

Anemia in Pregnancy

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Abstract

Anaemia is defined as the decreased oxygen carrying capacity of the blood and it can present with myriad of symptoms like fatigue, weakness, shortness of breath, palpitations, and maybe asymptomatic till the patient gets into the severe category. It's a widespread disease and WHO estimates that nearly one-fourth of the world's population is affected by the very treatable disease. It is still the number one cause of maternal mortality globally especially in the low middle income countries. There are different varieties of anaemia of which iron deficiency anaemia is the most common cause globally. Anemia needs to be investigated thoroughly, and then treatment should be done according to the type and cause of anemia.

Keywords: Anemia; causes of anemia; management of iron deficiency anemia; oral iron therapy; Anemia Mukd Bharat; Poshan Abhiyan; megaloblastic anemia; vitamin B₁₂ deficiency.

PHYSIOLOGICAL CHANGES IN PREGNANCY

- ♦ There is a progressive increase in plasma volume throughout pregnancy.
- ♦ Majority (50%) increase happens by 34 weeks and correlates positively with the birthweight of the baby.
- ♦ The expansion in plasma volume is more than the increase in red blood cell (RBC) mass, there is a fall in the hemoglobin (Hb), packed cell volume (PCV) and red cell count.
- ♦ Despite hemodilution, there is no change in mean corpuscular volume (MCV) or mean corpuscular hemoglobin concentration (MCHC).
- ♦ The platelet count progressively falls during normal pregnancy, though it remains within normal limits. In 5–10%, the count will reach $100\text{--}150 \times 10^9/\text{L}$ by term, without any pathological process. So, thrombocytopenia in pregnancy is only when the platelet count is $<100 \times 10^9/\text{L}$.
- ♦ Pregnancy causes a two-to-threefold increase in the iron requirement (for hemoglobin synthesis for certain enzymes and for the fetus). Folate requirement increases by 10-to 20-fold and vitamin B₁₂ by twofold.
- ♦ Coagulation system changes during pregnancy produce a physiological hypercoagulable state.

Definition

- ♦ Anemia is defined as decrease in the oxygen-carrying capacity of the blood and refers to quantitative and qualitative decrease in RBC count and/or hemoglobin, in relation to age and sex.
- ♦ The World Health Organization (WHO) defines it as hemoglobin concentration of less than 11 g/dl or PCV less than 33%.

- ✦ The Centers for Disease Control and Prevention (CDC) defines anemia during pregnancy as:
 - Hb <11 g/dl in the first and third trimesters
 - Hb <10.5 g/dl in the second trimester
- ✦ Indian Council of Medical Research (ICMR) classification

Grading	Hemoglobin (g/dl)
Mild	10–10.9
Moderate	7–9.9
Severe	<7
Very severe	<4

Causes of Anemia

- ✦ Physiological anemia (usually mild)
- ✦ Nutritional anemia (most prevalent)
 - Iron deficiency (most common nutritional anemia)
 - Folic acid deficiency (next commonest cause)
 - Vitamin B₁₂ deficiency
 - Dimorphic anemia
- ✦ Anemia due to blood loss (hemorrhagic anemia)
 - Antepartum hemorrhage, bleeding piles, hookworm infestation.
- ✦ Hemolytic anemia
 - Sickle cell anemia, thalassemia and hereditary spherocytosis
 - Malaria
- ✦ Others
 - Aplastic anemia (bone marrow insufficiency)
 - Neoplasms
 - Chronic renal disease
 - Tuberculosis.

Causes of Iron Deficiency Anemia in Pregnancy

- ✦ Decreased intake of iron
 - Inadequate diet intake due to hyperemesis gravidarum
 - Faulty dietary habits like pica and poor dietary iron content
 - Inadequate iron supplementation
- ✦ Decreased absorption
 - Due to malabsorption syndrome and giardiasis
- ✦ Increased loss of iron
 - Hookworm infestation (0.2 ml blood loss/worm/day), *Necator americanus* (0.3 ml blood loss/worm/day), schistosomiasis, tapeworm
 - Bleeding piles, malaria, etc.
- ✦ Increased demand during pregnancy
 - Increase in total iron requirement during pregnancy
 - Multiple pregnancy: Loss of 650 mg of iron equivalent to 1300 ml of blood is lost
- ✦ Inadequate storage of iron
 - Repeated and frequent childbirths
 - Menorrhagia.

Investigations

Aim is to know the type, severity and cause of anemia.

- ✦ Complete blood count
 - Hemoglobin estimation—severity of anemia

- Hematocrit (PCV)
- Red cell indices—MCV, mean corpuscular hemoglobin (MCH) and MCHC (most sensitive red cell index) (Table 1.1)
- Total RBC count
- Total and differential WBC count (elevated in infections)
- Platelet count
- Reticulocyte count

Table 1.1: Hematological parameters in different types of anemias

	<i>Normal values in pregnancy</i>	<i>Iron deficiency anemia</i>	<i>Thalassemia</i>	<i>Macrocytic anemia</i>
Hb (g/dl)	12–16	<11	Decreased	<10 g/dl
RBC count (million/mm ³)	4–5	<3.2		
PCV (%)	32–36	<30		<33%
MCH (pg):Hb/RBC	26–31	<25	Reduced to very low levels	>33 pg
MCV (fl):PCV/RBC	75–95	<75	Reduced to very low levels	>96 fl
MCHC (%): Hb/PCV	30–35	<30	Reduced to very low levels	Within normal range
Serum iron (μg/dl)	60–120	<60		
Serum ferritin (μg/L)	15–200	<15		
TIBC (μg/dl)	300–400	>400		
Transferrin saturation (%)	20–50	<10		
Mentzer index (MCV/RBC)	13	>13	<13	

- ✦ Peripheral smear examination (Leishman stain is used)
 - Morphology of RBCs—type of anemia (Table 1.2)
 - Hemoparasites—malarial parasite and filaria
 - Abnormal cells—blast cells in leukemia and burr cells in renal failure
 - Evidence of hemolysis
 - Manual platelet count
- ✦ Blood grouping and typing

Table 1.2: Peripheral smear findings in various types of anemia

<i>Type of anemia</i>	<i>Peripheral smear findings</i>
Iron deficiency anemia	Microcytic hypochromic anemia (RBCs are smaller in size with central pallor), anisocytosis (variation in size) and poikilocytosis (variation in shape)
Folic acid and vitamin B ₁₂ deficiency	Macrocytic anemia (10–20% pancytopenia, cabot rings, macro-ovalocytes are diagnostic), hypersegmented neutrophils (5% neutrophils show five lobes or more or a single neutrophil with six or more lobes), nucleated RBCs, Howell Jolly bodies in RBCs
Dimorphic anemia	All three types of erythropoiesis can be seen—hypochromic, megaloblastic and normoblastic—the latter being most common
Hemolytic anemia	Schistocytes, target cells
Leukemia	Abnormal cells such as blast cells
Renal failure	Burr cells

- ✦ Serum and red cell folate levels (macrocytic anemia)
- ✦ Serum iron profile (to differentiate iron deficiency anemia from other microcytic anemias)
 - Serum iron ($<12 \mu\text{mol/L}$)
 - Serum ferritin (accurate assessment of stores $<12 \mu\text{g/L}$ – iron deficiency/ $<50 \mu\text{g/L}$ – requires iron supplementation) (Table 1.3)
 - Serum transferrin saturation ($<15\%$)
 - Total iron-binding capacity (increased)

Note: All decreased in iron deficiency anemia but MCV increased in macrocytic anemia

Table 1.3: Stages of iron deficiency anemia (IDA)

Stage	Finding	Inference
I	Decreased serum ferritin	Depleted iron stores
II	Decreased serum iron and increased TIBC	Deficient erythropoiesis
III	Effects of decreased iron on Hb and RBCs	Iron deficiency anemia

TIBC: Total iron-binding capacity

To Evaluate the Cause

- ✦ Urine: Albumin, sugar, and microscopy for pus cells, casts, and deposits [chronic kidney disease (CKD)]
- ✦ Urine: Culture and sensitivity [chronic urinary tract infections (UTIs)]
- ✦ Stool: Ova/cyst/parasites/occult blood
- ✦ Serum total proteins (associated hypoproteinemia, especially in liver diseases)
- ✦ Electrocardiography (ECG) and echocardiography (ECHO) – to rule out cardiac disease (especially, if breathlessness and pedal edema with cardiac murmur).

Other Routine Antenatal Investigations

- ✦ Oral glucose tolerance test (OGTT), HIV, HBsAg, and VDRL.
- ✦ Ultrasonography (USG)—to assess fetal biometry and well-being.

Indications for Bone Marrow Study in Anemia

- ✦ Aplastic anemia (suspected in patients with pancytopenia)
- ✦ Refractory anemia (nonresponders to iron therapy)
- ✦ Suspected kala-azar.

Other investigations for evaluation of anemia other than iron deficiency anemia are shown in Table 1.4.

Table 1.4: Special investigations for evaluation of anemia other than iron deficiency anemia

Type of anemia	Investigation
Megaloblastic anemia	Serum folate, RBC folate, serum vitamin B ₁₂
Autoimmune hemolytic anemia	Coombs test, serum bilirubin
Hereditary spherocytosis	Serum osmotic fragility test
Sickle cell anemia	Sickle cell testing, hemoglobin electrophoresis
Hemoglobinopathies (thalassemia)	Hemoglobin electrophoresis by high performance liquid chromatography (HPLC)

Complications of Anemia during Pregnancy

Severe anemia during pregnancy may have adverse effects on the mother and the fetus. The complications during antenatal, intrapartum and postpartum are summarized in Table 1.5.

Table 1.5: Complications of anemia during pregnancy

<i>Antenatal</i>	<i>Intrapartum</i>	<i>Puerperium</i>	<i>Fetus and neonate</i>
▫ Infections ▫ Pre-eclampsia ▫ Preterm labor ▫ Congestive cardiac failure (around 30–32 wks)	▫ Congestive cardiac failure ▫ Postpartum hemorrhage and shock	▫ Cardiac failure ▫ Puerperal sepsis ▫ Subinvolution ▫ Failed lactation ▫ Venous thrombosis	▫ Prematurity ▫ FGR ▫ Low birth weight ▫ Decreased neonatal iron reserves

Management of Iron Deficiency Anemia during Pregnancy

- ✦ Aim of treatment is to achieve a hemoglobin level of a minimum of 8 g%, at the time of delivery to reduce the complications.
- ✦ Confirm the diagnosis, severity (ICMR grade), type and cause of anemia (by peripheral smear and RBC indices).
- ✦ Oral or parenteral iron therapy or blood transfusion are given depending upon the gestational age and the severity of anemia.

Admission Criteria

- ✦ Women with mild-to-moderate anemia without other complications can be managed on OPD basis.
- ✦ Women with severe anemia (<7 g/dl) and women near term need to be hospitalized (Table 1.6).

Table 1.6: Management of iron deficiency anemia

<i>Mild anemia</i> (10–10.9 g/dl)	<i>Moderate anemia</i> (7–9.9 g/dl)	<i>Severe anemia</i> (<7 g/dl)
Oral iron therapy is recommended ▫ Parenteral therapy if intolerant, noncompliant or malabsorption is present	Oral iron therapy can be given if no other complications Parenteral therapy if ▫ Intolerant, noncompliant or malabsorption is present ▫ >32 weeks of gestation ▫ PCC transfusion if <8 g% and near term	Packed cell transfusion

Oral Iron Therapy

Indications

Mild-to-moderate anemia

- ✦ Therapeutic dose—180–200 mg/day elemental iron is given in divided doses (60 mg TDS or 100 mg BD).
 - Iron is best absorbed on an empty stomach/with water or fruit juice, about 1 hour before or 2 hours after meals. To minimize the possible gastrointestinal (GI) side effects, it can be consumed with food or immediately after meals.
 - Avoid tea and coffee for at least 2 hours.
 - Calcium, salts and antacids decrease iron absorption—gap of at least 2 hours between intake of both (Table 1.7).

Table 1.7: Factors influencing the iron absorption

Factors which favour iron absorption	Factors which decrease iron absorption
▫ Acidity ▫ Ascorbic acid (vitamin C) ▫ Absorption of heme iron is more than twice that of nonheme iron ▫ Increases during pregnancy ▫ Iron deficiency anemia	▫ Phytates (cereals) ▫ Oxalates (leafy vegetables) ▫ Phosphates (egg yolk) ▫ Calcium salts ▫ Tea, coffee, antacids, and H₂ receptor blockers

- Hemoglobin starts rising in 2–3 weeks and reaches a normal value approximately after 6 weeks of treatment.
- To replenish the iron stores, iron therapy is continued for 3 months after the hemoglobin levels return to normal.
- Various iron preparations are shown in Table 1.8.
- ✦ Other drugs given along with oral iron therapy are the following:
 - Folic acid 5 mg/day
 - Vitamin C 500 mg/day (helps in absorption of iron)
 - Deworming with oral albendazole 400 mg stat dose or mebendazole 100 mg BD for 3 days.

Table 1.8: Oral iron preparations

Ferrous salt (most effective preparation)	Ferric hydroxide (iron) polymaltose complex	Carbonyl iron
<i>Ferrous sulfate</i> (200 mg contains 60 mg elemental iron) ▫ Higher elemental iron ▫ Cheaper ▫ Good bioavailability but with GI side effects <i>Ferrous fumarate</i> (300 mg tablet has 100 mg elemental iron) ▫ Has similar efficacy and GI tolerance to ferrous sulfate ▫ It is a commonly used salt in commercial preparation <i>Ferrous gluconate</i> (300 mg tablet contains 30 mg elemental iron) ▫ Well-tolerated but has low iron content <i>Ferrous ascorbate</i> (contains 100 mg elemental iron) ▫ Has high amount of elemental iron ▫ Converts ferric to ferrous iron, thereby increases iron absorption ▫ Formation of insoluble iron complexes is inhibited	▫ It is a combination of ferric iron with polymaltose molecules and is anionic. Does not stain teeth ▫ No metallic taste ▫ No interaction with food or other drugs ▫ Less absorption than ferrous salts ▫ Try as an alternative to those who do not tolerate ferrous salts	▫ 100% elemental iron ▫ Higher bioavailability in presence of dietary inhibitors ▫ Less GI side effects

Side Effects of Oral Iron Therapy

Metallic taste, staining of teeth, nausea, and gastric discomfort, constipation, diarrhea, and flatulence.

Signs of Improvement (Table 1.9)

Table 1.9: Symptoms and laboratory parameters of improvement in anemia

General symptoms	Laboratory parameters
▫ A sense of well-being ▫ Improved appetite ▫ Improvement in associated symptoms like breathlessness and pedal edema	▫ 5–7 days: Increase in retic count to up to 5% (normal 0.2–2%) (reticulocytosis is the earliest hematological response to iron therapy) ▫ 2–3 weeks: Increase in Hb (0.7–1 g/dl/week) ▫ 6–8 weeks • Hb to normal level • Peripheral smear shows normocytic, normochromic RBCs • Serum ferritin level increases

Causes for Failure of Oral Iron Therapy

- ✦ Noncompliance
- ✦ Intolerance
- ✦ Malabsorption
- ✦ Inaccurate diagnosis of the cause of anemia (e.g. anemia due to thalassemia/dimorphic anemia will not improve with iron supplementation)
- ✦ Ongoing blood loss—hookworm infestation, hemorrhoids
- ✦ Coexisting infections (infection impairs erythropoiesis)
- ✦ Coexisting deficiencies—folic acid deficiency.

Parenteral Iron Therapy

Indications	Advantage of parenteral iron over oral iron
▫ Noncompliance to oral iron ▫ Intolerance to oral iron ▫ Malabsorption—peptic ulcer, inflammatory bowel disease, etc. ▫ Moderate anemia >32 weeks and more	▫ Certainty of administration—predictable absorption rate ▫ Ensured compliance, especially with moderate anemia >32 weeks and beyond

Formulas for calculation of total requirement of parenteral iron:

- ✦ $[\text{Hb deficit} \times \text{BW (kg)} \times 2.2] + 1000 \text{ mg}$ (to replenish iron stores)
- ✦ $[\text{Hb deficit} \times \text{BW (kg)} \times 4.4] + 50\%$ for stores
- ✦ $(\text{Hb deficit} \times 250) + 50\%$ for stores
- ✦ $[\text{Hb deficit} \times 0.3 \times \text{BW (lb)}] + 1000 \text{ mg}$ (for stores)

Hb deficit = Target or desired Hb – Patient's Hb (target Hb usually taken as 11 g/dl in pregnancy).

Prepregnancy body weight (BW) is used.

The various iron preparations used for therapy are summarized in Table 1.10. Parenteral iron preparations are available for intramuscular and intravenous use.

Table 1.10: Parenteral iron preparations

Iron dextran (imferon)— 50 mg elemental iron in 1 ml (both IM and IV use) IM dose by Z tract technique	Iron sucrose (dextran- free preparation)— 100 mg in 5 ml	Ferric carboxymaltose (dextran-free prepa- ration)—IV infusion only (500 mg/10 ml)	Iron sorbitol- citrate complex (Jectocos)—IM only (50 mg in 1 ml)
The calculated total dose can be given as single large dose [total dose infusion (TDI)] or as divided multiple dose regimen on daily/alternate days Total dose infusion (single day) - Initial IV test dose of 0.5 ml is given slowly - The total dose—IV infusion in 500 ml normal saline over 6–8 hours (5% dextrose can lead to phlebitis) - If the total dose is > 1000 mg—two divided doses on alternate days - Not given due to increased risk of anaphylactic reactions Multiple dose regimen - Initial IV test dose of 0.5 ml (25 mg) is given slowly - Repeated doses of 2 ml (100 mg)—either as IV infusion by diluting in 250 ml of saline, over 30–60 minutes, or as undiluted slow IV push at a maximum of 20 mg/min on daily/alternate-day basis	- May be given undiluted as slow IV at 20 mg/min (maximum dose of 100 mg) - Alternatively, 5 ml containing 100 mg iron is diluted in 100 ml normal saline and administered over 20 minutes. The initial 25 ml is given slowly to look for any reactions. A maximum dose of 200 mg can be given at a time - Infusion can be repeated on alternate days Advantage: Hypersensitivity and anaphylactic reactions are very rare with minimal side effects Disadvantage: Multiple doses are required	1000 mg is diluted in 100 ml normal saline and is administered over 15–20 minutes - Subsequent doses after 7 days Advantages: - Large dose up to 1000 mg can be administered over 15–20 minutes - Hypersensitivity and anaphylactic reactions are very rare with minimal side effects - Test dose is not required - Good safety and efficacy profile - If it has to be given in pregnancy, use is restricted to second and third trimesters	- Single dose injection—1.5 mg/kg, max. 100 mg Disadvantage: - Multiple doses are required - Test dose is required - Painful - Stain the skin - Abscess formation

Parenteral Iron Therapy

The advantages and disadvantages of parenteral iron therapy are discussed in Table 1.11.

Blood Transfusion

Indications

- ✦ Severe anemia at any POG
- ✦ Moderate anemia with Hb <8 g% near term

Table 1.11: Parenteral iron therapy

Advantages	Side effects	Disadvantages of IM iron over IV
▫ Certainty of iron administration as parenteral iron predictable absorption rate ▫ Side effects of oral iron are avoided ▫ Risk of transmission of infections and transfusion reactions with blood transfusion are avoided	▫ Local—pain, skin discoloration, and abscess formation with IM preparations, and thrombophlebitis with IV administration ▫ General—myalgia, arthralgia, fever, lymphadenopathy, and anaphylaxis ▫ Possibility of iron toxicity in conditions like thalassemia	▫ More painful ▫ Skin stain and abscess formation at the injection site ▫ Irregular absorption

- ✦ Anemia due to acute blood loss such as antepartum hemorrhage
- ✦ Nonresponding refractory anemia to oral or parenteral iron therapy.

Advantages

- ✦ Improves oxygen-carrying capacity of blood
- ✦ Stimulates erythropoiesis
- ✦ Each unit of packed cell improves hemoglobin by 1 g/dl.

Disadvantages

- ✦ Possibility of transfusion reactions
- ✦ Risk of transfusion transmitted infections such as HIV, HBsAg
- ✦ Can precipitate CCF
- ✦ Can precipitate preterm labor.

Precautions to be Taken during Blood Transfusion

- ✦ Packed cell transfusion is preferred to whole blood (prevents volume overload).
- ✦ Clinical parameters (pulse, respiratory rate, and intermittent chest auscultation for crepts) must be regularly monitored every 15–20 minutes.
- ✦ Check bag number and blood group and type and match with the patient.
- ✦ Diuretic such as furosemide 20 mg is given IV before transfusion to prevent volume overload and congestive cardiac failure.
- ✦ Blood transfusion must be administered slowly over 4–6 hours.
- ✦ Stop blood transfusion immediately if patient complaints of itching, breathlessness or palpitations etc. (transfusion reaction).

Management of Women with Anemia in Labor

First Stage

- ✦ Strict aseptic precautions should be followed.
- ✦ IV line is secured, investigations like CBC and blood is cross-matched and released.
- ✦ Propped-up position if in cardiac failure, otherwise in left lateral position.
- ✦ Oxygen is given by face mask.

- ✦ Adequate analgesia for pain relief.
- ✦ Restrict IV to <75 ml/h to prevent volume overload and encourage oral hydration.
- ✦ Monitor for symptoms and signs of CCF (tachycardia, raised JVP, fine crepitations in base of lungs).
- ✦ Restrict the number of vaginal examination to prevent infections (monitor descent of fetal head by abdominal palpation of fetal poles—partogram to be maintained).
- ✦ Consider prophylactic antibiotics (increased risk of infection).
- ✦ Monitor FHR by continuous electronic fetal monitoring or intermittent auscultation every 15 minutes in the first stage and every 5 minutes in the second stage.
- ✦ Concentrated oxytocin can be given for augmentation of labor (to avoid fluid overload).
- ✦ Cesarean section is done only for obstetric indications. Regional anesthesia is preferred over general anesthesia.

In women with preterm labor, beta-agonists and steroids must be given with caution in anemic patients to prevent pulmonary edema.

Second Stage

- ✦ Consider forceps or vacuum for shortening second stage to reduce maternal straining, especially in women with CCF.
- ✦ Consider injection frusemide in severely anemic women to prevent cardiac failure.

Third Stage

- ✦ Restrict IV fluids.
- ✦ Active management of the third stage of labor (AMTSL) (to prevent PPH).
- ✦ Concentrated oxytocin is the drug of choice for AMTSL.
- ✦ Methergin 0.2 mg IV/IM is not contraindicated except in cases with severe anemia in failure (can lead to volume overload).
- ✦ Aggressive management of PPH (small amount of blood loss can lead to decompensation).

Postpartum

- ✦ Intensive monitoring is done for the initial 24 hours following delivery as there is a risk of CCF.
- ✦ Antibiotics are given to prevent infections, especially if episiotomy has been given.
- ✦ Consider parenteral iron/blood transfusion if required.
- ✦ 6 months of oral iron therapy to replenish the iron stores.
- ✦ Contraceptive counseling.
- ✦ Advice spacing of at least 2 years between pregnancies.

Prevention of Iron Deficiency Anemia during Pregnancy

Measures to prevent iron deficiency anemia include the following:

- ✦ Provision of iron prophylaxis to all preschool children and adolescent girls.
- ✦ Deworming with albendazole or mebendazole every 6 months for children and adults (MoHFW, Government of India guidelines—a single dose of albendazole 400 mg after the first trimester, preferably in the second trimester).
- ✦ Hemoglobin estimation should be done every 3–4 weeks (14–16 weeks/20–24 weeks/26–30 weeks/30–34 weeks).
- ✦ Iron and folic acid prophylaxis.

- ✦ Detection and treatment of any underlying infections like malaria and hookworm infestation.
- ✦ Advice on diet rich in iron.
- ✦ Fortification of food with iron like wheat flour, sugar, salt, and cereal-based food.

National Nutritional Anemia Control Program

MoHFW, Government of India (2013) recommends prophylaxis with 100 mg elemental iron as ferrous sulfate and folic acid 500 µg for at least 100 days during pregnancy from 14–16 weeks of pregnancy followed by the same dose for 100 days in the postpartum period.

Additionally:

- ✦ For children 6–60 months: 20 mg elemental iron and 100 µg folic acid per day for 100 days/year
 - ✦ For children 6–10 years: 30 mg elemental iron and 250 µg folic acid per day for 100 days/year
 - ✦ For children 11–18 years: 100 mg elemental iron and folic acid 500 µg for 100 days/year
- 12 by 12 initiative (2007):* Every child has a hemoglobin of 12 g by the age of 12 years.

WHO recommends: 60 mg elemental iron with 400 µg of folic acid for 6 months during pregnancy in countries with prevalence of anemia less than 40%, and additional 3 months during postpartum in countries with prevalence of anemia greater than 40%.

ANEMIA MUKT BHARAT INITIATIVE (2018)

- ✦ To solidify the existing mechanisms and devise newer strategies for tackling anemia.
- ✦ Focus is on six target beneficiary groups through six interventions and six institutional strategies—POSHAN Abhiyan.
- ✦ *Beneficiaries:* Children (6–60 months); adolescent girls and boys (15–19 years); Reproductive age, pregnant and lactating women.

Interventions

- ✦ Prophylactic iron and folic acid supplementation
- ✦ Deworming
- ✦ Intensified year-round behavior change communication campaign (solid body, smart mind) with a focus on four key behaviors
 - Improved compliance to iron folic acid supplementation
 - Suitable infant and young child feeding practices
 - Increase in iron-rich food intake through diverse diet in terms of quantity, frequency and or fortified foods harnessing locally available resources
 - Ensuring delayed cord clamping after institutional delivery.
- ✦ Testing using digital methods and early point-of-care treatment, with special attention to pregnant women and school-going adolescents
- ✦ Mandatory provision of fortified foods in government-funded public health programs
- ✦ Intensifying awareness, screening and treatment of non-nutritional causes of anemia in endemic pockets, with special focus on malaria and hemoglobinopathies.

Poshan Abhiyaan or National Nutrition Mission

- ✦ A flagship program of Government of India, launched in 2018 to improve nutritional outcomes in children, pregnant women, and lactating mothers.
- ✦ The focus of Abhiyaan is to lay emphasis on nutritional status of children (0 to 6 years), adolescent girls, pregnant women and lactating mothers.

Megaloblastic Anemia

It is characterized by macrocytic blood picture and megaloblastic bone marrow.

- ✦ Mechanism: Folic acid and vitamin B₁₂ are coenzymes required for red cell DNA synthesis. Deficiency of vitamin B₁₂ and/or folic acid leads to impaired DNA synthesis. The DNA synthesis is impaired while the cytoplasmic maturation is normal, leading to formation of megaloblasts or macrocytosis (Table 1.12).
- ✦ The two main causes for megaloblastic anemia are deficiencies of vitamin B₁₂ and folic acid deficiency (Table 1.13).

Table 1.12: Diagnosis of megaloblastic anemia

Hemoglobin	< 10 g/dl
Hematocrit	< 33%
MCV	> 96 fl
MCH	> 33 pg
MCHC	Within normal range
Peripheral smear	Macrocytes and megaloblasts, hypersegmented neutrophils, nucleated RBCs, Howell Jolly bodies
Unconjugated bilirubin and serum LDH	May be elevated

Table 1.13: Confirmatory tests for folate and vitamin B₁₂ deficiency

Deficiency	Serum levels
Vitamin B ₁₂ deficiency	Serum B ₁₂ level < 100 pg/ml
Folate deficiency	✦ Serum folate level < 2 ng/ml ✦ Fasting serum folate level < 6 µg/L ✦ RBC folate < 165 µg/L ✦ Fasting folate and RBC folate levels are more specific, as there is no interference by food

Folic Acid Deficiency

- ✦ Megaloblastic anemia in pregnancy is almost always secondary to folate deficiency.
- ✦ Folic acid is absorbed in jejunum.
- ✦ Folate stores last only for 2–4 months and deficiency occurs in 6 months with reduced intake.
- ✦ Dietary sources of folic acid include yeast, liver, green leafy vegetables, and fruits.
- ✦ *Treatment:* Folic acid 5 mg orally daily during pregnancy, continued till 3 months postpartum.

Vitamin B₁₂ Deficiency

- ✦ Intrinsic factor which is secreted by mucosal cells of stomach is required for B₁₂ absorption. Vitamin B₁₂ deficiency is most often due to malabsorption; therefore, it is usually administered in parenteral form.

- ✦ Vitamin B₁₂ has a high quantity of storage in the body and hence deficiency is manifested only after a prolonged period of reduced intake of 3–4 years.
 - ✦ Dietary sources of B₁₂ are meat, poultry, fish, and dairy products (animal sources mainly). Hence, deficiency is common in strict vegetarians.
 - ✦ Treatment: Vitamin B₁₂ (hydroxycobalamin) 1000 µg is given as IM injection on alternate days for 2 weeks followed by 1000 µg IM every month for 6 months.
- Along with folate or B₁₂ therapy, iron preparations are also given, as demand for iron increases with increase in erythropoiesis.

CASE DISCUSSION

Salient Points in History

Patient Details

- ✦ Age (anemia is common in teenage pregnancy)
- ✦ Occupation (e.g. agricultural workers prone to hookworm infestation resulting in anemia)
- ✦ Socioeconomic status (more common in low socioeconomic group)
- ✦ Religion (anemia is less common in red meat-eating population).

Presenting Complaints and History of Presenting Complaints

History of symptoms of anemia: Easy fatigability, tiredness, weakness, lethargy, breathlessness, palpitation (rule out cardiac disease), and swelling of feet. Elaborate with details such as onset, duration, and progression of symptoms.

History of Possible Causes for Anemia

- ✦ History of bleeding per rectum, melena (colon cancer), hematuria, hematemesis, and hemoptysis
- ✦ History of worms in stools
- ✦ History of chronic diarrhea (malabsorption)
- ✦ History of burning micturition [to rule out recurrent/chronic urinary tract infection (UTI)]
- ✦ History of fever with chills and rigors (to rule out malaria)
- ✦ History of chronic diarrhea (gastric surgery/malabsorption)
- ✦ History of other causes of breathlessness
- ✦ History of cardiac symptoms such as chest pain, palpitation, orthopnea, paroxysmal nocturnal dyspnea, and syncopal attack (to rule out cardiac causes of breathlessness)
- ✦ History of bronchial asthma.

History of Other Causes of Swelling of Feet

- ✦ Pre-eclampsia
- ✦ Cardiac disease
- ✦ Renal disease

History of Present Pregnancy

- ✦ Regular iron supplementation
- ✦ History of bleeding P/V, especially in second and third trimester

Menstrual History

History of menorrhagia or polymenorrhea in previous menstrual cycles.

Past Obstetric History

- ✦ Parity (repeated pregnancy is a likely cause of anemia)
- ✦ Spacing between pregnancies (spacing of at least 2 years is required to replenish iron stores)
- ✦ History of hematinic intake during pregnancy
- ✦ History of blood transfusion
- ✦ History of postpartum hemorrhage (PPH)
- ✦ History of puerperal sepsis
- ✦ History of low-birth-weight baby
- ✦ Whether taken postnatal iron supplementation.

Past Medical and Surgical History

- ✦ History of chronic medical illness, especially chronic kidney disease
- ✦ History of any gastric surgeries

Nutritional/Diet History (Very Important)

- ✦ In detail along with protein and calorie intake and deficiency (24 hr recall method).
- ✦ Sources of iron rich food

Family History

Family history of sickle cell anemia and thalassemia

Salient Points in Examination

Consider the following relevant points during examination in cases of anemia during pregnancy.

General Examination

- ✦ Nutrition
- ✦ Weight (serial weight gain may be less in malnourished women)
- ✦ Pallor—clinical grading is shown in Table 1.14
- ✦ Pedal edema [congestive cardiac failure (CCF)/hypoproteinemia in liver disease]
- ✦ Icterus (may be present in hemolytic anemia)
- ✦ Signs of vitamin deficiency such as dry lusterless hair, glossitis, and angular stomatitis
- ✦ Platonychia (flat nails), koilonychia (spoon shaped nails), and brittle nails (in chronic anemia)
- ✦ Dark palmar creases.

Vitals

- ✦ Pulse rate (tachycardia–hemorrhage/CCF; high-volume pulse is present in anemia)
- ✦ Blood pressure

Table 1.14: Clinical grading of pallor

Mild	Pallor of conjunctiva and/or mucous membrane
Moderate	Pallor of conjunctiva and/or mucous membrane + pallor of skin
Severe	Pallor of conjunctiva and/or mucous membrane + pallor of skin + pallor of palmar creases

Systemic Examination

Cardiovascular System

- ✦ Jugular venous pressure (JVP; may be elevated in CCF)
- ✦ Hyperdynamic apex beat
- ✦ Ejection systolic murmur in pulmonary area (due to volume overload).

Respiratory System

Basal lung crepitations secondary to CCF.

Gastrointestinal Tract

Look for hepatosplenomegaly (may be present in malaria, leukemia, lymphomas, and hemolytic anemia).

Obstetric Examination

Fundal height and symphysio-fundal height (SFH) may be normal or less than period of gestation (POG) if associated with FGR.

How to Write the Case Diagnosis in Anemia

An example of writing diagnosis in cases of anemia in pregnancy is given below.

Example: A woman of 32 years of age, G4P3L3 at 30 weeks, with moderate anemia with a single live fetus in cephalic presentation, not in failure, not in labor, admitted for further evaluation and management.

VIVA VOCE

Q.1. What are the causes of microcytic hypochromic anemia?

- Ans.** ✦ Iron deficiency anemia
- ✦ Thalassemia
 - ✦ Sideroblastic anemia
 - ✦ Anemia due to chronic diseases
 - ✦ Lead poisoning.

Q.2. What are the causes of normocytic normochromic anemia?

- Ans.** ✦ Acute blood loss
- ✦ Bone marrow failure.

Q.3. What are the causes of macrocytic anemia?

- Ans.** ✦ Vitamin B₁₂ deficiency
- ✦ Folic acid deficiency
 - ✦ Hereditary spherocytosis.

Q.4. What is physiological anemia of pregnancy?

- Ans.** ✦ Physiological anemia occurs in pregnancy due to relative increase in plasma volume more than the increase in red cell mass leading to apparent decrease in hematocrit.
- ✦ It starts by 7–8 weeks and reaches maximum at 32 weeks.

Q.5. How does hemodilution benefit pregnancy?

- Ans.** + Reduces blood viscosity, thereby enhancing placental perfusion and facilitating oxygen delivery to the fetus
 + Reduces work load on the heart
 + Reduces postpartum loss of RBCs.

Q.6. What are two forms of dietary iron?

- Ans.** + Heme iron: Meat and meat products (5–10% of dietary iron; most bioavailable source)
 + Nonheme iron: Cereals, pulses, and vegetables (90–95% of dietary iron)

Q.7. What are the dietary sources of iron?

- Ans.** + Rich sources: Organ meat like liver, heart, kidney, fish, egg yolk, and dry beans
 + Good sources: Green leafy vegetables, cereals, pulses, ragi, and dates
 + Poor sources of iron: Milk.

Q.8. What is the iron requirement during each trimester of pregnancy?

- Ans.** + First trimester: 2 mg/day
 + Second trimester: 4–6 mg/day
 + Third trimester: 6–8 mg/day
 + Only 10% of dietary iron is absorbed. Daily diet contains 10–20 mg of elemental iron, of which only 10% is absorbed (1–2 mg)

Q.9. What should be done if the patient does not tolerate oral iron?

- Ans.** + Take oral iron along with meals.
 + If no response—change the iron salt preparation.
 + If still no response—parenteral route.

Q.10. What is Z-track technique?

- Ans.** + Deep IM injections in the upper outer quadrant of buttocks with 2- or 3-inch long 20-gauge needle.
 + Left lateral position for the patient
 + Slide the skin at the injection site with nondominant hand
 + The needle inserted at right angle to the skin till bony resistance is felt and then withdrawn slightly so that tip of the needle is in the muscle
 + The plunger is withdrawn to check for any blood
 + Superficial tissues are then slid back into place (Fig.).

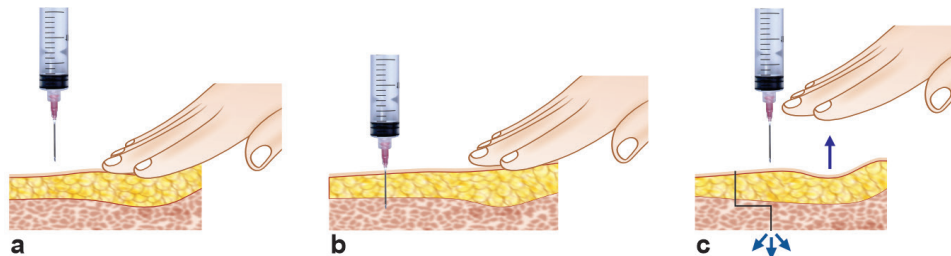


Fig.: Z-track technique for deep intramuscular injections: (a) The skin over the injection site retracted and held; (b) muscular injection given; (c) skin released

Q.11. Discuss iron metabolism.

Ans. See the following Flowchart.

