JPSIM Journal of Pakistan Society of Internal Medicine

Medical Guidelines

# A 3-Step Approach to the Diagnosis of Anaemia

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**How to cite this:**

Rehman AU. A 3-Step Approach to the Diagnosis of Anaemia. J Pak Soc Intern Med. 2022;3(4): 359-360

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DOI: https://doi.org/10.70302/jpsim.v3i4.2272

Anaemia is extremely prevalent in our country due to various reasons all centering on poverty. Due to gradual onset and subtle symptomatology, it often remains undiagnosed and untreated. Or it is regarded as a part of general weakness. The commonest cause is chronic iron deficiency for one or the other reason. In menstruating women, menorrhagia added to the background of poor nutrition is very common. Chronic blood loss due to haemorrhoids, acid peptic disease and hook worm infestations also common. Although a large segment of our population suffers from malnutrition contributing to anaemia, even well to do people are also not immune to iron deficiency as iron is not widely distributed in our diet. The best source of iron is haem that come in red meat. Iron that is present in vegetables is not readily absorbed. Hence people in the middle class may also have iron deficiency. In addition, folic acid and vitamin B12 deficiencies are also common. They are also mostly related to poor nutrition. All these conditions can be treated by supplementing diet with haematinic which typically contains iron, folic acid and vitamin B12. But it is also important to address the underlying cause responsible for anaemia. In addition, some patents might have other types of anaemias like thalassaemia, bone marrow depression and haemolytic anaemia, they need to be diagnosed properly and offered appropriate treatment. The list of causes of anaemia is actually very long. This document will provide a basic framework to guide a physician to diagnose common anemias with limited laboratory tests. It should also help to identify those who might require specialized testing. All this is possible with a careful inspection of CBC that is done by an auto-analyzer. These reports are often system generated and are presented on a very un-impressive chit. But they have a wealth of information if examined in these simple 3 steps as outlined below.

## Step No. 1: Diagnosis of Anaemia

History and physical examination may be very suggestive of anaemia, but a laboratory confirmation is needed. So, first of all you should look at the Hb% or Haematocrit. If these values are less than the given reference range, the diagnosis of anaemia is made. You must rule out haemodilution because that can also give the same picture in the absence of anaemia.

## Step No 2: RBC Morphology

Once we know that anaemia is there, we need to decide which of the three main categories it falls in. These categories are defined based on RBC morphology, particularly mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCV) and mean corpuscular haemoglobin concentration (MCHC). Out of the three, MCV carries the maximum weightage. If there is discordance among three values, the decision should be made as per MCV. The three categories and their differential diagnosis is as below.

1. Hypochromic Microcytic Anaemia. A low MCH (hypochromic) and low MCV (microcytic) is the hall mark of this group. Two main etiologies are chronic iron deficiency state or thalassaemia minor. Thalassaemia major is usually not included in this differential diagnosis as it has gross clinical signs and present very early in age. Out of the 2 possibilities, iron deficiency is so much commoner than thalassemia that the diagnosis can be taken for granted. It would be appropriate to go for iron studies to formally diagnose iron deficiency. These studies include serum iron, total iron binding capacity, transferrin saturation and serum ferritin. Ideally all should be done as they have limitations, and no single test is clearly diagnostic. Those with hypochromic, microcytic anaemia without the evidence of iron deficiency should be further investigated for thalassaemia. The investigation of choice is haemoglobin electrophoresis. In this context, elevated HB-F & HBA2 should confirm the diagnosis of beta thalassemia. Electrophoresis is expected to be normal in alpha thalassemia. After ruling out

iron deficiency and beta thalassaemia, the diagnosis of alpha thalassaemia is made by exclusion. However, a DNA analysis if available, can be used to confirm this diagnosis.

2. Macrocytic Anaemia. In the setting of anaemia, a high MCV will characterizes macrocytic anaemia. MCH may be normal, but MCHC is typically low. The differential diagnosis includes folic acid deficiency, vitamin B-12 deficiency, Vitamin B6 deficiency and hypothyroidism. Actual differential diagnosis is much wider but further discussion is beyond the scope of this document. History may provide important clues to the actual etiology but assays of Vit B12, folic acid vit 6 be performed to confirm the relevant deficiency. TSH alone is usually sufficient to rule out hypothyroidism.
3. Normochromic Normocytic Anaemia. In the context of anaemia, a normal MCV and a normal MCH would imply normochromic normocytic anaemia. Acute blood loss can also give rise to similar picture but that can be easily ruled out clinically. In this condition, lesser number of RBCs are made, but those cells are normal in size and haemoglobin concentration. The differential diagnosis is mostly related to bone marrow disorders. Important clues to the bone marrow etiology can also be obtained from CBC in step-3.

### Step No 3: WBC Count & Morphology

In step 3, you should check the total leukocyte count (TLC), differential leukocyte count (DLC), RBC count and platelet count. If all are low (pancytopenia), aplastic anaemia is a very strong diagnosis. All cell lines are affected as bone marrow isn't simply producing enough cells. You should also notice a reversed polys/lympho ratio. In aplastic anaemia, lymphocytic count is predominant as they are produced in extra-medullary tissues whereas polys are made in bone marrow only. A high TLC and presence of abnormal premature cells should indicate the possibility of leukemia and secondary bone marrow insufficiency.

Haemolytic anaemia also falls in this group of normochromic and normocytic picture. Absence of pancytopenia should point toward this possibly. Some individuals would exhibit mild macrocytic picture as younger RBC which come to the circulation as a result of haemolysis are usually slightly bigger in size. The differential diagnosis of haemolytic anaemia is very long. Initial investigations to substantiate this diagnosis include reticulocyte count, haptoglobin, LDH, differential bilirubin. Further testing should be done based on the results of these basic investigations.

With this simple 3 step approach to anaemia based on careful inspection of CBC should give you important clue to the diagnosis. Never overlook history and physical findings. In some cases, diagnosis may be difficult if CBC picture is altered by partial treatment, mixed etiologies and blood transfusions. Rare cases however must be dealt with in specialized centers.

**Fig. 1. A 3-Step Approach to The Diagnosis of Common Anaemias**