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Iron Deficiency Anemia: An Update

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Abstract

Anemia affects one fourth of the world's population, and iron deficiency is the most common cause of anemia. Iron deficiency anemia is only a part of the spectrum of iron deficiency syndrome. In this review we are discussing about the evaluation and management of iron deficiency anemia.

Keywords: iron deficiency, serum ferritin, refractory iron deficiency anemia, obscure GI bleed

Introduction

Iron deficiency anemia (IDA) is the most prevalent forms of anemia. Globally it accounts for approximately 50% of anemia. In developing countries 30-70% of the population is iron deficient. IDA is thought to affect the health of more than 1 billion people worldwide [1].

Iron metabolism

Duodenum and proximal jejunum is the major sites of iron absorption. Adult men have about 1 g of storage iron mostly in liver, spleen, and bone marrow. Only a small amount of iron enters and leaves the body on a daily basis [2]. Most iron is recycled from the breakdown of old red blood cells by macrophages of the reticuloendothelial system. (See **Figure 1**)

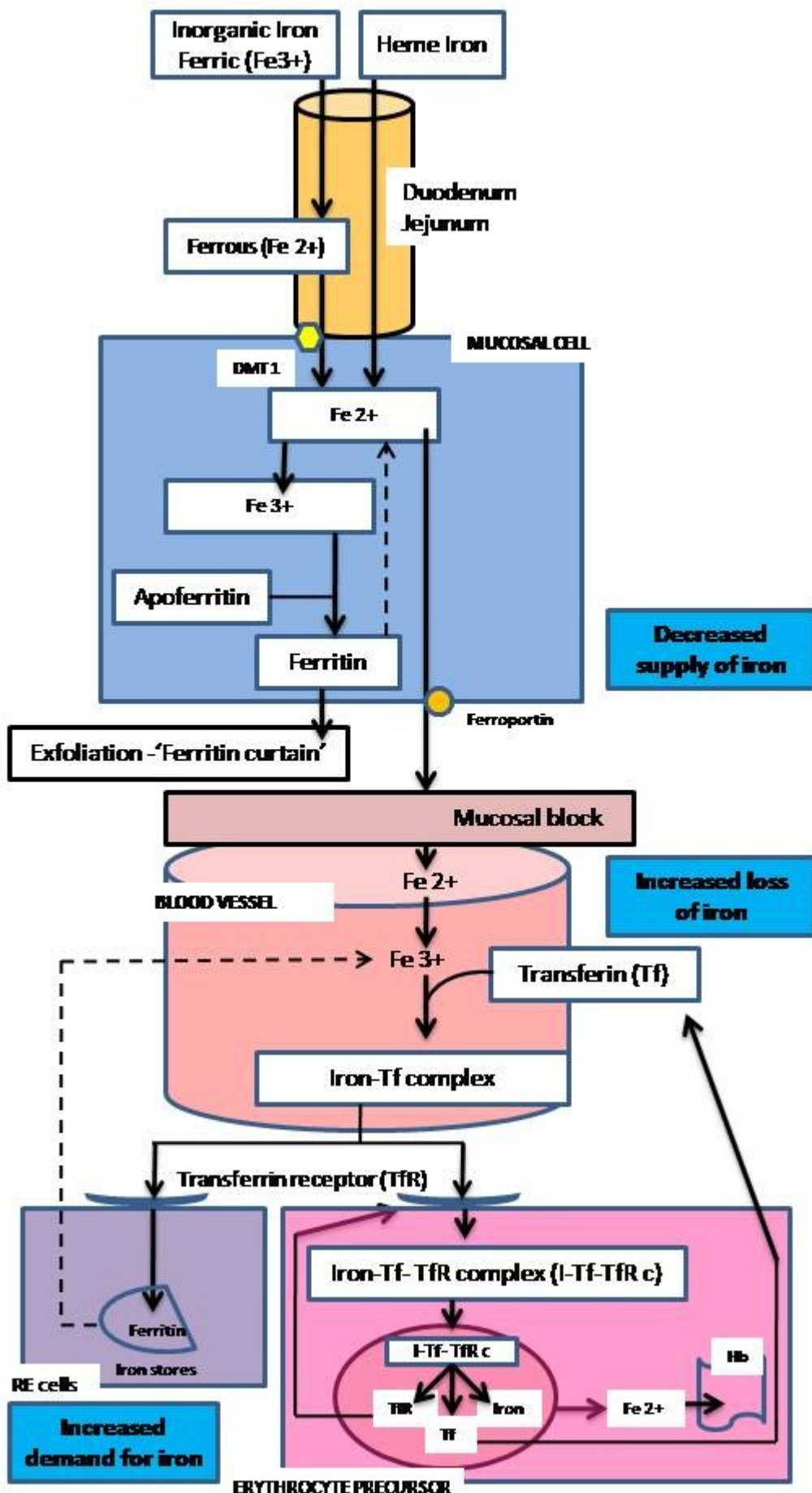


Figure 1: Iron metabolism and mechanism of iron deficiency anemia

The normal iron content of the body is approximately 3 to 4 g. It is distributed in the body as follows:

1. Hemoglobin in circulating red cells and developing erythroblasts - about 2.5 g
2. Iron-containing proteins (eg, myoglobin, cytochromes, catalase) - 400 mg
3. Plasma transferrin-bound iron - 3 to 7 mg
4. The remainder is storage iron in the form of ferritin or hemosiderin

Causes of iron deficiency

Common causes of iron deficiency includes [3]:

- a) Increased demand for iron - Infancy, adolescence, pregnancy, erythropoietin therapy
- b) Increased loss of iron - Blood loss, menses, phlebotomy
- c) Decreased supply of iron - Poor dietary intake, malabsorption

Stages of iron deficiency anemia

Progression of iron deficiency to anemia can be divided into three stages. The 1st stage is the stage of negative iron balance, where the iron demand exceeds body's ability to absorb iron from the diet. This may be due to blood loss, pregnancy, rapid growth spurts during adolescence or decreased dietary intake [4]. During this period iron stores are depleted. Serum ferritin and stainable iron stores in the bone marrow (BM) are reduced.

With continued deficiency serum ferritin begins to fall and once the serum ferritin falls <15ug/dl, the iron stores become depleted. Once transferrin saturation falls to 15 - 20%, hemoglobin synthesis become defective. This stage is called as the *stage of iron-deficient erythropoiesis* [5].

With further declines in iron level, hemoglobin level begins to fall and this stage is called as the *stage of iron deficiency anemia*. At this point transferrin saturation usually falls to 10-15%. (**Table 1**)

Early iron stores depletion can be assessed by measuring marrow iron stores, serum ferritin and TIBC. Iron deficient erythropoiesis can be recognized from additional abnormalities in serum iron, percent transferrin saturation and red cell protoporphyrin level.

Clinical presentation of Fe deficiency anemia

Common symptoms of IDA include tiredness, easy fatigability, breathlessness on exertion, giddiness, leg pain, hair fall and worsening of co-existing disease such as angina. Restless legs syndrome (RLS) or Willis-Ekbom disease is also associated with iron deficiency. Common signs include mucous membrane pallor, tachypnoea, tachycardia, postural hypotension, ankle oedema and presence of flow murmurs. Koilonychia and cheilosis are signs of advanced iron deficiency. Pica is commonly seen in children. Pica is perverted appetite for substance not fit as food. Clinical features of iron deficiency depend on the severity and chronicity of anaemia [6]. Sometime symptoms related to the cause of iron deficiency will be there like abdominal pain, menorrhagia or bleeding per rectum.

Table 1: Stages of iron deficiency anaemia and iron studies

		Normal	Stage of negative Iron balance	Stage of Iron deficient erythropoiesis	Stage of Iron deficient anemia
1	BM iron stores	1-3+	1 0-1 +	Absent 0	0
2	S.Ferritin (mg/L)	50 +200	1<20	< 15	< 15
3	S.Fe (mg/dl)	50-150	N	1<50	<30
4	TIBC (mg/dl)	300-360	N (> 360)	1>380	> 400
5	Transferrin saturation %	30-50	N	< 20	< 10
6	Red cell protoporphyrin	30-50	N	>100	> 200
7	Red cell morphology	NL	NL	Normal/ microcytic -Hypochromic reticulocytosis	1RDW - Hypochromic microcytic anaemia -

Differential diagnosis

In patients presenting with iron deficiency anemia, other causes of microcytosis should be considered as differential diagnosis (**Table 2**). The diagnostic workup include two steps; that is confirmation of the diagnosis of iron deficiency anemia from other microcytic anemia and identifying the cause for iron deficiency especially when the cause of anemia is not clinically evident.

Table 2: Causes of microcytic anemia

CAUSES OF MICROCYTIC ANAEMIA
1. Reduced iron availability: iron deficiency, the anemia of chronic disease, copper deficiency
2. Reduced heme synthesis: lead poisoning , sideroblastic anemias
3. Reduced globin production: thalassemic disorders , hemoglobinopathies

Investigations

1. Complete blood count

Complete blood count shows low hemoglobin and red cell counts. MCV and MCH are also reduced. The mean corpuscular volume (MCV) is the volume of the "average" red blood cell, stated in

femtoliters (fL). MCV can be calculated as:

$$\text{MCV (femtoliters)} = 10 \times \text{HCT(percent)} \div \text{RBC (millions}/\mu\text{L)}$$

The normal range for the MCV in adults is 80 to 96 fL. RBCs are considered microcytic if MCV <80 fL.

2. Red blood cell distribution width (RDW)

RDW determine the dispersion of RBC size about the mean. It is calculated as follows:

$$\text{RDW} = \text{Standard deviation of RBC size} \div \text{MCV}$$

The normal range for the RDW is 11.5 to 14.5 percent. An increased RDW indicates the presence of increased variability in red cell size (anisocytosis). An increased RDW is commonly found when there is a nutritional deficiency like iron, folate, and vitamin B12 deficiency (**Table 3**). This is because the nutrient levels available to red cell precursors may vary widely during any 24 hour period, resulting in variability in red cell endowment and, therefore, size [7].

Table 3: Causes of high RDW

Normal RDW	High RDW
1. Thalassemia minor	1. Iron deficiency
2. Anemia of chronic disease	2. Hemoglobin H disease
3. Some hemoglobinopathy traits	3. Some anemia of chronic disease
	4. Some thalassemia minor
	5. Fragmentation hemolysis

3. Reticulocyte production index (RPI)

Reticulocyte production index (RPI) is a measure of the marrow response to anemia. It involves two corrections to the reticulocyte count, one for the degree of anemia (normalized to a HCT of 45 percent or Hb of 15) and another for the reticulocyte maturation time (RMT), which varies from 1.0 days for a hematocrit of 45 percent to 2.5 days for a hematocrit of 15 percent.

$$\text{RPI} = \text{Reticulocytes (percent)} \times (\text{HCT} \div 45) \text{ or } (\text{Hb} \div 15) \times (1 \div \text{RMT})$$

The normal RPI is approximately 1.0. RPI in excess of 2.0 is considered increased, representing an adequate marrow response to anemia. If RPI is < 2 in patients with anemia, a defect in the erythroid marrow proliferation or maturation must be present.

Common causes of Microcytic anemia with RPI < 2 are given in **Table 4**

4. Peripheral smear

Peripheral smear shows microcytic hypochromic blood picture. Unlike thalassemia, target cells are not usually present and anisocytosis and poikilocytosis are not marked. It lacks intra-erythrocytic crystals (rod-shaped cells containing hemoglobin C crystals) seen in hemoglobin C disorders.

Combined folate deficiency and iron deficiency shows a population of macrocytes mixed with microcytic hypochromic cells. This condition can normalize MCV. Platelet count is usually increased [8].

Table 4: Common causes of microcytic anemia with RPI < 2

Common causes of microcytic anemia with RPI < 2
Iron deficiency anemia
Anemia of chronic disease
α Thalassemia
β Thalassemia
Sideroblastic anemia
Lead poisoning

5. Serum Ferritin

Ferritin is the chief iron - storage protein in the body. Serum ferritin measurement is helpful in the diagnosis of iron deficiency or excess, which correlate with total body iron stores. It is decreased in iron deficiency anemia. Normal levels are 15-400 ng/ml in males and 10-200 ng/dl in females. For ferritin levels in the range from 50 to 500 ng/mL, there appears to be a direct quantitative relationship between the ferritin concentration and iron stores as follows:

Iron stores (mg) \cong (8 to 10) x ferritin (ng/mL)

It is an acute phase reactant. Elevated or normal serum ferritin level can be seen in patients having iron deficiency with co-existent illness like liver disease, infection, inflammation and malignancy. The effect of inflammation is to elevate serum ferritin approximately three fold. So divide serum ferritin value by 3 and if the resulting value is 20 or less it might suggest concomitant iron deficiency in patients with other acute illness [9].

6. Serum iron

Serum iron level reflects Fe³⁺ bound to transferrin. Normal value is 56-150ug/dl and it is decreased in IDA, anemia due to infection and anemia of chronic disease. Serum iron level shows diurnal variation - higher values in the mid morning, low values in the mid afternoon and very low values near midnight.

7. Serum transferrin

Transferrin is the iron binding glycoprotein that determines the level of free iron in the body. Transferin transports circulating Fe³⁺ molecules, normally only about 13 of iron - binding sites are occupied. The remainder is called unsaturated iron binding capacity. S.Transferin levels are increased in IDA and decreased in iron overload states.

8. Total iron binding capacity

TIBC is an indirect measure of the circulating transferin. It is calculated as follows

TIBC = transferin (mg/L) x 0.025 .

The difference between TIBC and S.iron (ug/dl) indicate unsaturated iron-binding capacity (UIBC). TIBC normal value is 250 – 370ug/dl. It is increased in IDA.

9. S. Transferrin saturation

It is calculated as follows:

$$\text{Transferrin saturation} = (\text{S.iron}/\text{TIBC}) \times 100$$

Normal transferrin saturation is 25-50%. This figure represents the amount of iron - binding sites that are occupied. Iron deficiency status is usually associated with levels less than 18%.

10. Bone marrow iron

In iron deficiency, BM iron stores are absent. But S.ferritin measurement has largely supplanted bone marrow examination for determination of iron stores [10].

11. Soluble transferrin receptor

It is an indirect measure of erythropoiesis and is increased in patients with iron deficiency anemia. It is the cleaved extracellular portion of transferrin receptor 1 that is released into serum. It is unaffected by inflammatory states and can help to identify concomitant iron deficiency anemia in patients with anemia of chronic disease. Thus it is helpful in conditions where there is increased inflammation and serum ferritin measurement is unreliable.

12. Erythrocyte protoporphyrin levels

Its levels are increased in iron deficiency anemia. Erythrocyte protoporphyrin is a heme precursor and accumulates in the absence of adequate iron stores.

Differentiating features of iron deficiency anemia from other microcytic anemia are given in **Table 5**.

Table 5: Differentiating features of iron deficiency anemia from other microcytic anemia

	Fe deficiency anemia	Anemia of chronic Inflammation	Thalassemia	Sideroblastic anemia
Smear	Micro/Hypo	Normal Micro/Hypo	Micro Hypo an targeting	Variable
SI	<30	<50	N / η	N / η
TIBC	> 360	<300	Normal	Normal
%, saturation	<10	10-20	30-80	30-80
S.Ferritin	<15	30-20	50-300	50-300
Hb pattern	N	N	Abnormal	N
RDW	Increased		De	

Treatment of iron deficiency

The cause of anemia should be identified and corrected along with the administration of iron.

Empirical deworming appears justified in view of high prevalence of hook worm infection, which is the commonest cause of occult GI blood loss.

Oral iron therapy

It is the treatment of choice and the most economical and effective medication in the treatment of iron deficiency anaemia. Among the various iron salts, ferrous sulphate is most commonly used. The recommended daily dose for the treatment of iron deficiency in adults is about 150 to 200 mg/day of elemental iron. Prophylactic dose is 30 mg daily.

Common iron preparations are:

Ferrous fumarate - which contain 106 mg elemental iron/tablet

Ferrous sulfate - which contain 65 mg elemental iron/tablet

Ferrous gluconate - which contain 28 to 36 mg iron/tablet

Other oral iron preparations includes colloidal ferric hydroxide, ferrous succinate, ferrous aminoate etc.

There is no evidence that one iron preparation is more effective than another for the treatment of iron deficiency anaemia. The reported low incidence of side effects for some preparations can be explained by their low elemental iron content.

A single 325 mg ferrous sulfate tablet taken orally three times daily between meals provides 195 mg of elemental iron per day. This regimen should lead to a modest reticulocytosis beginning in approximately seven days and a rise in the haemoglobin concentration of approximately 2 g/dL over the ensuing three weeks.

There is no clear recommendation regarding the duration of treatment. Some stop treatment with iron when the haemoglobin level becomes normal, but some others prefer to treat for at least six months after the haemoglobin has normalized to replenish the iron stores in the body.

Iron is absorbed best from the duodenum and proximal jejunum. Therefore, enteric coated or sustained release capsules, which release iron further down, are less efficient sources of iron.

Iron salts should not be given with food because phosphates, phytates, and tannates in food bind with iron and impair its absorption. Iron should be given two hours before, or four hours after, ingestion of antacids.

Common side effects of oral iron therapy include nausea, constipation, epigastric discomfort and vomiting. Gastrointestinal tract symptoms are directly related to the amount of elemental iron ingested. Patients with persistent gastric intolerance to oral iron tablets may tolerate ferrous sulfate elixir, which provides 44 mg of elemental iron per 5 mL. Patients can titrate the dose up or down to the level at which the gastrointestinal symptoms become acceptable [11].

Recently there has been a thought that oral iron intake should be once a day on alternate days as compared to multiple daily doses. It is believed that iron intake causes an increase in serum hepcidin levels which block iron absorption on the next day and hence fractional absorption of iron is decreased [13].

Parenteral iron therapy

It is expensive and has greater morbidity than oral preparations of iron therapy. Indications for parenteral iron therapy are:

1. Unable to absorb oral iron
2. Increasing anaemia despite adequate doses of oral iron
3. Level of continued bleeding, exceeds the ability of the gastrointestinal tract to absorb iron
4. Unable to tolerate even modest doses of oral iron
5. Patients on dialysis
6. Cancer patients with anaemia receiving treatment with erythropoietin.

Dose of parenteral iron can be calculated as follows:

$$\text{Total iron deficit (mg)} = \text{BW [Kg]} \times (\text{Target Hb} - \text{Actual Hb}) [\text{g/dl}] \times (0.24) + 500 \text{ mg}$$

or

$$\text{Total iron deficit (mg)} = \text{BW [Kg]} \times (\text{Target Hb} - \text{Actual Hb}) [\text{g/dl}] \times (2.145)$$

The volume of iron injection can be calculated as follows:

$$\text{Volume of product required (mL)} = \text{BW} \times (14 - \text{Hgb}) \times (2.145) \div C$$

Where C is the concentration of iron preparation in mg/ml

Common Iron preparations are:

1. Iron dextran can be given either IM or IV
2. Ferric gluconate complex only approved for IV use
3. Iron sucrose only approved for IV use
4. Ferric carboxymaltose is a novel stable iron complex for IV use

Intravenous iron is commonly administered and Intramuscular iron is less preferred because of slow and occasionally incomplete mobilization of iron from intramuscular sites. Iron sucrose and sodium ferric gluconate (Ferrlecit) have greater bio-availability and a lower incidence of life-threatening anaphylaxis compared with iron dextran [12].

Blood transfusion

Blood transfusion is indicated only if the

1. Patient is symptomatic with extreme fatigue or dyspnoea on exertion

2. Patient has cardiac illness and Hb <8 g/dl even if asymptomatic
3. Patients with anemia undergoing emergency surgical intervention
4. Transfusion is recommended in pregnant women with hemoglobin levels of less than 6 g per dL because of potentially abnormal fetal oxygenation resulting in non-reassuring fetal heart tracings, low amniotic fluid volumes, fetal cerebral vasodilatation, and fetal death.

Each unit of packed cells with a volume of 300 mL contains approximately 200 mL of red cells and 200 mg of iron in the form of heme. Transfusion of one such unit to an adult will raise the hematocrit by roughly 3 to 4 percentage points (and the hemoglobin by about 1 gm/dl) unless there is continued bleeding.

Therapeutic trial of iron

A presumptive diagnosis of iron deficiency anemia is made in a patient with anemia, if there is a positive response to a trial of oral iron therapy, characterized by a modest reticulocytosis beginning about 5-7 days, followed by an increase in hemoglobin at a rate of about 2-4g/dl every 3 weeks until the hemoglobin concentration is normal. Hb increase by 0.25 - 0.4g/dl /day in the 1st 7-10 day followed by 0.1g/dl /day subsequently to reach level > 11g/dl in 3-4 wks. Usually IDA will be about half corrected in 3 wks and fully corrected by 8 weeks. In most patients with IDA who respond to iron supplementation, hemoglobin concentration usually returns to normal level by 2 months. But it may take up to 4 months for body iron stores to return to normal.

The limitation of this approach occurs if there is no response, or the response is incomplete. In this setting, we cannot differentiate among poor patient compliance, inability to absorb the iron preparation, an incorrect diagnosis, continued bleeding, or a coexisting condition such as the anemia of chronic disease or renal failure that blocks the full reticulocyte response [14]. The common causes for failure to respond to iron therapy are given in **Table 6**.

Table 6: Causes for failure to respond to therapeutic trial of iron

Causes for failure to respond to therapeutic trial of iron
<p>A. Coexisting disease interfering with marrow response</p> <ul style="list-style-type: none"> Infection Inflammatory disorder (e.g., rheumatoid arthritis) Concomitant malignancy Coexisting folic acid and/or vitamin B12 deficiency Bone marrow suppression from another cause
<p>B. Diagnosis is incorrect, possible correct diagnoses include</p> <ul style="list-style-type: none"> Thalassemia Lead poisoning Anemia of chronic disease (anemia of chronic inflammation) Copper deficiency (zinc toxicity) Myelodysplastic syndrome/refractory sideroblastic anemia
<p>C. Patient is not taking the medication regularly</p>
<p>D. Poor absorption of iron</p> <ul style="list-style-type: none"> Rapid intestinal transport bypasses area of maximum absorption Enteric coated product: coating is not dissolving Patient has malabsorption for iron (e.g., sprue, atrophic gastritis) Medication taken in association with an agent interfering with absorption (e.g., antacids)
<p>E. Continued blood loss or need in excess of iron dose ingested</p> <ul style="list-style-type: none"> Cause of blood loss treatable (e.g., bleeding peptic ulcer) Cause of blood loss not treatable (e.g., Osler Weber Rendu disease) Need cannot be met by oral iron preparation (e.g., renal failure responding to erythropoietin)

Refractory iron deficiency anemia (RIDA)

IDA is a common health issue resulting in microcytic blood picture. Even though most of them are due to decreased intake in comparison to iron requirement, some cases are now recognized where dietary intake is adequate but the deficiency occurs due to some defect in absorption of iron or mobilization of iron from stores. Two important causes are sideroblastic anemia and iron refractory iron deficiency anemia (IRIDA).

RIDA is defined as IDA persisting despite adequate oral iron intake for at least 3 months. It accounts for about 15% of all IDA.

Possible cause of refractory iron deficiency anemia

1. Inadequate / inappropriate iron intake or non-compliance
2. Obscure bleed
3. Disorders of iron malabsorption
4. Genetic mutation
5. Wrong diagnosis
6. Adult celiac disease
7. Autoimmune atrophic gastritis
8. Mutation of Tmprss6 gene
9. H. pylori infection [15]

Hersh et al identified celiac disease, autoimmune gastritis, H pylori infection, poor drug compliance, diet rich in tannates like tea, medicines that rise gastric pH like antacids as a cause of RIDA [16]. Annibale et al could establish causes in 85% cases with RIDA, 37% were related to bleeding and rest due to iron malabsorption [17].

Obscure GI bleed

In patients with bleeding from gastrointestinal tract, where the cause cannot be found out after extensive investigations including upper endoscopy, colonoscopy, and radiologic evaluation of the small bowel is called Obscure GI bleed. Obscure bleeding is subdivided into overt or occult, depending upon the presence or absence of clinically evident bleeding. Patients with occult bleeding presents with a positive fecal occult blood test (FOBT) result and iron-deficiency anemia (IDA), in the absence of any evidence of visible blood loss [16]. It could be due to lesions that are overlooked in esophagus, stomach or colon. The small intestine accounts for majority of potential site of bleed in patients with negative examination of colon and upper GIT. Capsule endoscopy may be helpful in identifying small bowel pathologies like vascular ectasia, ulcers and mass lesions.

A complete GI evaluation is obligatory in all adult males and post menopausal females with unexplained IDA. All subjects with moderate to severe iron deficiency anemia not responding to oral iron needs evaluation for occult blood loss [17].

Iron**malabsorption**

Diseases which can lead to iron malabsorption include celiac disease, autoimmune gastritis and H. Pylori infection. Diagnosis can be made by non invasive tests like anti endomysial antibodies, gastric and parietal cell antibodies and urease breath test.

Four serologic studies have been described to aid in the diagnosis of celiac disease:

1. IgA endomysial antibody (IgA EMA)
2. IgA tissue transglutaminase antibody (IgA tTG)
3. IgA antigliadin antibody (IgA AGA)
4. IgG antigliadin antibody (IgG AGA).

Serum IgA endomysial and tissue transglutaminase antibody testing have the highest diagnostic accuracy.

Urea breath testing: Urea breath testing (U.B.T) is based upon the hydrolysis of urea by H. pylori to produce CO₂ and ammonia. A labeled carbon isotope is given by mouth; H. pylori liberate tagged CO₂, which can be detected in breath samples. It can be performed in 15 to 20 minutes. The sensitivity and specificity of UBT is approximately 88 to 95 and 95 to 100 percent, respectively [18].

Possible mechanism of IDA secondary to H.pylori infection include occult GI bleed (due to hemorrhagic gastritis, peptic ulcer disease and gastric adenocarcinoma), competition for dietary iron by the bacteria, decrease in gastric acidity and impaired absorption.

Another group of microcytic anemia is atypical inherited microcytic anemia which is due to (i) defects of intestinal iron absorption (ii) impaired erythroblast iron uptake due to disorders of the transferrin receptor cycle (iii) defects of mitochondrial iron utilization for haem or iron sulphur cluster synthesis and (iv) defects of iron recycling [19].

Mutation of TMPRSS6 gene

It is a rare cause of iron refractory iron deficiency anemia (IRIDA). The transmembrane protease serine 6 (TMPRSS6) gene is located on chromosome 22 and encodes matriptase-2, a transmembrane type II serine protease, mainly expressed by hepatocytes that suppresses hepcidin secretion by cleaving membrane-bound hemojuvelin (mHJV), a surface co-receptor in BMP-6-SMAD signaling pathway. Hepcidin blocks the exportation of iron from hepatocytes, macrophages and from the GIT, by binding to ferroportin (FP 1) resulting its degradation. TMPRSS6 is essential for normal systemic iron homeostasis in humans [20]. About 40 different mutations have been described in this gene. A genetic mutation as a cause of refractory iron deficiency anemia can be suspected when there is a relatively early onset of iron deficiency, history of family members or siblings with iron deficiency, very low MCV and MCH compared to the degree of anemia, absence of organomegaly and other stigmata of iron deficiency. Treatment includes oral iron and vitamin C for six to eight weeks. Consider intravenous iron therapy if not responding.

Iron deficiency anemia during pregnancy

Iron deficiency anemia in pregnancy is an important public health issue in both developed and developing countries. The chance of development of iron deficiency during pregnancy depends upon the pre pregnancy status of the female and the amount of iron absorbed during pregnancy. The iron requirement increases during pregnancy but it is not uniform. In the first trimester the iron

requirement actually decreases and it is increased to between 4 and 6 milligram per day during second and third trimester of pregnancy. In the last 6 to 8 weeks it increases as much as 10 milligram per day.

The increased iron requirement during pregnancy is to meet the increased demand due to increase in the fetal blood volume, requirement of growing fetus and placenta and the blood loss during delivery.

Iron deficiency anemia is very common in pregnancy and postpartum period which can lead to serious maternal and fetal complications. Measuring serum ferritin is the most sensitive and specific test to diagnose IDA, provided there is no associated inflammation. When serum ferritin and Hb is low a diagnosis of iron deficiency anemia can be made. If serum ferritin is normal inflammatory pathologies has to be ruled out. Also when serum ferritin is normal and MCV is low it can be thalassemia, which can be confirmed with further evaluation.

Most of the pregnant women are asymptomatic and symptoms develop when the severity increases. Most commonly they present as fatigue, low physical capacity, leg cramps, palpitation, breathlessness, mucosal paleness and angular stomatitis. Various maternal and fetal problems due to anemia during pregnancy is given in **Table 7**.

Table 7: Maternal and fetal problems due to anemia during pregnancy

Maternal problems	Fetal problems
Risk of a decrease in maternal blood reserves during birth	Premature birth
Need for transfusion in cases of heavy blood loss	Intrauterine developmental retardation
Cardiac stress	Placental problems
Symptoms of anemia	Decrease in newborn iron storage
Prolonged hospital stay	
Decreased maternal breast milk production	
Maternal depletion of iron stores during and after the postpartum period	

Prophylactic oral iron is given to all pregnant women even with normal Hemoglobin levels to meet the increased demand during pregnancy. Oral iron preparations are preferred for IDA, but in certain circumstances parenteral iron is indicated like severe anemia associated risk of fetus and if emergency treatment is required, in non-compliance or intolerance to oral iron and inadequate response to oral iron. Oral preparation can be used throughout pregnancy but intravenous iron is recommended during second and third trimesters.

Conclusion

Iron deficiency anemia is a common health issue that has to be differentiated from other anemia like anemia of chronic disease, sideroblastic anemia etc which have similar blood picture. IDA not responding to iron therapy is a challenging clinical situation where further evaluation is required.

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