Ethiop. J. Health Biomed Sci., 2008. Vol.1, No.1

ORIGINAL ARTICLE

CLINICAL PATTERNS OF VISCERAL LEISHMANIASIS IN PAEDIATRIC AGE GROUP UNIVERSITY OF GONDAR REFERRAL HOSPITAL, NORTH-WEST ETHIOPIA

Sisay Yifru[1*], Belaynew Wasie[2]

ABSTRACT

Introduction: *Visceral Leishmaniasis(VL) is a highly morbid and incapacitating infection which usually presents with prolonged fever, weight loss and hepato-splenomegaly. Annually 500,000 cases of VL occur in a 200 million population at risk. In Ethiopia, VL is caused by species of the leshmania donovani complex including L.donovani and L.infantum and is transmitted by Phlebotomus orientalis, martini and celiae. It is mainly distributed in the lowlands of the Northwest and Southwest. Generally at least forty localities report cases of VL and new foci, like Libokemekem in South Gondar which has now become endemic for VL. The main objective of this study is to determine the clinical pattern of visceral leishmaniasis among children admitted to UoG Referral Hospital.*

Methods: *A total of 91 children admitted with a diagnosis of VL were studied over a period of three years from September, 2004 to October, 2007. Data which was collected using a pre-tested and structured questionnaire, was cleaned,entered and analysed using SPSS version 13 for windows. Percentages were used to describe the outcomes.*

Results: *The mean age of patients was 9.0 years (ranging from 3 to 14 years). More patients 24 (26.4%) came from Addis Zemen. This was followed by Metema 18 (19.8%), Belesa 13 (14.3%) and Armachiho 11 (12.1%). The rest were from Humera and Gondar town 3 and 2 cases, respectively. Most of them (86.8%) were from farmer households. The commonest clinical presentations were chronic fever and hepatosplenomegaly (96.7%) each followed by weight loss (93.4%), pallor (90.1%), with severe pallor contributing 35.2%, bleeding tendency 54.9%, cardiac findings (including ejection systolic murmur, gallop rhythm) 38.5%,leg edema 36.3%, lymphadenopathy 16.5%, and Ascites 2.2%.*

Conclusion: *VL commonly presents with chronic fever,hepatosplenomegally,pallor and anemia with severe anaemia in a significant proportion of the patients. Early initiation of treatment and proper care of patients are required for the management of this fatal disease and to reduce the case fatality rate.*

Key words: leishmaniasis, clinical presentation,Gondar

INTRODUCTION

Visceral leishmaniasis(VL) is a highly morbid and incapacitating infection. The most severe form of the disease usually presents with prolonged fever, weight loss,pancytopenia and hepato-splenomegaly.It is commonly seen in children and young adults . Despite the availability of effective treatment, the disease can have a high mortality even at referral centers. If left untreated, Visceral Leishmaniasis has a mortality rate of almost 100% (1,2).

The etiologic agent of VL in Africa is L. donovani. In Ethiopia VL is caused by species of the leshmania donovani complex which includes L.donovani and L.infantum. The main vectors are families of sand fly, Phlebotomus orientalis, Martini and Celiae(2,3, 4). Kalazar mimics a series of diseases like malaria, tropical splenomegaly syndrome, shistosomiasis, typhoid fever and tuberculosis. There needs to be a high index of suspicion for diagnosis and confirmation(2).

Annually 500,000 cases of VL occur in a 200 million population at risk. In Ethiopia VL is mainly distributed in lowlands, Metema and Humera in the Northwest, the Segen valley, Konso, and the lower Omo plain in the Southwest. On the whole, a minmum of forty localities report cases of VL and new foci like Libokemekem in South Gondar which has now become endemic for VL (2,5). A study conducted to describe the clinical and epidemiological features of VL in children and adolescents with VL in Georgia found out that the main clinical and laboratory presentations were hepatosplenomegaly, anemia, and

[1] *Department of Paediatrics, College of Medicine and Health Sciences, University of Gondar, E-mail: sisaydr@yahoo.com*

[2] *Department of Epidemiology and Biostatistics, College of Medicine and Health Sciences, University of Gondar, E-mail:bewassie@yahoo.com*

[*] *Correspondence Author: Sisay Yifru, E-mail: sisaydr@yahoo.com, Tel: +251 918 77 06 94*

pancytopenia (84.5%). Among the associated diseases, the most frequent were bronchitis, pneumonia (7.0%) and jaundice (3.5%) (6).

Studies in Turkey, Abottabad, Malta and Brazil also showed that the common features at presentation were fever (>95%), pallor (96%), hepatosplenomegaly (86-97%), weight loss and bleeding diathesis. The commonest laboratory findings included thrombocytopenia, anemia (95%), leucopenia (89.4%), and elevated erythrocyte sedimentation rate (77.7%) of the cases (7-11).

Morbidities and concomitant infections are also associated with visceral leishmaniasis among which the commonest ones are malnourishment (44.5%), pneumonia, cardiac failure and sepsis (10.9%) (8). The case fatality rate in visceral leishmaniasis commonly ranges from 10-12%. The main immediate causes of death are associated infections like pneumonia and sepsis, bleeding and multi-system organ failure (8, 11, 14).

Management of leishmaniasis includes antileishmanials mainly Sodiumstibogluconate, blood transfusion, treatment of malnutrition and antibiotics which if used properly will significantly improve outcome in about 90% of the patients (9,11,15). A study conducted at a leishmaniasis treatment center in Tigray revealed that the median age was 2.5 years (10 months to 77 years). The male to female ratio was 11:1. Children under the age of 15 had a lower mortality rate (3%,) than those aged 15 and over (21%).The main presentations were splenomegaly (97%) , fever (93%), cough (64%), diarrhea (52%), hepatomegaly (41%),vomiting (28%), hemorrhage (22%), oedema (16%) and BMI <16 (30%)(16).

The clinical pattern of VL among children in Ethiopia, in general and in Gondar in particular is not well investigated. The purpose of this study is therefore to determine the clinical pattern, identify the most common associated problems and determine the case-fatality rate and causes of death of visceral leishmaniasis.

METHODS

Study design and area: Institution based descriptive cross-sectional study involving patient record review and interview of parents/care takers at the time of discharge was conducted at UoG Referral Hospital Pediatric Ward for about three years from 2004-2007. UoG Referral Hospital is located 727 km North-West of Addis Ababa. This hospital serves patients coming from Gondar, Gojjam and some parts of Tigray. It provides services that include diagnosis for kalazar and blood transfusion.

Study subjects:Subjects were all children admitted to the pediatric ward from September, 2004 to October, 2007 with a diagnosis of VL with or without additional problems. All cases of VL coming to the hospital during the study period were studied. A child was studied only once and repeat admissions were not included in the study. We interviewed parents and reviewed the charts after the patient had completed treatment and was to be discharged. Repeat interviews were avoided via the cross-checking of identification numbers from the registration during the data collection. Patients who disappeared immediately after admission were not included for they did not complete the diagnostic workup making it impossible to observe treatment outcomes.

Diagnosis of visceral leishmaniasis: Patients were examined by a medical intern and general medical practitioner. Clinical data and laboratory results were used to diagnose VL and complications. A fine needle aspiration of the spleen was used for then confirmation of the diagnosis and bone marrow aspiration as well as direct agglutination tests were used where splenic aspiration was contraindicated. General investigations such as a differential white cell count, hematocrit, urinalysis, and chest X-ray were used to identify complications of VL. ELISA was done to test for HIV infection among children of volunteer parents/caretakers.

Variables: The outcome variable of the study was the clinical pattern of the occurrence of visceral leishmaniasis described as improved, same or dead. The independent variables of the study were family income, age, sex, platelet count, WBC count, concomitant/superimposed disease and nutritional status.

Data Collection: Data was collected from both patient care takers and record reviews during discharge by medical interns practicing in the Pediatric Ward using a structured and pre-tested questionnaire. Interviews were made to complement data from patient cards and characteristics related to parents, such as monthly income. The completed questionnaire was checked by a pediatrician.

Statistical analysis: Data was cleaned, entered and analyzed using the SPSS version 13 statistical package for windows. Descriptive outcomes were calculated using percentages.

Ethical issues: Permission was obtained initially from the Medical Director's Office of UoG Referral Hospital. Informed verbal consent was obtained from parents/caretakers of patients. Proper counseling was given during HIV testing for the caretakers/patients and those tested positive were referred to the ART clinic. Data obtained from the clients was kept confidential. Patients identified with problems were managed properly in the hospital. Any patient/caretaker was allowed to withdraw from the study at any time.

RESULTS

A total of 91 children (62.7% male and 37.3% female) with VL were included in the study. The age range of patients was from 3 to 14 years with a mean age of 9.0 years and median 9.0 years. The family size of the households of the patients ranged from 3 to 12 members with the average family size of (6.7± 2.1) persons per household. The majority of the children were from farmer families (86.8%) and only two cases had government-employee parents. The rest were merchants (9.9%) and daily labourers (1.1%) of smaller towns in areas outside Gondar (table-1).

Table-1: Socio-demographic characteristics of patients admitted to paediatric ward of UoG referral hospital with visceral leishmaniasis from September 2004-October 2007.

Characteristic		Number	%
Age	<5	11	12.1
	5-10	50	54.9
	10-15	30	33.0
	Total	91	100.0
sex of child	Male	57	62.6
	Female	34	37.4
Occupation	Farmer	79	86.8
	Merchant	9	9.9
	Government employee	2	2.2
	Other	1	1.1
	Total	91	100.0

The study found out a new focus of infection as many patients came from Addis Zemen 24(26.4%) followed by Metema 18(19.8%), Belessa 13(14.3%), Armachiho 11(12.1%). Two cases came from Gondar town and only 3 from Humera(Figure-1).

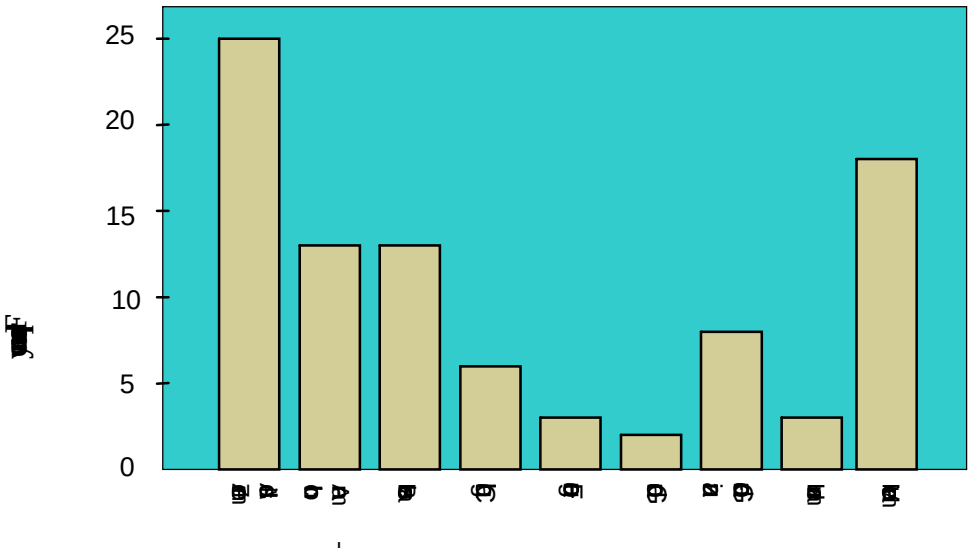

Figure-1: Residence of patients admitted with VL to pediatric ward of University of Gondar referral hospital, Gondar, September 2004-october 2007.

Clinical patterns of Visceral Leishmaniasis : The commonest clinical presentations were chronic fever and hepato-splenomegaly (96.7%) each, followed by weight loss (93.4%), pallor (90.1%) with severe pallor contributing 35.2%,bleeding tendency 54.9%, cardiac findings (including ejection systolic murmur, gallop rhythm) 38.5% (who also had cardiomegally on chest X-ray), leg edema 36.3%, lymphadenopathy 16.5% and ascites 2.2%. Recent fever at presentation was detected in 88% of the patients and high grade fever in 63.7% with a mean temperature of 37.81^{o}c (Table-2).

Table-2: Clinical presentation of patients admitted to the Pediatric Ward of UoG Referral Hospital with visceral leishmaniasis from September, 2004-October, 2007.

Clinical presentation		No of children	%
Splenomegally	yes	88	96.7
	no	3	3.3
Fever	yes	88	96.7
	no	3	3.3
Weight Loss	yes	85	93.4
	no	6	6.6
Pallor	no	9	9.9
	some	50	54.9
	severe	32	35.2
Bleeding Tendency	yes	50	54.9
	no	41	45.1
Lymphadenopathy	yes	17	18.7
	no	74	81.3
Leg Edema	yes	33	36.3
	no	58	63.7
Chronic Cough	yes	27	29.7
	no	64	70.3

During the study, there were 7 deaths giving a case fatality rate of 7.7%. Three patients disappeared and the rest recovered. Sepsis was the commonest cause of death (3 patients) followed by cardiac failure, severe anaemia and respiratory failure following severe pneumonia.

The commonest laboratory finding was anemia 90.1% (mean HCT 23.52%) the lowest hematocrit being 10% followed by leucopenia (WBC<4000cells/mm^3) 63.7% (mean 3441.2cells/mm^3) with a minimum value of 500/mm^3 and thrombocytopenia 52.7% (mean 140241.22 cells/mm^3) with 6.6% severe thrombocytopenia, (platelet count less than 20,000 cells/mm^3).

Fine Needle Aspiration (FNA) of the spleen was indicated for 87 patients and LD bodies were identified from direct microscopy. FNA was not done for four patients because of the presence of bleeding tendency. For these diagnosis was made by direct agglutination test and bone marrow aspiration. ELISA was done for 15 patients and one positive result was obtained. Stool microscopy was done for 74 patients and 30(40.5%) tested positive. The parasites observed were hook worm, giardia, amoeba trophozoites and ascaris ova. Urinalysis results were reported as positive for many 'white blood cells' and bacteria in 19 out of the 64 tested patients.

Chest X-ray was ordered for 50 patients for different reasons. Half of them had no findings; cardiomegally was observed in 10 patients followed by consolidation (7), infiltration (4), opacity (3). Pleural effusion was seen in one patient (Table-3).

Table-3: Common laboratory findings of patients admitted to the pediatric ward of UoG Referral Hospital with visceral leishmaniasis, September 2004-October 2007.

		Frequency	Percent
HEMATOCRIT (%)*	≤15	10	11.0
	>15	81	89.0
	Total	91	100.0
WHITE BLOOD CELL COUNT**	<4000	58	63.7
	≥4000	33	36.3
PLATELETE COUNT***	<20000	6	6.6
	20,000-150,000	60	65.9
	>150000	25	27.5
Stool microscopy	Positive	30	33.0
	Negative	44	48.4
	Not done	17	18.7
Urinalysis	Positive	19	20.9
	Negative	45	49.5
	Not done	27	29.7
Chest X-ray	Cardiomegally	10	11.0
	Consolidation	7	7.7
	Infiltration	4	4.4
	Pleural effusion & other opacity	4	4.4
	No finding	25	27.5
	Not done	41	45.1

Keys: *minimum value=10%
**minimum=500/mm^3
***minimum =1900/mm^3

Wasting was found in 56 cases with moderate wasting accounting for 41.8% and severe wasting for 19.8% of the patients. Stunting was observed in 47 (51.6%) children. Using the Harvard Standard and NCHS, malnutrition was identified among 61 children with kwashiorkor and marasmus accounting for 5.2% and 3.9%, respectively (Table-4). We found out congestive heart failure in 17 (18.7%), tuberculosis in 14 (15.4%), gastroenteritis in 10(11.0%), pneumonia in 21(23.1%) and intestinal parasitosis in 32 (35.2%) of the patients.

Table-4: Nutritional status of children admitted with a diagnosis of visceral leishmaniasis to the pediatric ward of Gondar University Hospital, September 2004 -October 2007(n=77).

Nutritional Status	Number	Percent
No malnutrition	16	20.8
Underweight	54	70.1
Kwashiorkor	4	5.2
Marasmus	3	3.9

Concerning the treatment given for patients, antileishmanial drugs were given to all patients. Transfusion was required for 34(37.4%) patients for severe anaemia. 39(42.8%) patients were treated with broad spectrum antibiotics mainly for sepsis, pneumonia and other bacterial infections. Four patients were treated with anti-malaria and anti-TB.

DISCUSSIONS

Male predominance (62.7%) was observed in this study. A similar condition was reported from Segen and Woyto areas (2, 5). The majority of these children were from farmer families**.** These findings focus on farmers and children at around the age of 9 who mostly spend the nights either in small huts or on the tops of watch towers to keep their animals and properties. Their life style expose, the people to the bite of sandfly.

The fact that most of the patients came from Addis Zemen indicated the appearance of a focus which was different from what had been hither to reported. This might be due to the seasonal migration of workers to endemic areas bringing the disease to unaffected sites since no cases were reported before the year 2005 in Libo Kemkem(17). Other sites were Metema (19.8%), Belessa (14.3%) and Tach Armachiho(12.1%)(Figuer1). This finding was observed in other reports (2).

As seen in this study, the commonest clinical presentation was chronic fever and hepatosplenomegaly accounting for 96.7% each followed by weight loss (93.4%), pallor (90.1%) and bleeding tendencies manifested by epistaxsis and petechiae in 54.9% of the cases. The finding is comparable to results from other studies (7-11). Lymphadenopathy which is (16.5%) in this study is a less common finding when compared to reports from other sites in South-West Ethiopia and countries like the Sudan in which most of patients present with it (5, 12).Congestive heart failure, anemia, tuberculosis, gastroenteritis, pneumonia, urinary tract infections and intestinal parasitosis occur as a complication or concomitant diseases in VL. Similar results were observed in other studies (8, 15). As seen in this review (Table 2), malnutrition accounts for 79.2% of the cases with severe malnutrition contributing 28.9%. A similar finding was seen elsewhere (8, 15).

In this study the common hematological findings (shown in Table 3) were similar to those found out in other areas and are characterized by anemia (90.1%), leucopenia(63.7%) and thrombocytopenia (52.7%).The minimum HCT was 10%, minimum WBC count 500/mm3 and minimum platelet count 1,900/mm3 with 6.6% having a platelet count of less than 20,000/mm3(8-11). As most of our patients were from low socioeconomic groups, poor sanitation contributed to the acquisition of intestinal infestations which were reflected by a positive stool microscopy in 40.5% of the cases. The commonest parasite obtained in this study was hook worm which again added a haemodynamic burden to the heart by causing anemia.

All of the patients were treated with sodiumstibogluconate; transfusion was required in 37.4% cases of severe anemia which was unlike a study conducted in Malta (9). The low rate of transfusion seen in this study might be due to smaller number of patients presenting with advanced stages of diseases like severe pallor and leg edema 35.2% and 36.3%, respectively. Antibiotics and anti-TB were common drugs used because sepsis pneumonia and tuberculosis were the commonest associated problems identified in this study. Similar findings were observed in other centers (8, 11, 14).

Seven deaths were reported in the study period with a case fatality rate of 7.7%, the commonest cause of death being sepsis and cardio-pulmonary failure due to CHF and Pneumonia. These findings were consistent with a study done at Tigray Leishmaniasis Center where mortality due to visceral leishmaniasis in

the age group of below 15 years was less than in those who were 15 and above (16). The lower case fatality rate observed in this study as compared to results absorbed in Brazil (10.5%) and Abbotabad (11.2%) might be attributed to the early introduction of treatment, earlier presentation of patients to hospital justified by many patients with non advanced stage of the disease and the availability of a transfusion set up resulting in good recovery(8,11,14).

In conclusion, leishmaniasis is commonly seen among male children which can be due to the increased tendency of the male child in rural families to spend most of the time outside home where he may be bitten by phlebotomus. A new focus of transmission is found out in this study in addition to the previously known transmission sites with the commonest clinical presentations of fever, hepatosplenomegally, pallor, pancytopenia and weight loss. Moreover, most of the patients in this setting present with hepatosplenomegally more than lymphadenopathy that can be seen in other sites. The demonstration of LD bodies by splenic aspirate remains the golden tool to make a diagnosis of visceral leishmaniasis while bone marrow aspiration and direct agglutination tests are alternatives when the former is contraindicated. Thus, early detection and treatment of cases including concomitant illnesses and pancytopenia are vital parts of patient care. Ongoing surveillance system shall be strengthened to detect new transmission sites as the disease pattern is changing over time and further prospective studies on clinical picture, predisposing factors and epidemiology of VL including vector studies in different sites are very important for the control of this severe disease as there are no detailed studies among a pediatrics patients.

ACKNOWLEDGEMENTS

We would like to thank the patients and the care takers for their cooperation in the data collection and the data collectors for taking their time to do the job. We are also grateful to UoG for allowing us to use resources.

REFERENCES

1. Malatesha G, Mathur P , Kaushal M, et al. Profile of fatal visceral leishmaniasis at an Indian tertiary care center. J Trop Gastr; 28 (1):28-31.
2. Federal Ministry of Health (FMOH). Visceral leishmaniasis diagnosis and treatment guideline for health workers in Ethiopia. Addis Ababa;June 2006.
3. Pahwa R, Fupta SK, Singh T, Nigam S. Acute fulminant visceral leishmaniasis in children--a report of two cases. Indian J Pathol Microbiol. 2004 Jul; 47(3):428-30.
4. Jonathan B. Visceral leishmaniasis in the New World & Africa. Indian J Med Res 123. March 2006; 289-294.
5. Lindtjorn and Fuller et'al. Kalazar in Segen and Woyto,South-West Ethiopia. Eth Med J. 1983; 21:35.
6. Zenanishvili OP, Bakashvili LZ, Pagave EK, et'al. Visceral leishmaniasis: clinical and epidemiological features among children and adolescents in Georgia. Georgian Med News. 2005 Dec; 129: 85-7.
7. Gönül T, Aysegül TÖ, Eda D. Pediatric visceral leishmaniasis in Turkey. Ped Int. 2006; 48 (1): 66–69.
8. Márcia JA, João GB, Jailson B. Correia.visceral leishmaniasis: clinical and epidemiological features of children in an endemic area. J Pediatr. (Rio J.), Mar. /Apr. 2004; 80(2):141-146. ISSN 0021-7557.
9. Victor G, Joseph M, Mariella M, Cecil V. Visceral leishmaniasis in Malta: an 18 year paediatric population based study. Arch Dis Child. 2000 May;82:381-385.
10. Maltezou HC, Siafas C, Mavrikou M, et al. Visceral leishmaniasis in immunocompetent children and the role of pentavalent antimonials. Abstr Intersci Conf Antimicrob Agents Chemother. 1999 Sep 26-29; 39: 698 (Abstract No. 2230).
11. Zardad MT, Manzoor ER, Abdus SK. Clinical presentation and management of visceral leishmaniasis. J Ayub Med Coll Abbottabad. 2005;17(4).
12. Pera WA, Ancelle T, Moren A, et al. Visceral Leishmaniasis in Southern Sudan. Trans R Soc Trop Med Hyg. 1991 Jan-Feb; 85(1):48-53.
13. Pasquale P, Marco R, Carolina R, et al.Mediterranean visceral leishmaniasis in hiv-negative adults: a retrospective analysis of 64 consecutive cases (1995–2001). J Antimicrob Chemoth. 2003; 52: 264–268.
14. Fuller Ck, Lemma A, Haile T, Gemeda N. Kalazar in Ethiopia: survey in South-West Ethiopia. Ann Trop Med Parasit. 73: 417-431.
15. Marlet MV, Wuillaume F, Jacquet D, et'al. A neglected disease of humans: a new focus of

visceral leishmaniasis in Bakool, Somalia. Trans R Soc Trop Med Hyg. 2003; 97: 667–671.
16. Suzi L, Hans V and Jean L. Visceral leishmaniasis and HIV in Tigray, Ethiopia. Trop Med Int Health. 2003 August; 8(8):733–739.
17. Jorge A, Seife B, Daniel A. Kala-azar outbreak in Libo Kemkem, Ethiopia: Epidemiologic and parasitologic assessment. Am J Trop Med Hyg. 2007; 77(2):275-282.