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Original Article

Epidemiological Features of Visceral Leishmaniasis in Fars Province, Southern Iran

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Abstract

Background: To describe the epidemiological features of pediatric visceral leishmaniasis in southern Iran.

Methods: This retrospective study was carried out using local hospital records of VL patients from 2001 through 2009. Data such as age, gender, place of residence, clinical signs and symptoms, treatment, history of recurrence were recorded. The collected data were statistically analyzed using SPSS software.

Results: A total of 260 cases of VL have been recorded during 2001 to 2009 in south of Iran, based on hospital records. Mean age of patients was 3.5 years with the highest prevalence in 2 years old patients. The diseases have been more common in males (60%). The main clinical signs and symptoms of the patients were fever (96.2%), hepatosplenomegaly (68.8%) and abdominal protrusion (71.9%). Most of cases were from Kazeroun County (17.5%) in Fars Province followed by Borazjan in Boushehr Province. Bone marrow aspirations have been performed in 178 of cases and *Leishmania* amastigotes were detected in only 50 (28.1%) cases. Glucantime has been the first drug treatment while 19.3% of cases have been treated with amphotericin B. Mortality rate was 6.2% and children under 1 year old have been the main victim of the disease. Relapse has been noted in 7.3% of patients.

Conclusion: VL is still endemic in South of Iran, especially in Fars Province with a noticeable mortality rate. Moreover, cases of the diseases are reporting from neighboring provinces and this might be due to the spreading of the diseases to the adjacent provinces.

Keywords: Epidemiology, Visceral Leishmaniasis, Iran

Introduction

Visceral leishmaniasis (VL) is caused by *Leishmania donovani* complex including *L. donovani* in the Indian subcontinent and Eastern Africa, *L. infantum* in Mediterranean area and Middle East and *L. chagasi* in Latin America. More than 65 countries are currently affected by VL and approximately 500,000 new human cases occur annually. Visceral leishmaniasis accounts for 75,000 deaths per year (1).

Leishmaniasis represents a major health problem in the Eastern Mediterranean Region (EMR) of the World Health Organization (WHO) (2). Cutaneous and visceral leishmaniasis are present in 14 of the 22 countries of the region. Zoonotic visceral leishmaniasis, caused by *L. infantum*, occurs in most countries of the region (2).

Northwest and Southern of Iran is the focuses of VL in Iran. The main focus of VL is located in

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Meshkin Shahr and Ardabil in Northwest and Kazeroun, Nourabad, Firouzabad and Darab in southwest of the country. Between 1998 and 2001, 1,062 human cases of visceral leishmaniasis have been reported from the rural district of Meshkin-Shahr in the mountainous, northwestern Iranian province of Ardabil (3).

A new focus of the disease has also been detected in Kohgiloyeh and Booyerahmad Province in southwest of the country. In a cross-sectional seroprevalence study, which was carried out in children in Booyerahmad district, anti-*Leishmania* antibodies were detected in 50 out of 1628 children (3.1%) by direct agglutination test (4). The causative agent of VL in south and north of Iran is *L. infantum* with canine (dogs, foxes and jackal) as reservoirs. In some VL-endemic areas in Iran (e.g. Meshkin-Shahr) more than 10% of the reservoirs (dogs) have anti-*Leishmania* antibodies in their serum (3). Asymptomatic infected dogs play an important role in epidemiology of VL in endemic areas and are the source of infection for both human and animals (5).

L. tropica and *L. major* which are the causative agent of cutaneous leishmaniasis have been reported from VL patients in Iran (6-8). The purposes of this retrospective study were to describe the characteristics of pediatric visceral leishmaniasis in southern Iran.

Patients and Methods

Hospital records of VL patients in university-affiliated hospitals in Shiraz, capital of Fars Province, were evaluated. Patients with positive IFA or positive parasitological tests (bone marrow aspiration) were considered as VL. All selected medical records were persistently reviewed and epidemiological data such as age, sex, place of residence and clinical data including signs and symptoms, physical examination, diagnostic tests, treatment and outcome of treatment were recorded. Collected data were analyzed using SPSS software.

Results

The total numbers of VL patients from 2001 to 2009 were 260 cases. From these, 156 (60%) were male and 104 (40%) were female. Their age ranged from one month to 36 years and the mean of age was 3.5 years. Ninety cases (34.6%) of patients were under 1 year and 77.7% of patients were under 5 years of age. The highest rate of disease was seen in 2 years old children. Table 1 shows the age distribution of patients.

Table 1: Age distribution of VL patients from southern Iran, 2001-2009

Age (yr)	Frequency	Percent	Cumulative Percent
0-1	90	34.6	34.6
1.01-5	112	43.1	77.7
5.01-10	11	4.2	81.9
10.1-20	14	5.4	87.3
20.1-30	7	2.7	90.0
>30.1	26	10.0	100.0
Total	260	100.0	

Most cases have been seen in winter (32.8%) followed by spring (32.4%) while the lower cases were seen in summer (17.7%) and autumn (16.9%).

Considering the place of residence, the majority of cases (77.6%) were from Fars Province followed by Boushehr (15.2%) and Kohgiloyeh and Boyerahmad (10.54%) provinces. In Fars Province, most of cases were from Kazeroun (45 cases) followed by Firouzabad (23 cases) and Darab (23 cases) whereas in Boushehr Province most of cases were from Borazjan (27 cases from 39 cases). Ten cases of the disease were from Mamasani, a new focus of VL in Fars Province.

Most cases of the diseases reported in year 2008 (16.2%) and the annual rate of the diseases was 28.8 cases. Fig. 1 shows the number of VL cases in each year from 2001 to 2009.

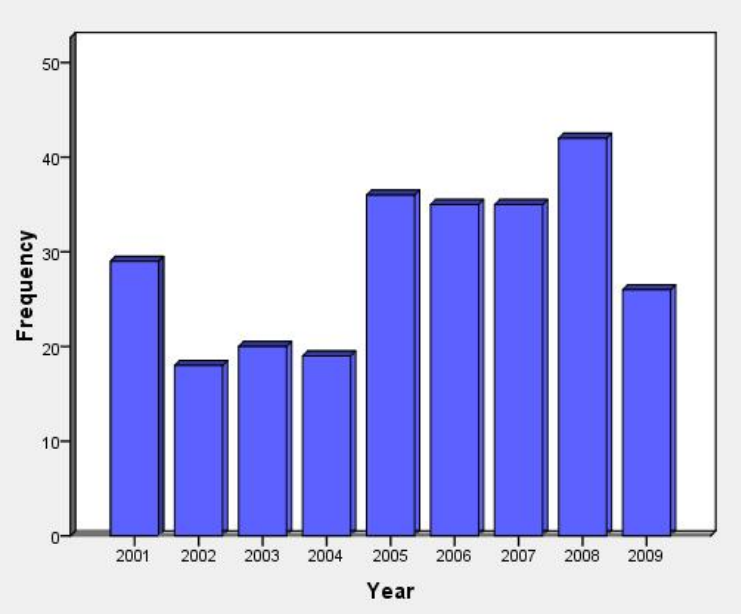

Fig. 1: Frequency of VL cases from southern Iran based on year, 2001-2009

The main and common clinical findings of patients were abdominal protrusion (71.9%), poor feeding (23.1%), anorexia (20.4%) and vomiting (15%). Majority of patients (96.2%) presented with a long history of fever. Other noticeable clinical features were chilling, sweating, lethargy, diarrhea, weight loss, and jaundice.

Of 178 bone marrow aspiration, only 50 were positive for *Leishmania* parasites. Diagnosis and treatment have been based on clinical signs and symptoms plus positive serological tests.

Titer of 1/128 has been considered as positive for IFA. Titer of higher than 1024, were recorded in some cases.

Most of patients (79.6%) were treated with glucantime (mean dose 20 mg antimony/kg/day). Mean duration of treatment was 21 days. Second line drug for treatment has been amphotericin B (1 mg/kg/day for 15 days). Relapse has been reported in 19 (7.3%) of cases. Most of relapses were seen in children aged 1-5 years old and the difference of relapse in age groups was statistically significant ($P<0.05$). Table 2 shows the frequency of relapse in VL cases in different age group.

Table 2: Frequency of relapse in VL cases from southern Iran, 2001-2009

Age group (yr)	Relapse		
	Yes	No	Total
0-1	3	87	90
1.01-5	9	103	112
5.01-10	2	9	11
10.1-20	2	12	14
20.1-30	0	7	7
>30.1	1	25	26

$X^2=14.7$ $df=7$ $P=0.039$

Mortality rate in these patients were 6.2%. Most of death cases were from children under 1 year old. Death rate was more in male than female and this difference was statistically significant ($P< 0.05$). The causes of death in these patients were reported to be secondary bacterial infection.

Discussion

Leishmaniases are endemic diseases in 88 countries in the world (1). In Iran, human leishmaniasis is present in at least 20 of the 30 provinces, with

human VL, endemic in the southern province of Fars and the eastern provinces of East Azarbaijan and Ardabil (9-10). Nourabad, Kavar, Kazeroun, and Darab in Fars and Kalaybar, Azarshahr, Meshkin-Shahr and Ardabil in East Azarbaijan and Ardabil province are known to be the main foci for the disease (6, 10-13).

From 1985-1990, 1051 cases of VL has been reported in Meshkin-Shahr (10). In a study in northwest, the average incidence rate of infection was 2.8% per year. One in 13 infections in children led to VL and this ratio decreased significantly with age. The focus of Meshkin-Shahr seems to have the highest incidence of the disease since in this population of less than 200,000 over 1000 cases have been reported in 5 years (12).

The focus of the diseases in south of the country is the second focuses of VL in Iran. Kadivar reported 367 cases of VL in southwest of Iran from 1996-2006 (13).

In a recent comprehensive study conducted by Mohebali et al., 9396 sera samples collected from humans from four distinct geographical locations of Iran have been evaluated for anti-*Leishmania* antibodies and antibody have been detected in 4.3% of cases. Physical examinations of 142 sero-positive cases revealed that the predominant clinical signs and symptoms of patients were fever (94.4%), paleness (67.6%) and hepato-splenomegaly (42.2%). The highest sero-prevalence rate (1.55%) has been reported in children ≤ 5 years old (14).

Mediterranean type of the disease is present in Iran. In the current study, more than eighty percent of the cases were from children under 10 years old. Median age of VL patients was found to be 2 years. Same scenario is present in northwest of the country where 90% of VL cases are under 5 years old children (10).

The main causative agent of VL in south of Iran, as diagnosed by molecular methods and isoenzyme, are *L. infantum.* This is the causative agent of VL in northwest of the country as well (15-16).

Other species of *Leishmania* (*L. major* or *L. tropica*) have been reported to cause VL in Iran, but these are just a few case reports (7-8).

Dogs have been considered the main reservoir of *L. infantum* in Iran (2). Although *Leishmania infantum* infected cats have been reported from Iran but their role in epidemiology of VL is still unclear (17).

In the current study, most new cases of VL appeared from February to May. This is contributed to the incubation period of VL which ranged from 6 months to 6 weeks and the sand flies activation period which is from mid June through mid October (18).

The pentavalent antimonia compounds, such as sodium stibogluconate and meglumine antimoniate have been the mainstay of antileishmanial therapy for more than 40 years with response rate of about 90%. In contrast to African and Indian forms of VL, resistance to antimonial agents is rare in Mediterranean VL (15). Although resistance to antimonial agents has been reported for cutaneous leishmaniasis in Iran**,** such data is not available for VL (19). Most of patients in this study have been treated with glucantime and the second line drug for treatment has been amphotericin B. Unresponsiveness to the treatment (mainly with glucantime) was noticed in few cases since relapse has been found in 7.3% of cases. This in turn raises an alarm that drug resistance to glucantime might be present in VL patients in this area. Possible correlation between high relapse rate and too short treatment (21 days) needs further investigation.

The mortality rate of VL in this study (6.2%) is equal to other reports in VL endemic areas. Bacterial super infection is one of the major complications in VL which leads to death in patients and this has been the case in our study as well (20).

Taken together, findings of the current retrospective study demonstrated that infantile VL is still prevalent in a few districts in southern Iran and its prevalence rate has not been significantly decreased over the last decade. Integration of VL surveillance system in primary care for children and timely treatment of cases could decrease the annual incidence of VL in the area, as this has been found to be effective in Meshkin-Shahr district, one of the focuses of VL in Iran (21).

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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