human visceral leishmaniasis in the city of Teresina as compared to Campo Grande and Belo Horizonte (Table 3).

Based on observations, the change in the transmission pattern of visceral leishmaniasis from the countryside to cities, associated with the interiorization of AIDS in Brazil, has led to *L. chagasi*/HIV coinfection. According to SINAN data, the number of cases of coinfection increased from 21 in 2001 to 86 in 2005. This trend indicates that the juxtaposition of visceral leishmaniasis risk areas and HIV/AIDS may lead to

Figure 1

Stratification of visceral leishmaniasis areas according to transmission risk. Brazil, 2005.



Source: Health Surveillance Secretariat, Ministry of Health.

an increase in cases of visceral leishmaniasis in young adults, thereby altering the profile of the disease in Brazil.

A recent evaluation of the SINAN, visceral leishmaniasis, and AIDS databases showed 176 cases of visceral leishmaniasis/AIDS coinfection. Mean age was 37 years and median age was 38 (± 1.1), predominantly affecting males (78%), with black individuals accounting for 53.4% of cases. Among the exposure categories for HIV/AIDS, heterosexuals accounted for 56.3% of the cases, with a statistically significant difference between the genders ($p < 0.001$). The States with the highest shares of the total number of patients with visceral leishmaniasis/AIDS coin-

fection were: Maranhão (16.5%), Minas Gerais (14.8%), São Paulo (13.6%), and Mato Grosso do Sul (9.1%)²⁶.

The objectives of visceral leishmaniasis surveillance are to reduce the disease's morbidity and mortality rates through early diagnosis and treatment of human cases and to decrease the risk of transmission by controlling the populations of domestic reservoirs and vectors¹².

The control strategies used in Brazil should be integrated and focused on diagnosis and adequate treatment of human cases, monitoring and euthanasia of seroreactive dogs, environmental management, and chemical control¹². A consultation of experts on visceral leishmaniasis held

Table 3

Cases of visceral leishmaniasis according to age bracket in the municipalities of Teresina (Piauí), Campo Grande (Mato Grosso do Sul), and Belo Horizonte (Minas Gerais), Brazil, 2001-2005.

Age bracket (years)	Teresina		Campo Grande		Belo Horizonte	
	n	%	n	%	n	%
< 5	294	63.2	102	28.4	97	25.6
5-19	52	11.2	85	23.7	86	22.7
20-49	102	21.9	122	34.0	163	43.0
≥ 50	17	3.7	50	13.9	33	8.7
Total	465	100.0	359	100.0	379	100.0

N.B.: p-value for comparison of Teresina and Campo Grande < 0.001; p-value for comparison of Teresina and Belo Horizonte < 0.001.

Source: Database on Reportable Diseases (SINAN).

by the Pan-American Health Organization in November 2005 presented, discussed, and approved these guidelines for the Americas²⁷.

Among the measures recommended for visceral leishmaniasis control, euthanasia of infected dogs is still a controversial point, but studies indicate that the disease in dogs precedes the appearance of human cases and that the odds of infection for humans increase in areas with high prevalence rates of canine infection where the vector is present²⁸. It was also shown that elimination of infected dogs is the single most cost-effective measure for reducing human incidence²⁹.

As for vector control measures, insecticides are widely used, but they vary as to efficacy^{30,31}, duration of impact, and the resources required for different endemic areas³². The combination of chemical treatment of buildings and environmental management has proven effective in reducing vectors in the intradomiciliary setting³³. Data from a recent study on control strategies in an urban area showed that chemical control and elimination of infected dogs, singly or jointly, reduced the incidence of human infection in 18 months by 24% to 39%³⁴.

Despite well-defined guidelines for the control of visceral leishmaniasis and the investments made in organizing services and developing the proposed activities, vectors and reservoirs in urban areas pose the greatest challenges for the program to control the disease, given the need for better understanding of the vector's behavior in the urban setting, operational difficulties for per-

forming the activities in sufficient time to impact the results, and the high cost of implementing the proposed measures. In relation to the vector, it is necessary to identify the factors that actually impact the control of *Lu. longipalpis*, given its high capacity to recolonize the urban environment and the complexity of identifying the sites with immature forms of the sand flies. Use of information like the vector's presence or absence, abundance, and infestation in the intra- and peridomicile is still limited for estimating the risk of transmission of visceral leishmaniasis, since there are no established parameters for such indicators.

The international scientific literature has presented some alternatives for visceral leishmaniasis vector and reservoir control, such as: dipping dogs with insecticides, vaccines, and pyrethroid-impregnated collars, among others. Some of these alternatives have shown satisfactory results, while for others the results are still inconclusive, and investment in further research is needed.

In recent years, the Brazilian Ministry of Health has invested in the search for new knowledge and alternatives for the control of this endemic. The main lines of research focus on the implementation of human and canine laboratory diagnosis, treatment of visceral leishmaniasis patients, evaluation of the effectiveness of vector and reservoir control strategies, and new technologies that can contribute to the implementation of surveillance and control measures for visceral leishmaniasis in the country.

Resumo

*A urbanização da leishmaniose visceral tem sido relacionada a modificações ambientais causadas por ações antrópicas, pelo rápido processo migratório, pela interação e mobilização de reservatórios silvestres e cães infectados para áreas sem transmissão, e pela adaptação do vetor *Lutzomyia longipalpis* ao peridomicílio. Entre 1980 e 2005, o Brasil registrou 59.129 casos de leishmaniose visceral, sendo 82,5% na Região Nordeste. Gradativamente, a leishmaniose visceral expandiu-se para as regiões Centro-Oeste, Norte e Sudeste, passando de 15% dos casos em 1998 para 44% em 2005. Entre 1998 e 2005 foram registrados casos autóctones em 1.904 (34,2%) diferentes municípios brasileiros. O controle vetorial e de reservatórios representam os maiores desafios para o controle da doença, dada a necessidade de melhor conhecer o comportamento do vetor no ambiente urbano, as dificuldades operacionais e o alto custo de execução. Nos últimos anos, o Ministério da Saúde tem investido em pesquisas sobre diagnóstico laboratorial humano e canino, tratamento dos pacientes, avaliação da efetividade das estratégias de controle, bem como de novas tecnologias que possam contribuir na implementação das ações de vigilância e controle da leishmaniose visceral no Brasil.*

Reservatórios de Doenças; Controle de Vetores; Leishmaniose Visceral; Urbanização; Vigilância Epidemiológica

Contributors

A. N. S. Maia-Elkhoury was responsible for the literature review, analysis of part of the data, and the article's overall description. J. M. Sena was responsible for the entomological information. M. L. Sousa-Gomes prepared the databanks. W. A. Alves was responsible for the information on reservoirs. E. A. Luna conducted the overall revision of the article and made contributions to all the sections. All the authors reviewed the final version.

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