Clinical Choices and Use of Appropriate Iron Therapy

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Definition of Anaemia:
Anaemia is defined as reduction in circulating haemoglobin below 11gm percent, however in India and most of the other developing countries 10 gms % is considered as critical level.

Degree's of Anaemia:
- mild degree (8-10 gm%),
- moderate (6-8 gms%)
- severe (4-6gm %)
- very severe (<4gm %)

Incidence:
Anaemia in pregnancy is present in very high percentage of pregnant women. According to WHO, the prevalence of Anaemia in pregnancy in south East Asia is around 56%. In India incidence of anaemia pregnancy has been noted as high as 40-80%. Iron deficiency anemia is the most common form of anemia. second highest cause of maternal mortality and perinatal morbidity.

It Causes
In Antenatal period: Poor weight gain, preterm labour, PIH, placenta previa, accidental haemorrhage, eclampsia, premature rupture of membrane (PROM).

In Intraanatal period: Dysfunctional labour, intranatal hemorrhage, shock, anaesthesia risk, cardiac failure.

In Post partum period: PPH (primary & secondary), hemorrhagic shock, infection, sepsis, subinvolution, embolism.

Physiological anaemia: Pregnancy causes a state of hydramic plethora → disproportionate increase of plasma volume → apparent reduction of RBC, haemoglobin and haematocrit value → normochromic and normocytic

Anaemia due to: Dysfunctional uterine bleeding. Excessive Menstrual Blood Flow (> 80 ml)

Acquired- Nutritional
a) Iron deficiency anaemia (60%)
b) Macrocytic anaemia (10%) due to deficiency of folic acid and vitamin B12
c) Dimorphic and protein deficiency anaemia (30%) both due to deficiency of iron and folic acid and/or vitamin B12
d) Protein deficiency due to extreme malnutrition
Risk factors
- Sociodemographic factors (age, level of formal education, marital status, areas and cities of residence)
- Obstetrical factors (gravidity, parity, history of previous preterm or SGA deliveries, plurality of pregnancy multiple or singleton)
- Behavioral factors (smoking or tobacco usage, alcohol usage, utilization of prenatal care services)
- Medical conditions (diabetes, renal or cardio-respiratory diseases, chronic hypertension)

Clinical presentation:
- Women with mild anaemia may be asymptomatic or have
- Weakness, fatigue, loss of appetite, weight loss, digestive upset etc
- Headaches.

As the anemia gets worse, symptoms may include:
Angular stomatitis, glossitis, koilonychias, platynychia, pallor, dyspnoea, palpitation, odema.
Obsterical complications: LBW, SGA, IUGR, Preterm labour, PROM, Infections (URTI & UTI).

Investigations for diagnosis of Iron Deficiency anaemia:
- Full clinical history and physical examination including Obstetrical.
- Hematocrit and hemoglobin
- RBC & PCV
- Peripheral smear (microcytic hypochromic RBC, Anisopoikilocytosis)
- Reticulocyte count: window to bone marrow
- When RBC production is less
- in hemolysis
- Prognostic value after iron therapy
- S.Ferritin: Imp. for Iron store
- TIBC
- Urine & stool examination
- Bone marrow
- Serum iron levels
- Urea and electrolytes,
- Liver function tests
- Ultrasound
- Transferrin Receptor study & MRI

Treatment:
Taking supplements and eating iron-rich foods are important parts of treating iron deficiency anaemia. Iron-rich foods include:

- Chicken
- Eggs (yolk)
- Meats (liver is the highest source)
- Soybeans
- Whole-grain bread
- Greens
- Dried lentils, peas, and beans
- Fish
- Peanut butter
- Jaggery
- Grams
- Grains

Other sources include: Oatmeal, raisins, prunes, and apricot, spinach, karela, and other greens

Oral Iron therapy clinical choice's and use:
are as follows:
- Safe, inexpensive and effective way to administer iron.
- Oral route should be the route of choice in routine cases.
- If all pregnant women receive routine iron and folic acid, it is possible to prevent nutritional anaemia
in pregnant women.
• It is suggested that 120 mg of elemental iron and 1 mg folic acid are the optimum daily doses. The higher dose in Indian women is required as they start pregnancy with low or absent iron stores due to poor nutrition and frequent infection like hookworm and malaria.

How to select the iron salt:
• Ferrous sulphate is least expensive

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<th>Table - I</th>
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<td><strong>Types of Oral Iron</strong></td>
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<tr>
<td>Ferrous Sulphate</td>
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<tr>
<td>Ferrous Fumerate</td>
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<tr>
<td>Ferrous Lactate</td>
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<tr>
<td>Ferrous Carbonate</td>
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<tr>
<td>Carbonyl Iron</td>
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<tr>
<td>Iron Polymaltose / Polysucrose</td>
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<tr>
<td>Ferrous Ascorbate</td>
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**Ferrous ascorbate is a better clinical choice in oral iron therapy** than other salts. It is available as 100 mg elemental iron per tablet and is an effective, safe & well-tolerated therapy. It reduces Fe+3 to Fe+2, promotes iron absorption, reverses inhibitory effect of calcium, phytates & tea. Once or twice a day therapy, better absorbed on empty stomach (avoid antacids).

What makes it different....?

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<tbody>
<tr>
<td>Stable Complex of Iron and Ascorbate ↓</td>
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<td>No dissociation on entering GI Tract due to the stable chelate of Iron with ascorbate. ↓</td>
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<tr>
<td>No action of food inhibitors as the complex does not dissociate. ↓</td>
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<tr>
<td>No oxidation to ferric forms as Ascorbate maintains the Iron in Ferrous form. ↓</td>
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<td>Much higher absorption!!</td>
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**Side effects of Oral Iron Therapy:**
Heart burns, nausea, upper GI disturbances, constipation, diarrhea, teeth stains.

Iron salt should be selected based on compliance of the patient, tolerance, side effects, clinical situation of the patient and availability of a particular salt. Oral iron must be continued for 3-6 months after haemoglobin has come to normal levels. Addition of vitamin C in medicine or in the diet enhances iron absorption. If the predictable rise in haemoglobin does not occur after oral iron therapy, one must find out the possible reasons.

**Parenteral Iron Therapy Clinical Choice's and Use:**
are as follows
1. Cannot tolerate side effects of oral iron
2. Patient does not comply
3. Patient near term

**Iron Dextran** is a colloidal solution of ferric oxyhydroxide complexed with polymerized dextran. Advantages of iron dextran is the ability to infuse the patient's total iron requirement (Total dose infusion).

**IM route**: 50 mg/ml (2 ml.amp.), Z technique on upper and outer quadrant of buttocks
- Painful, staining of skin.
- Fever, Joint pain, Lymphadenopathy, sweating, dyspnoea, palpitations as S/E

**IV route**: TDI in 500 ml. of saline maximum upto 2500 mg.
- Can be given as bolus slowly

**Response**: Rise of 0.15 gm % per day

A 25-mg test dose should be given to all new patients

Total dose of infusion of iron is calculated by various formula's

Patients should be monitored for adverse effects for 1 hr after a test dose

The rate of infusion should not exceed 50 mg/min. Iron dextran is the only parenteral iron product that can administered by the intramuscular route.

**TDI reaction:**
Anaphylaxis, Immediate vascular collapse, tachycardia, dyspnoea, cyanosis, vomiting, pyrexia, etc.

**Iron Sucrose** is an iron hydroxide sucrose complex in water. It's US FDA approved (November 2000) and India FDA approved in 2005. Intravenous route should be reserved for those who do not wish to have frequent intramuscular injections. Iron sucrose is administered by intravenous injection or infusion. No test dose is required.

- The recommended schedule is to administer 100 mg intravenously in 5 min. , 1-3 times weekly until 1,000 mg has been administered.
- Administration based on total iron deficit:

  *Pregnancy Anaemia*: \[ TID = BW \times (Target \: Hb - Actual \: Hb) \times 2.4 + 500 \] Stores need to be “refilled”
  *Post-partum Anaemia*: \[ TID = BW \times (Target \: Hb - Actual \: Hb) \times 2.4 \]

**Contraindication of parenteral iron therapy**: Nephritis, cardio respiratory disease, allergy.

**Conclusion:**
1) Iron dextran IM injectons : lower cost , but has more adverse side effects like dreadful anaphylactic reaction then Iron sucrose injections .multiple IM injections are cumbersome to the patient. Test dose is a necessary must.
2) For patients intolerant of iron dextran, Iron sucrose offer safe and effective alternatives, although their costs are slightly higher IV infusions totally replete iron stores with these products.
3) For ferric gluconate and iron sucrose, the package insert guidelines should be followed regarding total dose administered per infusion.
4) Transferrin saturation and serum ferritin measurements are useful in deciding on the frequency of repeat parenteral iron infusions except in treating functional iron deficiency.
5) Patients with functional iron deficiency receiving recombinant erythropoietin supplementation may require iron replacement despite normal iron indices. Adequate iron replacement can enhance the response to erythropoietin and decrease erythropoietin requirements.
6) Appropriate use of parenteral iron will eliminate the necessity for transfusing red blood cells in most patients with iron deficiency anaemia.