

INTRODUCTION

Anaemia is one of the most frequent observed nutritional deficiency diseases in world, affecting around 800 million children and women, with pregnant women at particular risk. The World Health Organization (WHO) 2011 data shows that anemia in pregnancy is a significant problem throughout the world with a prevalence of 38.2% (32 million) for pregnant women. Anaemia in pregnancy is one of the major causes of maternal complications, morbidity and offspring mortality in almost all the developing countries of the world. In India, National Family Health Survey -3 in 2005-2006 shows that 55% of women are anaemic; more prevalent in breastfeeding and pregnant (59%) women.

ANAEMIA IN PREGNANCY**Pathophysiology**

Nutritional Iron Deficiency (ID), accounting for more than half the cases is the commonest cause of anaemia during pregnancy. A 55 kg pregnant woman is estimated to need approximately an additional 1200 mg of iron over the whole pregnancy. The daily iron requirement increases from approximately 0.8 mg in the first trimester to 4–5 mg during the 2nd trimester and > 6 mg in the 3rd trimester.

Types of Anaemia

Several types of anaemia developed during pregnancy are:

- A. Physiological anaemia of pregnancy: During pregnancy there is a disproportionate increase in plasma volume, RBC volume and haemoglobin mass as plasma volume increases more than RBC mass hemodilution occurs.
- B. Nutritional deficiency:
 1. Iron deficiency Anemia (IDA) - IDA can occur as a result of low dietary intake of iron, less absorption from diet rich in phytates and phenolic compounds, deficient iron stores from adolescence to postpartum stage due to multiple pregnancies,

increased physiological demands, chronic blood loss due to inflammation and infections like malaria, HIV, Tuberculosis and worm infestation.

2. Vitamin B12 & folic acid deficiency - Vitamin B12 and folate deficiency can affect DNA replication leading to derangement of red cell maturation with production of abnormal precursors known as megaloblasts. Combined deficiency of iron and Vitamin B12 or folic acid produces dimorphic picture on peripheral smear.
3. Protein deficiency - Caused due to malnutrition and less dietary protein intake
- C. Hereditary - Hemoglobinopathies of genetic origin such as Sickle cell disease and Thalassemia; Hereditary hemolytic anaemias (RBC membrane defects); Microangiopathic haemolytic anemia (HELLP syndrome.)
- D. Aplastic anaemia – Bone marrow hypoplasia or aplasia due to radiation, drugs or idiopathic.

Clinical features of iron deficiency anaemia

The clinical features depend on the degree of anaemia and majority of patients with mild to moderate anaemia may be symptomatic with the entity being an accidental finding during examination. The categories of anaemia in pregnancy are listed in Table 1.

Symptoms – Lassitude and a feeling of exhaustion or weakness, indigestion and loss of appetite. Other features are palpitation, dyspnoea, giddiness, pedal oedema and rarely, generalized anasarca and even cardiac failure in severe cases.

Signs- Pallor of varying degree, glossitis, stomatitis, oedema of the legs due to hypoproteinaemia. A soft systolic murmur in the mitral area due to hyper dynamic circulation.

Diagnosis

The underlying reason for the reduced Hb production should be sought by taking a detailed medical history, proper clinical assessment or by means of further investigations.

TREATMENT OF IRON DEFICIENCY ANAEMIA IN PREGNANCY**Prophylactic**

1. Avoidance of frequent child births, teenage pregnancy and high parity.

Table 1: WHO categories of anaemia in pregnancy

Category	Hb level (gm/dl)
Non -anaemia	11 or higher
Mild	10-10.9
Moderate	7- 10
Severe	< 7

Table 2: Diagnostic workup for diagnosis of anaemia

Lab. Parameters	Comment
Haemoglobin & Erythrocyte indices	A typical iron deficiency anaemia shows following: Hb - < 10gm%, RBC - < 4 million/cmm ³ , PCV - < 30%, MCV < 75fl, MCH < 25 pg.
Peripheral Smear	In typical iron deficiency anaemia, Peripheral smear shows, anisocytosis, poikilocytosis, microcytic, hypochromic picture. If the MCV is >100 fl, and the peripheral blood picture suggests the possibility of folate or Vitamin B12 deficiency, appropriate investigations should be carried out to establish the diagnosis
Serum ferritin	Levels of < 15 µg/L confirm the presence of iron deficiency regardless of the Hb level.
Serum iron, transferrin saturation(TSAT), transferrin receptors(sTfR)	Iron deficiency – serum iron < 60mg/dl, TSAT <15%, sTfR > 8.5mg/L
Bone marrow examination	ID - Absence of hemosiderin granules; helps to rule out kala azar and aplastic anaemia
Stool & Urine examination	To rule out worm infestation and schistosomiasis

2. A balanced diet, rich in iron and protein should be prescribed. The foods rich in iron include liver, meat, egg, green vegetables, green peas, figs, beans, jaggery, whole wheat etc. Iron utensils should preferably be used for cooking.
3. Iron Supplementation: Government of India, Ministry of health and family welfare recommends 100 mg of elemental iron and 500 µg of folic acid daily for 100 days during pregnancy, followed by same dose for 100 days in the post-partum period.
4. Adequate treatment to eradicate hookworm infestation, malaria, bleeding piles and urinary tract infection. All infections and chronic inflammatory conditions should ideally be controlled prior to pregnancy.

Curative

An accurate diagnosis (Table 2) of the cause of anaemia and type of anaemia should be made before starting treatment. At present the main treatment options for

anaemia include oral iron, parenteral iron, erythropoiesis stimulating agents and blood transfusion.

Oral iron therapy

For mild to moderate anaemia, oral iron therapy is gold standard treatment. For therapeutic iron supplementation various iron preparations are available – iron salts e.g. Ferrous sulphate, ferrous ascorbate, ferrous gluconate, ferrous fumarate, ferric ammonium citrate; Iron complexes e.g. Iron dextran complex, Iron polymaltose complex. Depending upon anaemia severity international guidelines recommend elemental ferrous iron 120 mg daily or 100-200 mg daily for IDA treatment. Haematologically, there is reticulocyte response in 5-10 days with a rise in Hb concentration from 0.3 gm to 1.0 gm per week and haematocrit subsequently. If clinical or haematological improvement does not occur within 3-4 weeks, diagnostic re-evaluation is needed.

Oral therapy, however, can suffer from compliance issues (up to 10% of patients). About a third of women also suffer with significant gastrointestinal side effects like epigastric pain, nausea, vomiting, diarrhoea or constipation which make some women intolerant of oral iron. Depending on the degree of anaemia and iron deficit, especially in the presence of risk factors for IDA; like inflammatory bowel disease, multiple pregnancy, a short inter-pregnancy interval, teenage status, grand-multiparity oral iron may not successfully correct anaemia before birth of the baby.

Parenteral Iron Therapy

The indications for the parenteral administration of iron Include:

- Insufficient or no response to oral iron
- Severe anemia
- Insufficient absorption of oral iron due to intestinal disease
- Intolerance of oral iron
- Poor compliance
- Combination with rhEPO (for the prevention of functional iron deficiency)

Deficit can be calculated using Ganzoni's formula-

Body weight (target Hb – Actual Hb gm/dl) 2.4 + 500 (for refilling body stores)

Various parenteral iron formulations are available for correcting iron deficiency e.g. Iron dextran (low molecular weight), iron gluconate, iron sucrose, ferric Carboxymaltose, iron isomaltoside, ferumoxytol. Iron dextran is associated with risk of anaphylactic reactions, so a test dose is needed prior to infusion. Iron sucrose causes rapid rise in Hb levels and replenish iron stores faster. The introduction of newer intravenous formulations like Ferric Carboxymaltose, iron isomaltoside, Ferumoxytol offer administration of higher doses in single administration making it as an effective, rapid and safe treatment for IDA avoiding the use of blood transfusion. However a

careful risk/benefit evaluation is required before use in pregnancy.

Blood transfusion is required in patients with severe anaemia after 36 weeks, associated infection, refractory anaemia, to correct anaemia due to blood loss and to combat post-partum haemorrhage.

Megaloblastic Anaemia

It occurs due to deficiency of either Vitamin B₁₂ or folate or both. Vitamin B₁₂ deficiency is rare in pregnancy. Folate deficiency can occur as a result of inadequate intake, diminished absorption or increased demands. A prophylactic dose of 400 µg is recommended for all women, in the preconception period and throughout pregnancy. Treatment of established folic acid deficiency by giving 5 mg oral folate per day which should be continued for at least 4 weeks in puerperium. When response to folic acid is not adequate supplementary intramuscular vitamin B₁₂ 100 µg daily or on alternate days may be added.

CONCLUSION

Iron deficiency anaemia is a major public health problem, especially in countries like India, and is associated with increased maternal and perinatal morbidity and mortality. Majority of women do not have adequate stores of iron to meet the increased demands during pregnancy. Strategies like nutritional education, iron & folic acid supplements and ensuring maximum compliance, deworming, treatment of chronic diseases and universal antenatal care to pregnant women will help in overcoming this serious issue.

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