Trend in cumulative cases and mortality rate among visceral leishmaniasis patients in Eastern Sudan: a 14-year registry, 2002–2015

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SUMMARY

Background: Leishmaniasis is one of the neglected infectious diseases of the world. This disease largely affects individuals of low socio-economic level, mainly in developing countries.
Methods: The aim of this study was to investigate the cumulative number of cases, case fatality rate, and trend in incidence and mortality rate of visceral leishmaniasis (VL) in Eastern Sudan. A retrospective descriptive study was performed through analysis of the database managed by the Ministry of Health in Gadarif State, which includes all cases of VL.
Results: Over the 14-year study period (2002–2015), a total of 51 773 patients were registered in Gadarif State with clinical and laboratory evidence of proven VL. The trend in VL was considerably higher over the years 2003–2005 as compared to the last 5 years of 2011–2015. The highest fatality rate was observed in 2002 (4.8%) and it had declined in 2014 (1.1%) and 2015 (1.7%). Rural residence was statistically associated with death related to VL ($p = 0.021$).
Conclusions: This study showed a high number of cumulative cases of VL in Eastern Sudan. The fatality rate was found to be highest among rural residents and has declined in the last 5 years. Thus immediate interventions are needed in terms of health education and the implementation of preventive measures, with a specific focus on people residing in rural areas.

1. Introduction

Leishmaniasis is one of the neglected infectious diseases of the world. It largely affects individuals of low socio-economic level, mainly in developing countries.[1–3] Clinically, the disease is characterized by a diverse spectrum of manifestations that develop after infection with protozoan parasites of the genus *Leishmania*. Features of the disease vary widely, but are often divided into three distinct clinical syndromes, namely visceral leishmaniasis (VL)/kala-azar with its dermatological sequelae (post kala-azar dermal leishmaniasis, PKDL), cutaneous leishmaniasis (CL), and mucosal leishmaniasis (ML).[4] VL places a huge burden on society in terms of morbidity, mortality, and economic burden. Worldwide, more than 90% of VL cases occur in six countries: Bangladesh, Brazil, Ethiopia, India, South Sudan, and Sudan.[1,4]

VL is a disseminated protozoan infection, transmitted by sand fly bites, in which macrophages of the liver, spleen, and bone marrow are preferentially parasitized with intracellular replication.[5] *Leishmania donovani* is the primary cause of VL in Sudan and East Africa.[6] Epidemiological and entomological studies have confirmed *Phlebotomus orientalis* to be the vector in several parts of Sudan, typically associated with *Acacia seyal* and *Balanites aegyptiaca* vegetation.[7]

In Sudan, VL is primarily anthroponotic.[8] Sudan has a population of 36.4 million, VL is endemic in seven states and 17 localities, and all clinical forms exist (VL, PKDL, CL, ML). During the period 2002–2011, a total of 29 700 cases were reported, with a case fatality rate of 3.7%.[8,9] Gadarif State in Sudan is highly endemic for VL, thus the current study was performed to investigate the cumulative number of cases, case fatality rate, and the trend in incidence and mortality rate of VL, with the aim of providing program managers with the fundamental data necessary for interventions and the implementation of a strategic plan to reduce the incidence rate of this disease in Sudan.

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2. Methods

2.1. Study area

Gadarif State is one of the most important states in Sudan and plays a significant role in the economic and agricultural activities of the country. It has a population of 1 727 401 residents, covers 75 000 km^2, and lies between latitude 14 and 16 north and longitude 33 and 36 east. The average rainfall is 612 /millimeter. Four rivers pass through the state (Atbara, Elrahad, Saitit, and Basalam) and there are many forests, which provide an excellent environment for the sand fly vector. There are 10 centers for the diagnosis and treatment of VL in the State.

2.2. Study design

To investigate the cumulative number of cases, case fatality rate, and trend in the incidence and mortality rate of VL, a retrospective descriptive study was performed through an analysis of the database managed by the Ministry of Health of Gadarif State, which includes all cases of VL. This database is based on registration at the Department of Infectious Diseases of the Ministry of Health, Gadarif State, Eastern Sudan. The data include personal and social information, the clinical presentation, type of leishmaniasis, follow-up, and the outcome. The outcome is registered as complete recovery, relapse, lost during follow-up, or death; death is registered without further explanation (disease-related or not disease-related). All cases reported during a 14-year period (January 1, 2002 through December 31, 2015) were collected. For each case, the following data were retrieved: sex, age, residence, occupation, and outcome. In accordance with the Sudanese health system, patients aged ≤18 years were considered children.

2.3. Patient management

According to the World Health Organization (WHO), a case of visceral leishmaniasis is a person showing clinical signs of the disease (mainly prolonged irregular fever, splenomegaly, and weight loss) and with confirmation, based mainly on bone marrow aspiration, through direct microscopic visualization or PCR detection.[10] The WHO guidelines were applied for all identified leishmaniasis patients; these guidelines are based on the internationally agreed strategies for the control of the disease.[6] The recommended treatment regimen in Sudan consists of intravenous sodium stibogluconate 20 mg/kg plus intramuscular paromomycin 15 mg/kg for 17 days as the first-line therapy. In cases with severe side effects, liposomal amphotericin B (Ambisome 3 mg/kg for 10 days) is the second option.

2.4. Analysis

Data were entered into a computer database and SPSS version 16.0 software (SPSS Inc., Chicago, IL, USA) and double-checked before analysis. Trends in the incidence rates and mortality were analyzed by linear regression. Means and proportions of the socio-demographic characteristics were compared between the study groups (patients who died and those who survived), and $p < 0.05$ was considered significant.

2.5. Ethics

The study received ethical clearance from the Research Board Committee, Gadarif University.

3. Results

3.1. General characteristics

During the 14-year study period (2002–2015), a total of 51 773 patients were registered in Gadarif State with clinical and laboratory evidence of proven VL. Their mean age was 24.1 (standard deviation 18) years. The majority of these patients had less than a secondary level of education (49 201, 95%), were male (37 002, 71.4%), and lived in a rural area (35 611, 68.7%). More than half of the study sample were adults (29 183 adults (56.4%) and 22 590 children (43.6%)). With regard to environmental factors, the majority of the adult study subjects were farmers (75.2%); housewives made up the lowest percentage (7.7%). Out of the 51 773 VL cases, 48 395 (93.5%) recovered completely, 1686 (3.3%) died, 1581 (3%) relapsed, and 111 (0.2%) were lost during follow-up.

3.2. Cumulative number of cases and fatality rate

Table 1 shows the cumulative number of cases and the case fatality rates. The highest fatality rate was observed in the year 2002 (4.8%); this rate had declined in 2014 (1.1%) and 2015 (1.7%) (Figure 2).

3.3. Trend in VL

As seen in Figure 1, the trend in VL was considerably higher over the years 2003–2005 as compared to the last 5 years of 2011–2015. There were three incidence peaks at different intervals (2003, 2010, and 2014).

3.4. Socio-demographic factors associated with death related to VL

With regard to the socio-demographic factors associated with death related to VL, this study revealed that there was no significant difference in age, education level, or sex between those who died and those who survived. However residence in a rural area was statistically associated with death related to VL ($p = 0.021$) (Table 2).

4. Discussion

This study provides a 14-year review of the epidemiological trends and patient characteristics of leishmaniasis in Eastern Sudan. This appears to be the largest report of VL for the country. The main finding of this study was the high number of cumulative cases of VL in Eastern Sudan. There was a clear decline in the

Table 1
Cumulative number of cases, new cases, and case fatality rate of visceral leishmaniasis in Gadarif State, Eastern Sudan—2002–2015

Year	New cases	Cumulative cases	Deaths	Case fatality rate
2002	4006	-	192	4.8%
2003	7304	11 310	228	3.1%
2004	7004	18 314	264	3.8%
2005	4138	22 452	186	4.5%
2006	2792	25 244	109	3.9%
2007	2751	27 995	98	3.5%
2008	3277	31 272	89	2.7%
2009	4097	35 369	143	3.5%
2010	5050	40 419	142	2.8%
2011	2660	43 079	73	1.4%
2012	2022	45 101	45	2.2%
2013	1897	46	51	2.6%
2014	2818	49	31	1.1%
2015	1957	51 773	35	1.7%