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RESEARCH

Aspectos clínicos e epidemiológicos da leishmaniose visceral em crianças

Clinical and epidemiological aspects of visceral leishmaniasis in children

Aspectos clínicos y epidemiológicos de la leishmaniasis visceral en niños

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ABSTRACT

Objective: describing the epidemiological and clinical profile of Visceral *Leishmaniasis* (VL) in hospitalized children. **Method:** this was a documentary and retrospective research performed from January 2001 to December 2009, at a hospital in Fortaleza - Ceará. There were evaluated the variables such as: cases per year, age, weight and symptoms. For analysis of the correlation between the variables the Spearman's coefficient was calculated. The study was approved by the Ethics Committee (CEP 42/2005). **Results:** the largest number of cases occurred in 2007, with 23, 5% (46) cases. The predominant age range was between 0 and 2 years old. A part of the children 47,96% (94) were malnourished and 47,4% and 49% had diarrhea and weight loss, respectively. Clinical manifestations were: fever, swollen spleen and liver. **Conclusion:** although the incidence of cases of VL is decreasing along the years, the number of children affected by VL remains a source of concern, due to the susceptibility of this age range. **Descriptors:** visceral leishmaniasis, child, epidemiology.

RESUMO

Objetivo: descrever o perfil clínico e epidemiológico da *Leishmaniose* Visceral (LV) em crianças internadas. **Método:** pesquisa documental e retrospectiva realizada no período de janeiro de 2002 a dezembro 2009 em um hospital de Fortaleza - Ceará. Foram avaliadas variáveis como: casos por ano, idade, peso e sintomas. Foi calculado o coeficiente de Spearman para investigar a correlação entre variáveis. O estudo foi aprovado pelo Comitê de Ética, sob o protocolo (CEP 42/2005). **Resultados:** o maior número de casos ocorreu em 2007, com 23,5% (46) casos, a faixa etária predominante foi entre 0-2 anos. Parte das crianças, 47,96% (94), era desnutrida e 47,4% e 49% apresentaram diarreia e emagrecimento, respectivamente. Manifestações clínicas: febre, esplenomegalia e hepatomegalia. **Conclusão:** embora a incidência de casos de LV seja decrescente com o decorrer dos anos, observa-se, ainda que a quantidade de crianças acometidas pela LV ainda é preocupante devido à suscetibilidade dessa faixa etária. **Descritores:** leishmaniose visceral, criança, epidemiologia.

RESUMEN

Objetivo: este estudio tiene como objetivo describir el perfil clínico y epidemiológico de la *Leishmaniasis* Visceral (LV) en niños internados. **Método:** investigación documental y retrospectiva hecha entre enero de 2002 y diciembre de 2009 en un hospital de Fortaleza-Ceará. Las variables fueron evaluadas: casos por año, edad, peso y síntomas. Para investigar la correlación de las variables fue calculado el coeficiente de Spearman. El estudio fue aprobado por el Comité de Ética (CEP 42/2005). **Resultados:** el mayor número de casos ocurrió en 2007, con 23,5% (46) casos. El grupo de edad predominante fue entre 0-2 años. Una grande parte de los niños, 47,96% (94) era desnutrida y 47,4% y 49% tuvieron diarrea y pérdida de peso, respectivamente. Manifestaciones clínicas: fiebre, esplenomegalia y hepatomegalia. **Conclusión:** aunque la incidencia de casos de LV está descendiendo en los años, el número de niños afectados por el LV es todavía preocupante debido a la susceptibilidad de este grupo de edad. **Descriptor:** leishmaniasis visceral, niño, epidemiología.

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INTRODUCTION

Visceral Leishmaniasis (VL) is a vector-borne zoonosis, which if not treated properly, provides high levels of lethality. Thus, control strategies should be instituted with emphasis on epidemiological surveillance, environmental sanitation, chemical control, surveillance and monitoring canine with euthanasia of seropositive dogs. Early diagnosis and appropriate treatment of human cases are also very important to minimize the deleterious effects caused by the condition.¹

With overall mortality estimated at 59.000 deaths per year, the VL remains an important public health problem in many countries of the world. The Brazilian real has been showing an expansion of human cases with outbreaks in towns and cities in development. In Ceará, the disease is in an increasing trend of incidence, with periodic outbreaks. In 2008, 586 cases that reached all age groups, predominantly in the range 1-4 years old (41,1%) were confirmed. The municipalities with the highest number of reported cases were: Fortaleza (247), Sobral (88) and Caucaia (36). The fatality rate is high (5,6% in 2008) and requires early diagnosis and treatment of cases for its reduction.²⁻³

Since the 80s, in the Northeast, the incidence in patients under five accounted for 49% of cases in Natal, 64% in Maranhão, and only 28% in Belo Horizonte, which shows that there is a new expansion area of VL in Brazil. The high proportion of children under one year in Fortaleza (12%) patients could be explained by household transmission of *L. chagasi* in urban and peri-urban areas, as in Belo Horizonte and São Luís.⁴

The VL is a reportable disease, predominantly in rural areas, although recently also established in urban areas, due to changes in the environment and constant migrations determined by the impoverishment of rural areas and the prospects for further development in major centers urban. The disease manifests itself mainly in the outskirts of large cities, where the vector of the disease meets environmental conditions for the maintenance of your cycle life.⁵ Other reasons for the continuous increase in VL are lack of diagnostic methods and awareness of professional health on the importance of investigating this disease.⁶

The clinical aspect of the disease is characterized by irregular and long lasting fever, weight loss, asthenia, malaise, anemia and chronic and systemic manifestations. Generally the clinical suspicion of VL should be raised when the patient has fever and splenomegaly with or without hepatomegaly. In untreated cases, death can reach 90%.⁴

In reference to Communicable Diseases (DT), at the Ceará State hospital, the record is expressive on the disease in children, it is necessary to evaluate the factors related to the disease. Thus, it appears the relevance of investigating the clinical and epidemiological features of VL in this age group and check for associations with socioeconomic, nutritional and clinical factors.

Given the incidence and persistence of VL cases in children, it is important to hold knowledge about the dynamics of the disease in endemic areas and populations at risk, as is the case of malnourished children. That's because in this context there is an increased complexity of cases of infection, which can lead to a worsening of morbidity in the pediatric age group. It is hoped that this study covers the clinical and epidemiological knowledge of VL, allowing prevention and health promotion can be put into practice, facilitating control of the disease.

Thus, this study aimed to establish a clinical and epidemiologic profile of children with VL, analyzing the nutritional, socioeconomic and symptoms of these children treated at a referral hospital in Infectious Diseases in Fortaleza features.

METHOD

This is a documentary research, retrospective, quantitative and of epidemiological character, developed into a referral hospital for infectious diseases in the city of Fortaleza/Ceará - Brazil.

The study population comprised the medical records of children aged zero to 12 years old admitted to this hospital with a diagnosis of VL, from January 2002 to December 2009. 450 records were identified between VL cases of confirmed or not. After excluding the records of individuals aged 12 years and unconfirmed cases of VL, we reached a total of 196 records.

The data collection occurred from January to June 2010. The data collection instrument used was a structured form with the following variables: age, gender, county of residence, time elapsed between the first symptoms and diagnosis, diagnostic methods, clinical manifestations and outcome. Initially, a pre-test to evaluate the instrument in which the need for adjustment was performed was observed. After using the pre-test, there was a need to add some variables such as area (urban, rural), body weight (Kg), mean length of hospitalization, symptoms reported by family members, use of any medicine before diagnosis, presence of dogs in the house or neighborhood and the case was relapse.

Nutritional status was assessed by Gomez⁷ criterion, which uses the relationship between weight and height of children of female and male from zero to 12 years old classifying them as normal weight, malnutrition 1st level, 2nd level malnutrition or undernutrition the 3rd level.

The collected data were organized and tabulated in Excel and processed in SPSS software version 17.0, having been grouped and made the crossing of the variables. To investigate the correlation between the incubation periods and hospitalization with age and body weight, the Spearman correlation coefficient was calculated. Data were organized in tables that show the absolute and relative frequencies.

The project complied with Resolution 196/96 and was approved by the Ethics Committee at the Hospital São José, and was approved under the protocol 42/2005. As this

is a retrospective study of medical records with information was asked to grant a term of trustee to validate the use of information from medical records for research purposes.

RESULTS AND DISCUSSION

There was a higher prevalence of VL cases in 2007, with a frequency of 23,5% (46). In the first four years, we identified the similarity of cases with less than 10% and a frequency range from 13 to 18 affected children.

Table 1 - Annual distribution of cases and deaths of children hospitalized for VL in the period from 2002 to 2009. Fortaleza/CE - Brazil, 2010.

Year	Cases	%	Deaths	%
2002	14	7,14	-	-
2003	13	6,63	-	-
2004	15	7,67	2	1,02
2005	18	9,18	-	-
2006	07	3,59	-	-
2007	46	23,46	-	-
2008	44	22,44	-	-
2009	39	19,89	-	-
Total	196	100,0	2	1,02

The case fatality reviews was observed in 2004 with 1,02% (2) deaths, with probable cause, in the first case, respiratory failure, sepsis, bacterial pneumonia and varicella, and in the second case, respiratory failure and sepsis. In 2009, there was a decrease in the number of cases compared to 2007, when it found the highest incidence of cases (Table 1).

Table 2 - Distribution of cases by age group, gender, nutritional status, municipality and region of children hospitalized during 2002 LV to 2009. Fortaleza/CE - Brazil, 2010.

Characteristics	f	%
1. Age (years)		
< than 2	65	33,2
Between 2 and 4	57	29,0
Between 4 and 7	34	17,4
Between 7 and 12	40	20,4
2. Gender		
Male	107	54,6
Female	89	45,4
3. Nutritional Situation		
Normal	102	52,0
Malnutrition of 1 st level	68	34,7
Malnutrition of 2 nd level	24	12,3
Malnutrition of 3 rd level	2	1,0
4. Municipality of residence		
Fortaleza and the metropolitan region	115	58,7
Cities of the countryside	81	41,3
5. Zone		
Metropolitan	124	63,3
Rural	72	36,7

The most affected age group referred to under 2 years old with 33,2% (65) of the cases, the average age was 6 years (SD = 38,096), the youngest child identified in the medical records was nine months. Regarding gender, 54,6% (107) of the children were male

and 45,4% (89) were female. As for the weight, it was found that most children with normal nutritional status were - 52,0% (102). In geographic distribution, 58,7% (115) of children living in Fortaleza and in the metropolitan area and 63,3% (124) were in the metropolitan cities of the State of Ceará (Table 2).

Table 3 - main symptoms and clinical manifestations of children admitted with VL in the period from 2002 to 2009. Fortaleza/CE - Brazil, 2010.

<i>Symptoms</i>	<i>f</i>	<i>%</i>
Fever	196	100
Slimming	96	49,0
Increase in abdomen	128	65,3
Asthenia	74	37,8
Cough	83	42,3
Diarrhea	93	47,4
Vomit	42	21,4
<i>Clinical findings</i>		
Splenomegaly	191	97,4
Hepatomegaly	182	93,0
Malnourishment	94	48,0
Pallor	52	26,5

There were identified from the registry of the records of the main symptoms: fever in all children; abdominal enlargement in 65,3% (128), and diarrhea in 47,4% (93), among others. Have the main clinical manifestations were: splenomegaly in 97,4% of children (191), hepatomegaly in 93,0% (182), and malnutrition in 48.0% (94) and paleness, 26,5% (52) (Table 3).

Table 4 - Correlation between variables, age and body weight versus incubation time and average time of hospitalization of children admitted with VL, from 2002 to 2009. Fortaleza, CE, Brazil, 2010.

	Incubation time	Average time of hospitalization
Age	R=0,118 p=0,371	R=0,100 p=0,940
Body weight	R=0,144 p=0,272	R=0,024 p=0,855

On Table 4, there was no correlation between incubation time and age ($p = 0,371$) and weight ($p = 0,272$). The average hospital stay did not correlate with age ($p = 0,940$) and weight ($p = 0,855$). It was expected that the time between onset of symptoms and diagnosis suffer interference of age and weight, as it is believed that the higher this time, the greater the clinical worsening of this child. Similarly, it was expected an interference ratio of the average length of stay with age and weight, is thought to be the lower age group and precarious nutritional situation of children, would be his worst prognosis and, consequently, the greater the length of stay.

The increasing number of cases during the study period is estimated due to the expansion of endemic areas, resulting in the onset of disease in the outskirts of large cities, in which it is most of the poor and with little information about the disease, a fact that makes the diagnosis and leads to an increase in mortality cases. The seasonality of the disease occurs mainly in northeastern states, where VL is historically a public health

problem. Allied to this, climate change affecting this region contribute to people to agglomerate in large urban centers, where the vector of the disease is adapted.⁸

In the period 1995-2002, one study⁸ evaluated children with VL treated at a children's referral hospital in the State of Ceará. At the time, 450 children were analyzed, 22% (99) residents of Fortaleza and 27% (121) of the metropolitan area. This study presents similarities with what was done in this study, so we could emphasize that no concentration of cases of VL in large centers, associated with poverty and housing. Note that 1995 is the last year in which it was observed that the number of reported cases of VL was higher in rural areas than the urban area. This points out to a weakness of the health of the population, since it is believed that urban centers indicate the best living conditions and access to health services.

As for the two deaths reported in this study, who were children under seven was found, had a normal weight and the other of first degree malnutrition, which were from Fortaleza and residing in urban areas, and that they spent little time hospitalized 3 and 4 days, respectively. The causes directly responsible for the deaths were respiratory failure, sepsis, bacterial pneumonia and chickenpox. A study⁹ found a rate of 9,3% of deaths when VL researched in the Federal District. The causes of death were pulmonary infection, respiratory failure, and gastrointestinal bleeding, with circulatory failure, noting the high susceptibility of children to acquire these opportunistic infections due to immunosuppression.

In another investigation in Mato Grosso do Sul, the causes that contributed to death were: bacterial infections, respiratory failure, liver failure, hemorrhage (gastrointestinal, lung, epistaxis and gingival bleeding) and cardiac arrhythmia.¹⁰

VL is a serious disease that is associated with protein-energy malnutrition, anemia, hepatosplenomegaly, and coagulopathy infectious processes. The main causes of death include infection, bleeding, anemia and failure in liver metabolism.¹¹ The difficulty of access to health services, too, is a risk factor for the occurrence of death, because it delays early diagnosis and hinders the effectiveness treatment because of impairment of body.¹²

Deaths caused by VL cases are preventable through a vaccine prevention reducible, for adequate control during pregnancy and childbirth, prevention, early diagnosis and treatment and also through partnerships with other setores.¹³ Classic VL affects people of different ages however, in most endemic areas, 80% of reported cases occurred in children under the age of 10.⁹

An important feature of VL is, the higher the incidence of the disease, the greater the risk to children (indeed already been documented in Brazil), since it develops a long-lasting immunity with age. Thus, it is likely that the higher incidence of illness and death in the younger group of patients depends on the increased susceptibility to infection in this age group.¹¹

Study describing the epidemic of VL in Campo Grande, 2002 to 2006, found that children under five years were at higher risk, with an incidence ranging from 11,3 to 64,3 cases.¹²

The VL is one of the six most important endemic diseases in the world, given the incidence and mortality rates, rather than lack of treatment at the right time, in malnourished children and HIV-positive individuals who are immunosuppressed.¹¹

Susceptibility to children may be related to frequent contact with animals of the same, unlike adults, and also due to the fact that students have higher rates of nutritional deficiency and immune status are still under development.¹⁴

A tendency for masculinization of the disease, with male/female ratio of approximately 2:1.¹⁵ In this study, there was a predominance of males, 54,6% (107), corroborating the findings of other studies in the literature, despite disagreement with studies that identified higher rate in females. This emphasizes the problem of higher prevalence among males, yet no scientific savvy, believing in the existence of hormonal factor related to gender or exposition.⁵

Most children, 52% (102) had no malnutrition. However, 34,7% (68) of all investigated showed stunting of first level, 12,3% (24), malnutrition 2nd level, and 1% (2), third level of malnutrition. Numerous authors have reported that the clinical course of the disease may depend as much on factors related to the nature of the host immune response and the virulence of the parasite, as well as the low age and nutritional status of the patient, because the lower the nutritional status of the child, more likely it will enable the evolution of the disease to a worse prognosis, especially because the VL is an infection that leads to immune-depression.^{7,16} Furthermore, children are still exposed to numerous infections, gastrointestinal and respiratory, providing a longer period instability of immunity in this age group, contributing to cases of weight loss and malnutrition.

The cases included in the sample were from throughout the State of Ceará, having its origin concentrated in inner cities and urban areas, reflecting the high incidence of VL, and Ceará an endemic area for the disease. The disease, once restricted to rural areas of northeast Brazil, spread to other unaffected areas, including reaching the outskirts of large urban centers, becoming increasingly worrying.⁹

The main clinical manifestations of VL mentioned in this study were similar to those found by several scholars of this topic, both the symptoms reported by the family regarding the findings of the physical examination at admission, stood out fever, enlarged liver and spleen, pallor, decreased appetite, cough, weight loss, asthenia, and abdominal pain are classic symptoms of the disease.^{10, 12}

Thus, it can be identified as differential for VL and the prolonged course of enterobacteriosis diagnoses, malaria, brucellosis, typhoid fever, schistosomiasis hepatoesplenic the acute form of Chagas disease, lymphoma and sickle cell anemia.^{7,13}

There was no relationship between the incubation time of symptoms and admission to the variables body weight and age. Disease duration from onset of symptoms to diagnosis ranged from 3 to 215 days, featuring an average of 37,55 (SD±38,830). This duration ranged from 2 to 365 days with a mean of 42.7 days (SD±45). This long time for the discovery of the disease may be related to different levels of awareness of the disease by families, probably due to lack of information of the same and the fact that its symptoms are similar to several other existing diseases in endemic areas; over 50% of women who used any medication before diagnosis of the disease, especially antibiotics. The average length of hospital stay was 22,25 days (SD=9,198), ranging 3-54 days.^{5,18}

The Brazilian program for control of VL bases its strategy in three steps, with the first of them is eminently curative: 1) detection and treatment of human cases, 2) control of domestic reservoirs, and 3) vector control. What sustains the use of vector control and

reservoirs as intervention strategies on VL is the conjecture that the incidence of infection in humans is directly related to the number of infectious dogs and entomological factors.¹⁹

It is also an intervention to control the disease vaccination of dogs, especially in endemic areas. The dog is the largest reservoir of the parasite inhabits and easily between people. Studies show positive serology in apparently healthy dogs without clinical signs and symptoms, reinforcing their potential for optimal reservoir.²⁰

The multidisciplinary team should be trained in early recognition of the disease as well as clinical and laboratory monitoring of patients during treatment of VL, in order to identify potential complications early.^{10,12} The educational actions with primary care approach to disease, the clinical manifestations and prevention methods are needed to control and decrease the number of cases reporting.^{14,21}

CONCLUSION

Although the incidence of VL cases is decreasing with the years, even if observed high number of affected children and clinical complications with the disease, due to the persistence of cases in children under two years of age, no correlation was found between the incubation period and the variables age and body weight. The average hospital stay was not correlated with age and body weight, the mean hospital stay was independent of time of the symptoms. Thus, it is noteworthy that the incubation period is independent of age and body weight, as well as the effectiveness of treatment depending on the nutritional situation.

It is paramount attention from healthcare professionals, primarily from community health workers, nurses and physician for early recognition and treatment of VL, considering the precariousness of basic health network of municipalities, signaling the importance of multidisciplinary treatment quality to improve the customer user of the health service.

Studies show that clinical and epidemiological reality are important for understanding the VL in the study population, facilitating the identification of inaccuracies, in order to support the improvement and/or construction of health care strategies focused on this disease.

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