Time series of visceral leishmaniasis in Aracaju, state of Sergipe, Brazil (1999 to 2008): human and canine aspects

Série temporal da leishmaniose visceral em Aracaju, estado de Sergipe, Brasil (1999 a 2008): aspectos humanos e caninos

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Support: MCT/CNPq/MS-SCTIE-DECIT – Process 410481/2006-8

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Abstract

Introduction: Considered as a neglected disease by the WHO, **visceral leishmaniasis** (VL) has expanded and urbanized. Its transmission and expansion have been linked to several factors. **Objective:** To evaluate the epidemiological aspects of VL in the city of Aracaju/SE, through retrospective studies of the historical series of human and canine VL in the 1999-2008 period. **Methods:** Secondary data from SINAN (Information System for Reportable Diseases) for human cases were used. Data from canine surveys and from the Zoonosis Control Center´s (ZCC) passive demand were used for canine cases. **Results:** 192 autochthonous cases of human VL were reported, and 63.5% were male. Children aged 1-4 years were the most affected (29.2%), followed by adults aged 20-29 years (15.6%) and children aged 5-9 years (15.1%). General mortality was 8.9%, and it was higher for the 60-69 year age group (60%); 32.3% of autochthonous cases performed serology for HIV, with a 6.9% positivity. Laboratory results were confirmed mostly by indirect isolated immunofluorescence (71.1%). 58,161 dogs were serologically tested for VL, with a positivity rate of 5.4%, while 87.0% of the surveys conducted annually by the ZCC, have a 4.4%positivity rate for VL. Of the 7,501 dogs that were brought to the ZCC for multiple complaints, the serological test was positive in 12.0%. **Conclusion:** Data show the endemicity of VL in the city, revealing the need for actions to reduce the risk of the population, mostly for the group with higher incidence and mortality, such as improvement in the diagnosis of VL and its HIV-associated infection, along with monitoring of the dog population, among others.

Keywords: Visceral leishmaniasis. Epidemiological profile. Urbanization. Concomitant diseases. Zoonose. Fatality.

Resumo

Introdução: Considerada doença negligenciada pela OMS, a Leishmaniose visceral (LV) tem se expandido e urbanizado, sendo sua transmissão e expansão associadas a diversos fatores. **Objetivo:** Avaliar aspectos epidemiológicos da LV no município de Aracaju/SE, por meio de estudo retrospectivo da série histórica de LV humana e canina no período de 1999-2008. **Métodos:** Foram utilizados dados secundários do SINAN para os casos humanos, e o resultado dos inquéritos caninos e atendimentos da demanda passiva do Centro de Controle de Zoonoses (CCZ). **Resultados:** Foram notificados 192 casos autóctones de LV humana, sendo 63,5% do gênero masculino. Crianças entre 1 e 4 anos foram mais acometidas (29,2%), seguidas de adultos entre 20-29 anos (15,6%) e de crianças entre 5-9 anos (15,1%). A letalidade geral foi de 8,9%, sendo mais acentuada em pessoas entre 60 a 69 anos (60%); 32,3% dos casos autóctones realizaram sorologia para HIV, com positividade de 6,9%. A confirmação laboratorial foi realizada principalmente mediante a imunofluorescência indireta isolada (71,1%). Dos 58.161 cães que realizaram sorologia a positividade foi de 5,4%, sendo 87,0% dos inquéritos realizados anualmente pelo CCZ, com uma positividade de 4,4%. Dos 7.501 cães trazidos ao CCZ por diversas queixas, o exame sorológico foi reagente em 12,0%. **Conclusão:** Os dados denotam o caráter endêmico da LV no município, mostrando a necessidade de ações que permitam a diminuição do risco para a população, principalmente aquela onde a incidência e a letalidade são maiores, como melhorias no diagnóstico da LV, assim como na co-infecção com HIV e no monitoramento da população canina, entre outros.

Palavras-chaves: Leishmaniose visceral. Perfil epidemiológico. Urbanização. Doenças concomitantes. Zoonose. Letalidade.

Introduction

Visceral leishmaniasis (VL) is endemic in 70 countries in tropical and subtropical areas of four continents. The main sources of human infection are located specifically in Southeast Asia (300,000 cases in 2006) in western Africa (about thirty thousand cases in 2006) and the Americas (four thousand cases in 2006). New outbreaks have emerged in Africa and its incidence has increased, despite high rates of underreporting[2]. Worldwide, over 90% of cases occur in six countries - Banglandesh, Brazil, Ethiopia, India, Nepal and Sudan. According to WHO estimates for the year 2007, there are about 500,000 new VL cases per year and over 50,000 deaths[1,4]. The mean mortality rate in the period of 1984 to 2004 was 6.3%. However, at this period it´s seen an increase of 100%, from 3.6% in 1984 to 7.4% in 2004[3].

The essentially sylvatic transmission cycle of VL in rural areas in recent decades has shown changes in its pattern as a result of socio-environmental changes, such as deforestation and the migration process product of the rural exodus to the suburbs of big cities. This dynamic is variable in the different places of occurrence as a function of variables related to parasites, vectors, ecosystems and social processes of production and use of the land[5]. In Brazil the VL is currently distributed in five regions, although the Northeast still focus about 56% of human cases[6]. On the other hand, the VL as urban epidemic has been observed in several cities, and it has been verified including in concomitant and opportunistic infections in individuals affected by HIV/AIDS, similar to what is found in southern Europe[7,8].

The role of dogs as domestic host of VL is well established. The canine infection precedes the onset of human cases. Most dogs that have positive serology don´t show symptoms of the disease but act as excellent hosts with high virulence for vectors[9]. On the other hand, in urban areas the canine enzootic diseases have manifested themselves with a higher prevalence than in men.

In the wild environment, the main hosts are foxes and marsupials[16].

The VL popularly known in Brazil as calazar, although it present itself in an endemic way in our country, it reveals an epidemic potential and a great chance of urban occurrence. The current epidemiological profile of VL, both in areas where transmission occurs in natural enzootic foci and those in periurban and peridomestic transmission, involving domestic hosts, is different from that which was seen years ago[10,11]. The disordered human occupation of the suburbs of cities, still bordering the sylvatic forest, proliferates precarious houses with gardens which are home of domestic animals and livestock, favoring the contact host-vector-man and therefore the onset of cases, thus contributing to the increase of the incidence of the disease[12].

In urban areas of developing countries, the way the population is organized into large settlements with houses without adequate sanitation, are increasing the chance of transmitting diseases such as leishmaniasis, leading to what has been reported by some authors as "ruralization of the living conditions" in some urban areas of cities. Somehow, this type of urbanization contributes to the overall increase in morbidity[13,14]. In the process of urbanization of the VL in Brazil, besides the environmental changes caused by human actions and current rural-urban migration, it is seen a constant adaptation of L. longipalpis, the main vector responsible for transmission of the disease to the human peridomestic[15,16].

In the state of Sergipe, since the first description of a human case of VL by Evandro Chagas, it has been identified new ocurrences. In the '30s, 40s and 50s, 28 cases were recorded. In the period from 1972 to 1998, 1874 cases were reported, while from 1999 to 2006, 433 cases of the disease were reported in the state. In this latter period, until the year 2003 there is a downward trend in the number of cases, but thereafter the incidence is rising[17,18].

Considering the importance of VL in Aracaju / SE, capital under intense process of urban expansion, it is essential to better understand the dynamics of the transmission of this parasitic infection. In this context, this study aimed to assess the main epidemiological features of VL in the city of Aracaju / SE in the period from 1999 to 2008.

Methods

Study area. Municipality of Aracaju, capital of Sergipe state, located in northeastern Brazil. Aracaju has a population of 460,898 inhabitants spread over an area of 181.8 km², with a population density of 2,535.19 inhabitants per km². According to the IBGE of 2000, 53% of Aracaju´s inhabitants are female, and they are distributed according to following age group: 8.9% from 0 to 4 years, 8.8% between 5 and 9 years, 21.5% between 10 and 19 years, 20.1% between 20 and 29 years, 15.6% between 30 and 39 years, 11.2% between 40 and 49 years, 6.8% between 50 and 59 and 7.1% higher than 60 years[33].

The distribution of average annual rainfall is 1590 mm with an average annual temperature of 26 ° C. The rainy season is from March to August[19].

The municipality for health care is divided into eight health regions and has a coverage of approximately 90% of family health strategy.

Data sources. For the assessment of human VL there were used data on confirmed cases reported in the Information System for Notifiable Diseases (SINAN) for a period of ten years (1999-2008), from the Coordination of Epidemiological Surveillance of the Aracaju´s Municipal Secretary of Health.

Data for canine infection in the period of 1999-2008, originated by the passive demand and active search (canines' surveys), were obtained along with the Center for Zoonosis Control (CCZ) in Aracaju, linked to the Municipal Secretary of Health.

The human population of the city under study used in the calculations of incidence rates was obtained from the IBGE databases and their projections. Data on population

and geographical area of the districts were obtained from the Municipal Secretary of Planning. These data are grouped according to the eight health regions, used by the Municipal Secretary of Health for planning and implementing actions related to public health in the municipality.

Statistical Analysis. The data were extracted from SINAN with the use of the application TABWIN (DATASUS). It was performed a descriptive analysis from graphs and tables, and calculated incidence, relative risk (RR) and frequency distributions coefficients. It was applied the Pearson correlation test to investigate possible correlations between age, gender, and incidence coefficients.

Results and Discussion

A temporal series of VL in Aracaju/SE, between January 1st of 1999 and December 31th of 2008, reveals the notification of 270 human cases, 192 (71.1%) of them natives. The annual average of 19.2 cases ranks the municipality as an area of intense transmission of VL. The annual incidence rate ranged from 1.1 to 9.0 cases per 100 000 inhabitants during the studied period (Figure 1A), showing a cyclical epidemic behavior observed in VL, with an increase in the number of cases every five years. In most of the decade, the incidence rate remained higher than the average Brazilian mean, which is 2 cases per 100 000 inhabitants[8].

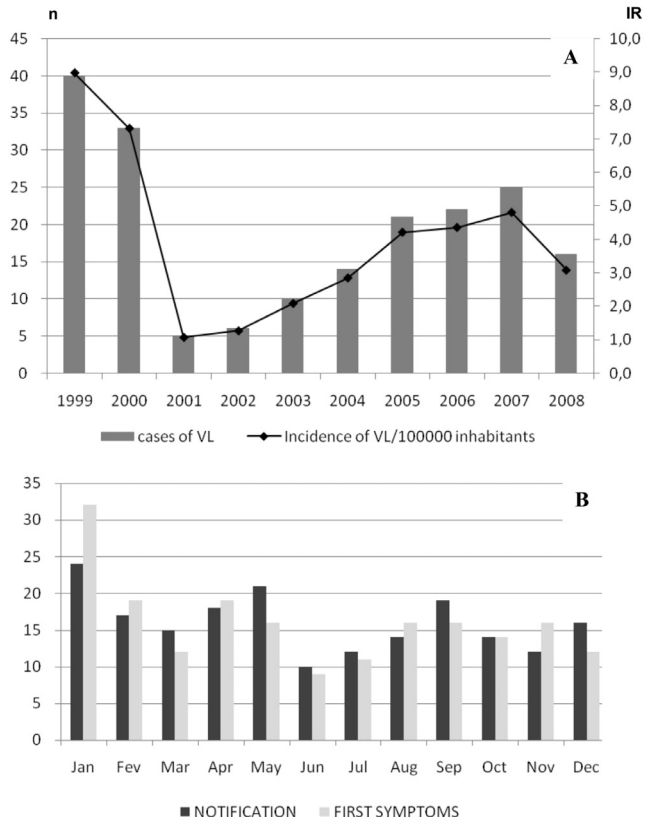
The correlation between the emergence of human cases of VL and seasons is very difficult due to the long incubation period of disease, the subacute clinical manifestations and the elapsed time between the onset of symptoms and the diagnosis. The annual curve of the disease´s onset shows that VL occurred in all months of the decade (Figure 1B), with the highest concentration of reports in the month of January. As in other studies it is observed a homogeneous distribution of cases during the months of the year, regardless of weather changes, which hinders the establishment of a more appropriate time for vector control interventions based only on the occurrence of human cases[21, 22, 23].

192 of the autochthonous cases of human VL in Aracaju, 63.5% (122) were male. Excepting the years 2003 and 2007 in all other years of the series, the relative risk of illness by VL was higher in males (RR = 1.98, p <0.00001). When evaluated as incidence and gender rates of individuals affected by the VL, it was found a strong correlation between the male and the increase in CI (p <0.028).

Several studies indicate a higher susceptibility of males to this parasitosis, not only proportionally, but also when assessing the annual incidence rates by gender (Figure 2A). However, this differential susceptibility between the genders was not observed in children under four years. Hormonal factors linked to exposure to the vector have been blamed for the increased risk in males older than four years[21, 6, 24].

VL presented itself more frequently in children between 1-4 years, with 29.2% (56) of the total cases, followed by adults aged 20 to 29 years with 15.6% (30) and children aged 5 to 9 years with 15.1% (29) (Table 1). The coefficients of annual incidences were higher in children up to 9 years, confirming the risk of illness caused by VL in this age group in almost every year in this historic series (Figure 2B). The reason for the higher susceptibility of children has been explained by the relative immaturity of immune aggravated by malnutrition so common in endemic areas of VL in the Northeast[25]. When calculating its incidence in the age group 1-4 years in the studied period, it confirms the risk increased four times in this population group, with 152.9 cases per 100 000 inhabitants. The Pearson correlation test showed a negative correlation, which shows that with increasing age, the incidence of VL decreases (P <0.001).

The overall fatality rate in the period was 8.9% (17), which was more pronounced in individuals aged 60 to 69 years with 60% and between 50 and 59 (55.8%). In young adults (20-29 years) it was observed a high mortality rate (20%), similar to reports from

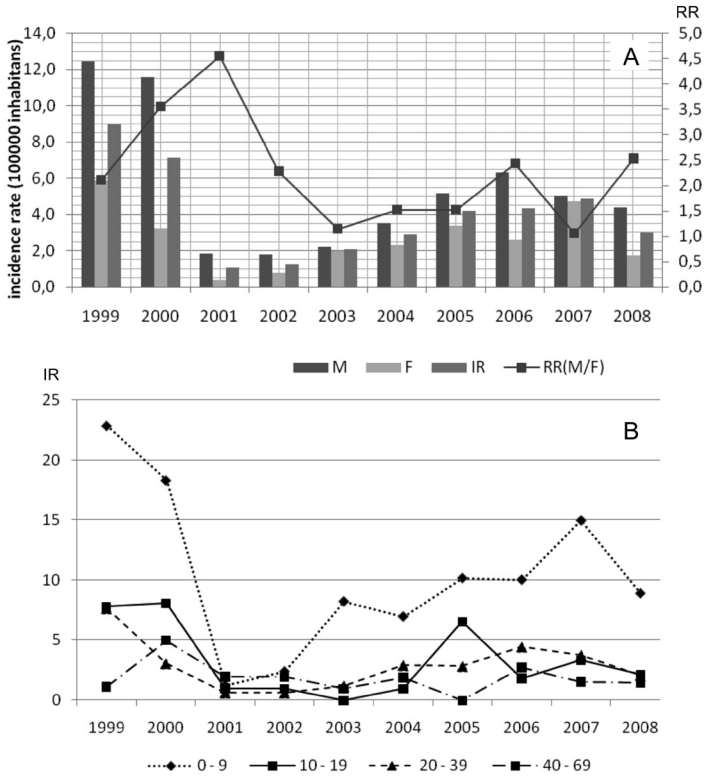


Figures 1 - A - Number of autochthonous cases and incidence rate of annual human visceral leishmaniasis in Aracaju/SE, from 1999 to 2008. **B** - Monthly distribution of autochthonous cases of human VL by month of onset of symptoms and diagnosis in Aracaju/SE, 1999 to 2008.
Figuras 1 - A *- Número de casos autóctones e coeficiente de incidência anual de leishmaniose visceral humana em Aracaju/SE, 1999 - 2008.* ***B*** *- Distribuição mensal de casos autóctones de LV humana,segundo o mês de início dos sintomas e de diagnóstico em Aracaju/SE, 1999 a 2008.*

other states' capitals such as Belo Horizonte (8-17%), São Luís (6.7%), Natal (9.0%) And Brasília (9.2%)[34]. In the latest years, VL mortality rate in Brazil has increased gradually, from 3.2% in 1994 to 6.9% in 2005, representing an increase of 117%[29,8]. Among the main factors that contribute to increase the mortality rate are late diagnosis and the epidemic expansion affecting groups of individuals with co-morbidities. Infectious complications and bleeding are the major risk factors for death in VL[26, 27, 28, 29, 24].

In the studied period, only 32.3% (62) of autochthonous cases of human VL had HIV serology, with a positivity of 6.9% (4). HIV co-infection has been reported in 212% of VL cases worldwide, but it can reach rates of 15-30%, as in Ethiopia [30, 31, 4]. In Brazil, according to SINAN´s data, the number of co-infection cases of VL/HIV has increased from 21 in 2001 to 86 in 2005. The states where this association was most frequently reported were Maranhão (16.5%) Minas Gerais (14.8%), São Paulo (13.6%) and Mato Grosso do Sul (9.1%). These findings show the risk increasingly present of a superposition of the risk areas for VL and HIV / AIDS in Brazil[8,35].

The most frequent symptoms in reported cases of VL in Aracaju-SE was fever (95.8%), followed by splenomegaly (83.2%), lose of weight (78.2%), weakness feelings (76.5%) hepatomegaly (68.1%) and cough (52.1%). In endemic areas, the entire clinical picture that present itself with hepatosplenomegaly fever should be investigated as a suspicion of LV. Findings with lymphadenopathy, commons in India and Sudan,



Figures 2 - A - Annual incidence rate of human VL by gender (CIM – male gender, CIF – female gender), overall and relative risk (RR) of masculine gender in relation to the feminine gender in Aracaju/SE, 1999-2008. **B** - Annual incidence rate of human VL by age group in Aracaju/Se, 1999-2008.
Figuras 2 - A *- Coeficientes de incidência anual de LV humana por gênero (CIM – gênero masculino, CIF – gênero feminino), geral e risco relativo (RR) do gênero masculino frente ao gênero feminino em Aracaju/SE, 1999-2008.* ***B*** *- Coeficientes de Incidência anual de LV humana por faixa etária em Aracaju/Se, 1999-2008.*

Table 1 - Distribution of cases of visceral leishmaniasis by age and gender, accumulated incidence rates, deaths, fatality rates and relative risks. City of Aracaju/SE, from 1999 to 2008.
Tabela 1 *- Distribuição dos casos de leishmaniose visceral por faixa etária e gênero, coeficientes de incidência acumulada, óbitos, taxas de letalidade e risco relativo (RR). Município de Aracaju/SE, 1999 a 2008.*

Age	Male		Female		Total		IR (100000 inhab)	Deaths	Mortality rate	RR
	N	%	n	%	n	%				
<1 year	1	0.8	3	4.3	4	2.1	43.7	1	25.0	1.2
1 - 4	29	23.8	27	38.6	56	29.2	152.9	0	0	5.3
5 - 9	17	13.9	12	17.1	29	15.1	64.3	0	0	1.8
10 - 14	11	9	5	7.1	16	8.3	31.4	2	12.5	0.8
15 - 19	11	9	6	8.6	17	8.9	28.9	0	0	0.7
20 - 29	20	16.4	10	14.3	30	15.6	29.2	6	20.0	0.7
30 - 39	15	12.3	5	7.1	20	10.4	25.0	0	0	0.6
40 - 49	5	4.1	1	1.4	6	3.1	10.4	0	0	0.3
50 - 59	8	6.6	1	1.4	9	4.7	25.8	5	55.6	0.6
60 - 69	5	4.1	0	0	5	2.6	25.7	3	60.0	0.7
Total	122	100	70	100	192	100	37.5	17	8.9	

n = número absoluto *[absolute number]*
CI = coeficiente de incidência (por 100 mil habitantes) *[incidence rate (per 100,000 inhabitants)]*
RR = risco relativo de cada faixa etária frente ao restante das faixas etárias *[relative risk per age group compared to the remaining groups]*

were not described in the studied cases, as in other studies conducted in Brazil[32, 27,23].

The main criterion for confirmation of suspected cases of VL was the positive response in the indirect immunofluorescence (IIF) lonely (71.4%) or combined with cytological examination (6.3%), followed by parasitological (myelogram) isolated (5.8%). Also noteworthy is the fact that in 29 patients (15%), the case confirmation was based only on clinical and epidemiological studies.

A percentage of 81.6% of the 38 districts of Aracaju had at least one case of human VL in the studied series. In the first health region, the expansion zone of the municipality, during the period of 1999-2003, there was 45.7% (43) of autochthonous VL cases of Aracaju, with an incidence of 84.06 cases per 100 000 inhabitants in this period. In the period of 2004-2008, however, there was a reduction of human cases of VL in this region, and there were reported 26.5% (26) of the total cases, with an incidence of 35.37 cases per 100 000 inhabitants. In the fourth health region opposite phenomenon was observed both in the percentage increase in the number of cases, widening of 11.7% (11) to 24.5% (24), and in an increase in the incidence rate of 15.17 to 30.70 cases per 100 000 inhabitants, showing a change in the epidemiological pattern of transmission. This change may be due to changes in the profile of the municipality´s landscape, especially in Mosqueiro´s district, located on the first health region, which was characterized as peri-urban with rural aspect and is gradually turning into a residential area, which has caused deforestation in the area and possible migration of the VL vector.

The calculation of the density of VL cases per area in the municipality revealed that the highest densities are found in neighborhoods Novo Paraíso (9.91 cases/km^2), América (8.92 cases/km^2), Cirurgia (8.05 cases/km^2) and Pereira Lobo (7.85 cases/km^2).

The dog is the main host responsible for the epidemiological cycle of transmission of VL in urban environment, and it is known that canine infection precedes the occurrence of human cases. During the studied period, 58,161 dogs were submitted to serological tests for leishmaniasis, with an overall positivity of 5.4%.

Of the total number of examined dogs 87.0% (50,660) were collected through annual surveys conducted by the Center for Zoonosis Control (CCZ), with a positivity of 4.4%. 7,501 of the dogs that were brought passively to CCZ for several complaints, the serologic test was positive in 12.0% (897) of them. This higher positivity shown by the passive demand can be attributed to canine cases that are brought to the CCZ already showing some symptoms. The annual surveys were not conducted in all districts, because they follow the planning of the Municipal Secretary of Health, based on local epidemiological situation. Thus, the percentages presented in this study do not reflect the prevalence in dogs, since the examined dogs are not part of a representative sample of the whole municipality.

It is observed that both the passive demand and in the canine surveys conducted by CCZ there were an increment in the positivity of leishmaniasis, with an increase in of 2.7 times in passive demand and 3.5 times in active search, when compared the periods 1999-2003 and 2004 -2008 (Table 2). In the health regions that concentrated the highest number of cases of human VL, it was observed the highest positivity rates, both in canines' surveys and in passive demand (Figure 3). Another important aspect of canine VL is that dogs do not always look sick in the beginning of the infection, and even asymptomatic, they may also be infective to the vectors 11.

The visceral leishmaniasis is a significant public health problem in the municipality of Aracaju, with a high incidence coefficient of human cases, high mortality rate and widespread distribution in several city environments. Besides that, the canine seropositivity has also distributed itself throughout the territory, and the expansion zone of the city has the highest incidence coefficients, but as it represents 43% of the territorial capital of Sergipe, it shows a low density of

Table 2 - Incidence rate and percentage of positivity of serological tests for leishmaniasis performed in dogs residing in Aracaju during surveys and passive demand for each health region, Aracaju/Se, 1999 to 2008.
Tabela 2 - *Coeficientes de Incidência e percentual de positividade dos exames sorológicos para leishmaniose realizados em cães domiciliados durante inquéritos caninos e demanda passiva por região de saúde, Aracaju/SE, 1999 a 2008.*

Health	1999 - 2003			2004 - 2008			Total		
region	IR	% DP	% AS	IR	% DP	% AS	IR	% DP	% AS
1	84.1	13.5	4.5	35.4	21.3	11.6	93.9	19.0	7.8
2	25.2	8.5	1.2	16.0	12.3	4.1	37.3	9.7	2.1
3	6.4	6.7	*	1.9	9.1	0.0	7.5	7.9	0.0
4	15.2	4.8	3.1	30.7	20.3	6.5	44.8	13.7	6.0
5	10.4	5.6	0.5	5.9	23.9	7.5	16.2	11.1	4.9
6	12.7	6.1	0.7	16.8	21.4	6.2	28.0	10.7	1.4
7	13.6	5.0	*	20.5	17.1	2.7	33.4	11.5	2.7
8	14.1	4.2	0.8	13.4	8.5	5.1	26.9	6.4	1.5
Total	22.4	6.5	2.1	20.7	17.8	7.4	40.5	12.0	4.4

IR – coeficiente de incidência de LV humana *[incidence rate of human VL]*
%DP – percentual de positividade da demanda passiva *[percentage of positivity of passive demand]*
%AS – percentual de positividade da busca ativa *[percentage of positivity of active surveillance]*
*inquéritos não realizados *[*surveys not performed]*

human cases. Given the modifications that have been occurred in the area with the increase of housing sprawl, it is important that the health authorities maintain the epidemiological surveillance in order to detect and act against the possible occurrence of outbreaks of VL.

Although the information presented in this study is relevant, in order to classify the municipality of Aracaju as a region of active transmission of VL, some factors limit the lineation of the epidemiological profile in the capital of Sergipe. In Brazil, there is a high percentage of under-reporting of human VL, as well as disparities in secondary data when analyzed different information systems (SINAN, SIH, SIM), which can interfere in epidemiological indicators36. In the case of canine VL, underreporting is a reflection of the demand for positive dogs (active

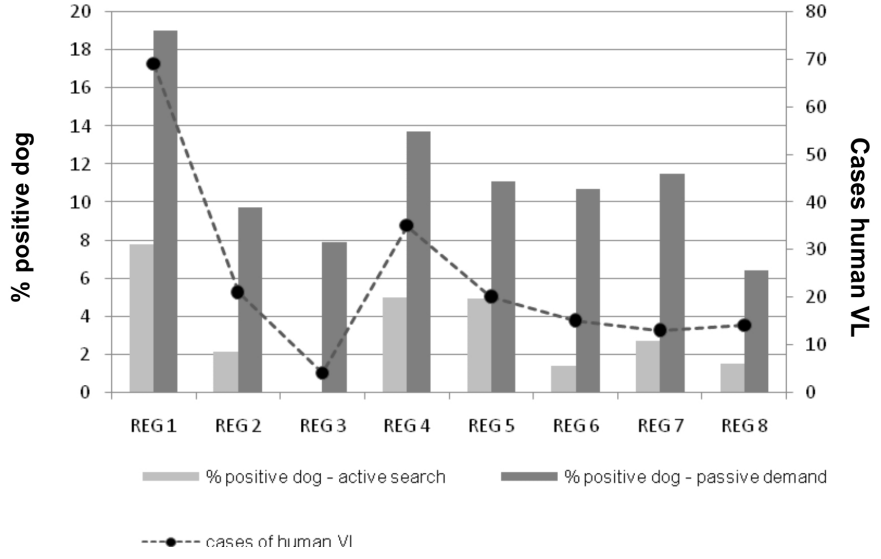


Figure 3 - Distribution of autochthonous cases of human VL by region and positive canine VL in passive demand and active surveillance. Aracaju/SE, from 1999 to 2008.
Figura 3 *- Distribuição dos casos autóctones de LV humana por região e positividade para LV canina na demanda passiva e busca ativa. Aracaju/SE, 1999 a 2008.*

search) in certain areas be performed only when there is notification of human cases in the location. On the other hand, the lack of studies regarding the indices of vector infestation and its positivity makes it difficult to have a more embracing discussion on the main epidemiological links of VL.

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Received: 11/23/2009
Final version: 06/09/2010
Approved: 04/11/2011