

# Epidemiological aspects of visceral leishmaniasis (kala-azar) in Ceará in the period 2007 to 2011

## *Aspectos epidemiológicos da leishmaniose visceral (calazar) no Ceará no período de 2007 a 2011*

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**ABSTRACT:** *Introduction:* Visceral leishmaniasis (VL; kala-azar) is a serious zoonosis that can be lethal, especially in untreated patients. Due to the fact that the State of Ceará is still an important area of transmission of VL, and based on the constant reports of the urbanization process of the disease in the country, it was necessary to monitor the occurrence of cases of leishmaniasis through epidemiological surveillance. *Objectives:* To describe the epidemiology of leishmaniasis cases in Ceará, Brazil. *Methods:* We conducted an epidemiological survey of secondary data provided by SINAN/MS from January 2007 to December 2011. *Results:* VL is an endemic disease in the State of Ceará, with cases notified in approximately 88% of the municipalities, with an average of  $596.8 \pm 29.6$  cases, an incidence of 6.1 cases/100,000 inhabitants and prevalence of 7.1 cases/100,000 inhabitants. The Metropolitan Region of Fortaleza is the microregion with the largest number of cases reported in state (51.9% of cases), with the capital, Fortaleza, being the municipality with the highest number of cases in the country. Traditionally, the main age group affected by the disease are children; however, a reversal has been observed in the profile from 2008, when the population of adult patients exceeded the pediatric population. *Conclusion:* Ceará is still an endemic area for VL, and the city of Fortaleza reported the highest number of cases in the country. In the State, a change in the profile of patients with the disease has been observed, now affecting primarily adults.

**Keywords:** Leishmaniasis, visceral. Kala-Azar. Zoonosis. Epidemiology. Communicable Diseases. Epidemiological Surveillance.

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**Conflict of interests:** nothing to declare – **Financial support:** Coordination for the Improvement of Higher Education Personnel (CAPES).

**RESUMO:** *Introdução:* A leishmaniose visceral (LV; calazar) é uma zoonose grave que pode ser letal, principalmente em doentes não tratados. Devido ao fato de o Estado Ceará ainda ser uma importante área de transmissão da LV e com base nos constantes relatos do processo de urbanização da doença pelo País, fez-se necessário o acompanhamento da ocorrência dos casos de calazar através da vigilância epidemiológica. *Objetivos:* Descrever o perfil epidemiológico dos casos de calazar no Estado do Ceará. *Metodologia:* Realizou-se uma avaliação epidemiológica a partir dos dados secundários disponibilizados pelo SINAN/MS no período de janeiro de 2007 a dezembro de 2011. *Resultados:* A LV é uma doença endêmica no Estado do Ceará, tendo sido notificados casos em aproximadamente 88% dos municípios, com uma média anual de  $596,8 \pm 29,6$  casos, incidência de 6,1 casos/100 mil habitantes e prevalência de 7,1 casos/100 mil habitantes. A Região Metropolitana de Fortaleza foi a microrregião que notificou a maior quantidade de casos da moléstia no Estado (51,9% dos casos), sendo a capital Fortaleza o município que registrou a maior quantidade de casos de calazar no País. Tradicionalmente, o principal grupo etário afetado pela doença são as crianças; entretanto, no Ceará observou-se uma inversão no perfil a partir de 2008, quando a população de doentes adultos ultrapassou a população infantil. *Conclusão:* O Ceará ainda é uma área endêmica para a LV, tendo a cidade de Fortaleza como o município que registrou a maior quantidade de casos. Foi observada uma alteração no perfil dos doentes, com a doença afligindo prioritariamente indivíduos adultos.

*Palavras-chave:* Leishmaniose visceral. Calazar. Zoonoses. Epidemiologia. Doenças Transmissíveis. Vigilância Epidemiológica.

## INTRODUCTION

Visceral leishmaniasis (VL), popularly known as kala-azar, has parasites from the *Leishmania donovani* complex as its etiologic agent. Clinically, it is a chronic systemic disease characterized by fever of long duration, with weight loss, asthenia, and anemia, among other symptoms, and it has a high mortality rate in untreated patients, malnourished children and HIV-infected individuals<sup>1-3</sup>.

Worldwide, it is estimated that approximately 350 million people live in areas at risk for leishmaniasis, diagnosed in 88 countries, 72 of which are developing countries. Approximately 90% of the world's cases of visceral leishmaniasis are concentrated in India, Bangladesh, Sudan and Brazil. In Brazil, the disease is endemic in rural areas and many outbreaks have been reported in the Northeast region of the country. Currently, it is observed that the disease has shown an expansion to medium and large-sized urban areas, making it a growing public health problem in frank geographic expansion<sup>1,4</sup>.

The State of Ceará, geographically located in the Brazilian Northeast region, has approximately 8.5 million inhabitants and a land area of 148,920.472 sq km<sup>2</sup> divided into seven mesoregions, 33 microregions and 184 municipalities<sup>5</sup>.

As in the whole Northeastern region, Ceará has a high rate of social inequality, where approximately 37% of the population aged ten or more have no income, 54.4% earn less than two minimum wages and only 8.5% earn above two minimum wages<sup>6,7</sup>. The state

also has a share of approximately 17.8% of its population living in extreme poverty or misery, a condition defined as insufficient income to meet basic food needs of a person, with a monthly household income per capita of up to R\$ 70 (approximately US\$ 30)<sup>8</sup>. Associated with the low level of development of the region, there is still a complex of factors favoring the spread of the disease, such as reduced investment in health and education, discontinuity of control actions, adaptation of the vector to environments modified by humans, new immunosuppressive factors, such as HIV infection and the difficulties of controlling the disease in large urban areas, where problems of malnutrition, housing and sanitation are often present<sup>9</sup>.

This conjuncture of factors provides favorable conditions for the spread of the VL in the State of Ceará.

## METHODOLOGY

VL is a reportable disease in the whole national territory, as established by Brazilian Law no. 6259 of 30/10/1975<sup>10</sup> and GM/MS Ordinance no. 104 of 25/01/2011<sup>11</sup>. The Ministry of Health provides a database on the Internet, the Notifiable Diseases Information System (SINAN), which is fed primarily by the reporting and investigation of cases of diseases and conditions that appear on the national list of notifiable diseases, as regulated by GM/MS Ordinance No. 201 of 03/11/2010<sup>12</sup>.

Using the database provided by the Ministry of Health, through SINAN, an epidemiological study of all cases of cases of VL reported in Ceará for the period from January 2007 to December 2011 was conducted. Data collection was held from January 2nd to 30th, 2013 and was revised on November 10, 2013 to rank the cities in the categories of VL transmission, the following criteria were used: sporadic transmission – cities with an average of less than 2,4 cases; moderate transmission – cities with average  $\geq 2.4$  and  $< 4.4$  cases; intense transmission – cities with average  $\geq 4.4$  cases<sup>13</sup>.

Using these data, the epidemiological profile of VL in Ceará was established through the identification of epidemiological descriptors by meso, microregion and/or municipalities in the state.

The following parameters were evaluated:

- distribution of the disease by age, gender, education level, disease progression, mortality, incidence and prevalence;
- cases of HIV-VL coinfection and VL in pregnant women were described according to geographic distribution, age range and lethality.

The endemic level of the disease in each microregion was calculated using the control diagram for the graphical representation of the monthly distribution of mean and standard incidence values, which express the maximum expected limit for each region for the period,

as described by the Ministry of Health<sup>13</sup>. For the calculation of incidence and prevalence, annual projections for the population were used, according to the Brazilian Institute of Geography and Statistics (IBGE)<sup>6,7</sup>.

The maps were created and data were collected into spreadsheets generated by the system through the TabWin32 software, version 3.6b, and exported to Excel 2007 and GraphPad Prism version 5.0. Statistical analysis was performed using the GraphPad Prism v.5.0 software. The collected data are expressed as mean  $\pm$  standard error of the mean (SEM) and were accepted as statistically significant when  $p < 0.05$  using the unpaired t-test (binary analysis) or analysis of variance (ANOVA) followed by Student-Newman-Keuls as a post hoc test (for multiple comparisons).

Since the study was conducted using secondary, open access data, submission and approval by an ethics committee was not required.

## RESULTS

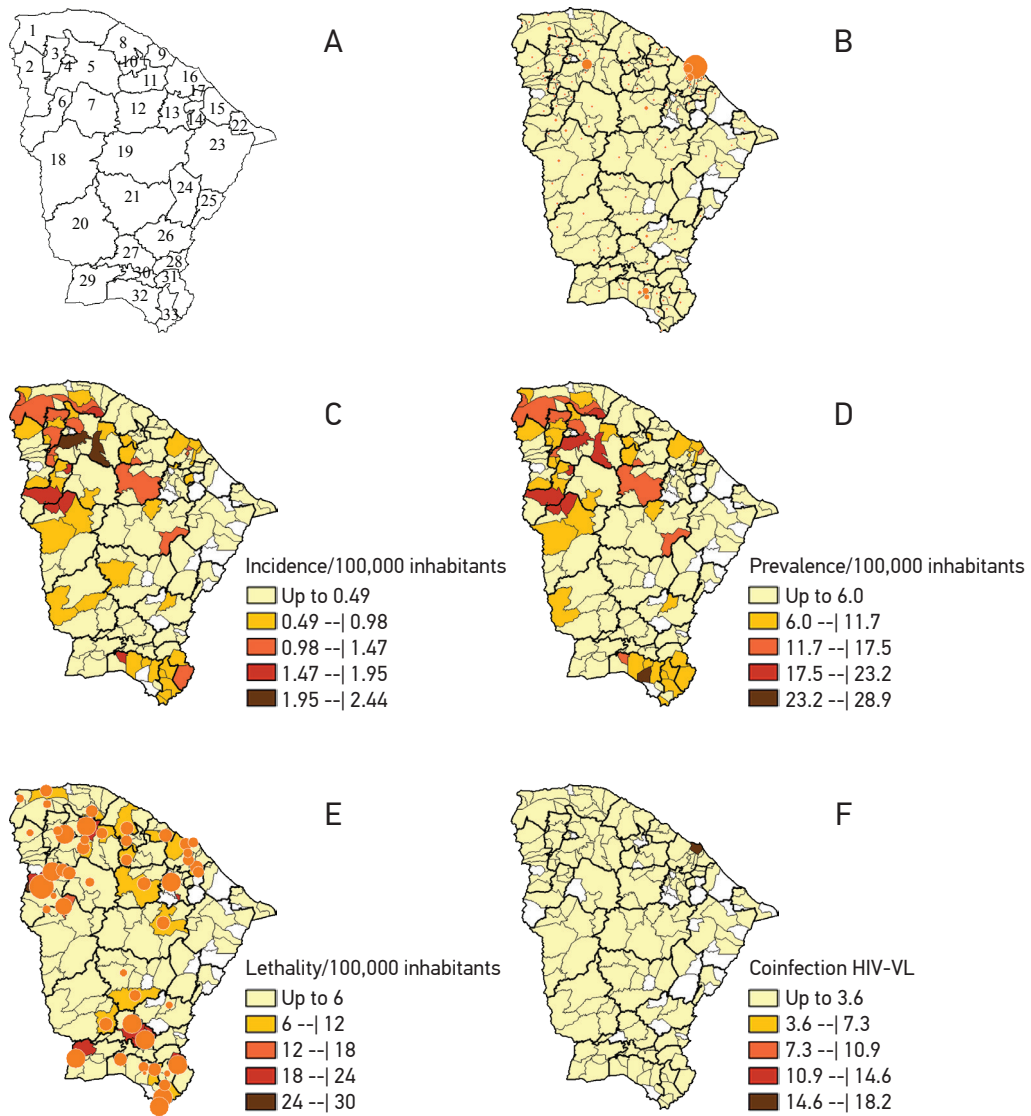
VL is endemic in the State of Ceará, having been reported in the period analyzed in all seven mesoregions, 33 microregions (Figure 1A) and in 162 of all 184 municipalities. During this period, an annual average of  $596.8 \pm 29.65$  cases was observed, which corresponds to approximately 15% of cases in the country, with an incidence of 6.1 cases/100,000 inhabitants and prevalence of 7.1 cases/100,000 inhabitants. Table 1 shows existing cases new cases, incidence and prevalence, distributed per each microregion of Ceará.

Of the 184 municipalities of Ceará, 16 municipalities have intense disease transmission, 23 municipalities have moderate transmission and 123 municipalities have sporadic transmission.

Figure 1A shows the geopolitical division of the mesoregions (thicker line) and microregions of Ceará (thinner lines). It is possible to highlight that of the seven mesoregions, it is observed that the Metropolitan Region of Fortaleza (composed of 11 municipalities) presents the largest number of cases, with approximately 51.9% of the total, followed by the mesoregions: Northwest Ceará (47 municipalities), with approximately 19.7% of cases; South Ceará (25 municipalities), with approximately 12.1% of cases; Ceará Backcountry (30 municipalities), with approximately 7.3% of cases; North Ceará (36 municipalities), with approximately 5.2% of cases; South-Central Ceará (14 municipalities), with approximately 2.1% of cases; and Jaguaribe (21 municipalities), with approximately 1.7% of cases.

The capital, Fortaleza, is the municipality with the highest number of cases in the country, with approximately 5.6% of national cases. Approximately 51.4% of the cases in the State were recorded in the microregion of Fortaleza, which corresponds to about 7.9% of cases in the country (Table 1, Figure 1B).

The highest incidence of the disease was recorded in the municipalities of Barbalha, Sobral, Ipueiras and Varjota (Figure 1C, Figure 2A), and the higher prevalence is located in Barbalha, Sobral, Ararendá and Morrinhos (Figure 1D, Figure 2B).



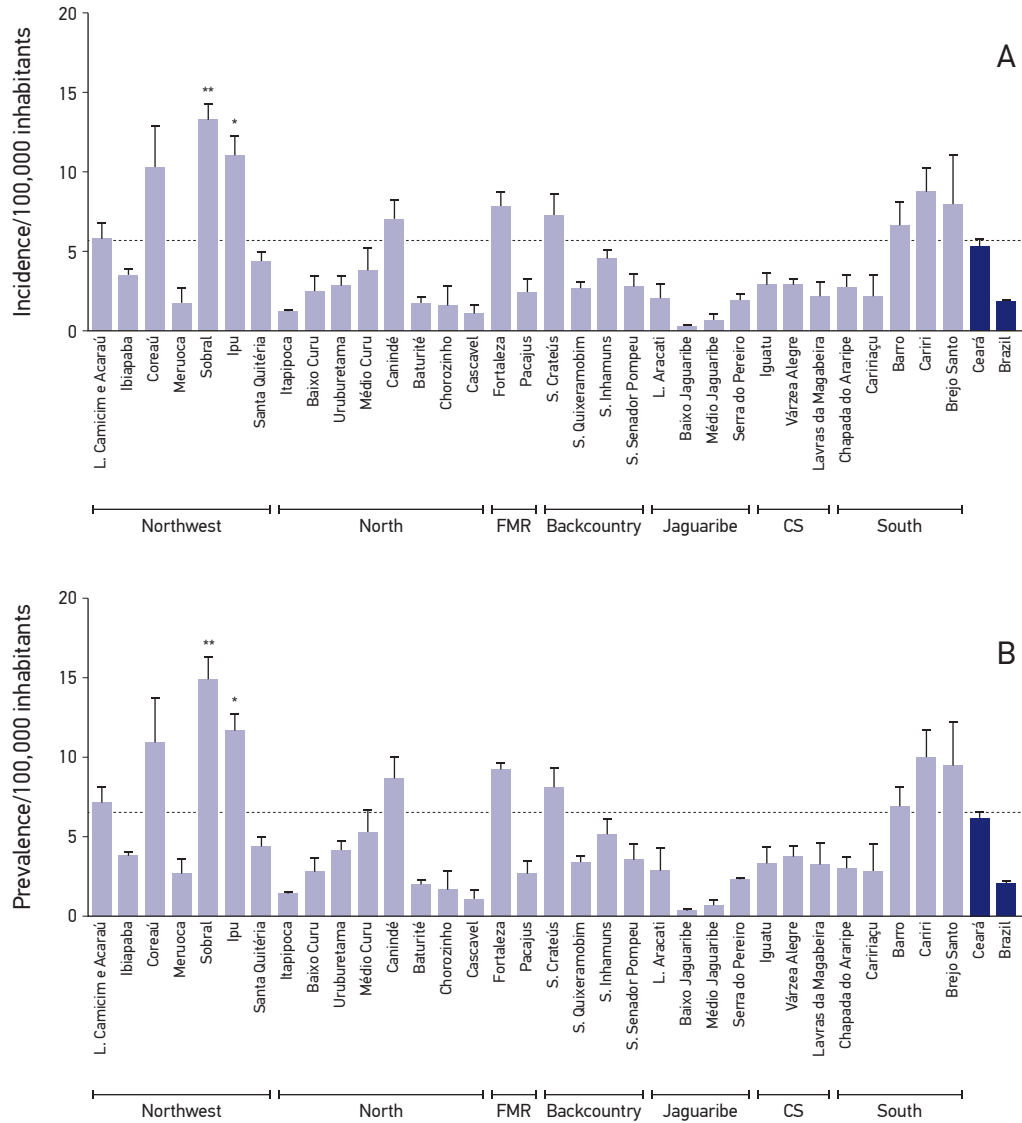
(Northwest: 1 - Camocim e Acaraú; 2 - Ibiapaba; 3 - Coreaú; 4 - Meruoca; 5 - Sobral; 6 - Ipu; 7 - Santa Quitéria; North: 8 - Itaipococa; 9 - Baixo Curu; 10 - Uruburetama; 11 - Médio Curu; 12 - Canindé; 13 - Baturité; 14 - Chorozinho; 15 - Cascavel; Metropolitan Region of Fortaleza: 16 - Fortaleza; 17 - Pacajus; Ceará's hinterlands: 18 - Sertão de Crateús; 19 - Sertão de Quixeramobim; 20 - Sertão dos Inhamuns; 21 - Sertão de Senador Pompeu; Jaguaribe: 22 - Litoral de Aracati; 23 - Baixo Jaguaribe; 24 - Médio Jaguaribe; 25 - Serra do Pereiro; Mid-South: 26 - Iguatu; 27 - Várzea Alegre; 28 - Lavras da Magabeira; South: 29 - Chapada do Araripe; 30 - Caririáçu; 31 - Barro; 32 - Cariri; 33 - Brejo Santo). The diameters of the circles are directly proportional to the number of cases and are located in the county seat.

Figure 1. (A) Mesoregion and microregion of Ceará. (B) Cases by county. (C) Incidence by county. (D) Prevalence by county. (E) Lethality by county. (F) Cases of co-infection HIV-VL.

Table 1. Cases, new cases, incidence and prevalence of Visceral leishmaniasis national, state and distributed by microregions of Ceará.

Mesoregion	Microregion	Cases	New Cases	Incidence <sup>#</sup>	Prevalence <sup>#</sup>
Northwest	Litoral de Camocim e Acaraú	25.0 ± 4.2	20.6 ± 3.6	5.7 ± 1	7 ± 1.2
	Ibiapaba	11.0 ± 0.8	10.4 ± 1.0	3.5 ± 0.3	3.7 ± 0.3
	Coreaú	6.2 ± 1.6	5.8 ± 1.5	10.2 ± 2.6	10.9 ± 2.8
	Meruoca	0.6 ± 0.2	0.4 ± 0.2	1.7 ± 1	2.5 ± 1
	Sobral	55.8 ± 6.1	49.8 ± 4.4	13.2 ± 1.1**	14.8 ± 1.5**
	Ipu	16.0 ± 1.4	15.2 ± 1.6	11 ± 1.2*	11.6 ± 1*
	Santa Quitéria	3.2 ± 0.5	3.2 ± 0.5	4.3 ± 0.6	4.3 ± 0.6
North	Itapipoca	2.8 ± 0.4	2.4 ± 0.2	1.2 ± 0.1	1.4 ± 0.2
	Baixo Curu	2.8 ± 1.0	2.6 ± 1.0	2.5 ± 0.9	2.7 ± 0.9
	Uruburetama	4.0 ± 0.7	2.8 ± 0.7	2.8 ± 0.7	4 ± 0.7
	Médio Curu	4.4 ± 1.3	3.2 ± 1.2	3.8 ± 1.4	5.2 ± 1.5
	Canindé	10.8 ± 1.8	8.8 ± 1.6	7 ± 1.2	8.6 ± 1.4
	Baturité	3.6 ± 0.7	3.2 ± 0.8	1.7 ± 0.4	1.9 ± 0.3
	Chorozinho	1.0 ± 0.8	1.0 ± 0.8	1.6 ± 1.2	1.6 ± 1.2
Fortaleza M.R.	Cascavel	1.4 ± 0.7	1.4 ± 0.7	1 ± 0.5	1 ± 0.5
	Fortaleza	306.6 ± 17.9	261.8 ± 31.9	7.8 ± 0.9	9.1 ± 0.5
Backcountry	Pacajus	3.0 ± 1.0	2.8 ± 1.0	2.4 ± 0.8	2.6 ± 0.8
	Cratêus	19.6 ± 3.3	17.8 ± 3.4	7.3 ± 1.4	8 ± 1.3
	Quixeramobim	9.0 ± 1.1	7.2 ± 1.1	2.7 ± 0.4	3.4 ± 0.4
	Inhamuns	7.4 ± 1.5	6.6 ± 0.8	4.5 ± 0.6	5.1 ± 1
Jaguaribe	Senador Pompeu	7.6 ± 2.3	6.0 ± 1.9	2.7 ± 0.9	3.5 ± 1
	Litoral de Aracati	3.0 ± 1.5	2.2 ± 1.0	2 ± 0.9	2.8 ± 1.4
	Baixo Jaguaribe	5.8 ± 0.6	4.2 ± 0.6	0.3 ± 0.03	0.4 ± 0.04
	Médio Jaguaribe	0.4 ± 0.2	0.4 ± 0.2	0.6 ± 0.4	0.6 ± 0.4
Central south	Serra do Pereiro	1.0 ± 0.0	0.8 ± 0.2	1.8 ± 0.5	2.3 ± 0.03
	Iguatu	7.4 ± 2.3	6.4 ± 1.8	2.9 ± 0.8	3.3 ± 1
	Várzea Alegre	3.6 ± 0.7	2.8 ± 0.4	2.9 ± 0.4	3.7 ± 0.7
South	Lavras da Mangabeira	1.8 ± 0.7	1.2 ± 0.5	2.2 ± 0.9	3.2 ± 1.3
	Chapada do Araripe	2.8 ± 0.7	2.6 ± 0.7	2.7 ± 0.8	2.9 ± 0.8
	Caririáçu	1.6 ± 1.0	1.2 ± 0.8	2.1 ± 1.4	2.8 ± 1.7
	Barro	6.2 ± 1.1	6.0 ± 1.3	6.6 ± 1.4	6.9 ± 1.2
	Cariri	52.2 ± 8.1	45.4 ± 7.7	8.7 ± 1.6	10 ± 1.6
Ceará	Brejo Santo	9.2 ± 2.9	7.8 ± 3.1	7.9 ± 3.1	9.4 ± 2.8
		596.8 ± 29.6	514 ± 45.2	6.1 ± 0.5	7.1 ± 0.3
Brazil		3.881 ± 120.5	3.433 ± 101.6	1.8 ± 0.1	2.0 ± 0.1

Data are expressed as mean ± SEM of the parameters analyzed. \*p < 0.05, \*\*p < 0.001 versus Ceará (ANOVA, Student-Newman-Kuels). <sup>#</sup>per 100 thousand inhabitants.



\*p < 0.05; \*\*p < 0.001 versus Ceará. ANOVA, Student-Newman-Kuels. Results are expressed as mean ± SEM of incidence or prevalence of national, state or each microregion of Ceará. The dotted line represents the state's mean + SEM of the disease.

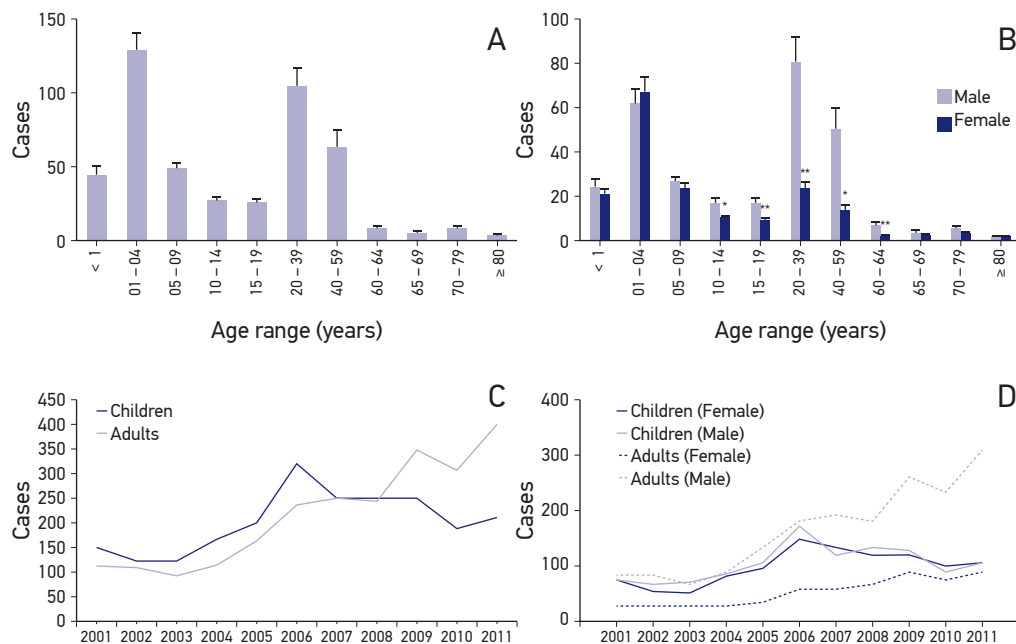
Figure 2. (A) Incidence of Visceral leishmaniasis. (B) Prevalence of Visceral leishmaniasis.

The average mortality rate of VL in Ceará was 5.1%, with an annual average of 30.8 ± 4.9 deaths, with approximately 39.6% of the deaths recorded in individuals living in Fortaleza (Figure 1D). There was a yearly average of 31.8 ± 6.0 individuals presenting HIV-VL coinfection in the state, with approximately 57.2% of the cases in the city of Fortaleza (Figure 1F). The recurrence rate of VL among patients with HIV was of 15.5% of

cases, which corresponds to the total of 30% of recurrences. In addition, it was found that in the period 2007 – 2010, the average mortality rate in this group was 4.7%, reaching rates of 21.2% in 2011 and exceeding approximately 4.5 times the mortality rate of the previous period, with deaths occurring in individuals aged 20 to 59 years.

During the study period, regarding pregnant women affected by VL, seven cases were reported in the cities of Fortaleza (three cases), Nova Olinda, Crato, Croatá and Caucaia (one case/each), with a mortality rate of 14.3 %. In 71% of reported cases, affected individuals were aged between 10 and 19 years. The distribution of the monthly average incidence per mesoregion and the maximum limit expected for each period were calculated from the control diagram (data not shown), revealing that, in all mesoregions of Ceará, except Jaguaribe, the disease behaves endemically, being transmitted in every month of the year.

Regarding age, the VL has a bimodal distribution, where it is possible to separate the population into two groups: children (0 – 14 years) and adults (15 years and over). The most affected group is children aged between 1 – 4 years and adults aged 20 – 39 years (Figure 3A). The disease notably affects males, notably in the 14 – 64 years age group (Figure 3B).



\* $p < 0.01$ ; \*\* $p < 0.001$  versus male.

Results are expressed as mean  $\pm$  SEM, unpaired t-test (A and B) or all cases (C and D).

Figure 3. (A) Distribution of cases by age group. (B) Sex of patients according to age group. (C) Distribution of cases of children and adults. (D) Distribution of cases of children and adults, and gender.



The population of sick children was higher than that of adults until 2006, when there was a match between populations and an increase in adult cases from 2008 on (Figure 3C). Stratifying the results by gender, it is observed that there was an increase in cases mainly in the adult male population (Figure 3D).

Among the cases in adults, there is a low level of education, with approximately 6.5% of the individuals being illiterate and 57.5% with only primary education (Figure 4A). In approximately 28% of cases, the level of education was not informed, and therefore excluded from the analysis.

Considering the evolution of the disease, it is observed that approximately 83.7% of VL cases progressed to the cure, with lethality in approximately 5.7% of cases (Figure 4B). In the period from year 2007 to 2010, there was an annual average of  $26.3 \pm 2.5$  deaths; however, only in 2011, 48 deaths were reported in the state, representing an increase of approximately 60% lethality (Figure 4C). The increase in deaths occurred mainly in the city of Fortaleza, which increased from  $10 \pm 1.5$  deaths from 2007 to 2010 to 21 deaths in 2011, representing an increase of approximately 110% over the deaths registered in the municipality.

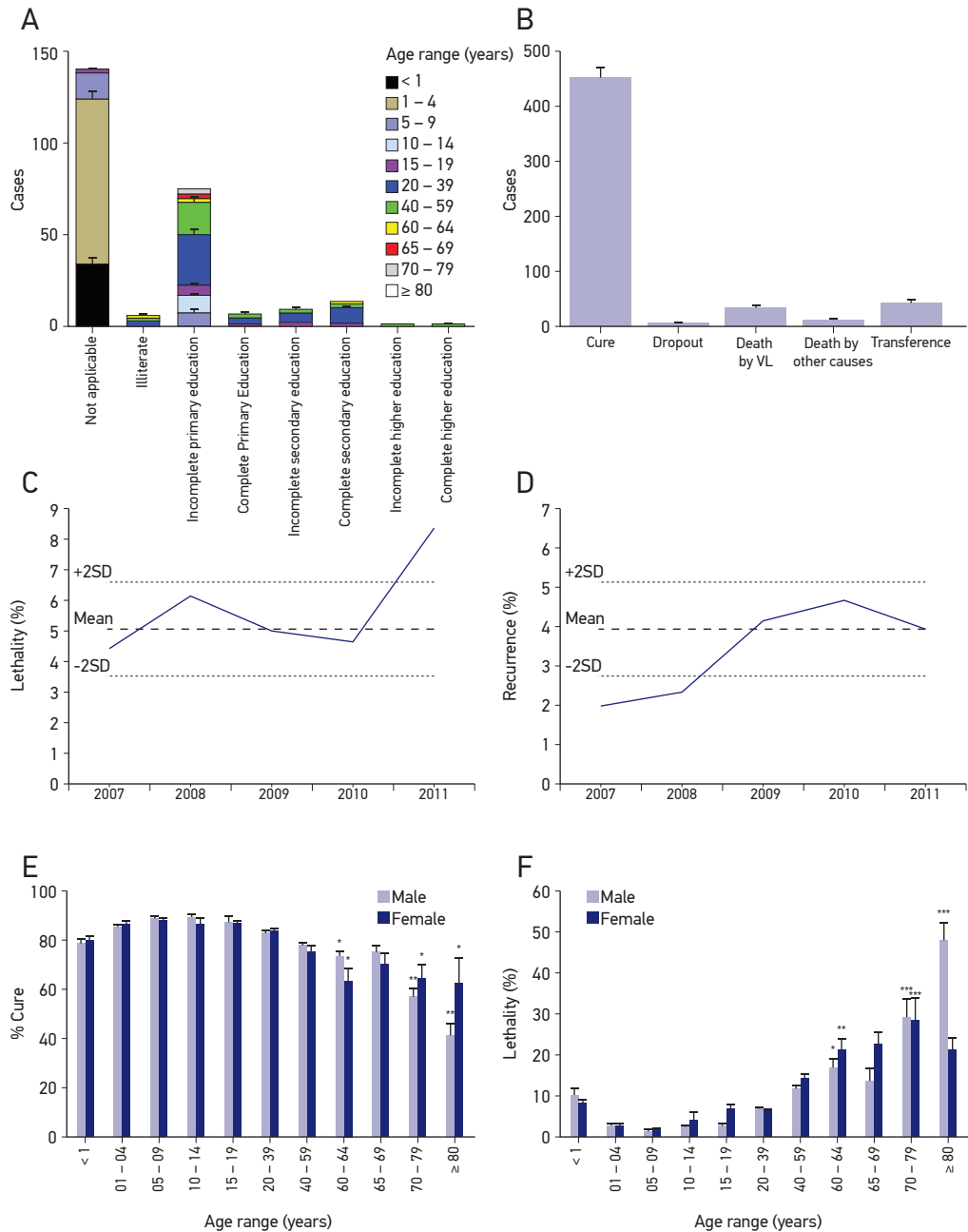
During the analyzed period, the affected individuals had recurrence of the disease in  $3.4 \pm 0.5\%$  of cases (Figure 4D).

Since population presents a bimodal distribution (figure 3A), it was divided into two groups to evaluate the lethality and cure. The first, group 1 – 4 years for comparisons among children groups and the second, the age group 20 – 39 years for comparisons among adult groups. The evolution to cure has a tendency to be lower in children under one year of life and is significantly reduced in people older than 60 years (Figure 4E). Lethality, in turn, is strongly influenced by age: an increasing trend in children under one year of life and a significant increase after 60 were observed (Figure 4F).

## DISCUSSION

VL is an endemic disease in Brazil, where, in the period 1984-2002, approximately 66% of cases occurred in the states of Bahia, Ceará, Maranhão and Piauí. In the 1990s, approximately 90% of cases occurred in the Northeast. With the geographic expansion of the disease, the share of the Northeast region was reduced to approximately 48% of cases in the following decade<sup>13,14</sup>.

Systemic fight against leishmaniasis in Ceará and other Brazilian states began in 1950 through the National Department of Rural Endemic Diseases (DENERu), was discontinued in 1964 and resumed only in 1980 by the former Superintendence of Public Health Campaigns (SUCAM). Since 1990, with the extinction of SUCAM, combating diseases became the responsibility of the National Health Foundation (FUNASA)<sup>15</sup>.



\*p < 0.05; \*\*p < 0.001 versus 20 to 39 years old

\*p < 0.05; \*\*p < 0.01; \*\*\*p < 0.001 versus 20 to 39 years old

Results are expressed as mean ± SEM, unpaired *t*-test (A, B, E and F) or mean of cases (C and D).

Figure 4. (A) Level of education distributed by age. (B) Evolution of the disease. (C) Annual fatality rate of VL. (D) Percentage of annual recurrence of the disease. (E) Percentage of cure distributed by gender and age. (F) Percent case fatality distributed by gender and age.

To combat VL, the Brazilian government developed the Visceral Leishmaniasis Control Program (PCLV) with the aim of reducing mortality and morbidity rates of the disease through early diagnosis and treatment of cases, as well as reducing the risk of transmission through the control of reservoirs and vectors<sup>13</sup>.

Despite public actions against VL started more than 60 years ago, Ceará still presents itself as an endemic area for VL, with approximately 15% of all cases in the country having been registered in the State. Except for the Jaguaribe Mesoregion, an active transmission of the disease can be observed in all mesoregions during all months of the year, and it is possible to realize a wide geographical distribution of the disease in state, with about 20% of municipalities reporting severe or moderate transmission.

No Nationwide, it is observed that, traditionally, there is a greater prevalence of the disease in males, and the main group affected is children under ten years old, which represents a total of up to 58% of cases<sup>13</sup>. In Ceará, a reversal in the epidemiology profile of the disease was detected since 2008, when the population of adult patients surpassed the child population.

Historically, the city of Sobral presents itself as an endemic region for VL, being the first city to record an outbreak of the disease in Brazil<sup>16</sup>. In the 1950s, it was observed that 96% of patients infected by VL in the city of Sobral were infected in rural areas<sup>17</sup>. Currently, it is observed that the microregions of Sobral and Ipu have the highest rates of incidence and prevalence of the disease in the State.

VL is traditionally a rural disease, however, it has been observed in recent decades a trend of change in this pattern. Epidemiological data have revealed a suburbanization and urbanization of the disease, with records of outbreaks in the cities of Rio de Janeiro (RJ), Belo Horizonte (MG), Araçatuba (SP), Santarém (PA), Corumbá (MS), Teresina (PI), Natal (RN), São Luis (MA), Fortaleza (CE), Camaçari (BA), Três Lagoas (MS), Campo Grande (MS) and Palmas (TO)<sup>13,18</sup>.

In this context of urbanization of VL in Brazil, it is observed that the Metropolitan Region of Fortaleza has the largest number of cases in the State, and the city of Fortaleza is the municipality with the largest number of cases in the country. In this scenario, it is possible to observe the progression of the disease through cities with high rates of municipal development (MDI) and high rates of municipal human development (MHDI).

From the MHDI for the year 2010 of the Ceara Institute of Research and Economic Strategy (IPECE), it appears that the cities of Fortaleza, Sobral and Crato have the highest MHDIs, ranging from 0.700 to 0.799<sup>19</sup>. However, despite the good human development indicators, these municipalities are still among ten with the largest number of cases in the state.

Using the MDI ranking for the year 2010 by IPECE<sup>20</sup>, one can observe that the ten cities with the highest MDI account for around 38% of the population<sup>7</sup> and for approximately 55% of cases of VL occurring throughout the state.

Education, health and income are the pillars for calculating the human development index (HDI) of a given region<sup>21</sup>. In this scenario, education serves as a tool for health promotion

because it enables individuals to learn about methodologies for disease prevention, adequate means of hygiene and nutrition. In VL, education also appears to influence disease prevention, since the majority of patients (approximately 64%) show a low level of education.

In addition, as one of the pillars of the HDI<sup>21</sup>, the level of education of individuals affected by VL was used to estimate the degree of socioeconomic development of the population affected by the disease, in the absence of the other parameters.

Thus, from the data obtained, it can be suggested that, although the majority of cases occur in municipalities with higher levels of development (MDI and MHDI), the disease must be occurring particularly in deprived areas of the most developed cities, we agree with Rey et al., who attempt to explain this change in the profile of VL from rural to urban and peri-urban areas for the rural exodus of impoverished peasant families who take infected dogs with them<sup>18</sup>.

Regarding the evolution of the disease, it is observed that the cure has a tendency to be decreased and mortality tends to be increased when VL affects children under one year old and seniors over 60 years old.

Since AIDS is the leading cause of immunodeficiency in the world, HIV infection seriously increases the risks of coinfection with VL, with a mortality rate of approximately 21% of individuals being observed in 2011, and the aggravation of such coinfection is evidenced by increased mortality in adults (20 – 59 years), because lethality is low in this age group in the absence of HIV. The occurrence of HIV-VL coinfection was reported in approximately 5.4% of VL cases, with a predominance of cases occurring in the city of Fortaleza.

When compared to previous studies, it was found that in the period 1995-2002, there was a mortality rate of approximately 8.7% for VL in a reference public pediatric hospital in Fortaleza, with deaths mostly in children under one year of age<sup>18</sup>. In the period 2005 – 2006, it was observed, in the same hospital, an increase in mortality to 13.3%<sup>17</sup>. Despite efforts to reduce the lethality of the disease in Brazil, mortality increased from 3.4% in 1994 to 5.5% in 2008, representing an increase of 61.8%<sup>13</sup>. The observed increase in the lethality of VL is a worrying indicator and should be evaluated with more appreciation as to its possible causes (late diagnosis, treatment failure, treatment dropout, comorbidities, etc.).

Another very delicate condition occurs when pregnant women are affected by VL, because it imposes risks of treatment to the mother and fetus, as well as the possibility of abortion or vertical transmission of the disease<sup>13,22,23</sup>. In Ceará, there was an annual occurrence of VL in pregnant women at approximately 1.9% of patients (in the group of women aged 10 – 59 years), which corresponds to approximately 0.65% of the total female cases, with high prevalence in adolescents and young adults (between 10 and 19 years old). However, in Brazil and worldwide, there are no official estimates of VL in pregnant women, with few reports in the literature, and, from the data available, cases are from known endemic areas for the disease<sup>24</sup>.

## FINAL CONSIDERATIONS

VL is a serious disease, often neglected, and requires special attention from public health authorities. More effective control of the disease is needed in Ceará, aiming to identify early cases and decrease transmission through control of reservoirs and vectors, in order to reduce related morbidity and mortality.

Ceará is still an endemic area for VL, and the capital Fortaleza is the city with the highest number of cases in the country. Though most cases are recorded in the most developed cities of the State, it is suggested, based on social indicators, that transmission occurs mainly in poor areas of large cities.

Besides the urbanization of VL in Ceará, a change in the disease profile was also observed, with a tendency to affect primarily adult individuals.

Although the vast majority of cases progress to clinical cure, mortality is still high in children and individuals over 60 years old, as well as in young adults and in cases of HIV-VL coinfection, a worrying increase in the lethality of disease was noted in 2011.

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Received on: 07/23/2013

Final version presented on: 11/27/2013

Accepted on: 02/03/2014