

26. HAEMATOLOGIC DISORDERS

Haematological disorders are frequently encountered in PLWHA. In addition to the haematological problems caused by opportunistic infections and the toxic effects of drugs, including antibiotics and antiretrovirals, HIV affects the haematologic system by invading stem cells.

26.1 Anaemia

Anaemia is defined as a haemoglobin level less than 13.8g/dl for men and less than 11.7g/dl for women. Anaemia of chronic disease is very common in the HIV-infected persons. Treatment of anaemia leads to an improved quality of life. However, very rarely is there a need for intervention when the haemoglobin level is above 10g/dL and thorough investigation at these levels is not necessary in persons with HIV infection. Patients with haemoglobin levels less than 6g/dL are invariably symptomatic and need investigations.

26.1.1 Clinical features

Patients who have gradual declines in haemoglobin may be asymptomatic even at very low haemoglobin levels. Patients may complain of weakness, palpitations, and dyspnoea on exertion, dizziness, headache and malaise. It is important to check for fever, weight loss, pain and other symptoms suggestive of infectious or neoplastic aetiology. Always review the list of drugs that the patient is taking. Examine the patient and note any abnormal findings such as lymphadenopathy, hepatosplenomegaly, tumours, tachycardia and pallor. Confirm anaemia with a full blood count; check the reticulocyte count, the MCV and peripheral blood smear. Table 26.1 gives guidance on the approach to the investigation of anaemia based on the reticulocyte count and the MCV.

26.1.2 Investigation of anaemia

A full blood count and haematologic indices together with haematinic assays, i.e., serum iron, folate and vitamin B₁₂ levels should be performed in anaemic patients. Depending on the results of such tests, further tests may need to be carried out to establish the cause of anaemia.

Bone marrow aspirates and trephine biopsies should be examined for morphology and cellularity and should be stained by the Ziel Nielsen method and examined for tuberculosis. An examination of the buffy coat may reveal parasites. In persons with HIV infection and AIDS the bone marrow is hypercellular and dysplastic in 80%, and hypoplastic in 20%.

Table 12.1 summarises the investigations that need to be carried out in anaemic persons with HIV infection.

Table 26.1 Investigating anaemia in persons with HIV infection			
Low reticulocytes and low MCV	Low reticulocytes and normal MCV	Low reticulocytes and high MCV	High reticulocytes
Iron deficiency from blood loss from neoplasm, GI infection, e.g., CMV, or from menorrhagia. Reduced intake in very ill patients.	Cause may be drugs (atovaquone, dapsone, primaquine, pyrimethamine, ganciclovir, amphotericin, flucytosine, others); neoplasm; infections; renal failure; anaemia of chronic disease. Marrow aplasia. Combined haematinic deficiencies.	May be due to B12 or folic acid deficiency; malabsorption; liver disease; ART and other drugs; autoimmune process. Marrow aplasia.	Consider hemolysis due to oxidant drugs; if the RBCs are fragmented and thrombocytopenia is present, DIC or TTP may be causing the problem
<p>Further tests:</p> <ul style="list-style-type: none"> ▪ Stool for occult blood x 3; if positive may need endoscopy to determine cause of bleeding ▪ Iron studies, including, ferritin, transferrin, TIBC. Ferritin often elevated in anaemia of chronic disease, but low level will confirm iron deficiency. ▪ Haemoglobin electrophoresis (for patients with 	<p>Further tests:</p> <ul style="list-style-type: none"> ▪ AFB and fungal blood cultures ▪ Look for OIs ▪ Fever work up ▪ Biopsy or fine needle aspiration of lymph node to exclude neoplasm, mycobacteria ▪ Refer for bone marrow test for suspected lymphoma, neoplasm, B-19 parvovirus 	<p>Further tests:</p> <ul style="list-style-type: none"> ▪ B12 level ▪ RBC folate ▪ Direct Coombs test 	<p>Further tests:</p> <ul style="list-style-type: none"> ▪ Peripheral blood smear, ▪ Platelet count ▪ Direct Coombs test

normal iron studies)			
▪ Bone marrow studies			

NOTES:

- Additionally, for symptomatic patients, or those with declining haemoglobin levels < 7, arrange for urgent transfusion.
- Discontinue offending drugs, if appropriate substitutes available, and monitor FBC.
- Treat appropriately if infectious pathogen identified (see applicable treatment guidelines), or if neoplasm detected.
- With B-19 parvovirus infection, the patient is likely have a reticulocyte count of <0.2%, and a profound isolated anaemia, compared to fungal, parasitic, or mycobacterial infections, in which the patient usually has pancytopenia
- An elevated LDH, low haptoglobin, or increased indirect bilirubin would support the diagnosis of haemolysis
- Patients with HIV-related anaemia usually respond to control of viral replication using ART.
- Refer for treatment of neoplasm or bleeding.

26.1.3 Management of anaemia

The mainstay in the management of anaemia is correcting the cause where possible. Blood transfusion may be used as a temporary measure. It is important to withdraw drugs that may be implicated in causing anaemia. It is also important to search for infections. Androgenic steroids and erythropoietin are also used in treating anaemia.

NOTE:

- All antiretroviral may be used in patients with pre-existing anaemia

- Declining haemoglobin levels indicate need to review drugs prescribed and possible withdrawal of certain drugs such as zidovudine

In patients in whom no treatable pathology is identified, manage as follows: If normocytic and isolated anaemia (haemoglobin more than 10 g/dL), and patient with no unexplained constitutional symptoms, the most likely diagnosis is anaemia of chronic disease. Close follow-up and avoidance of haematotoxic medications is indicated.

Note: Patients with symptomatic anaemia and erythropoietin levels less than or equal to 500 IU/L may benefit from erythropoietin 100-200 U/kg given 3 times a week till RBC count normalizes. RBC must be checked weekly, as polycythaemia can occur. Injections are then given weekly. Patients who do not respond to erythropoietin may have occult iron, folate, or B12 deficiency, which must be corrected for response to occur.

26.2 Leucopenia

White cell abnormalities occur commonly in HIV-infected persons; leucopenia is found in 11%, neutropenia in 30%, lymphopenia in 32% and eosinophilia in 25% of cases.

In persons with severe neutropenia the management is with broad spectrum antibiotics when fever is also present. The use of colony stimulating factors, e.g., G-CSF "Neupogen", provides a transient rise in neutrophils and therefore should not be used in persons with neutropenia with septicaemia. Intravenous immunoglobulin has a role in limiting infections and stimulating an increase in white cells.

26.3 Thrombocytopenia

Thrombocytopenia occurs in 25% of patients with HIV infection. It is not an indication of disease severity on its own but is more severe in advanced AIDS. Thrombocytopenia occurs as a result of the effects of HIV infection on the bone marrow and also as a result of autoimmune processes suggestive of idiopathic thrombocytopenia (ITP). Thrombotic thrombocytopenic purpura (TTP) should be considered in cases where renal impairment and red cell fragmentation are present.

26.3.1 Management

Prednisolone 1mg/kg body weight is given daily for 10 to 12 weeks. Persons who do not respond to this should be treated with azathioprine. Failing this splenectomy should be considered together with the usual vaccines and antibiotic prophylaxis pre- and post-splenectomy should be given. There is little evidence that short-term immunosuppressive therapy and even splenectomy have an adverse effect on the outcome of the HIV.

26.4 Coagulation and thrombophilia

Lupus anticoagulant and phospholipid antibodies have been demonstrated in over 20% of HIV/AIDS patients. The presence of lupus anticoagulant results in a prolongation of the activated partial thromboplastin time (APTT). However lupus anticoagulant is clinically associated with thrombosis rather than haemorrhage and both arterial and venous thrombosis have been reported in persons with HIV infection.

26.4.1 Management

Thrombosis should be managed by anticoagulation, initially with heparin and then with warfarin, maintaining an INR around 2 to 4. Anticoagulation should be continued for 3 months. It is important to monitor the patients' platelet count as well.

Management of haemorrhage that may occur as a result of a coagulopathy due to the presence of other antibodies, is with transfusions of fresh frozen plasma and platelets. This management is reactive to, rather than elective, as there are no laboratory tests that predict bleeders.

26.5 Hypergammaglobulinaemia

Most patients with HIV/AIDS are hypergammaglobulinaemic until the very advanced stage of AIDS when they may become hypogammaglobulinaemic. The increase in gammaglobulin can lead to the hyperviscosity syndrome which is diagnosed by measuring the viscosity of plasma.