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# Variations in Hematology Associated With Visceral Leishmaniasis and Kala Azar

**Dr Malay Bajpai[1], Dr Mayurika Tyagi[2], Dr Swati Singh[3]**

[1] Professor, Department of Pathology, Santosh Deemed to be University, Ghaziabad

[2,3] Associate Professor, Department of Pathology, Santosh Deemed to be University, Ghaziabad

## ABSTRACT:-

Visceral leishmaniasis, also known as kala azar, is a chronic infectious disease that is caused by parasites of the Leishmania donovani complex. This disease can induce a variety of hematologic symptoms. Visceral leishmaniasis, also known as kala azar, is also known as VL. Fever, an enlarged liver and spleen, weight loss, pancytopenia, and hypergammaglobulinemia are some of the symptoms associated with this condition. The Indian subcontinent is home to this disease in its endemic form, and the states of Bihar and West Bengal are where it is most prevalent. Prior to acquiring the diagnosis of VL, patients with VL may present to the haematologist for a variety of disorders related to their blood or blood cells. The haematological symptom of VL that is seen most frequently is anaemia. Leucopenia, thrombocytopenia, pancytopenia, hemophagocytosis, and disseminated intravascular coagulation are all possible complications of VL. Within a week of starting treatment, patients will see an improvement in their haematological status, and after 4–6 weeks, they will experience a complete haematological response. Relapses are extremely uncommon, and there is no evidence that long-term follow-up results in an increased chance of being diagnosed with hematolymphoid malignancies.

**Keywords:** Anaemia, Kala Azar, Pancytopenia, Hematological changes.

## INTRODUCTION: -

Visceral, cutaneous, and mucocutaneous leishmaniasis are the three primary illness patterns associated with leishmaniasis, a protozoan parasite infestation. Visceral forms include several hematologic symptoms. Hematologists may encounter visceral leishmaniasis (VL) in the form of splenomegaly, hepatomegaly, fever, lymphadenopathy, or pancytopenia. VL, also known as Kala Azar, is endemic in more than 60 nations around the world [1], including the Indian subcontinent, Southern Europe, North Africa, the Middle East, and Central and South America. It is primarily endemic in the Indian states of Bihar and West Bengal, with a few isolated cases also occurring in Himachal Pradesh and the country's northwest [2].

The protozoan Leishmania donovani (LD) of the genus Leishmania is the cause of VL, a systemic infection of the reticuloendothelial system. Ross established the genus Leishmania in 1903. Charles Donovan and Sir William Leishman both identified the same parasite in spleen biopsy samples at the same time [3]. Aflagellate or amastigote and flagellate or

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promastigote are the two types of the parasite. It occurs and multiplies as an amastigote in the mononuclear phagocytic system (MPS), particularly in the spleen, liver, and bone marrow. This causes the MPS to hypertrophy, which causes problems in the phagocyte-bearing organs and results in haematological symptoms. Since the reticuloendothelial system is the target of parasitization, this condition is of concern to hematopathologists. Particularly, the spleen significantly enlarges. Other clinical signs of the illness include hepatomegaly, fever, and a strange grey colouring of the hands, feet, belly, and face that gave the illness the name "kala azar," or "black disease." It has been found that certain of the key haematological characteristics and spleen size correlate with each other. In their investigation of the impact of parasitaemia on bone marrow ultrastructure, Calvo et al. [4] found no connection between the level of parasitaemia and either the frequency or the structural abnormalities of the bone marrow in VL patients. Therefore, the key etiopathogenetic determinants in the formation of bone marrow alterations and peripheral cytopenias appear to be splenic sequestration and inefficient hematopoiesis [5].

In a recent article, Tripathi et al. [6] offered fresh insights into the fundamental immunological mechanisms regulating leishmaniasis and proposed that the IL-10 produced by leishmania-parasitized macrophages is essential for the development and spread of the illness. The Th1/Th2 paradigm of resistance/susceptibility seems to be oversimplifying a much more intricate web of regulatory/counter-regulatory interactions exhibited in these patients. However, a deeper comprehension of the immune system's reaction to the parasite might open the door to the creation of preventative and curative measures. This study will provide direction to the proper techniques of investigation to help in the timely identification of VL by summarising the connections of VL with both common and rare illnesses that may be of interest to haematologists.

## DISCUSSION:-

### Hematological Changes Seen in VL

**Anemia:** Hemoglobin values of 7–10 g/dl are typically detected, and normochromic normocytic anaemia is a frequent and clinically relevant characteristic of VL. In two significant patient series, the average haemoglobin levels were 8.3 and 7.8 g/dl [7, 8]. In patients younger than 18, it is more severe. Al-Jurrayan et al[9] .'s evaluation of 94 VL patients revealed that every single patient had anaemia. All 23 VL patients examined by Marwaha et al. [5] were moderately to severely anaemic (Hb = 4.3-8.1 gm/dl). Children in this study showed slightly lower Hb levels than adult patients (mean = 6.4 vs 7.3 g/dl). Red blood cell (RBC) sequestration and destruction in an enlarged spleen, immunological mechanisms, and changes in RBC membrane permeability have all been suggested as contributing factors to the anaemia found in these patients. Hemolysis is thought to be the main cause of anaemia in VL, according to red cell survival and ferrokinetic investigations [10, 11], while there may also be plasma volume expansion linked to a significantly enlarged spleen. However, very little evidence of inefficient erythropoiesis has been found in

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ferrokinetic experiments. Reticuloendothelial hyperplasia is thought to be associated with aberrant macrophage iron retention, which is typical of chronic illness anaemia, based on the reduced plasma iron level in the presence of significantly elevated iron storage [11]. This might reduce the marrow's ability to respond to hemolysis. A very quick onset of anaemia with hemolysis is frequently seen in the Mediterranean population [12].

**Leucopenia:** Leucopenia is a prominent and early sign of VL. Neutropenia is accompanied by relative lymphocytosis, and the differential diagnosis excludes VL in the presence of substantial eosinophil counts since eosinophils are nearly entirely absent. The mean TLC reported in two large series [7, 8] is 2.8 9 109 /l and 4 9 109 /l respectively. However, a lower TLC (2.4 9 109 /l) was reported in a series of VL patients studied at our centre [5]. About 75% patients with VL have been shown to have leucopenia in various studies [5, 7]. The main cause for its development has been attributed to hypersplenism.

**Thrombocytopenia:** After a prolonged illness, platelet levels are typically impacted. In their study, Marwaha et al. [5] found that patients with thrombocytopenia had considerably longer average sickness times than patients without thrombocytopenia.

**Pancytopenia:** Several groups of workers have reported varying degrees of incidence and severity [8, 13, 14]. It typically manifests itself after a protracted sickness. This happens as a result of blood cell sequestration in the spleen. The peripheral blood picture does in fact resemble aplastic anaemia in these situations, however the presence of reticulocytes and young white cells shows continuing blood regeneration and aids in distinguishing from aplastic anaemia. The clinical presentation of pancytopenia is similar to leukaemia when it is accompanied by fever, hepatosplenomegaly, and lymphadenopathy, but bone marrow testing can clearly distinguish between the two.

**ESR:** Erythrocyte sedimentation rate in VL consistently increases, most likely as a result of acute phase reactant release.

**Bone Marrow (BM) Changes:** Erythroid hyperplasia, an increase in plasma cells, and intracellular parasites (in amastigote form) in mononuclear phagocytes are frequent observations. Depending on the underlying deficiency, erythroid cells may exhibit mild to severe megaloblastosis, inadequate iron storage, or dual deficiency characteristics. There have been reports of no changes in the morphology of granulocytic and megakaryocytes other than a little increase in immature forms in specific circumstances. Leukophagocytosis (46%) and granulomatous response (25%) may also be present in varying degrees [9]. An instance of fatal hemophagocytosis owing to VL in a 4-year-old child was reported by Mathur et al. [15]. They stressed the need for a thorough investigation of the causative agent, particularly LD bodies, in patients with hemophagocytic syndrome in order to start prompt, vigorous, and successful treatment. Rajagopala and others [16]

**Coagulation Abnormalities**: A poor prognosis is associated with late-stage liver impairment that includes jaundice, ascites, and abnormal coagulation [17]. Protozoa can directly affect

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the liver or can have an indirect impact on it through the parasites' immune system. Ten (11%) of the 94 VL patients in Al-Jurrayan et al [9]. study had aberrant coagulation, as evidenced by extended PT and APTT, with four (36%) of these having disseminated intravascular coagulation.

Platelet Function Studies: Dube et al. [18] reported abnormal platelet function studies \sin their report on patients with VL. They conducted platelet \sfunction investigations on 25 parasitologically positive patients of \sIndian VL and 25 age and sex matched healthy controls. 92% of patients had thrombocytopenia of varying degrees; 44% of patients had platelets below 60,000 mm3. In 70% of individuals with VL, the platelet adhesive index was less than 30% (normal, 31–60%). In comparison to the controls, the platelet aggregation time with ADP and adrenaline was unusually protracted. In 40% of instances, platelet factor III availability was subpar. They discovered a moderate link between platelet adhesiveness and platelet factor III availability in these individuals, with poor platelet adhesiveness being associated with lower platelet factor III availability in 50% of patients.

However, further investigations on platelet function are needed \sto validate their findings.

**Diagnosis:** When leishmaniasis is suspected, serological testing are advised as the initial diagnostic procedure. In advanced stages of the illness, phagocytic cells in the spleen, bone marrow, lymph nodes, and occasionally blood can contain parasites. Morphological diagnostics offers a rapid, accurate, and economical diagnosis. However, bone marrow culture is a more accurate diagnostic method than microscopy. Aspiration samples are taken aseptically and cultured in Schneider's Drosophilia medium or Novy-MacNeal-Nicolle medium with calf serum. Promastigotes typically start to appear in cultures in 2 to 5 days.

The amastigotes, also known as Leishman Donovan—LD bodies, are directly seen to determine the presence of leishmania in the haematology laboratory [19]. Peripheral blood or aspirates from lymph nodes, bone marrow, spleen, or skin lesions should be spread thinly on a slide to create a smear before being stained with Leishman or Giemsa stain for 20 minutes. In peripheral blood and, less frequently, in neutrophils and macrophages from bone marrow aspirates, amastigotes are seen. They have a nucleus, a tiny rod-shaped kinetoplast, and small, spherical bodies that range in size from 2-4 lm. Extracellular free-lying LD entities that have been liberated from the damaged cells can frequently be seen as well.

We assessed a range of VL diagnosis tests. DAT's sensitivity and specificity on the basis of positive bone marrow aspirate results were 100%, whereas those of the rk39 strip test, ELISA, and other tests were 100% and 87%, respectively [20].

**Treatment:** Traditional leishmaniasis treatments include antimonial substances (sodium stibogluconate and meglumine antimonite). In areas of the world where antimonials are frequently resistant, amphotericin B is the most widely used substitute. The Institute of OneWorld Health has provided funding for the production of paromomycin as an orphan

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medication for use in the treatment of leishmaniasis, with initial usage in India. Paromomycin is a less expensive alternative to amphotericin and has fewer side effects.

The absence of parasites in two consecutive splenic aspirates obtained one week apart is the "Test of Cure" (to stop treatment) [21]. Patient must not have a fever, show clinical and haematological improvement, have a smaller spleen, and have a score of zero on the splenic aspirate in order to be considered cured. All patients whose response to acceptable therapeutic drugs is delayed should be checked for complicating diseases such pulmonary tuberculosis and AIDS.

## CONCLUSION:-

Hematological anomalies are frequent in VL. Pathogenesis is intricate and multifaceted. The most significant contributors seem to be hypersplenism, hemophagocytosis, chronic inflammation, and nutritional factors. Hematologists need to keep a high level of suspicion for VL and should consider it when making a differential diagnosis for patients who present with fever, hepato-splenomegaly, anaemia, leukopenia, thrombocytopenia, pancytopenia, or histiocytosis as well as DIC, especially in areas where the disease is endemic.

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