# DIAGNOSING ANAEMIA: AN OVERVIEW

Dei-Adomakoh YA<sup>1</sup>, Ekem I<sup>1</sup>, Segbefia CI<sup>2</sup>, Atiase Y<sup>3</sup>.

<sup>1</sup>Department of Haematology, <sup>2</sup>Department of Child Health, <sup>3</sup>Department of Medicine.University of GhanaMedical

School, Korle-Bu, Accra, Ghana.

## Summary –

The World Health Organisation (WHO) provides a definition for anaemia in both adults and children based on haemoglobin values determined in the laboratory. However, not all patients with haemoglobin values lower than these thresholds warrant investigation. The decision to investigate those with minor abnormalities must be based on clinical judgement, and from what is known about the individual's previous blood counts. Anaemia is therefore said to be present when the blood haemoglobin (Hb) value is below the reference value for the age, sex and place of residence (altitude) of the individual. Anaemia is a public health problem in most developing countries including Ghana and therefore important to thoroughly investigate these patients. This paper discusses the different types of anaemia and provides a simple overview of issues related to the investigation of different types of anaemia. It should serve as a guide for the practicing doctor in Ghana and elsewhere.

Key words: Anaemia, classification, investigation

# Introduction:

The global prevalence of anaemia in 2010 was estimated to be  $32.9\%^1$ . The under fives still have the highest prevalence (16.3% in males and 18.1% in females)<sup>2</sup>. The World Health Organization (WHO) defines anaemia in adults as haemoglobin levels lower than 13 g/dl (males) or 12 g/dl (females)<sup>3</sup>. In children, normal haemoglobin levels are highly dependent on age. At birth, the mean normal haemoglobin level is 18g/dl, dropping to a nadir of 10-12g/dl at two to three months of age in full term infants. In preterm babies, the haemoglobin nadir occurs earlier at six to eight weeks of age due to physiological and iatrogenic factors and may be as low as 7-8g/dl (often termed 'anaemia of prematurity')<sup>4</sup>. In children from 2 years to puberty, haemoglobin level of less than 11.0g/dl signifies anaemia. In the under 5 years, it has been defined by the WHO and the US Centers for Disease Control as haemoglobin level less than  $11g/dl^3$ . Anaemia is present when the blood haemoglobin (Hb) value is below the reference value for the age, sex and place of residence (altitude) of the individual<sup>3</sup>. Anaemia is always secondary to a disease or disorder including malnutrition, thus anaemia is not a diagnosis in itself, but an objective sign of disease or disorder which must be searched for if the anaemia is to be properly treated.

Author for Correspondence: Dr. Yvonne A. Dei-Adomakoh Department of Haematology, University of Ghana Medical School, Korle–Bu, Accra, Ghana. E mail: deiadom@yahoo.com In summary, anaemia could be caused by acute or chronic blood loss, increased destruction of red cells in haemolysis or decreased production due to nutritional deficiency, bone marrow failure, hereditary conditions or congenital anomalies. In investigating a patient with anaemia, it is important to take a good history, examine the patient thoroughly, request essential haematology blood tests, and order additional investigations and specialized tests as necessary. Depending on the person's age, sex, occupation and social standing, emphasis may be placed on certain aspects of the history, examination and investigations.

#### **History and Examination**

As in all areas of medical enquiry a detailed history and physical examination are essential, with particular attention to: Patient's diet. An adequate nutritious balanced diet is necessary for building up haemoglobin. Abnormal bowel habits such as diarrhoea and steatorrhoea impair absorption of nutrients necessarv for building haemoglobin. up Nutritionalhistory is very important in children, as well as pregnant and lactating mothers. In infants, it is important to obtain birth history, including gestational age at delivery, as these may affect the level of haemoglobin, the lower the gestational age, the lower the iron stores and thus the higher the chances of neonatal anaemia<sup>5</sup>.

Unusual bleeding or bruising, blood in stools, excessive menstrual blood loss, increased number of pregnancies are all important. Bleeding haemorrhoids must be specifically asked for as the information may not be volunteered. Presence of 'cola-coloured' urine may suggest intravascular haemolysis. Family history of anaemia is important in inherited forms of anaemia. Medication history may reveal drugs which are known to cause anaemia. Other co-existing medical problems eg acute infections, chronic non-infectious inflammatory diseases or other chronic diseases as in kidney disease may also contribute to the anaemia. Information on recent surgery may also be helpful<sup>6</sup>.

A thorough physical examination is important. Examination of the conjunctiva for pallor is an important start to anaemia investigation. The mouth should be checked for glossitis, stomatitis, gum disease and other changes; and nails for koilonychia. Koilonychia and pallor suggest iron deficiency. Pedal oedema which may be a sign of cardiac failure is usually seen in severe anaemia (Hb less than 7g/dl or worse in an adult). Note that this may not be present in young children even when severely anaemic. Jaundice may be suggestive of a haemolytic process. Signs of infection, purpura, and bruises may together suggest pancytopenia. Hepatosplenomegaly and lymphadenopathy are important for signs lymphoproliferative disorders. The abdomen and pelvis must be examined for liver, spleen, uterus and other masses; and rectal, scrotal and vaginal examination performed as appropriate.

#### Investigations

After the history and examination, working and differential diagnoses must be made and a decision taken as to what investigations should be done. In general the investigations can be divided into two broad groups: (a) those which help to confirm and classify the anaemia, (b) those which help to elucidate the cause. The first tests (essential haematology tests) to be requested are the full blood count (FBC), film comment and reticulocyte count. The results of these will confirm not only the anaemia, but also give parameters to enable its classification, give information on the activity of the bone marrow, and on occasion give the final diagnosis away.

# **Classification of Anaemia**

Anaemia may be classified in terms of the morphology of the red cells as seen on a blood film, assisted by red cell indices provided in an automated full blood count or in terms of its aetiology, or both. Understanding the figures in a full blood count will also assist in the understanding of anaemia.

#### Morphological classification of anaemia

This is based on the red cell size, shape and colour in a stained blood smear often correlating with the red cell indices as explained later in this article. Thus, the three main morphological distinctions are:

*Normocytic and normochromic anaemia*- the red cells have normal size, shape and colour but there are not enough of them. E.g. dilutional anaemia of pregnancy, haemolytic anaemia,uncomplicated anaemia of chronic disease.

*Microcytic and hypochromic anaemia* - the red cells are smaller and paler than normal, as in iron deficiency

#### and thalassemic states.

*Macrocytic anaemia* - the majority of the red cells are larger than normal e.g. folate or vitamin  $B_{12}$  deficiency<sup>7</sup>. Combinations of these three main morphological types are common in practice, making the diagnosis less obvious than one might presume. Other morphological and numerical changes in the red cells themselves, white cells and platelets give clues as to the aetiology of the anaemia e.g. sickle cell anaemia, acute eukaemia, aplastic anaemia etc.

#### Aetiological classification of anaemia

This is based on the underlying cause of the anaemia

1. Excessive loss of red cells as in chronic blood loss.

2. Excessive destruction of red cells as in haemolysis. Haemolysis may be due to inherited causes e.g. sickle cell disease, G6PD deficiency (favism, drug-induced or infection-provoked) or acquired causes such as autoimmune haemolysis, and infections like malaria and septicaemia.

3. Inadequate production as occurs in:

- i. Nutritional deficiencies like deficiencies of iron, folate, vitamin B12 and protein which are all vital to the synthesis of haemoglobin.
- ii. Bone marrow failure e.g. aplastic anaemia.
- iii. Infiltration of the marrow as in leukaemia.
- iv. Miscellaneous causes such as endocrine disorders, chronic renal failure, chronic inflammatory disease and cirrhosis of the liver<sup>7,8</sup>.

## The red cell indices

Red cell indices are specific parameters related to red cell morphology as determined with the aid of electronic equipment such as the Coulter machine, which has largely replaced manual methods. Without looking at the blood film, the red cell indices, particularly MCV (mean corpuscular volume), MCH (Mean corpuscular haemoglobin), and RDW (Red Cell Distribution Width) have been used to enhance the morphological classification of anaemia to a large extent, as follows:

**MCV (mean corpuscular volume)**: This describes the mean size of the RBC, the reference range is 76-96fl. Values above 100fl indicate macrocytosis, and microcytosis is indicated by values (usually) below 76fl.Values are (most) often raised in megaloblastic anaemia as mentioned above.

**MCH** (mean corpuscular haemoglobin): This defines the haemoglobin content of the red cell. The reference range is 27-30pg, hypochromia results from values below 27pg. Low MCH occurs in iron deficiency and the thalassaemias as mentioned below.

**RDW** (red cell distribution width): The extent of the red cell size variation is measured by the RDW i.e. it is a measure of the degree of anisocytosis as seen on a blood film. It is useful in distinguishing between iron deficiency and Beta–thalassaemia trait. A low MCV

with an increased RDW suggests iron deficiency and a low MCV with normal RDW suggest thalassaemia trait. It is also useful in differentiating high MCV due to aplastic anaemia from that due to megaloblastic anaemia – the RDW is normal in aplastic anaemia but high in megaloblastic anaemia. Its unit of measurement is either the coefficient of variation (CV) or standard deviation (SD). The normal range of RDW as CV is 11.6-13.0%. Values above 15% are regarded as increased<sup>9</sup>.

# **Other Essential Haematological Tests**

**Reticulocyte count** – this is raised in response to acute blood loss, and also in haemolysis or as a result of specific therapy for a deficiency of an essential nutrient.eg. Folic acid.

**Blood Film examination** – for fragments, spherocytes, polychromasia, blasts and nucleated red blood cells (NRBCs). This could be diagnostic such as in haemolytic anaemias or anaemia due to bone marrow failure. A leuco-erythroblastic picture (presence of immature red and white cells in peripheral blood) may be suggestive of bone marrow infiltration. E.g. by malignant cells.

In the next section, each morphological subtype as well as other tests will be discussed in more detail.

#### Microcytic anaemia i.e. Low MCV (<76fl)

1. *Iron deficiency anaemia* (low MCV, MCH and high RDW): This is the commonest cause of anaemia worldwide. Iron deficiency starts with inadequacy of iron (negative iron balance) leading to depletion of body stores, followed by functional iron deficiency in which there is inadequate iron for normal bone marrow activity and tissue function plus, sometimes mild anaemia. Further iron depletion causes frank iron deficiency anaemia.

Clinical assessment of the patient should include the diet, weight loss, indigestion, change in appetite, and bowel habits, including frequent fatty stools and bloody stools; genitourinary symptoms including menorrhagia, haematuria and abdominal symptoms. Poor dietary intake may be contributory if there is inadequate red meat intake. Iron is poorly absorbed from vegetable sources. Iron in haem molecules in meat is much better absorbed than the inorganic iron in vegetables, even spinach. Menstrual loss is the most common cause of iron deficiency anaemia in premenopausal women; in men and post-menopausal women, gastrointestinal (GI) blood loss is the most frequent cause.

Clinical examination should include weight and nutritional assessment, abdominal examination for GI malignancy, uterine fibroids, renal masses and assessment of any lymphadenopathy including supraclavicular nodes. Koilonychia (spoon-shaped nails) is occasionally seen.

2. *Thalassemic disorders*: This covers an entire spectrum of conditions ranging from thalassaemia

minima through thalassaemia trait (RDW is usually normal and the RBC count may be high) to thalassemia major. Their clinical manifestations range from completely asymptomatic microcytosis to profound anaemia that is incompatible with life and can cause intrauterine fetal death. In heterozygous alpha+ or alpha<sup>0</sup> thalassemia, or heterozygous beta thalassemia, the hypochromia is often less marked, in relation to the degree of microcytosis, than in iron deficiency. In homozygous beta thalassemia, there, is severe microcytosis, hypochromia and nucleated red cells are usually present on the thin blood flim.

Lifelong low or very low MCV and mean cell haemoglobin (MCH), with a normal or near normal haemoglobin, strongly suggests a thalassaemic disorder. The red cell count is often raised or may be normal while the Hb is low. The thalassaemic disorders are inherited disorders of reduced specific globin chain production, causing microcytosis and variable degrees of anaemia. If a patient with thalassaemia trait develops iron deficiency, both the haemoglobin and MCV will fall further.

3. *Sideroblastic anaemia:* as defined by the presence of ring sideroblasts in the bone marrow and occasionally the peripheral blood.

4. Anaemia of chronic disease: In the early stages this may be normocytic and normochromic, but with increasing cytokine production may become microcytic and hypochromic on account of poor iron utilization. Examples are chronic infection, such as tuberculosis, chronic inflammatory disease, such as rheumatoid arthritis and chronic renal disease.

## Macrocytic anaemia: i.e. MCV high (>100fl)

These include vitamin B12 or folate deficiency, hypothyroidism, liver disease, chronic alcoholism, myelodysplasia and high reticulocyte count (from any cause). Abnormal liver function, excess alcohol consumption and hypothyroidism can all cause macrocytosis without anaemia. Some drugs, such as azathioprine, zidovudine, methotrexate and hydroxycarbamide, cause significant macrocytosis due to interference with DNA synthesis.

When assessing patients with macrocytic anaemia, history taking must include diet, alcohol consumption, personal or family history of jaundice. Clinical examination should include search for peripheral sensory neuropathy, signs of chronic alcoholism and chronic liver disease, jaundice and splenomegaly. Firstline tests for further investigating the cause of a macrocytic anaemia are: serum vitamin B12 and folate, liver function and function thyroid tests. Myelodysplasia should be suspected in elderly patients with isolated macrocytic anaemia, neutropenia, thrombocytopenia or any combination of these. Review of previous results may show a progressive change over months or years. Sometimes there has been a macrocytosis for many years but neutropenia or anaemia has more recently developed.

The blood film may be diagnostic if it shows dysplastic neutrophils or macrocytic red cells. Features of myelodysplasia on a blood film include anisopoikilocytosis (variation in size and shape), hypogranular neutrophils (lack the usual quantity of granules), pseudo-Pelger or bilobed neutrophils (neutrophils with only two nuclear lobes, instead of the usual 3, 4 or 5 nuclear lobes).

#### Normocytic Normochromic Anaemia

In patients with normocytic anaemia, clinical assessment is essential to guide further investigations. The early phase of any cause of anaemia may be normocytic, but a significant change in the MCV can suggest developing iron or Vitamin  $B_{12}$  deficiency even while the MCV is still in the normal range. Causes include acute blood loss, anaemia of chronic disease, including renal disease and malignancy.

For all patients with normocytic anaemia, an abdominal ultrasound scan must be considered to look for splenomegaly, renal lesions, liver abnormalities, unsuspected malignancy and metastases. Chest X-ray must also be considered to look for malignancy and other pulmonary lesions.

The mechanisms of the anaemia of chronic disease, also called anaemia of inflammation, involve cytokines. Pro-inflammatory cytokines such as tumour necrosis factor are increased, so is hepcidin, a regulator of iron transport, whose increase results in reduced availability of iron for haematopoiesis. There is also decreased erythropoietin production and decreased response of red cell precursors in the bone marrow to erythropoietin.

Anaemia of chronic disease should be considered as a cause in patients with diabetes, heart failure, mild renal impairment, leg ulcers, inflammatory arthritis, polymyalgia rheumatica, etc. In practice, since the anaemia of chronic disease cannot be tested for directly, but is a diagnosis of exclusion, some patients are referred to a haematologist for further assessment, particularly if the haemoglobin is less than 10 g/dl and there is no obvious cause<sup>8</sup>.

# Other tests

- •Renal and hepatic function: Renal function tests are mandatory for all anaemia patients, especially normocytic normochromic anaemia. Inadequate production of erythropoietin in renal disease is the cause of the anaemia. Hepatic function is useful in the investigation of macrocytic anaemia and other red cell abnormalities
- ESR (Erythrocyte Sedimentation Rate) and CRP(Creactive protein): These are raised in plasma cell myeloma and inflammatory conditions.
- Serum vitaminB<sub>12</sub>/folate levels: In macrocytic anaemias.
- Iron studies: Serum Ferritin measurement is one of

the first-line tests to confirm iron deficiency and a significantly low level is diagnostic. However, a normal or high serum ferritin level does not exclude iron deficiency. Ferritin is an acute phase protein, and its level rises in infection, other inflammatory conditions and malignancy. It is good practice to check C-reactive protein at the same time. If this is raised, the patient may still be iron deficient despite having a serum ferritin level in the normal range.

- Where ferritin is not diagnostic, the next step is to test fasting serum iron and transferrin saturation. Transferrin may also indicate total iron-binding capacity. Low transferrin saturation indicates low levels of iron available to the bone marrow.
- Stool examination for intestinal parasites, especially hookworm ova, and stool occult blood especially in the elderly, for the possible presence of bleeding, be it from an ulcer or malignant tumour.
- Thick and thin blood films for malaria parasites which may cause haemolysis.
- Urine routine examination To demonstrate proteinuria, haemoglobinuria, haematuria and also the presence of excess urobilinogen in haemolytic anaemia.
- Coombs test to look for antibodies in autoimmune haemolytic anaemia.
- Sickling and haemoglobin electrophoresis for suspected haemoglobinopathies.
- Glucose 6 phosphate dehydrogenase screening tests and or assay in cases of intravascular haemolysis.

Patients with a red cell microcytosis who are not iron deficient will often require specialised tests (e.g. Hb electrophoresis and assays of other uncommon types of haemoglobins) and are best discussed with a consultant haematologist. Patients who have macrocytic anaemia with no evidence of megaloblastic anaemia should have the following done in addition to the tests above:

- Thyroid function tests (TSH). Macrocytosis may be seen in hypo or hyperthyroidisim.
- Serum protein electrophoresis (to look for a paraprotein) in multiple myeloma. The reported falsemacrocytosis may just be due to aggregation of red cells being assessed as single cellsin autoimmune haemolytic anaemias.
- Level and duration of alcohol intake should be documented. This can cause liver disease as well as have direct toxic effect on red cells.
- Investigations for haemolysis (Direct antiglobulin test, Lactate dehydrogenase (LDH) and haptoglobin). There is usually polychromasia in Romanowsky-stained blood smears due to increase in reticulocyte count in haemolytic anaemias and this causes an increase in MCV as well.

Patients who have significantly macrocytic red cell indices without a clear cause found after these tests should be discussed with a consultant haematologist.

# Case scenarios

# a. Patient with Haemolytic Anaemia:

Haemolytic anaemia is defined as anaemia due to shortened red cell lifespan. The most common causes are the haemoglobinopathies, red cell enzyme deficiencies e.g. G6PD deficiency, hereditary spherocytosis (HS) and autoimmune haemolytic anaemia (AIHA). The normal red cell lifespan is about 120 days but in some haemolytic states may be as short as ten days.

In haemolytic anaemia the following observations are important:

- Family history- to check for hereditary conditions and their mode of inheritance.
- Ethnic origin G6PD deficiency occurs worldwide but is most common in Mediterranean and Chinese populations.
- Drug history in association with G6PD deficiency as evidenced by dark urine etc.
- Favism: (haemolysis following ingestion of broad or fava beans). is also an important cause of haemolysis in certain types of G6PD deficiency.

Tests for patient with suspected haemolytic anaemia:

- Hb estimation (low Hb) reticulocyte count (raised); peripheral film examination for the presence of polychromasia, spherocytes, elliptocytes, irregularly contracted cells, schistocytes, or auto-agglutination.
- Direct Coomb's Test usually positive in immune haemolysis.
- LDH non-specific but is often raised in haemolysis.
- Haptoglobin a low level suggests haemolysis, especially the intravascular type.
- Liver function tests. This will show an increase in unconjugated bilirubin. Elevated unconjugated bilirubin and reticulocytosis suggest haemolytic anaemia.
- Osmotic fragility tests: Increased in conditions associated with red cell membrane loss, defect or damage.
- Urinary haemosiderin, especially in patients with intravascular haemolysis.
- Past history Neonatal jaundice may be indicative of congenital conditions as hereditary spherocytosis or G6PD deficiency.

• Triggering events- history of drugs, infections

Important Points to Remember

- Clinical findings seldom are sufficient to enable a definitive diagnosis of a particular haemolytic condition to be made.
- Lab investigations play a central role in the accurate diagnosis and assessment of severity of haemolytic anaemia.

# b. Patient suspected to be suffering from plasma cell myeloma

Myeloma should be considered if there is anaemia with bone pain in the middle aged and elderly, particularly vertebral pain or collapse, or new or worsening renal impairment.

- FBC and blood film: This will confirm anaemia and show the presence of excessive rouleaux formation and occasionally plasma cells (seen only in advanced cases).
- Serum protein electrophoresis may detect the presence of a monoclonal band
- Urine for Bence Jones Protein: About 30% of myeloma cases do not have a paraprotein but instead show hypogammaglobulinaemia (low serum immunoglobulins), serum free light chains and have detectable urinary light chains (Bence Jones protein)
- Skeletal survey for lytic lesions and extent of bone involvement.
- Bone marrow examination should normally reveal increase in percentage of plasma cells and can also be used for monitoring of disease.
- Serum free light chains are particularly important in patients with normal serum protein electrophoresis
- Serum Beta-2 Microglobulin is often raised and is a useful indicator of prognosis.
- Flow cytometry and cytogenetics if facilities available. Immunophenotyping by flow cytometry will confirm the presence of abnormal plasma cells in peripheral blood as well as bone marrow samples. The characteristic immunophenotype of malignant plasma cells is CD38high, CD138high and CD45low. Cytogenetics will detect chromosomal abnormalities<sup>9</sup>.

It is not necessary to try and complete all the tests before referring to the haematologist. Precious time is wasted that way. If any two or three of the above bullet points are suggestive, the haematologist should be called.

# c. Pregnancy

The mild anaemia of pregnancy is principally dilutional. The red cell mass increases by up to 32%, but the plasma volume expands even more, (40% at term). It is usual for the MCV to rise slightly in pregnancy. A tandem fall in both haemoglobin and MCV suggests developing iron deficiency. National Institute for Health and Care Excellence (NICE) Clinical Guideline 62 (2008) on antenatal care recommends checking the full blood count at booking and again at 28 weeks.

Haemoglobin below 11.5 g/dl at booking or 10.5 g/dl at 28 weeks should prompt investigation and treatment of anaemia. Iron deficiency constitutes 75% of cases of anaemia especially in developing countries<sup>6</sup>. Other known causes of anaemia in pregnancy include folate and vitamin B12 deficiency, hookworm infestation and malaria in endemic areas.

# d. The suspected bleeding patient

There should be a high index of suspicion of occult

bleeding in the individual with microcytosis and hypochromia as well as a high platelet count. The following tests and any specialized tests depending on the patient's presentation should be done.

- Stool tests for occult blood, especially in adults with iron deficiency anaemia to exclude hookworm infestation, ulcers or GIT malignancy.
- Coagulation screening tests, for inherited and acquired bleeding disorders
- Endoscopy/colonoscopy- if upper or lower gastrointestinal bleeding is suspected.
- Urine dipstick/urine for haemosiderin this is also seen in haemolytic anaemias with haemoglobinuria.
- Urine microscopy for red blood cells

Stool test for Helicobacter pylori antigen. This is important since the prevalence of H.Pylori in Ghanaians and other developing countries is high<sup>10,11.</sup> H.pylori may cause iron deficiency anaemia (refractory to iron therapy), immune thrombocytopenic purpura and mucosa associated lymphoid tissue (MALT) lymphoma.

#### e. Neonatal anaemia

Co-morbidities such as congenital infections, bacterial sepsis and repeated blood sampling in hospitalized neonates may worsen the physiologic drop in haemoglobin levels in both term and preterm babies. In addition, preterm babies have a diminished response to erythropoietin, shorter red cell survival, rapid postnatal growth and little or no iron stores, which contribute to anaemia of prematurity<sup>5</sup>. Haemolysis is also an important cause of anaemia in neonates e.g. from blood group incompatibility or red cell membrane or enzyme defects. Babies with underlying haemolytic disease may also be severely jaundiced and require exchange blood transfusions to both correct anaemia and lower bilirubin levels. Diamond-Blackfan anaemia, an inherited red cell aplasia often presents in the neonatal period. Detailed history of past and current pregnancies should be obtained. Any intra-partum complications that might have contributed to blood loss should be noted. Physical examination should include evaluation for any dysmorphic features or congenital anomalies such as abnormal skin pigmentation, dysplastic radii and thumbs, microcephaly, hypogonadism etc. Phlebotomy blood losses in the neonatal or babies' units should be monitored and minimized as much as practicable. Red cell transfusions may be considered at haemoglobin levels 9-12g/dl, depending on gestational age, postnatal age and need for respiratory support<sup>5</sup>.

## **Specialised Tests.**

- Serum erythropoietin levels (for patients with renal impairment)
- Bone marrow examination to establish a bone marrow infiltration such as leukaemia or carcinomatosis as the cause of anaemia.

- Paroxysmal Nocturnal Haemoglobinaemia (PNH) Screen - Hams test, glycerol lysis test, Fluorescent
  - labeled inactive toxin aerolysin test.
- Haemoglobin electrophoresis and quantification of haemoglobin fractions for the diagnosis of haemoglobinopathies.
- Red cell membrane/enzyme studies- For G6PD and pyruvate kinase deficiencies<sup>12</sup>.

## When to refer an anaemic patient

- Anaemias where the cause is unclear after initial routine investigations are best discussed further with a consultant haematologist
- When there is microangiopathic haemolysis (red cell fragments on film).
- Suspected leukaemia or myeloma
- Pancytopenia (anaemia with either a low platelet count or a low WBC count)
- Leucoerythroblastic blood picture on film comment
- All immune haemolytic anaemias
- Drug induced anaemias
- Congenital anaemias, including haemoglobinopathies
- Severe anaemia (Hb< 8 gm/dl) with no obvious cause after preliminary investigation

All patients requiring specialised tests like bone marrow examination, cell markers, cytogenetics, haemoglobin quantification etc.

# Conclusion

This paper provides a summary of the doctor's approach to diagnosis and management of anaemia, one of the most common global public health problems which is often underdiagnosed and undertreated. It is important to give it the necessary attention as that would contribute in good measure to reducing morbidity and mortality resulting from its neglect. Since anaemia is always secondary to a disease or disorder, it is imperative to aim at diagnosing the underlying cause. Doctors are encouraged to take a good history, examine the patient thoroughly, request essential blood tests ie FBC, reticulocyte count and blood film comment. Additional investigations and specialized tests must be carried out where necessary and the Specialist or Consultant Haematologist must be consulted in cases where the underlying cause is not clear.

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