BRIEF COMMUNICATION

CLINICAL AND HEMATOLOGICAL FEATURES AND TREATMENT OUTCOMES OF VISCERAL LEISHMANIASIS PATIENTS ADMITTED TO GONDAR UNIVERSITY HOSPITAL

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ABSTRACT

Back ground: *Visceral leishmaniasis (VL) is zoonotic or anthroponotic protozoal infection acquired from sand fly bite, which causes substantial morbidity and mortality in endemic areas. We conducted the study to look at the clinical characteristics and outcome of VL patients in Gondar University Hospital.*

Objective: *The study aims to evaluate clinical characteristics of VL as related to presenting features, poor prognostic indicators and treatment outcome.*

Methods: *This is a retrospective review of medical records of patients admitted with the diagnosis of VL to the Medical Ward of Gondar University Hospital (GUH) from Sep.10, 2005 to June 30, 2007.*

Results: *During the 2- year review period, 81 patients were admitted with a diagnosis of VL. The diagnosis was made on patients who presented with fever > 2 weeks with splenomegaly and/or wasting, and confirmed by demonstration of parasite in tissue aspirate of bone marrow or spleen. The mean age of patients was 24 ± 7.18 yrs. The average duration of symptoms was 2.8 ± 2.1 months. The majority of the patients (67/81) presented with a complaint of fever. The most frequent clinical features were fever, cough, weight loss, pallor, hepatosplenomegaly and pancytopenia. Of all patients, five VL patients (16.1%) were co-infected with HIV and were clinically indistinguishable from HIV-negative patients. Pneumonia, otitis media and sepsis of gastro intestinal and pulmonary foci were the commonly encountered secondary bacterial infections. Among a total of 81 patients, 15 (18.5%) died and the rest discharged improved. The major cause of death was sepsis with septic shock, and drug-related hepatic, renal and pancreatic toxicities.*

Conclusions: The clinical and laboratory features including fever, cough, weight loss, hepatosplenomegaly and pancytopenia were the typical features of VL in our study. Secondary bacterial infections were commonly encountered in our hospitalized patients.

The major cause of death in this study was inter-current bacterial infection and drug-related organ dysfunction.

INTRODUCTIONS

Visceral Leishmaniasis (VL) is a protozoal infection of the reticuloendothelial system caused by Leishmania spp, acquired from sand fly bite. The majority of VL cases are from the Indian Subcontinent, the Mediterranean Region, Asia, Latin America and East Africa including Sudan, Kenya and Ethiopia (1-7).

The two most endemic foci in Ethiopia are Metema and Humera in Northwest Ethiopia, and Konso and Hamer areas in Southern Ethiopia (7-10). The clinical features of VL such as fever, wasting, hepatosplenomegaly, lymphadenopathy, pancytopenia and skin hyperpigmentation were described by various studies in the world including Africa (1-6,8-12).

Studies reported that VL was one of the protozoal opportunistic infections coexisting with HIV/AIDS and frequently manifesting atypically with frequent relapses after treatment and associated with high mortality (13-17). Andrade *etal* in Brazil showed that secondary bacterial infections frequently co-existed in 60% of their VL patients. Kager *etal* in Kenya reported respiratory infection to be the commonest complication in hospitalized VL patients. Berhe N *etal* as well documented inter-current or concurrent

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bacterial infection occurred in 17-32 % of VL patients treated in various hospitals of Ethiopia (18,19). The drug treatment currently used for VL cases in East Africa is parenteral sodium stibogluconate which is effective in most cases, unlike a report from Bihar, India, in which failure rate for treatment of VL is more than 50% (11,17,20,21). The purpose of this study is to describe the clinical characteristics, poor prognostic indicators and treatment outcomes of VL, as the aforementioned information is scarce in the study locality.

METHODS

This study was a retrospective analysis of 81 VL patients admitted to Gondar University Hospital (GUH) from Sept. 10, 2005 to June 30, 2007.

Diagnosis of VL was made on clinical evaluation (Case definition: fever more than two weeks with splenomegaly and/or wasting (WHO 1990) and confirmed by demonstration of the parasite from splenic or bone marrow aspirate).

Patients who completed and survived the treatment course (Sodium stibogluconate 20mg/kg IV for 30 days) and discharged were considered improved based on clinical and hematological parameters (fever-free, sense of wellbeing, regression of splenomegaly and rise in hematocrit).

Inter-current infection was considered as a concomitant presence of infection during the course of treatment.

HIV testing was performed using determine HIV-1/2 (Abbott, USA) and capillus HIV-1/2 (Trinity Biotech, Ireland). Those patients who had consecutive positive results with both tests were considered HIV-positive. HIV testing was voluntary and pre and post-test counseling was made.

Socio-demographic, clinical and laboratory data were obtained by chart review, and statistical analysis was performed using EPI info 2002 statistical soft ware package.

RESULTS

A total of 82 VL patients (79 males, 3 females) were admitted to the Medical Ward of GUH from Sept 10, 2005 to June 30, 2007. Of these, one HIV-positive male patient with the diagnosis of relapsed VL was excluded from the study because of atypical presenting features and less responsiveness to Sodium stibogluconate in HIV-associated relapsed VL patients.

Therefore 81 patients with first diagnosis of VL were included.

The mean and median age of the study subjects was 24.9 ± 7.18 yrs and 22 yrs respectively (range: 12-52 yrs).

Sixty-eight patients were non-immune, young migrant daily laborers who traveled to Metema and Humera, North West Ethiopia, for agricultural work; the rest were residents of a VL endemic area.

The average duration of symptoms was 2.8 ± 2.10 months, ranging from 2 weeks to 13 months. Presenting complaints were fever in 67 patients, awareness of abdominal mass in 7, cough in 3, easily fatigability in 3 and epistaxis in 1.

The frequent clinical symptoms and signs were fever, cough, weight loss, pallor, splenomegaly and hepatomegaly. The mean splenic size at presentation was 12cm below the left costal margin along the splenic growth line. Hepatomegaly was present in 49 patients with a mean size of 4.9cm below the right costal margin along the right midclavicular line (table 1&2).

Table 1: Frequency of symptoms of visceral leishmaniasis in 81patients

Symptoms	No. of patients	%
Fever	81	100
Cough	57	70
Weight loss	53	65
Leg swelling	42	52
Abdominal swelling	39	48
Epistaxis	39	48
Diarrhea	13	16

Table 2: Frequency of signs of visceral leishmaniasis in 81 patients

Signs	No. of patients	%
Fever	81	100
Splenomegaly	80	99
Pallor	77	95
Hepatomegaly	49	61
Wasting	30	37
Jaundice	15	19
Lymphadenopathy	0	0

Hematological data was determined and 81/81 (100%) of the patients presented with anemia, 77/80 (96%) with leucopoenia and 50/52 (96%) with thrombocytopenia. At presentation 36/81(44%) patients had severe anemia (Hct<21%), 3/52 (6 %) severe thrombocytopenia (Platelet<20,000/ml) and 52 patients pancytopenia (table 3).

Table 3: Hct level, and WBC and Platelet counts

Hct level(%)	No. diagnosed/ Denominator	%
<21.0	36/81	44
21.0-30.0	41/81	51
30.1-41.0	4/81	5
WBC count	**No. diagnosed/ Denominator**	**%**
<1500	26/80	32
1500-3000	39/80	49
1500-3001	12/80	15
>4500	3/80	4
Platelet count	**No. diagnosed/ Denominator**	**%**
<20,000	3/52	6
20,000-50,000	20/52	38
50,000-150,000	22/52	42
>150,000	7/52	14

Aminotransferases, AST and ALT, were determined for 58 patients and were found to be significantly elevated (>3xULN) in 5/58 (9 %) and 11/58 (19 %) patients respectively, indicating hepatic injury. Serology for HIV was done using rapid tests for 31 VL patients and 5/31 (16.1%) were co-infected with HIV.

The inter-current infections detected were pneumonia in 12 patients, otitis media in 6, sepsis in 6, tuberculosis in 4 and bacterial diarrheal diseases in 3. Congestive heart failure secondary to anemia was detected in 15 patients (table 4).

Table 4: Inter-current/Concurrent infections in 81 patients with visceral leishmaniasis

Infections	No. of patients	%
Pneumonia	12/81	15
Otitis media	6/81	7
Sepsis	6/81	7
Tuberculosis	4/81	5
Bacterial diarrheal disease	3/81	4

Among a total of 81 patients, antibiotics and blood transfusion was given for 40 (50.6%) and 48 (59.3%) patients, respectively.

Fifteen patients (18.5%) died, and 66 (81.5%) discharged improved and appointed to return to the follow-up clinic after three months. Two among five HIV-positive VL patients died during their stay in the hospital.

Sepsis with septic shock (usually GI and pulmonary focus) in 5 patients, severe pneumonia in 2, hemorrhage in 1 and drug-related hepatic, renal and pancreatic toxicities in 5 were the presumed clinical causes of death. The causes of death for 2 patients were not documented (table 5).

Table 5: Cause of death in 15 patients with visceral leishmaniasis

Cause of death	Frequency	%
Sepsis	5	34
Pneumonia	2	13
Acute hepatic failure	2	13
Acute pancreatitis	2	13
Acute renal failure	1	7
Hemorrhage	1	7
Unknown	2	13

A concomitant presence of sepsis ($P< 0.01$), and development of drug-induced acute hepatic failure ($P < 0.001$) and acute pancreatitis ($P < 0.05$) were significantly associated with mortality.

DISCUSSION

Most of the study subjects were non-immune, young, male migrant daily laborers who traveled to the kala-azar endemic area because of enormous agricultural development in the Ethio-Sudanese border.

The study subjects displayed the classical symptoms and signs of VL, such as fever, cough, weight loss, pallor and hepatosplenomegaly which were similar to reports from India, Sudan and Ethiopia (8,9,10,12,16).

No significant lymphadenopathy was seen in any of our patients. This was similar to other Ethiopian studies (9,10) but a common finding in India and a typical feature of VL in Sudanese cases (36-80 %) (5).

In general, the laboratory results in this series were typical of those in VL patients in other parts of the world. Anemia, leukopenia and thrombocytopenia were commonly present (1,2,3,6,8,9,10,12).

Inter-current/ concurrent infections with VL occurred in 38.3 % of our patients, higher than a report by Berhe etal which was 16.6% and 32.3% in a regional hospital and Addis Ababa referral hospitals, respectively. This difference could be explained by differences in patient characteristics and infection control systems in hospital settings (18).

Seven out of fifteen patients (47 %) died because of inter-current bacterial infections. This was similar to a report by Stephenson in which the majority of deaths of VL patients was associated with a concomitant presence of infections.

The case fatality rate in this study (18.5%) was the same as that of the Medicines Sans Frontiers (MSF) Programme in Tigray Region (18.5%) and close to an earlier report by Maru in the same hospital (16.6%) (8,16).

At presentation, HIV co-infected VL patients were clinically indistinguishable from HIV-negative VL patient, which was congruent with a study by Lyons *etal* and a report by Russo *etal* (13, 16).

The HIV co-infected VL patients had higher mortality rate of 2/5 (40 %) than HIV-negative VL patients 1/26 (3.8 %) which was similar with a study done in MSF treatment center in Tigray Region, which reported a mortality rate of 33.3% and 3.6% in HIV co-infected and HIV-negative VL patients (17).

In conclusion, the clinical and laboratory features including fever, cough, weight loss, hepatosplenomegaly and pancytopenia were the typical features of VL in our study.

Secondary bacterial infections were commonly encountered in our hospitalized patients.

The major cause of death in the study was inter-current bacterial infection and drug-related organ dysfunction. This study would like to recommend prompt evaluation of VL patients for the presence of secondary bacterial infection and for early detection of life threatening adverse events, which had significantly affected patients' survival.

The study has several weaknesses. First, the retrospective nature of the analysis resulted in incomplete data and a potential for observation bias. Furthermore, the sample size was small and might have not been powerful enough for the differences observed.

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REFERENCES

1. Herwaldt BL. Leishmaniasis. Lancet 1999; 354 (9185):1991-99
2. Piscopo TV, Azzopardi CM. Leishmaniasis. Post grad med J 2007; 83:649-57
3. Davidson RN. Leishmaniasis. Med Edu Res Afr 2006; 24:16-21
4. Badaro R, Jones TC, Lorenco R. A prospective study of visceral leishmaniasis in an endemic area of Brazil. J Infect Dis 1986; 154(4):639-49
5. Zijlstra EE, El-Hassen AM. Visceral leishmaniasis in Sudan. Trans Royal Soc Trop Med Hyg 2001; 95:S27-S58
6. Osman OF, Kager PA, Oskam L. Leishmaniasis in the Sudan: a literature review with emphasis on clinical aspects. Trop Med Int Health 2000;5 (8):553-562
7. Ayele T, Ali A. The distribution of visceral

leishmaniasis in Ethiopia. Am J Trop Med Hyg 1984; 33(4):548-52
8. Maru M. Clinical and laboratory features and treatment of visceral leishmaniasis in hospitalized patients in North West Ethiopia. Am J Trop Med Hyg 1979; 28(1):15-18
9. Ayele T, Tefera M, Muluneh M, Ali A, Hailu A. The clinical features of visceral leishmaniasis in Ethiopia. EMJ 1987; 26:69-76
10. Haile T, Anderson SD. Visceral leishmaniasis in Northern Ethiopia. EAMJ 2006; 83(6):63-66
11. MOH. Visceral leishmaniasis: Diagnosis and treatment guideline for health workers in Ethiopia (1st Edition). Addis Ababa. 2006;1-35
12. Sud A, Varma N, Marwaha RK, *etal*. Visceral leishmaniasis in non-endemic area in India. Trop Doc 2004; 34:247-49
13. Russo R, Laguna F, Lopez-Verez R, *etal*. Visceral leishmaniasis in those infected with HIV. Clinical aspects and other opportunistic infections. Annal Trop Med Para 2003; 97:S99-S105
14. Laguna F, Garcia-Samaniego J, Soriano V. Gastrointestinal leishmaniasis in HIV-infected patients: Report of five cases and review. Clin Infect Dis 1994; 19(1):48-53
15. Ali A. Leishmaniases and HIV/AIDS co-infections. Review of common features and management experiences. EMJ 2002; 40:S37-S49
16. Lyons S, Veeken H, Long J. Visceral leishmaniasis and HIV in Tigray, Ethiopia. Trop Med Int Health 2003; 8(8):733-739
17. Ritmeijer K, Veeken H, Melaku Y, *etal*. Ethiopian visceral leishmaniasis: Generic and proprietary sodium stiboglucanate are equivalent; HIV co-infected patients have a poor outcome. Trans Royal Soc Trop Med Hyg 2001; 95:668-72
18. Berhe N, Hailu A, AbrahamY, *etal*. Inter-current and nosocomial infections among visceral leishmaniasis patients in Ethiopia: an observational study. Acta Tropica 2001; 80:87-95
19. Andrade TM, Carralho EM, Rocha H. Bacterial infections in patients with visceral leishmaniasis. J Infect Dis 1990; 162(6):1354-9
20. kager PA, Rees PH, Manguyo FM, *etal*. Clinical hematological and parasitological response to treatment of visceral leishmaniasis in Kenya: a study of 64 patients. Trop Geo Med 1984; 36:21-35
21. Thakur CP, Deder JP, Narain S, Pratlong F. Leishmaniasis species, drug unresponsiveness and visceral leishmaniasis in Bihar,India. Trans Royal Soc Trop Med Hyg 2001; 95:187-89