VOLUME-8, ISSUE-10, OCTOBER-2019 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Pathology

INTERPRETATION OF SERUM IRON PROFILE AND CBC FINDINGS IN IRON DEFICIENCY ANEMIA

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ABSTRACT

BACKGROUND: Iron deficiency anaemia is most common anemia worldwide. It is most common in female. In male IDA occurs most commonly due to gastrointestinal disease. Diagnosis of IDA on clinical suspicion is easy with CBC report and iron profile .Few dimorphic anemias and anemias in complex clinical settings pose difficulty in diagnosis, thus other investigations are also needed.

MATERIALS AND METHODS: we prospectively collected clinical data, CBC findings and iron profile results of patients of IDA in tertiary teaching institutes of Bihar. EDTA peripheral blood samples were run on Sysmex XT-1800i and CBC findings were noted, whenever needed peripheral blood smears were made to know morphology of red blood cells; serum samples of all cases were run for serum iron profile (iron, ferritin and transferritin saturation) and values noted and tabulated.

RESULT: All patients have both decreased serum iron and ferritin. They revealed classical microcytic hypochromic picture with raised RDW. Female outnumbered male. Male female ratio was 1:1.4. In this study CBC findings (MCV, MCH and RDW) were well correlated with iron profile findings. Minimum hemoglobin level was 5.4gm/dl.

CONCLUSION: Iron deficiency anemia is major public health problem worldwide .In majority of cases, CBC and iron profile study can clinch the diagnosis, however few cases need further investigations and clinical correlation.

KEYWORDS : IDA, Ferritin, Iron, CBC, Peripheral Blood Smear, Hemoglobin

INTRODUCTION:

The diagnosis of anemia is simple and objective: the World Health Organization (WHO) defines anemia as the decline in blood hemoglobin to a concentration below 13 g/dL in men and 12 g/dL in women. However, to confirm that iron deficiency (ID) is the origin of the anemia is not always easy (1,2). Usually, the simple complete blood count (CBC) strongly suggests this origin with typical pattern of microcytic hypochromic and elevation of red cells distribution width (RDW). However, microcytic hypochromic picture may be found in other anemias, like thalassemia, sideroblastic anemia and also in anemia of chronic inflammation. Few pure and many dimorphic IDA cases are normocytic. Therefore, a normal mean corpuscular volume (MCV) does not exclude ID from being the cause of the anemia. Moreover, the presence of microcytosis does not necessarily imply ID and can be produced by other anemias (chronic process, sideroblastic anemia) and diseases (e.g. thalassemia). RDW measures the degree of anisocitosis (size difference) of the population of red cells and its elevation is neither sensitive nor specific for ID (3, 4, 5). The next step is to determine the so-called iron metabolism (in addition to all other necessary determinations, including levels of vitamin B12 and folic acid) and in many cases the level of C-reactive protein. A typical pattern is a decrease in decreased serum iron (sideremia) serum ferritin, and transferrin saturation. However, this is not the usual case. Serum ferritin, in the absence of inflammation (usually defined as a normal C-reactive protein level), reflects total body iron deposits. Thus, a low serum ferritin (< 30 ng/mL) unequivocally means ID, whether accompanied by anemia or not. However, as serum ferritin is an acute phase reactant, a normal or even elevated ferritinemia does not exclude the presence of ID (6, 7,8). Thus, in the presence of an inflammatory process (usually defined by an elevated C-reactive protein level), ID could exist even with levels of ferritin up to 100 ng/mL. Another parameter of the normal "iron metabolism", especially useful when the determination of ferritin is equivocal, is the transferrin saturation index. This shows the percentage of transferrin that transports iron and thus a decrease (< 20%) implies ID, either absolute or functional.

In some cases, even taking into account all these determinations, ID can be difficult to diagnose. It generally occurs in situations where the anemia has a multifactorial origin. This is typical in cases of anemia of mixed origin, a chronic process that coexists with ID, which is a frequent scenario in gastrointestinal inflammatory disease or cancer (9,10,11). These other factors include the determination of soluble transferrin receptor, reticulocyte hemoglobin concentration, the percentage of hypochromic red cells, the concentration of erythropoietin and even the determination of hepcidin(12,13,14). The soluble transferrin receptor is one of the most useful as it is the least influenced by the presence of inflammation and it correlates well with concentration of transferrin receptor in the cell plasma membrane. If the levels are high, ID is likely to be a major component of anemia, while in those cases with normal or low levels; anemia is probably not associated with ID (15, 16).

Patients with inflammatory conditions such as inflammatory bowel disease (IBD), chronic heart failure (CHF), and chronic kidney disease (CKD) have high rates of iron deficiency with adverse clinical consequences. Under normal circumstances, serum ferritin levels are a sensitive marker for iron status but ferritin is an acute-phase reactant that becomes elevated in response to inflammation, complicating the diagnosis. Proinflammatory cytokines also trigger an increase in hepcidin, which restricts iron absorption and promotes sequestration of iron by ferritin within storage sites. Patients with inflammatory conditions may thus have restricted availability of iron for erythropoiesis and other cell functions due to increased hepcidin expression, despite normal or high levels of serum ferritin. The standard threshold for iron deficiency (<30 g/l) , therefore does not apply and transferrin saturation (TSAT), a marker of iron availability, should also be assessed. A serum ferritin threshold of <100 g/l or TSAT < 20% can be considered diagnostic for iron deficiency in CHF, CKD, and IBD. If serum ferritin is 100–300 g/L, TSAT < 20% is required to confirm iron deficiency. Routine surveillance of serum ferritin and TSAT in these at-risk groups is advisable so that iron deficiency can be detected.

The clinical picture varies greatly from one case to another. Pallor of varying grades may be found. It is produced both by the anemia and by the lack of iron, which is essential for cellular energy metabolism. Symptoms depend greatly on the speed of onset of anemia, its severity and the characteristics of the patient. Thus, IDA or ID can be detected in a person with symptoms that include general weakness, fatigue, irritability, poor concentration, headache, and intolerance to exercise. Some iron-deficient patients, with or without anemia, might have alopecia, atrophy of lingual papillae, or dry mouth due to loss of salivation. Other symptoms, such as weakness or koilonychia, chlorosis, or the syndromes of Plummer-Vinson or Paterson-Kelly (dysphasia with esophageal membrane and atrophic glossitis) have virtually disappeared. These changes were caused by reduction of iron-containing enzymes in the epithelia and the gastrointestinal tract. Pica can cause iron deficiency.[17,18,19].

MATERIAL AND METHODS:

we prospectively collected clinical data, CBC findings and iron profile results of 11 patients of IDA in tertiary teaching institutes of Bihar. EDTA peripheral blood samples were run on Sysmex XT-1800i and CBC findings were noted, whenever needed peripheral blood smears were made to know morphology of red blood cells; serum samples of all cases were run for serum iron profile (iron, ferritin and transferritin saturation) and values noted and tabulated. Further investigations were done in those Patients that had normocytic and dimorphic blood picture with clinical features of iron deficiency and or dimorphic anemia .In few cases, bone marrow study was also done to know cause of microcytic anemia, especially in oral iron refractory patients.

Table 1.IRON PROFILE IN IRON DEFICIENCY ANEMIA

CASE NO.	IRON µg/dL	FERRITIN ng/mL	TIBC	Transferrin Saturation %	RETIC %	AGE/SEX Year
1	17	8.6	337	5.0	1.0	5/M
2	28	3.6	371	8.0	1.5	22/F
3	20	7.5	355	10.0	1.0	40/F
4	18	9.0	354	9.5	1.4	20/M
5	17	8.5	353	7.9	1.2	35Y/F
6	19	8.0	355	7.6	1.5	3/F
7	18	9.0	388	8.6	2.0	78/F
8	17	8.5	380	8.7	2.0	80/M
9	16.9	7.4	389	7.7	1.0	67Y/F
10	16.9	7.4	389	7.7	1.0	30/F
11	18	4.1	272	8.0		60Y/M

RESULT:

Male female ratio was 1:1.4. In this study CBC findings (MCV, MCH and RDW) were well correlated with iron profile findings. Minimum hemoglobin level was 5.4gm/dl. Severity of anemia i.e. hemoglobin concentration was proportional to MCV and MCH values. Serum ferritin level was well correlated with severity of microcytic hypochromic anemia. Minimum serum ferritin was 3.6mcg/L

Table.2 RBC INDEXEX IN IRON DEFICIENCY ANEMIA

CASE	RBC	HB	HCT	MCV	MCH	MCHC	RDW
1	3.8	7.1	25.3	66.6	18.7	28.1	18.7
2	3.3	5.4	20.6	64.0	18.3	29.6	16.8
3	3.5	5.6	20.8	65.0	18.3	28.5	19.0
4	3.6	7.8	21.5	63.0	17.5	27.9	18.5
5	3.7	6.8	22.0	62.5	18.0	28.0	19.0
6	3.5	6.6	23.8	63.0	19.5	27.7	18.8
7	3.6	7.0	22.9	63.0	18.9	26.00	19.6
8	3.9	7.5	23.8	63.0	17.0	27.0	19.0
9	3.7	7.2	23.5	62.0	16.0	26.0	18.0
10	3.4	5.7	20.1	64.0	18.1	28.2	18.5
11	3.3	5.8	21.0	64.5	18.5	29.0	19.0

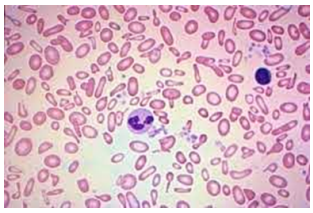

Figure 1. PBS shows microcytic hypochromic picture and tear drop cell

DISCUSSION:

Ferritin is the best indicator of iron deficiency and a low ferritin alone is diagnostic of IDA. Iron is stored intracellularly as ferritin and in the presence of infection, malignancy or chronic inflammation; the ferritin rises as acute phase protein. Therefore, the diagnosis of IDA is challenging when there is coexisting inflammation, as the ferritin can be up to 100 g/L, even in the presence of iron deficiency. In this case, further tests can help clarify the diagnosis. Total iron-binding capacity, transferrin saturation, serum iron, and serum transferrin receptor levels may be helpful if the ferritin level is between, 46 and 99 mcg/L (12,13).

Iron profile studies include serum iron level, transferrin saturations and total iron-binding capacity (TIBC) or transferrin concentration, in addition to ferritin. In the bloodstream, serum iron is carried bound to transferrin. The TIBC (expressed in g/dL) is the maximum iron that can be bound by transferrin if this were 100% saturated. The transferrin saturation is the concentration of iron that is bound to transferrin, expressed as a percentage of the TIBC. In IDA, the ferritin, serum iron and transferrin saturations are low, but the TIBC increases. The serum transferrin concentration (expressed in mg/dL) increases in IDA, as the body tries to compensate for low iron levels and this correlates positively with the TIBC. In contrast, in anaemia of chronic disease (ACD) the ferritin is raised, owing to an increase in the iron regulator hepcidin (14, 15,16). Studies have shown that hepcidin expression is unregulated when there is infection or inflammation, via inflammatory cytokines such as IL-6. Hepcidin binds to ferroportin (the iron exporter on cells) which results in internalization and degradation of this transporter, which reduces iron release from cells. This failure of release of iron from the ferritin stores results in a low iron, low transferrin saturation and low TIBC, with a high ferritin

The mean cell volume (MCV) and mean cell hemoglobin (MCH) are very sensitive for IDA in the absence of B12 deficiency or folate deficiency. However, they may also be reduced in ACD, haemoglobinopathies and sideroblastic anemia. The MCH may be more reliable than the MCV as it is less influenced by storage and the counting machine. In patients with an MCV disproportionately low for the Hb, Hb electrophoresis should be performed to exclude a haemoglobinopathy. If iron deficiency coexists with B12 or folate deficiency, the MCV can be high, normal or low. The red cell distribution width (RDW) is a measure of the variation in the diameter of the red cells. The normal diameter of a red cell is 6–8 m. A high RDW occurs in conditions such as IDA, B12 deficiency and folate deficiency. The RDW would be expected to be normal in ACD and haemoglobinopathies. Measurement of soluble transferrin receptor is more reliable at identifying IDA than TIBC and iron. The discovery of the iron-regulatory hormone hepcidin in 2001 has revolutionized our understanding of iron disorders. Nevertheless, promising applications can already be glimpsed, ranging from the use of hepcidin levels for diagnosing iron-refractory iron deficiency anemia to global health applications such as guiding safe iron supplementation in developing countries with high infection burden (18, 19, 20, 21).

CONCLUSION:

Iron deficiency anaemia is major public health problem. In majority of cases, CBC and iron profile study(serum iron, transferrin, ferritin and TIBC) can clinch the diagnosis, however few cases need further investigations and clinical correlation. Ferritin is the best indicator of iron deficiency and a low ferritin alone is diagnostic of IDA. It has not diagnostic importance in clinical setting of chronic inflammation and infection.

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