

Geographical Distribution of Visceral Leishmaniasis Among Children in Dhamar Governorate, Yemen

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Abstract: This is a retrospective study to describe the geographical distribution of *visceral leishmaniasis* among children in Dhamar governorate, Yemen and to assess the outcomes of the chemotherapeutic management. It was conducted at Al - Wahdah University Hospital, Mabbar, Dhamar governorate from April 2015 to March 2016. The study population were all the patients admitted to the hospital having the disease and the data sourced from the patients' charts using a performa sheet. Fifty-seven pediatric patients with confirmed *visceral leishmaniasis* were registered during the study period. The mean age was 3.51 ± 2.4 years and all cases were from Dhamar governorate. All cases presented with fever and splenomegaly. All children were severely anemic and the mean haemoglobin concentration was $(6.51 \pm 2.82 \text{ g/dl})$. The mean duration of symptoms prior to admission was 98.28 ± 10.6 days and the mean hospital stay was 22.07 ± 15.3 days. The cure rate after hospital management was 94.7%. Death had occurred in 3 cases (5.2%) mostly seen among younger age, and with prolonged illness prior to hospitalization. This study confirmed the presence of VL cases in Dhamar governorate, most frequently affected children below four years of age with excellent response to chemotherapeutic drug. The extension of *visceral leishmaniasis* infection to involve the highest central regions indicates that the disease tend to spread to other unusual parts of the country. Such a new distribution combined with lack of vital recording and reporting make the efforts to approximate the figure of true incidence difficult.

Keywords: Visceral Leishmaniasis, Paediatrics, Yemen

1. Introduction

Visceral leishmaniasis (VL) is the most severe form of *leishmaniasis* with high mortality if not treated. The disease is caused by protozoan parasites that belong to the genus *Leishmania* and is transmitted by the bite of certain species of sand fly [1]. It is estimated that over 200 million people around the world are at risk of acquiring the disease [2], and about 500000 new cases per year of VL globally are recorded [3]. VL is one of the seven most neglected tropical disease in the world [4]. The disease occurs in focal distribution and in remote locations, making extrapolation from official data sources difficult [5]. The prevalence of VL in pediatric population is high due to the higher susceptibility to infections and the immune-depressed state found in this population [6]. The majority of pediatric patients present with fever, anemia, hepatosplenomegaly, weight loss,

haemorrhage, lymphadenopathy and less frequently dry cough and diarrhea [7].

The diagnosis of VL is usually suggested by clinical and laboratory findings but the definitive diagnosis is based on identification of the parasites in bone marrow, liver, spleen or lymph node tissues [7, 8]. VL is considered endemic in our country and confined mainly to low-lying rural areas with high temperature [9]. Al-Selwi previous study on the topic [10] highlighted the extension of the VL foci towards some governorates which considered suburban regions. Recently, VL cases recorded among the central highlands that represent the highest area in the country. The aim of this study is to describe retrospectively the geographical distribution of *visceral leishmaniasis* among children in Dhamar governorate and to assess the outcomes of the chemotherapeutic management.

2. Patients and Methods

2.1. Study Design

This is a retrospective hospital-based study conducted at the paediatric unit in Al- Wahdah University Hospital, Dhamar governorate, Yemen from April 2015 to March 2016.

2.2. The Study Area

Dhamar, is one of the high land governorates of Yemen. It is located 100 Km to the south of Sana'a governorate. It is administratively divided into 12 districts covering a surface area of 8,745 km² with a total population of 1,330,108 (Census 2004) (11).

2.3. Data Collection

The pediatric clinical data were obtained by the retrospective analysis of the medical records. The ethical clearance for the study was obtained from the university ethical committee. We included all pediatric patients who aged between 0 to 12 years. All patients were diagnosed as having VL based on the identification of *leishmania* donovani bodies (LDB) in smears obtained by Bone Marrow Aspiration from the posterior iliac crest or upper tibia. The clinical findings at time of admission were recorded and the history details, physical examination were retrieved from the patient's charts. The investigations reviewed were complete blood count including hemoglobin concentration, total leukocytes with differential, platelet count, erythrocyte sedimentation rate (ESR), smear for malarial parasites and urinalysis. The onset of symptoms and the duration of illness prior to admission, treatment, length of hospital stay, complications during the treatment course and the outcome were noted. In this study, we defined anemia as Hb (<11 g/dl), and severe anemia as (Hb <7 g/dl), neutropenia (<1500 / μ l neutrophils) and thrombocytopenia (<150000/ μ l platelets). Within the hospital, all pediatric patients received adjunctive treatment such as blood and blood products, symptomatic medication, and dietary support. Sodium stibogluconate was administered (20 mg/kg/day) intravenously for a total of 28 days. All cured pediatric patients were followed-up for 4 month after discharge.

2.4. Statistical Analysis

All statistical analyses were performed using SPSS version 21 (IBM, Inc, Chicago, IL). Categorical data were summarized as frequencies and percentages of subjects, continuous data as mean, standard deviation and range. Chi-square tests and t-student tests were applied where needed. Statistical significance was defined as P value of < 0.05.

3. Results

A total of 57 cases of pediatric confirmed VL were registered in Al Wahdah University Hospital during the study period. The

mean age was 3.51 \pm 2.4 years with almost 2/3rd \leq 4 years old. There were (59.6%) males. Table 1, summarizes the pediatric characteristic. All cases were from Dhamar governorate distributed amongst the highland settings in scattered villages. The majority of VL cases (45.6%) were identified in Anes district, (24.5%) from A'ns, (19.2%) from Wesab, (5.2%) from Al hada and (5.2%) from Automah. Figure 1.

Table 1. The characteristics of the pediatric patients (n=57).

| variable | Mean \pm SD or n (%) | P value |
|-------------------|------------------------|---------|
| Age (yr) | 3.51 \pm 2.4 | |
| \leq 1 | 4 (7) | <0.00 |
| 2-4 | 38 (66.6) | |
| 5-10 | 17 (29.8) | <0.00 |
| Sex | | |
| Male | 34(59.6) | 0.01 |
| Female | 23(40.3) | |
| Body weight (kg) | 9.93 \pm 4.1 | |
| Family occupation | | |
| Agriculture | 43 (75.4) | <0.00 |
| Others | 14 (24.6) | |

Fever was presented in almost all cases likewise, splenomegaly found among all affected children. Pallor (86%), abdominal distension (80.7%), hepatomegaly (77.1%), anorexia (56.1%) and loss of weight (40.3%) were the predominant clinical presentation (Table 2). The mean Hemoglobin concentration was 6.51 \pm 2.82 g/d with (61.4%) had Hb \leq 7 g/dl. Neutropenia was observed in 10 cases (17.5%) and platelet count <100 \times 10³ / μ l was observed in 29 cases (50.8%). Table 3 shows the main haematological findings.

The mean duration of symptoms before admission was 98.28 \pm 10.6 days (range 2-370) and the mean hospital stay was 22.07 \pm 15.3 days (range 7-46). The cure rate of medical management was (94.7%) and the death rate was (5.2%). The three cases who died were aged less than a year, and complicated by secondary infection, and hemorrhage (Table 4). There was no relapse recorded during the follow-up period.

Table 2. Clinical symptoms and signs of the affected children (n=57).

| Variable | no (%) |
|----------------------|-----------|
| Fever | 57 (100) |
| Splenomegaly | 57 (100) |
| Pallor | 49 (86) |
| Abdominal distension | 46 (80.7) |
| Hepatomegaly | 44 (77.1) |
| Anorexia | 32 (56.1) |
| Loss of weight | 23 (40.3) |
| Lower limb edema | 8 (14) |
| Chest infection | 6 (10.5) |
| Jaundice | 6 (10.5) |
| Lymphadenopathy | 3 (8.7) |

Table 3. Hematological findings of the affected children (n=57).

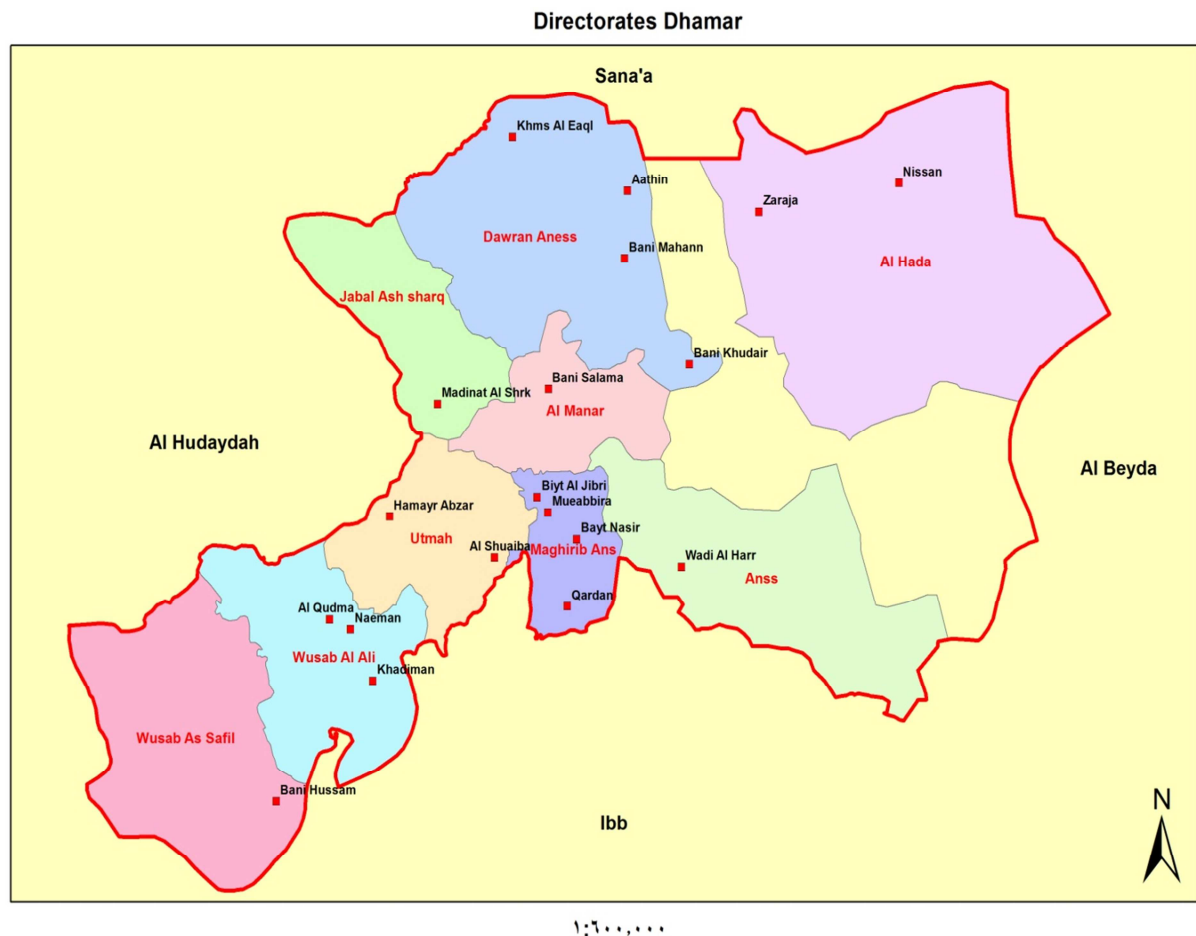
| Variable | mean \pm SD | 95% CI | P value |
|------------------------------------|-------------------|------------------|---------|
| Hb (g/dl) | | | |
| < 7 | 35 (61.4) | 3.2433 - 40.6211 | 0.01 |
| 7 – 11 | 22 (38.6) | | |
| Mean \pm SD | 6.51 \pm 2.82 | | |
| WBC (mm ³) | | | |
| < 4000 | 26 (45.6) | 32.34 - 59.33 | < 0.00 |
| Mean \pm SD | 4.28 \pm 3.87 | | |
| Neutrophil (mm ³) | | | |
| < 1500 | 10 (17.5) | 8.72 - 29.86 | < 0.00 |
| Mean \pm SD | 2848 \pm 511 | | |
| Platelet (1000 / mm ³) | | | |
| < 100 | 29 (50.8) | 37.22 - 64.30 | <0.001 |
| Mean \pm SD | 102.1 \pm 6.045 | | |
| ESR | 58.42 \pm 18.1 | | |

he data presented as means \pm SD or n (%) and range

Table 4. Duration of disease and outcomes.

| Variable | mean \pm SD | 95% CI | P value |
|---------------------------|------------------|--------------------|---------|
| Duration of illness (day) | 98.28 \pm 10.6 | 95.4674 – 101.0926 | <0.001 |
| Range | (2–370) | | |
| Hospital stay (day) | 22.07 \pm 15.3 | 18.0104 - 26.1296 | <0.001 |
| Range | (7–46) | | |
| Cured | 54 (94.7) | 85.33 - 98.88 | < 0.001 |
| Death | 3 (5.2) | | |

The data presented as means \pm SD or n (%) and range

**Figure 1.** Map of the affected districts with visceral leishmaniasis in Dhamar governorate.

4. Discussion

VL is an endemic disease in Yemen. The most notable finding of this study is the diagnosis of all 57 cases of VL within Dhamar governorate, the central highland area with at least 3000 kms above sea level. The majority of VL cases were identified in Anes district, A'ns, Wesab, Al hada and Automah. All of these districts represent the south west highlands of Dhamar and rising more than 2724 kms above the sea level. The characteristics of these regions are villages scattered over mountains overlapping with some foothills and valleys. The people are mostly farmers with widespread of wild animals including domestic dogs. In addition, they are poor, low educated, having inadequate public health infrastructure, and poor sanitation. The people earn their living from sales of the agricultural products, small-scale business or depend on their daily manual labor. VL have developed for long time in the hot regions of Northern and Western plains where malarial infection is coexisted. The observed cases of VL in the central highlands suggest increasing spread of the disease to unusual sites as reported by several studies [12, 1]. This could be explained at least in part by vectors adaptation to the changing climate observed recently.

The alternative explanation could be related to population displacement seen during the last five years due to political turmoil. Therefore, VL cases might have been exposed to *L. donovani* infection elsewhere. Population displacement during war has been described as a risk factor of increasing *leishmaniasis* cases in Iraq and Syria [13]. In Yemen, it is reported that the population movement from urban areas to villages, disrupted habitats of animal reservoirs and vectors due to current armed conflicts may be the most important risk factors for the increased transmission of the different forms of *leishmaniasis* [14]. In our setting, notification of VL cases is not demanding thus, the active foci cannot be followed and determined and the geographical distribution could not be mapped. Sharing of clinical features of VL with several feverish diseases, delay in the diagnosis and high lethality rate often before hospitalization further complicate the situation and account for underreporting the disease [15]. In the current study, it is found that the most frequent clinical presentations were fever and splenomegaly which affected all children. Abdominal distension was present in the majority of our patients reflecting the gross splenomegaly and / or hepatomegaly. These findings are consistent with other study [16]. It is reported that the hepatosplenomegaly could be the result of accumulation of mononuclear phagocytic cells causing hyperplasia of the reticuloendothelial cells, the principal involved system [17]. Hematological abnormalities in VL are common, chronic inflammation and dietary factors appear to be most common factors. Anemia was evident in all patients of this study with mean haemoglobin level of 6.51 ± 2.82 g/dl. This finding is similar to other studies [18, 16]. The causes of anemia in patients with VL are multifactorial factors such as sequestration and destruction of

red blood cells (RBC) in the enlarged spleen, immune hemolysis and alterations in RBC membrane permeability [19]. Neutropenia was less frequently found in our patients (17.5%) and more than half of our patients developed thrombocytopenia. The presence of very low counts of neutrophils and platelets has been reported to increase the risk of death three and twelve folds respectively [20].

There are different strategies applied to control the vectors transmission including among others spraying houses with insecticide and treated bed nets [21]. It is reported that in countries with endemic VL such as Sudan, the incidence has been sharply reduced after a community distribution of insecticide treated nets [22]. However, the control of the disease relies on the people in the targeted area [23]. In some communities like ours, the implementation of the control program is less likely to success owing to the people low education, socio-economic factor and most importantly lack of individual awareness. Furthermore, the controlling of the animal reservoir hosts appears difficult in such agricultural areas where the density of animals including domestic dogs is predominant and favourable by settlements. The increasing prevalence of VL and urbanization of the disease observed worldwide [1] should alarm the physicians as well as the health care system to go one step forwards. Nationwide notification of all VL cases plus some form of control programs is required. The current study showed a response rate to sodium stibogluconate treatment as 94.8%. This finding is similar to the data derived from Ethiopia that reported the initial cure rates of 95% [24]. The high cure rate observed in this study could be also attributed to aggressive adjunctive care provided for pediatric patients. The specific anti *leishmania* agents are only part of the treatment for VL patients. Supportive care including managing and preventing the complications of VL is very important [25]. All of patients in this study received blood products and dietary support. However, the sole dependence on chemotherapy is no more acceptable and the demand for the development of an efficient vaccine is needed [26].

Death was occurred in 3 cases (5.2%) of pediatric patients in this study and seen among patients with age below one year, prolonged illness prior to treatment, severe anemia and large spleen size. It is reported that the overall case-fatality rate of VL is around 10% [27].

5. Conclusion

This study confirmed the presence of VL cases in Dhamar governorate, most frequently affected children below four years of age with excellent response to chemotherapeutic drug. Existence of VL foci in the highest central highlands indicating that the disease tend to spread into other virgin parts of the country. Such a new distribution combined with lack of vital recording and reporting make the efforts to approximate the figure of true incidence difficult. Correction of the factors contributing to under reporting of VL and better surveillance system through collection of community-

based data are urgently needed.

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