# Clinical and hematological manifestations of visceral leishmaniasis in Yemeni children

*Yemenli çocuklarda visseral leishmaniasis'in klinik ve hematolojik belirtileri*

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## *Abstract*

**Objective:** In southeast Yemen, visceral leishmaniasis (VL) is endemic in Lahj and Abyan and also in Hagga and Sadah, the areas lacking adequate diagnostic facilities. This study describes the clinical and hematological features in 64 cases of childhood VL.
**Material and Methods:** All children below 12 years of age who were managed as inpatient cases from 1 January to 31 December 2005 were included in this study. The diagnosis of VL was established by demonstration of leishmania parasites in bone marrow aspiration. Demographic information, physical signs at presentation and results of complete blood count were recorded and bone marrow aspirations were done for LD bodies.
**Results:** Mean age of the patients was 30 months, and there were 33 females and 31 males. Fever was seen in 100% of children with duration before diagnosis of 56 days. Splenomegaly was present in all cases and hepatomegaly in 84.4%, with mean enlargement of spleen and liver of 9.3 and 3.5 cm, respectively. Mean hemoglobin level, white blood cell and platelet counts were 6.6 g/dl, $3.58x10^9$ /L and $71.7x10^9$ /L, respectively. Absolute neutrophil count was $<0.78x10^9$ /L and mean reticulocyte count was 1.7%.
**Conclusion:** Fever, hepatosplenomegaly and pancytopenia were the most common clinical and hematological manifestations in Yemeni children with VL. *(Turk J Hematol 2009; 26: 25-8)*
**Key words:** Leishmania, clinical, hematological

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## *Özet*

**Amaç:** Visseral leishmaniasis (VL), yeterli tanı hizmetlerinden yoksun olan Yemen'in güneydoğu bölgesinde yer alan Lahj ve Abyan'da ve ayrıca Hagga ve Sadah'da endemiktir. Bu çalışma 64 çocukluk çağı VL olgusunun klinik ve hematolojik özelliklerini tanımlamaktadır.
**Gereç ve Yöntemler:** Bu çalışmaya, 1 Ocak'tan 31 Aralık 2005 tarihine kadar hastanede tedavi görmekte olan 12 yaş altındaki tüm çocuklar dahil edilmiştir. VL tanısı kemik iliği aspirasyonunda leishmania parazitlerinin gösterilmesi ile konmuştur. Demografik bilgi, başvuru sırasındaki fiziksel bulgular, tam kan sayımı sonuçları kaydedilmiş ve LD cisimcikleri için kemik iliği aspirasyonları yapılmıştır.

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**Bulgular:** Hastaların ortalama yaşı 30 aydı. Otuz üçü kız ve 31'i erkekti. Çocukların %100 ünde tanıdan önce 56 gün süren ateş görüldü. Dalak ve karaciğerde sırasıyla 9.3 cm ve 3.5 cm ortalama büyüme ile tüm olgularda splenomegali ve %84,4'ünde hepatomegali vardı. Ortalama hemoglobin düzeyi, lökosit ve trombosit sayıları sırasıyla 6,6 g/dl, 358x$10^9$/l ve 71.7x$10^9$ /l idi. Mutlak nötrofil sayısı <0.78x$10^9$ /l ve ortalama retikülosit sayısı %1.7 idi.
**Sonuç:** Visseral leishmaniasis'li Yemenli çocuklarda ateş, hepatosplenomegali ve pansitopeni en sık görülen klinik ve hematolojik belirtilerdi. *(Turk J Hematol 2009; 26: 25-8)*
**Anahtar kelimeler:** Leishmaniasis, Klinik, Hematolojik

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## Introduction

Visceral leishmaniasis (VL) is caused by the parasites of Leishmania donovani and is transmitted by the bite of a Phlebotomus fly. VL is found in 47 countries of the world, most of them being developing countries. It is estimated that approximately 400.000 individuals are infected annually worldwide [1,2].

Visceral leishmaniasis is a parasitic disease of the reticuloendothelial system characterized by fever, hepatosplenomegaly, anemia and leukopenia, and progressive weakness and emaciation, which can result in death if left untreated. Children are at greater risk than adults of developing VL in endemic areas [3].

Visceral leishmaniasis is endemic in Yemen and most of the cases are registered in Lahj, Abyan, Hagga and Sadah governorates [4], the areas lacking adequate diagnostic facilities. The diagnosis is mostly missed or delayed for months or years and some patients are treated blindly.

The aim of this study was to document and identify the clinical and hematological changes in VL in Yemeni children and to determine the relation of parasitemia with hematological changes.

## Materials and Methods

This study was conducted at Al-Gamhouria Teaching Hospital in Aden, Yemen. It included 64 patients diagnosed as VL. The diagnosis was confirmed in all patients by identifying Leishmania donovani in bone marrow cytology (Figure).

Investigations performed in each patient included complete blood count (CBC), differential count and erythrocyte sedimentation rate (ESR). Bone marrow aspirates were taken for Leishmania donovani bodies (LD bodies) and evaluation of the hematological abnormalities.

Quantitation of LD bodies: The parasite load of LD bodies was calculated by counting the number of parasites (LD bodies per 100 consecutive oil-immersion fields [OIFs]). LD bodies were graded as follows: 1. High grade (>30 LD bodies/100 OIF); 2. Moderate grade (10-30 LD bodies/100 OIF); and 3. Low grade (< 10 LD bodies/100 OIF).

The processing of the obtained data was performed using the special statistical package of Epilnfo 2004 to findout the frequency, percentage, mean values, standard deviation and P values

## Results

Sixty-four cases were diagnosed as childhood VL during the period from 1 January to 31 December 2005. Thirty-three patients were female and 31 were male. Both sexes were affected. In infancy, males were affected more than females (66.7% and 33.3%, respectively), while after infancy there was no significant difference in the percentages of those affected according to gender.

Clinical examination of patients with VL revealed that all had fever and splenomegaly. Other common symptoms were weight loss and abdominal distension (67.2% for each) and fatigue (65.6%). The common signs were pallor (84.4%) and hepatomegaly (76.6%). Lymph node enlargement was seen in 17.2% (Table 1).

Blood investigation revealed hemoglobin concentration ranging from 2.4 to 10 g/dl (mean: 6.6±1.7 g/dl). The red blood cell count ranged from 0.8 to 3.5x$10^{12}$/L (mean: 2.4±0.6x$10^{12}$/L. Total white blood cell count ranged from leukopenia of 1.1x$10^9$/L to near normal count of 8.5 x $10^9$/L (mean: 3.5±1.6x$10^9$/L). The mean absolute neutrophil count was 0.78±0.56x$10^9$/L (range: 0.032 to 2.31x$10^9$/L). The platelets also showed a count ranging from thrombocytopenia of 5x$10^9$/L to normal range of 188x$10^9$/L (mean: 71.7±41x$10^9$/L) (Table 2).

The presence of peripheral pancytopenia was noticed in 45 patients (70.3%) with VL, while the remaining patients had anemia plus either leukopenia or thrombocytopenia.

The ESR ranged from 22 to 135 mm/hour (mean: 71.9±28.9 mm/hour). Reticulocyte count ranged from normal value of 0.2% to 6.5% (mean: 1.7±1.5%). Table 3 shows abnormalities of the blood smear in Yemeni children with VL and Table 4 presents the relation between hematological parameters and the level of parasitemia.

**Table 1. Clinical features in pediatric patients with visceral leishmaniasis**

| Clinical features | | Cases (n=64) | |
|---|---|---|---|
| | | No | % |
| Symptoms: | | | |
| | Fever | 64 | 100.0 |
| | Weight loss | 43 | 67.2 |
| | Abdominal distension | 43 | 67.2 |
| | Cough | 29 | 45.3 |
| | Anorexia | 24 | 37.5 |
| | Vomiting | 23 | 35.9 |
| | Diarrhea | 17 | 26.6 |
| | Bleeding | 5 | 7.9 |
| Signs: | | | |
| | Splenomegaly | 64 | 100.0 |
| | Pallor | 54 | 84.4 |
| | Hepatomegaly | 49 | 76.6 |
| | Lymph node enlargement | 13 | 20.3 |
| | Skin rash | 5 | 7.8 |
| | Pitting edema | 2 | 3.1 |

## Discussion

Visceral leishmaniasis (VL) is a major health problem in Yemen and affects predominantly infants and young children. According to the World Health Organization (WHO), leishmaniasis affects around two million people annually, 500.000 cases of which are of the visceral form. It is estimated that 350 million people are exposed to the risk of infection, with a global prevalence of 12 million infected individuals [4].

**Table 2. Clinical and hematological profile in pediatric patients with visceral leishmaniasis**

| Clinical and hematological profile | Cases (n=64) | | |
|---|---|---|---|
| | Mean | SD | Range |
| Age (years) | 2.6 | 2.01 | 2/12-12 |
| Duration of symptoms (weeks) | 8.0 | 5.0 | 2-21 |
| Spleen (cm) | 9.3 | 2.6 | 2-16 |
| Hemoglobin (g/dl) | 6.6 | 1.7 | 2.4-10.0 |
| Red blood cells (x$10^{12}$/L) | 2.4 | 0.6 | 0.8-3.5 |
| White blood cells (x $10^9$/L) | 3.5 | 1.6 | 1.1-8.5 |
| Neutrophils (x $10^9$/L) | 0.78 | 0.56 | 0.03-2.31 |
| Platelets (x $10^9$/L) | 71.7 | 41.0 | 5-188 |
| ESR (mm/hr) | 71.9 | 28.9 | 22-135 |
| Reticulocyte (%) | 1.7 | 1.5 | 0.2-6.5 |

**Table 3. Abnormalities of blood smear in Yemeni children with VL**

| Blood smear findings | Cases (n=64) | |
|---|---|---|
| | No | % |
| **Red Blood Cells** | | |
| Hypochromic microcytic | 32 | 50 |
| Macrocytic normochromic | 13 | 20.3 |
| Dimorphic 14 | 21.9 | |
| Anisocytosis | 24 | 37.5 |
| Poikilocytosis | 25 | 39.1 |
| Knizocyte 27 | 42.2 | |
| Schistocytes | 16 | 25.0 |
| Target cells 9 | 14.1 | |
| Rouleaux formation | 58 | 90.6 |
| **White Blood Cells/Platelets** | | |
| Decreased neutrophils | 50 | 78.1 |
| Increased lymphocytes | 6 | 9.4 |
| Decreased lymphocytes | 5 | 7.8 |
| Increased monocytes | 2 | 3.1 |
| Decreased platelets | 60 | 93.8 |

**Table 4. Blood parameters in relation to the level of parasitemia in children with visceral leishmaniasis**

| Parasitemia | Hemoglobin (g/dl) | WBC (X$10^9$/L) | Platelets (X $10^9$/L) |
|---|---|---|---|
| | Mean±SD | Mean±SD | Mean±SD |
| Low | 7.0±1.6 | 3461.1±1193.7 | 85555.5±39207.1 |
| Moderate | 6.0±1.8 | 3655.0±1886.6 | 74400±50956.5 |
| High | 6.9±1.6 | 3465.4±1597.2 | 59961.5±30588.2 |
| P value | P=0.10 | = 0.90 | = 0.10 |

**WBC:** White blood cells, **SD:** standard deviation

The characteristics of the current study are similar to previous studies, with VL predominating among five year olds, mainly the toddler (1-3 years) age group [5,6]. The mean age of children was 2.6 years. Children of both sexes were approximately equally affected, and a significant variation was not expected due to the similar rate of exposure in children regardless of sex difference [7].

The major clinical symptoms in this study were fever in 64 patients (100%), similar to results reported in other studies [8,9]. Abdominal distension was seen in 43 patients (67.2%), with similar reports in Bangladesh (67%) [10] and Saudi Arabia (76.8%) [8]. The mean duration of fever at presentation was 8 weeks (range: 2 to 21 weeks). Campose et al. [11] had reported a period of 1-6 months in 78% of patients and another study in Malta reported the mean duration as 4-8 weeks [12]. Splenomegaly was present in 100% of patients in this study and other similar studies [13,14]. The mean size of the spleen was 9.3 cm. Al-Orainey et al. [8] in a Saudi study found 85.9% of patients had spleen size of more than 5 cm. Other studies found the mean size of the spleen as 6.8 cm among Pakistani children and 11 cm in Somalia children [15]. The increased spleen size in Somalia and Yemeni children was probably due to the long duration of symptoms before presentation to the hospital [16]. VL with massive splenomegaly could be associated with hypersplenism and consequent anemia, leukopenia and thrombocytopenia [17].

Pancytopenia was the most frequent hematological abnormality in our patients (70.3%). Sud et al. [18] and Mathur et al. [19] found pancytopenia in 57.8% and 88%, respectively. The reason for the higher frequency of pancytopenia is probably the long duration of symptoms and splenomegaly before presentation to the hospital and increased peripheral destruction rather than bone marrow failure of production as suggested by the bone marrow hyperplasia [20]. Anemia of varying degrees was present in all cases with a multifactorial etiology, of which nutritional factors have an important bearing. This was obvious from peripheral smear findings of anisopoikilocytosis, macrocytosis, hypochromasia and polychromasia [19].

Leukopenia is found with great frequency among VL patients. In this study, leukopenia occurred in 67% of the cases and neutropenia in 78.1%, which may indicate that a relative lymphocytosis or monocytosis accounted for what appeared to be total leukocyte count within the normal range [8]. Increased neutropenia in VL children is strongly associated with massive splenomegaly [20]. Thrombocytopenia is a common finding in VL patients, and is exhibited in 40% to 65% of patients [5]. Helmi et al. [21] in Iraq and Rahim et al. [22] in Pakistan found thrombocytopenia in 80-90% of the patients, similar to our results. Although our results reported 90% thrombocytopenia, and the mean platelet count was 72x$10^9$ /L, the thrombopoiesis was normal in the majority of the bone marrow studied. It is postulated that the thrombocytopenia observed in the peripheral blood may have been due to hypersplenism, and partly due to poor platelet formation [23].

The relation between parasite load in the bone marrow and the degree of anemia, leukopenia, and thrombocytopenia has

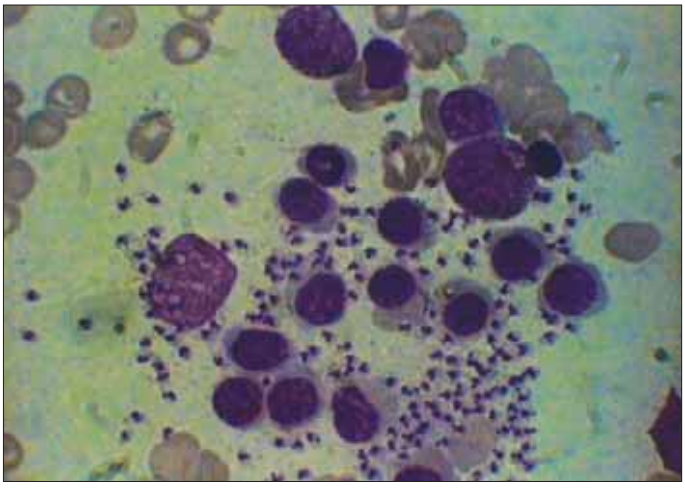

**Figure 1.** Bone marrow cytology with high-grade parasitemia

varied in different studies. Sud et al. [18] found a direct correlation of parasitemia and the degree of anemia; at the same time, there was no correlation of the parasite index with leukopenia or thrombocytopenia. On the other hand, Marwah [24] and other workers found that the hemoglobin level and platelet count were related to parasite load. In our findings, there was an increase in the parasite load in children with severe anemia, leukopenia and thrombocytopenia, but less significant than that reported by Sud et al. [18] and Marwah et al. [24].

In conclusion, in our study, the most common presentation was fever followed by abdominal distension, and the most common sign was splenomegaly followed by pallor and hepatomegaly. Pancytopenia was the most frequent hematological abnormality in VL patients. Leukopenia is due mainly to a reduction in neutrophils.

This study shows that VL in children, particularly in areas endemic for the disease, is a recognized problem. It is essential that the Ministry of Public Health be more aware of the condition in order to improve environmental sanitation and personal protective measures and to establish diagnostic laboratories for early and correct diagnosis and treatment.

## References

1. World Health Organization. The leishmaniasis. Technical report series no. 743. Geneva: World Health Organization, 1990.
2. World Health Organization. Life in twenty-first century: a vision for all world health. Switzerland: World Health Organization, 1998.
3. Kafetzis DA. An overview of pediatric leishmaniasis. J Postgrad Med 2003;49:31-8.
4. World Health Organization. Global health situation in selected infections and parasitic diseases due to identification organisms. Wkly Epidemiol Rec 1993; 641-8.
5. Queiroz MJA, Alves JGB, Correia JB. Visceral leishmaniasis: clinical and epidemiological features of children in endemic area. J Pediatr (Rio J) 2004;80:141-6.
6. Singh K, Singh R, Parija SC, Faridi MM, Bhatta N. Clinical and laboratory study of kala-azar in children in Nepal. J Trop Pediatr 1999;45:95-7.
7. Haidar NA, Abdul-Baset LD, El-Sheik AM. Visceral leishmaniasis in children in Yemen. Saudi Med J 2001;22:516-9.
8. Al-Orainey IO, Gasim IY, Singh LM, Ibrahim B, Ukabam SO, Gonchikar D, Shekhawat BS. Visceral leishmaniasis in Gizan, Saudi Arabia. Ann Saudi Med 1994; 14:396-8.
9. Elnour IB, Akinbami FO, Shakeel A, Venugopalan P. Visceral leishmaniasis in Omani children: a review. Ann Trop Paediatr 2001;21:159-63.
10. ICDDR, Center for Health and Population Research. Visceral leishmaniasis, Mymensingh, 2002, 2003;1:7-10.
11. Campose JD. Clinical and epidemiological features of kala azar in children. J Pediatr 1995;71:238-40.
12. Grech V , Mizzi J, Mangion M, Vella C. Visceral leishmaniasis in Malta - an 18 year paediatric, population based study. Arch Dis Child 2000;82:381-5.
13. Al-Jurayyan NA, Al-Nasser MN, Al-Fawaz, Al-Ayed IH, Al-Herbish AS, Al-Mazrou AM, Al-Sohaibani MO. The hematological manifestations of visceral leishmaniasis in infancy and childhood. J Trop Pediatr 1995;41:143-8.
14. Kefetzis DA. An overview of pediatric leishmaniasis. J Postgrad Med 2003;49:31-8.
15. Marlet MVL, Wuillaume F, Jacquet D, Quispe KW, Dujardin JC, Boelaert M. A neglected disease of humans: a new focus of visceral leishmaniasis in Bakool, Somalia. Trans R Soc Trop Med Hyg 2003;97:667-71.
16. Thakur CP, Kumar M, Pathak PK. Kala azar hits again. J Trop Med Hyg 1981;84:271-6.
17. Mehata BC. Approach to a patient with anemia. Indian J Med Sci 2004;58:26-9.
18. Sud A, Varma N, Marwaha RK, Patel FM, Trehan A, Singeh S, Varma S. Visceral leishmaniasis in a non-endemic area of India. Trop Doct 2004;34:247-9.
19. Mathur P, Samantaray J, Chauhan NK. Evaluation of a rapid immunochromatography test for diagnosis of kala azar & dermal leishmaniasis at a tertiary care centre of north India. Indian J Med Res 2005;122:485-90.
20. El-Hassan AM. Visceral leishmaniasis in the Sudan: clinical and hematological features. Ann Saudi Med 1990;10:51-6.
21. Helmi Ferial I, Al-Allawi Nasir AS, Al-Attar Adil M. Hematological changes in kala azar: a study of 82 Iraqi patients. J Community Med 1993;69:85-90.
22. Rahim F, Rehman F, Ahmed S, Zada B. Visceral leishmaniasis in District Dir, NWFP. J Pak Med Assoc 1998;48:161-2.
23. Dameshek W, Miller EB. The megakaryocytes in idiopathic thrombocytopenia purpura, a form of hypersplenism. Opera Omnia 1975;27-48.
24. Marwah N, Sarode R, Gupta RK, Garewal G, Dash S. Clinicohematological characteristics in patients with kala-azar. A study from north-west India. Trop Geogr Med 1991;43:357-62.