Iron Deficiency Anemia in Children — Diagnosis and Treatment

Iron-deficiency anemia (IAD) in children is the most common among other types of anemia. It is commonly presented in children aged between 6 - 36 months than at other age groups, according to a report. Pediatric iron-deficiency anemia might involve multiple etiological factors including low birth weight, nutritional deficiency, and gastrointestinal blood loss. Diagnosis is made on the basis of demonstration of microcytic hypochromic anemia, reduced serum iron, anisocytosis, and poikilocytosis.

Definition

Anemia refers to a state whereby the blood hemoglobin (Hb) is below the reference range for the age and sex of the individual according to WHO’s (World Health Organization) lower limits for hemoglobin. Iron-deficiency Anemia (IDA) develops when there is an insufficient amount of iron for hemoglobin synthesis. Despite medical advancements in diagnosing and managing iron-deficiency at a relatively low cost, pediatric iron-deficiency anemia still remained the most common anemia and nutritional disorder throughout the globe but more significantly in developing countries.
According to World Health Organization (WHO):

- In children aged between 6—59 months, the lower limit for Hb is 11 g/dL
- In children aged between 5—11 years, the lower limit for Hb is 11.5 g/dL
- In children aged between 12—14 years, the lower limit for Hb is 12 g/dL

In infants younger than 6 months, physiological anemia must be kept in mind while making a diagnosis; however, Hemoglobin is not expected to be lower than 9 g/dL in physiological anemia.

Epidemiology of Iron Deficiency Anemia

According to a report published in 2009, around 1.6 billion people throughout the world are anemic, out of which several million represents iron-deficiency anemia. The prevalence of anemia is unevenly distributed around the globe; it is more prevalent in developing countries as compared to developed countries.

In developing countries, according to World Health Organization (WHO), 30 % of the children up to 4 years of age have iron-deficiency anemia and 48 % of the children aged between 5—14 years are anemic. In developed countries, 30—40 % of the anemic cases are of iron-deficiency anemia in pre-school children. In the United States, there are approximately 5 million people having iron-deficiency anemia.

Etiology of Iron Deficiency Anemia

Pediatric iron-deficiency anemia might involve multiple etiological factors, including low birth weight, nutritional deficiency, and gastrointestinal blood loss. Moreover, these factors vary according to age.

In infants younger than 6 months

As there are many iron stores in the prenatal period to provide for body needs up to 6 months, in infants younger than 6 months, IDA develops due to low birth weight and perinatal blood loss/hemorrhage.

In children aged between 6—24 months

After six months, due to rapid growth, sufficient iron is needed to meet the need of the body. In this period, nutritional iron deficiency is common. In addition, cow’s milk leads to gastrointestinal losses of iron and therefore is another factor.

In children older than 24 months (2 years)

A major etiological factor in children older than 24 months leading to iron-deficiency anemia is chronic blood loss (ancylostomiasis). This might be due to a peptic ulcer, Meckel’s diverticulum or inflammatory bowel disease.

Classification of Iron Deficiency Anemia

Iron-deficiency anemia

Stage 1: Prelatent stage (Depletion of iron stores):
This stage is marked by the depletion or absence of iron stores alongside normal serum iron concentration, hemoglobin, and hematocrit. There is reduced or absent bone marrow iron stores and reduced serum ferritin level.

**Stage 2: Latent stage (Depletion of transport iron):**

The characteristic feature of this stage is that there is reduced serum iron and transferrin saturation. In addition, there are reduced iron stores while hemoglobin and hematocrit values are normal.

**Stage 3: Marked Iron-Deficiency Anemia:**

This stage is characterized by frank features of iron-deficiency anemia in which there are depleted iron stores and serum iron, and transferrin saturation, as well as a reduced level of hemoglobin and hematocrit and manifesting associated symptoms.

However, all these stages are overlapping and there is no clear cut boundary in the evaluation of them. Moreover, the change in variables presented with the passage of time with iron deficiency; therefore, one should be meticulous while evaluating these.

**Pathophysiology of Iron Deficiency Anemia**

The only source of iron in the prenatal period is through the placenta. In the last stage of pregnancy, the aggregate sum of iron in the fetus is 75 mg/kg. The level of iron in breast milk is at the most elevated level in the first month and the absorption of iron from breast milk is significantly high around 50%. Although the absorption of iron from breast milk is high, it is still inadequate for growth rate; therefore, the iron from the iron stores is extracted to meet the needs of a body.

In infants with normal weight, the iron stores are sufficient for 6 months. However, the iron stores of infants with low birth weight or blood loss depleted before six months. This eventually leads to iron-deficiency anemia. In addition, solid foods lacking an adequate amount of iron and consumption of cow’s milk further worsen the condition because they disrupt the absorption of iron from intestinal mucosa.

In older children, iron-deficiency anemia usually underlies some chronic causes. These might include gastrointestinal disruption, such as peptic ulcer, polyp or inflammatory bowel disease.

**Clinical Features of Iron Deficiency Anemia**

Mild iron-deficiency in children usually remains asymptomatic. Symptoms and signs vary according to severity. In general, in severe cases, children presented with common symptoms of anemia and specific signs of iron-deficiency anemia.

**Symptoms**

Symptoms appear in severe cases of iron-deficiency anemia. These might underlie the involvement of skin, musculoskeletal system, cardiovascular system, nervous system and gastrointestinal system.

**Note:** Pallor, fatigue, irritability, anorexia, diarrhea, and weakness are the common symptoms of iron deficiency anemia in children. Unhappiness, a lack of co-operation and shorter attention span demonstrating low infant
behavior record (IBR) and lower mental development index (MDI). However, both IBR and MDI go back to normal once the iron deficiency is corrected.

**Signs**

**Musculoskeletal disorder and weight gain**
- Effort capacity is decreased
- Exercise limitation
- Fatty children are seen in the wake of cow’s milk consumption that leads to weight gain and poor muscle tone

**Cardiovascular signs**
- Increased cardiac output
  - Tachycardia
  - Cardiomegaly
  - Congestive Cardiac Failure
  - Hemic murmur (soft systolic, intense near base and changing with position)

**Immune system dysfunction**
- Decreased resistance against infections
  - T lymphocyte and polymorphonuclear leukocyte dysfunction

**Gastrointestinal system signs**
- Splenomegaly
- Loss of appetite
- Dysphagia
- Pica

**Neurological signs**
- Iron-deficiency decreases expression of dopamine receptors and leads to dysfunctional neurotransmitters
  - Papilledema
  - Sleep disturbance
  - Attention deficit
  - Behavioral disorder

**Investigations of Iron Deficiency Anemia**

**Diagnosis of iron-deficiency anemia is made on the basis of demonstration of microcytic hypochromic anemia, reduced body/serum iron, anisocytosis, and poikilocytosis.** Hemoglobin in severe cases of IDA might be as low as 3—4 g/dL. The following investigations are significant in making.

**The following investigations are significant in making a diagnosis:**
**Complete Blood Count (CBC)**

- Hemoglobin and Hematocrit would be low according to age
  - RDW (Red cell Distribution Width): 14
  - RBC: Low
- MCV (mean corpuscular volume): Low according to age
- MCHC (mean corpuscular hemoglobin concentration): 30%
  - Thrombocytosis
  - Rarely Thrombocytopenia and leucopenia

**Peripheral Smear**

- Microcytosis
- Hypochromia
- Anisochromia
- Anisocytosis
- Pencil cells

**Iron Studies**

- Serum iron: < 30 mcg/dL (diagnostic)
- Serum ferritin: < 12 ng/mL
- TIBC (total iron binding capacity): > 480 mcg/dL
- Transferrin saturation (Iron/TBC x 100): < 16%

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### Differential Diagnosis of Iron Deficiency Anemia

Differential diagnosis of iron-deficiency anemia in children is needed to be made with other similar blood disorders and anemia showing a hypochromic microcytic picture. These include beta-thalassemia minor, anemia of lead poisoning and anemia accompanying chronic inflammations or infections.

#### Beta-Thalassemia minor

B-thalassemia minor has typically an elevated number of RBCs as compared to IDA. In addition, the index of MCV by the red cell count is under 13.

#### Anemia of lead poisoning

IDA differentiated from anemia of lead poisoning in lacking basophilic stippling of the red cells which is a characteristic feature in anemia of lead poisoning.

#### Anemia of chronic inflammation or infection

Anemia of chronic inflammation has low serum level, while iron-binding capacity is normal and serum ferritin level is normal or raised. On the other hand, anemia accompanying infections must be excluded by screening tests for infections.

### Management of Iron Deficiency Anemia

**Pediatric iron-deficiency anemia is almost always managed medically by iron replacing therapy through oral or parenteral routes.** Rarely, in life threatening cases, a blood transfusion is considered.

**Oral iron therapy**

The recommended dose of elemental iron is 3—6 mg/kg/day and it is administered in three divided doses.

**Common and easily available iron salts are:**
- **Ferrous sulfate**, containing 20% elemental iron and available as 200 mg tablets.
- **Ferrous gluconate**, containing 12% elemental iron and available in 250 mg dose.

However, **potential side effects could occur in the form of nausea, vomiting, diarrhea, constipation and epigastric pain**. Even the recommended dose can cause side effects in which case readjustment of the dose becomes essential.

**Note:** Optimal absorption of iron takes place when administered in between meals. Simultaneous administration of vitamin C has shown to increase its absorption. On the contrary, diets rich in phytates and phosphates, such as cereals and milk respectively decreases iron absorption from the gut.

**Duration of iron therapy usually ranges from 3 to 6 months.** Hemoglobin levels are expected to rise around 0.4 g/dL/day with.

**Factors involving in poor response to oral iron include:**
- Poor tolerance
- Insufficient time span of treatment
- Malabsorption
- Persistent bleeding
- Inadequate iron absorption due to concurrent phytates and phosphates
- Inadequate dose (< 3—6 mg/kg/day)
- Poor compliance

**Parenteral iron therapy**

**Parenteral route of administering iron is indicative in the following conditions:**
- Failure of oral iron administration in managing iron-deficiency anemia
- Incapability or intolerance to oral iron therapy
- Incompetence of patient with oral medication

However, some pediatricians prefer to start with parenteral iron administration. They might administer a few injections initially and put the patient on oral medication to prevent initial difficulties in treatment.

**Parenteral iron can be administered IM (intramuscularly) or IV (intravenously).**

**Note:** The following formula is significant in the calculation of total dose: Iron required = 2.5 × body weight (kg) × Hb deficit. Here, Hb deficit is the difference between the present and required values of Hb. Moreover, an additional 20—30% of the calculated dose is administered to refill the iron stores.

**Intramuscular (IM) Administration**

Iron dextran complex (Imferon) or iron-sorbitol (Jectofer) are considered in this regard. **A daily dose of intramuscular injection should not exceed 5 mg/kg i.e., 50 mg in infants and 100 mg in adolescents.**

The **recommended daily dose (upper limit of IM injection) in infants is 5 mg/kg i.e., 50 mg. In adolescents, it is 100 mg.** A suitable site for this is the upper and outer quadrant of the thigh. In addition, to prevent a repeated injection at the previous prick, it is recommended to administer in a Z fashion.
Side effects:
- Fever
- Pain
- Arthralgia
- Lymphadenopathy

**Intravenous (IV) Administration**

Iron-dextran complex (Imferon) or iron-sucrose injection (Venofer) is considered to administer by this route. Initially, a test dose is given to assess the sensitivity. After that, the total dose infusion (TDI) is given accordingly.

**Blood transfusion**

A blood transfusion is considered in critical and life threatening conditions of severe anemia whereby a rapid rise in hemoglobin is required as the only option.

**References**


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