

## HAEMATOLOGICAL FINDINGS IN RELATION TO CLINICAL FINDINGS OF VISCERAL LEISHMANIASIS IN HAZARA DIVISION

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**Background:** Visceral Leishmaniasis (VL) has worldwide distribution including Pakistan. The disease is characterized by a spectrum of clinical features along with serious complications in untreated cases. This study describes the correlation between clinical manifestations with haematological changes of VL in Hazara Division. **Methods:** This cross sectional study was carried out in the children wards of Women & Children Hospital an Ayub Teaching Hospital Abbottabad. Seventy cases were included in this study, Sign, symptoms, complications and haematological parameters were recorded in detail and their comparison was carried out. **Results:** Majority of the patients (98.57%) presented with fever followed by abdominal distension (47%) Pallor, (44%) weight loss (43%) diarrhoea (17%), vomiting (15%) and epitasis (8%) and hepatosplenomegaly was found in about 83% along with lymphadenopathy (20%) purpura (13%) and peripheral oedema (11%). Laboratory findings revealed anaemia in all the cases followed by neutropenia 43%, lymphocytosis 86% with thrombocytopenia 79%. Bone marrow in most of these cases showed myeloid hyperplasia with increased megakaryocytosis. **Conclusion:** There exists a new focus of visceral leishmaniasis in Hazara Division. The disease mainly affects children below 5 years and is more common in males than in female children. Bone marrow examination provides a reliable and simple tool for diagnosis of visceral leishmaniasis and the condition can be affectively managed with Sodium stibogluconate or meglumine antimoniate.

**Keywords:** Leishmaniasis, Visceral, Clinical, Haematological

### INTRODUCTION

Leishmaniasis is a clinical syndrome caused by obligate intracellular protozoa of the genus leishmania, while Visceral Leishmaniasis (VL) is a systemic disease caused by 'Leishmania Donovanii, described by Leishman and Donovan in 1903.

Leishmaniasis is a parasitic disease caused by obligate intracellular protozoa of the genus leishmania. Nearly 350 million people are at risk in 88 countries around the world. Currently an estimated 12 million people are infected and around 2 million infections occur each year. The most severe form of the disease is visceral leishmaniasis that affects the internal organs. Visceral leishmaniasis is fatal within two years if left untreated.<sup>1</sup>

In Pakistan, human VL was first reported in 1960 from Baluchistan. Afterward, various studies have been carried out in different parts of the country and a good number of cases were reported.<sup>2</sup>

The disease is characterised by fever, hepatosplenomegaly, anaemia, leucopenia and hypergammaglobulinemia. Serious complications are cancrum oris, dysentery, pneumonia, anaemia, agranulocytosis, jaundice, severe haemorrhage and anasarca. Pulmonary tuberculosis may occur with Kala-azar. Mortality is very high in untreated cases (90%).<sup>3</sup> Severe anaemia, thrombocytopenia and leucopenia is the rule in late cases and is due to extensive proliferation of the parasites, loaded

histiocytes in the bone marrow and in the enlarged spleen. In addition serum albumen is decreased and globulin increased.<sup>4</sup>

Demonstration of the parasite in the aspirates of spleen, liver, and bone marrow or in the lymph nodes is the only way to confirm VL.

Since Visceral Leishmaniasis has protean clinical manifestations reported by different authors we planed to study the clinical findings and reviewed the laboratory data of these patients in our setting.

### PATIENTS AND METHODS

It was a cross sectional study conducted in paediatric wards of women and children hospital and Ayub Hospital Complex, Abbottabad from October 1985 to 31<sup>st</sup> August 1999.

The paediatric units of these hospitals have a very wide catchment area including Hazara division (with an area of 17103 sq km. and population of 3,471,399) and Northern areas of Pakistan along with adjacent areas of Azad Jammu and Kashmir.

Suspected patients were admitted in the ward. After obtaining the consent of the parents detailed history was taken from them regarding the illness. Complete clinical examination along with laboratory investigations were carried out and a proforma was filled for each case.

Haemoglobin estimation was done by Sahli's method, total leucocyte count and platelet

count by visual methods using improved Neubaur chamber and differential leucocyte counts was performed after staining with May-Granurald Giemsa stain, Red blood cell morphology was done by visual method and ESR by Westergren tube.

Formal gel test was done by adding 2 drops of 4% formalin is 2 ml of patient's serum and test was taken as positive if milk white opacity like the white of a hard-boiled egg appeared within 20 minutes.<sup>5</sup>

Bone marrow aspiration under local anaesthesia with xylocaine was performed from upper end of tibia in patients less than two years of age and from posterior inferior iliac spine in older children (>2 years) using Sahli's bone marrow aspiration needle. At least 10 slides were prepared and were stained with Giemsa stain for morphology and Leishman Donovan (LD) bodies and Prussian blue reaction was used for iron stores. Diagnosis was based upon finding intracellular and/or extracellular amastigote forms of Leishmania donovani in the marrow smear. Except one patient, in whom marrow aspiration was unsuccessful, and diagnosis was established by examining a trephine biopsy all other cases were diagnosed on bone marrow aspiration.

## RESULTS

During this study 70 cases were diagnosed. Out of these 70 cases 48 (68.57%) were male and 22 (31.43%) were female with Male/Female ratio of 2.2:1. All the cases were below 10 years of age. Five (7.14%) were infants, 48 (68.57%) were of toddler's age, 13 (18.57%) were of pre-school age group while 4 (5.72%) were of school going age.

The detailed record of clinical features, complications and laboratory findings are given in Tables 1-6.

**Table-1: Symptoms and signs in the cases of visceral leishmaniasis (n=70)**

	No of Patients.	Percentage
<b>Symptoms</b>		
Fever	69	98.57
Abdominal Distension	33	47.14
Pallor	31	44.28
Weight Loss	30	42.86
Cough	24	34.28
Diarrhea & vomiting	12	17.14
<b>Signs</b>		
Splenomegaly	69	98.57
Anaemia	67	95.71
Hepatomegaly	60	85.71
Lymphadenopathy	14	20.00
Signs of Pneumonia	10	14.29
Petechia and or Purpura	9	12.86
Peripheral Oedema	8	11.43

**Table-2: Complications in cases of visceral leishmaniasis (n=70)**

Complications	Number	Percentage
Bleeding disorder	17	24.29
Gastroenteritis	12	17.14
Pneumonia	10	14.28
Dysentery	3	4.28
Cancrum Oris	1	1.43
Total patients with complications	43	61.43

**Table-3: Haematological findings in 70 cases of visceral leishmaniasis**

Parameter	No. of patients	Percentage
<b>Haemoglobin g/dl</b>		
8-12	12	17.14
4-8	48	68.57
<4	10	14.29
<b>Total Leukocyte Count/mm<sup>3</sup></b>		
4000 and above (normal)	40	57.15
4000-3000	11	15.71
3000-2000	13	18.57
<2000	6	8.57
<b>Neutrophil Count</b>		
Normal (40-75%)	33	47.14
Relative Neutropenia (<40% with normal TLC)	21	30.00
Absolute Neutropenia (<40% with ↓ TLC)	16	22.86
<b>Lymphocyte Count</b>		
Normal (20-45%)	9	12.86
Relative Lymphocytosis (>45% with normal TLC)	36	51.43
Absolute Lymphocytosis (>45% with decreased TLC)	25	35.71

**Table-4: Red blood cell morphology in 70 cases of visceral leishmaniasis**

Morphology	No. of Patients	Percentage
Microcytosis	28	40.00
Macrocytosis	21	30.00
Anisocytosis	17	24.29
Poiklocytosis	11	15.71
Hypochromia	55	78.57
Polychromasia	3	4.28

**Table-5: Erythrocyte sedimentation rate in 70 cases of visceral leishmaniasis**

	>100	50-100	20-50	<20
Number of patients	34	24	8	4
Percentage	48.57	34.29	11.43	5.71

**Table-6: Formal gel test in 14 cases**

Formal Gel Test	Positive	Negative
No of Patients	10	4
Percentage	71.43	28.57

## DISCUSSION

This study is one of the largest studies from NWFP on Visceral Leishmaniasis (VL). In our study we noted preponderance of VL, in males than in female and this is in accordance with studies carried by other authors.<sup>6,7</sup> This may be due to greater exposure of

male than females. Moreover in our society parents usually bring their male children for treatment.

All the 70 patients were below 10 years of age and this is in accordance with other studies from hilly areas of Pakistan. Majority of the patients were of toddler age group (1–3) years and similar age incidence has been reported by other workers from Pakistan.<sup>8,9,14</sup>

The pattern of disease that occurs in this area clinically resembles the Mediterranean (Chinese) type as against the Indian Kala-azar in which there is black pigmentation on extremities and trunk.<sup>10,15,16</sup>

The onset was insidious in almost all the cases, the child loose interest in play and become listless. This type of onset has been reported in various studies.<sup>8,9</sup>

Duration of symptoms was from few weeks to 2 years with an average duration of 6 months. Irregular fever was the commonest symptom. While abdominal distension pallor and weight loss were the other main symptoms recorded in more than forty percent of the cases. Pallor was reported in hundred percent patients by other workers from Pakistan thus favouring our study.<sup>8,9</sup>

As cough was noted in many studies as a symptom of respiratory tract infection it was also present in 34.28% of the patients in our study.

Splenomegaly was the most prominent and frequent sign and main cause of protuberant abdomen. It is consistent with various studies done on VL. It was found in 85.71% of patient in our study, whereas it was reported in hundred percent of patients by Hassan *et al.*<sup>8,9,13</sup>

Gastroenteritis, bronchopneumonia, petechia, purpura, ecchymosis and bleeding were present in a good number of patients in our study like other studies.<sup>17</sup> Laboratory investigations revealed anaemia in almost all the cases. Majority of them (68.57%) were having moderate anaemia (Table-3). Similar findings have been reported by various researchers.<sup>8,9</sup> Hypochromia, Anisocytosis, poikilocytosis were present in good number of patients. Size of the erythrocytes were also altered, 40% showed microcytosis, 30% macrocytosis while in 30% of the patients the cells were normocytic.

In this study, 42.86% patients showed leucopenia and 52.86% were neutropenic. Infections were common and severe in these neutropenic patients. A study from Armed Forces Institute of Pathology in 1986, showed leucopenia in 50% and neutropenia in 100% cases.<sup>9</sup>

Lymphocyte count was found to be above normal level (>45%) in 87.14% patients and more than seventy percent in 76% of cases in a study done by Hassan<sup>8</sup> while in our study the number of

patients were 51.43% whose lymphocytes were more than 70%.

Thrombocytopenia was noted in 55 (78.57%) patients. This thrombocytopenia was the main cause of bleeding in our patients. These findings about platelet count resemble the findings in the study done by Saleem (1986) in which 91% cases showed platelet count of <100,000/cmm.<sup>9</sup>

Erythrocyte Sedimentation Rate (ESR) was raised in 94.28% of the patients in our study. In a study from Pakistan Institute of Medical Sciences 1995 ESR was found to be raised in 88% of cases.<sup>8</sup> Definitive diagnosis was made by finding LD bodies in bone marrow and most of them (80%) were extracellular and were amastigotes. Promastigote forms of Leishmania were observed in three bone marrow smears and it is in contrast to other studies in which promastigote forms have not been reported in any single patient.<sup>2</sup>

Formal gel test was performed in all the cases and it was positive in ten cases (71.43%) and it was negative in four cases (28.57%). In most of the studies the researches depend upon finding LD bodies in bone marrow as a definitive proof of V.L. while some people prefer splenic aspiration upon bone marrow aspiration. Splenic aspiration though the most sensitive technique of confirming the diagnosis of Kala-azar, but there is great reluctance in doing the procedure because of fear of complication, like the splenic tears.

Majority of bone marrows showed normal erythropoiesis, myelopoiesis, and megakaryopoiesis. Majority of the cells were of the mature type, and very few precursors were present. All these marrow findings are in accordance with marrow cytology found in studies by Ahmed & Burney.<sup>2,11,12</sup>

On admission majority of the patients (61.43%) reported with complications. Two major categories of complications were infections of respiratory and gastro intestinal tract and bleeding disorders.

## CONCLUSION

It is concluded from the study of these 70 cases that a new focus of visceral leishmaniasis exists in Hazara Division. The disease mainly affects children below 5 years of age with its prevalence more in male than female children. Bone marrow examination is the most reliable and simple mean of diagnosing visceral leishmaniasis. Sodium stibogluconate or meglumine antimoniate along with the supportive treatment is the most useful method of management.

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