

# CLINICAL AND HEMATOLOGICAL PRESENTATION OF VISCERAL LEISHMANIASIS IN CHILDREN IN A TERTIARY CARE HOSPITAL

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## ABSTRACT

**Objectives:** To evaluate the clinical and hematological features of Visceral Leishmaniasis (VL) in children.

**Material and Methods:** It was a retrospective study, carried out at Pediatrics Department, Khyber Teaching Hospital, Peshawar. All the children admitted with splenomegaly, from January 2007 to December 2007 were evaluated clinically, with peripheral blood examination and bone marrow aspiration and trephine biopsy.

**Results:** Sixty-two children with splenomegaly, VL was seen in 13 (21%) cases with a mean age of 3.2 years. Hepato-splenomegaly and pallor was seen in all 13 cases, followed by abdominal distension (84%), fever and weight loss (46%) and Jaundice was seen in 23% cases. Bicytopenia was seen in 77% cases and pancytopenia i.e. anemia, leucopenia and thrombocytopenia was seen in 23% cases.

**Conclusion:** Childhood VL is not uncommon in Peshawar, and presents with pallor, splenomegaly, fever and cytopenias.

**Key Words:** Visceral, Leishmaniasis, splenomegaly, anemia, thrombocytopenia, Leucopenia.

## INTRODUCTION

Leishmaniasis is a parasitic disease caused by the obligate intracellular protozoan "Leishmania Donovanii" first described by Leishmann and Donovan in 1903. Infection can either lead to a milder cutaneous form, or a potentially fatal visceral form<sup>1</sup>. In Pakistan, Visceral Leishmaniasis (VL) was first reported in 1960 from Baluchistan but later on cases were reported from Azad Kashmir and Abbottabad areas<sup>2</sup>.

VL is characterized by chronic fever, hepato-splenomegaly, cytopenias, dysentery, pneumonia, jaundice and hemorrhages<sup>3</sup>. Mortality is very high in untreated cases (90%). Anemia, thrombocytopenia and leucopenia are the rule in late cases due to extensive proliferation of the parasites in macrophages of the bone marrow and spleen. Demonstration of the parasite in the aspirates of bone marrow, spleen, liver, and lymph nodes is the standard method to confirm VL. Although VL is seen throughout the world, 90% of the cases are from India, Bangladesh, Brazil, Nepal and Sudan, where epidemics are common<sup>4</sup>. About half

a million new cases are diagnosed each year and about 350 million people are at risk in 88 countries around the world. Currently an estimated 12 million people are infected. This is probably an under estimation because of poor surveillance system in third world countries. Moreover with the recent surge in HIV/ AIDS, there is 100-1000 times increased risk of the disease in endemic areas<sup>5</sup>.

The vector of VL is a sand-fly that belongs to the genus *Phlebotomus*<sup>6</sup>. It ingests amastigotes from the host and transforms them to the promastigotes in its gut. Certain parasitic and host factors may play their role in behavior and outcome of the disease<sup>7,8</sup>. The incubation period of the disease varies, ranging from days to years but the average period is 2-6 months<sup>9</sup>. Main species that causes VL are *Leishmania donovani*, *Leishmania infantum* and *Leishmania chagasi*. *Leishmania donovani* is common in India, Bangladesh, Middle East and East Africa, with its reservoir in humans. It causes disease in older children >5 years of age and is associated with high incidence of resistance to antimony compounds. *Leishmania infantum* is seen in Mediterranean basin, China and Pakistan with its reservoir in dogs, foxes and jackals. It causes VL in younger children <5 years of age, and resistance to antimony compounds is not known<sup>10,11</sup>. *Leishmania chagasi* is seen in Central and South America with its reservoir in dogs and foxes. Antimony compounds are the gold standard to treat VL.

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All Leishmania species have similar morphological appearance under a light microscope. In addition to clinical features and geographical distribution, isoenzyme study in a reference lab may be used to identify the species. VL may present with a variety of clinical and hematological manifestations, so we planned this study to evaluate the clinical and hematological data of our own patients from Peshawar, KPK.

## MATERIAL AND METHODS

This study was conducted in Paediatric ward of Khyber Teaching Hospital, Peshawar from January 2007 to December 2007. All the children below 12 years age admitted with splenomegaly irrespective of sex and race were included in the study. Other diseases known to cause splenomegaly e.g. Malaria, typhoid fever, leukemias, hemolytic anemias including thalassaemias and storage disorders were excluded. The diagnosis of VL was established by demonstrating amastigote forms of the parasites in bone marrow.

In all cases 2.5 ml EDTA blood was collected in commercially available vacutainer tubes and analyzed on hematology analyzer- Sysmex KX 21 with daily quality control. Peripheral blood slides were prepared and stained for smear examination. Bone marrow aspiration was performed under local anesthesia, from upper end of tibia < 2 years of age or from posterior iliac spine (PIS) in >2 years of age. Slides were prepared and stained with Giemsa, as described by Dacie and Lewis. Marrow aspirate slides were scanned for intracellular / extracellular amastigote forms of Leishmania Donovan (LD) bodies. Trephine biopsy was done only in > 2 years old children from PIS. All the cases were diagnosed on bone marrow aspiration, except in one case, in whom marrow aspiration was non diagnostic initially and the diagnosis was made on a trephine biopsy. Later on scanty amastigote forms could be seen on revisit of the diluted marrow. The unique feature on marrow aspirate in VL was a dirty look of the smear with a lot of debris in the background as a result of breakdown of fragile macrophages during smear preparation. All the data was entered and then analyzed using Microsoft Excel 2007. Results were presented in the form of charts and tables.

## RESULTS

A total of 62 children presenting with splenomegaly were analyzed during the specified period. Clinical features in cases of VL, are shown in Fig. 1. Mean age in our patients was 3.2 years with a range from 15 months to 08 years. Strangely, all the patients in our study were males. Seventy-seven percent children were Afghanis and rest 3/13 (23%) were from the surrounding tribal areas. On peripheral blood smear, 10 (77%) children presented with bicytopenia (Anemia/ thrombocytopenia and

leucopenia), and only 3 (23%) cases were having pancytopenia (Anemia, leucopenia & thrombocytopenia). Hematological features of 13 cases are shown in Table 1. Anemia (Hb < 12 gm/dl) was seen in all 13 cases with mild anemia (Hb 9-12 gm/dl in 7 (54%) cases and moderately severe anemia (Hb 6-9 gm/dl) in 6 (46%) cases. Moderate Leucopenia (TLC 1-4 X 10<sup>9</sup>/L) was seen in 3 (23%) cases. All the cases were having moderate thrombocytopenia (Platelet count 50- 100 X 10<sup>9</sup>/L). In all 13 cases, diagnosis of VL was confirmed by demonstrating intracellular/ extracellular Leishmania Donovan (LD) bodies on examination of bone marrow aspirate/ trephine biopsy.

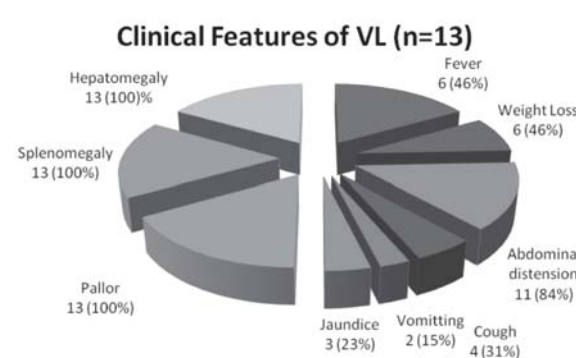


Fig. 1

Table 1: Hematological parameters in VL cases (n=13)

S. No.	Parameter	Mean ± 2SD
1.	Hb (gm/dl)	8.9 +/- 1.2
2.	TLC (/cmm)	5150+/-1950
3.	Platelets (/cmm)	82,000+/-12,000
4.	Anemia (Hb < 12. gm/dl)	13 (100%)
5.	Thrombocytopenia (Platelets Count < 150 X 10 <sup>9</sup> /L)	13 (100%)
6.	Leucopenia (TLC < 4000/cmm)	3 (23%)
7.	Pancytopenia (Anemia + Thrombocytopenia + Leucopenia)	3 (23%)
8.	Bicytopenia (Anemia/ Thrombocytopenia + Leucopenia)	10 (77%)

## DISCUSSION

In Pakistan, Cutaneous Leishmaniasis (CL) is reported from a large area of Balochistan, some areas of Sindh, tribal areas of Waziristan/ Kurram Agency, Karak, Bannu, Peshawar and in Afghan refugees<sup>13,14</sup>. Visceral Leishmaniasis (VL) has been reported mainly from hilly areas of Azad Kashmir, Abbottabad and Murree. VL has not been reported from Peshawar so far although there are reports of VL in Afghan refugees<sup>15</sup>. In the present study all the cases of VL were males, which may be just a chance finding. A study from Muzaffarabad showed a male to female ratio of 2:1<sup>16</sup>. Predominance of males in our study could be due to gender bias in the male dominant society or it may be due to greater exposure of our males than females.

Mean age was 3.2 years in our patients with a range from 15 months to 8 years. Most of the patients (90%) were below 5 years age, suggesting infection by *L. infantum*. This negates the common belief amongst our health professionals, that *L. donovani* is the cause of VL in our region like Indian kalaazar. Use of the term Leishmania Donovanii bodies (LD bodies) in reports of bone marrow aspirates supports it. Rab et al using indirect fluorescence and isoenzyme techniques have confirmed *L. infantum* in patients of VL from AJK and Northern areas<sup>17,18</sup>.

In our cases of VL, anemia was seen in all (100%) cases. Mild anemia (Hb 9-12 gm/dl) was seen in 7 (54%) cases and moderately severe anemia (Hb 6-9 gm/dl) in 6 (46%) cases. Total Leukocyte Count (TLC) was between  $1-4 \times 10^9/L$  in 03 (23%) cases. Moderate thrombocytopenia (Platelet count  $50-100 \times 10^9/L$ ) was seen in all the 13 cases and none of them suffered from bleeding. Pancytopenia i.e. anemia, leucopenia and thrombocytopenia was seen in only 03 cases (23%), while 10 cases (77%) were having bicytopenia (Anemia / thrombocytopenia and leukopenia), which is in contrast to a study done by Hassan et al, where pancytopenia was reported in 66%, anemia in 100% and thrombocytopenia in 90% cases<sup>19</sup>. This was probably because of late presentation of patients from AJK/ Muzaffarabad and relatively early presentation of our cases due to proximity to health care facilities in a tertiary care hospital at Peshawar.

In our cases, fever and splenomegaly was also seen in all the cases (100%). Abdominal distension was seen in 11 (84%) cases and jaundice in 3 (23%) cases. Vomiting was seen in 2 (15%) and cough in 4 (31%) cases. In a study by Rai<sup>21</sup> et al, majority of the patients (98%) presented with fever followed by abdominal distension (47%), Pallor (44%), weight loss (43%), diarrhea (17%), vomiting (15%) and hepato-splenomegaly (83%). In the same study lymphadenopathy (20%), purpura (13%) and peripheral edema (11%) was reported, which was not seen in our cases. Lymphadenopathy is a feature of

African/ Indian VL and is not seen in our cases<sup>20</sup>. Laboratory findings in the above study revealed a more severe disease with anemia in all, followed by thrombocytopenia (79%) and neutropenia (43%), which was less severe in our cases<sup>21</sup>.

## CONCLUSIONS

We conclude that childhood VL is not uncommon in Peshawar, KPK. Most of the children present with hepato-splenomegaly, pallor, abdominal distension, fever and weight loss. Hematologically they may present with bicytopenia or pancytopenia i.e. anemia, thrombocytopenia and leucopenia.

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