CLINICAL REFERENCE

# Anemia in Pregnancy

*A Comprehensive Clinical Guide to Diagnosis, Prevention & Management*

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Anemia in Pregnancy Module · 2026

NINE CHAPTERS

# Contents


01 Approach to Anemia in Pregnancy ..... 3
Dr Megha Karnik, Dr Nivedita Jha

02 Prevention of Anemia in Pregnancy ..... 28
Dr Sairem Mangolnganbi Chanu

03 Haemoglobinopathies: Diagnosis & Preconceptional Counselling ..... 46
Dr Divya MB, Dr Shruti P Shiradkar

04 Iron Deficiency Anemia in Pregnancy ..... 65
Dr Dhruva Halani

05 Sickle Cell Anaemia in Pregnancy ..... 89
Dr Deepika Dewani

06 Thalassaemia in Pregnancy ..... 109
Dr Amrita Datta

07 Megaloblastic Anaemia in Pregnancy ..... 123
Dr Neema Acharya

08 Transfusion in Pregnancy ..... 132
Dr Nivedita Jha, Dr Vijitha MP

09 Post-partum Care in Anaemic Women ..... 144
Dr Sheela Mane

CHAPTER 01

# Approach to Anemia in Pregnancy

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IN THIS CHAPTER

Severity & Classification | Prevalence | Clinical Evaluation | Investigations | Microcytic Anaemia | Macrocytic Anaemia

## Introduction

Pallor is the most common presentation of anaemia in pregnancy. Anemia is defined as a hemoglobin value less than two standard deviations below the median for a healthy matched population.[1] The Centers for Disease Control and Prevention (CDC) defines anemia in pregnancy as hemoglobin less than 11 g/dl (Hematocrit; Hct 33%) in the first and third trimesters and less than 10.5 g/dl (Hct 32%) in the second trimester, whereas the World Health Organization (WHO) defines anemia in pregnancy as Hb values less than 11gm/l. WHO defines anemia in postpartum females as Hb less than 10 g/dl.[2,3]

## Degree/Severity

According to WHO, Anemia is defined as haemoglobin levels less than 11.0g/dL during pregnancy and is classified into three levels of severity: mild anemia (Hb levels 9 to 10.9g/dL), moderate anemia (Hb levels 7 to 8.9g/dL), and severe anaemia (Hb levels less than 7g/dL).[4] This is the

standard to be accepted in India. The expert group also agreed upon the Indian Council of Medical Research (ICMR) classification for the severity of anemia.

| Severity of anaemia | Hb in g/dl |
|---|---|
| **Mild** | **10–10.9** |
| Moderate | 9.9–7 |
| Severe | 6.9–4 |
| Very severe | <4 |

## Prevalence

In India more than 15 states belong to the high prevalence (>%55) of anemia among socially backward groups in 2019–21. The anemia prevalence was high (>55%) in all social groups (SC & ST, OBC, general) observed in 7 states in NFHS-3, 4 in NFHS-4 and 11 states in NFHS-5.[5]

## Classifications

- Anemia broadly classified as physiological and pathological,
  - Physiological anemia of pregnancy
    - This condition should be considered in a previously non anaemic woman with mildly decreased Hb and/or RBC counts during pregnancy which is due to hemodilution.
- In practice, anemia classification based on fundamental red cell morphological metrics such as mean corpuscular volume (MCV) provides for a more rapid diagnostic approach.

- Based on this anemia can be classified as into three categories:
  1. Microcytic (MCV 82 fL, MCH less than 27pg, MCHc less than 32%),
  2. Normocytic (MCV = 82-98 fL, MCH 27 -32pg, MCHc 32- 35%), and
  3. Macrocytic (MCV > 98 fL, MCH more than 32pg, MCHc 32-35%)[6–8]
- Differential diagnosis of anemia in pregnant women

I. Microcytic anemia

1. Iron deficiency anemia

2. Thalassemia

II. Normocytic anemia

1. Hemolytic anemia

a. Microangiopathic hemolytic anemia (MAHA)

i. Thrombotic thrombocytopenic purpura (TTP)

ii. Hemolytic uremic syndrome (HUS)

iii. HELLP syndrome

b. Non-MAHA

i. Immune-mediated: autoimmune hemolytic anemia (AIHA)

ii. Nonimmune-mediated: pregnancy-induced haemolytic anemia (PIHA), intrinsic RBC disorders, for example, enzymopathy, membranopathy, paroxysmal nocturnal hemoglobinuria (PNH)

2. Nonhemolytic anemia

a. Physiologic anemia of pregnancy

b. Anemia of chronic disease

c. Bone marrow aplasia

III. Macrocytic anemia

1. Vitamin B12 deficiency

2. Folic acid deficiency

IV. Anemia associated with other organ dysfunction, for example, hypothyroidism, chronic liver disease

- Anemia can alternatively be characterized based on presentation as

1. **Acute** (typically with bleeding or hemolysis) or
2. **Chronic.** [9]

## Evaluation ➔ A practical approach

The strategy for establishing a diagnosis of anemia must follow a classic pattern that includes

***A detailed History:***[10,11]

- A detailed history can help us diagnose the cause of anemia, type of anemia and severity, which help us in the management.

| History elicited | Probable cause |
|---|---|
| Recurrent fever with chills and rigors, urinary complaints, prolonged cough | Presence of infections(Malaria, UTI,TB) |
| Bleeding gums, piles or worm infestation | Chronic loss of blood |
| Bulky stools , chronic diarrhea | Malabsorption |
| Petechiae, bruises, ecchymosis | Bleeding or coagulation disorder |
| Repeated blood or blood component transfusion in self or family | Hemoglobinopathies |
| High colored urine, yellow sclera , drug intake | Hemolysis |
| ***Detailed dietary history:***<br>cooking habits, cooking vessels etc. | Dietary deficiency |
| ***Menstrual history:***<br>Cycle length, duration, amount of bleeding, passage of clots, flooding etc. | Most common cause is iron deficiency |

| | |
|---|---|
| ***Obstetric history :***<br><br>**Abortions, repeated childbirth, any complications like APH, PPH, blood transfusion , etc. in previous or current pregnancies** | **Loss of reserve of iron , Vit.B12 , folate** |
| ***Contraceptive history :***<br><br>Use of IUCD/with heavy menstrual cycles | Most common cause is iron deficiency |
| ***Socioeconomic History:*** | Iron deficiency anemia more common in lower socioeconomic status |

## A basic physical examination12

- *General Physical Examination:*
- Built and nourishment
- Pulse rate, Blood pressure, Respiratory rate.
- Skin and mucosa: Pallor, Colour of palmar creases, Petechiae, ecchymosis.
- Eyes: pallor , icterus
- Oral cavity: glossitis, stomatitis, cheilosis.
- Nails: pallor , platonychia or koilonychias, clubbing
- Neck: Lymphadenopathy, JVP, Thyroid enlargement.
- Legs : Oedema , ulcers, peripheral neuropathy
- *Systemic Examination:*
- Chest examination: Sternal tenderness, any crepitation , fine basal or coarse apical.
- Cardiovascular system (CVS) murmurs.

- Per abdomen examination: Oedema of abdominal wall, hepatosplenomegaly, presence of free fluid.
- Obstetrical examination: Height of uterus, tone of uterus, Number of foetuses, presentation , amount of liquor, FHS.

## Investigations for cause of Anemia

- The Anemia work up includes a series of investigations which helps us to identify the cause, type and severity of anemia.

| INVESTIGATION | CAUSE OF ANEMIA |
|---|---|
| Peripheral smear | Malarial parsaite , sickle cells, spherocytes, evidence of hemolysis |
| Liver function tests | Liver disease , hemolysis |
| Renal function tests | Renal disease |
| Serum proteins, serum folic acid , vit b12, serum iron studies | Hypoprotenimea , folic acid , b12 and iron deficiency |
| Electrophoresis / high –performance liquid chromatography | Hemoglobinopathy |
| Urine examination | Urinary tract infection (UTI), occult hematuria, schistosomiasis |
| Stool examination(3 consecutive days ) | Ova and cyst , occult blood |
| Bone marrow aspiration | Abnormal cells, iron stores |
| Xray chest (after shielding abdomen) | Pulmonary tuberculosis |

The prevalence of anaemia was 22.9% according to WHO and 10.9% according to CDC. A significantly higher risk of low birth weight was found in children of women with anaemia, regardless of the diagnostic

criteria used, while a greater risk of having a small-for-gestational-age new born was seen only when the CDC criterion were applied.[13]

In country like India it's advisable to follow WHO criteria to diagnose and treat anaemia to improve antenatal care, which is also agreed upon by the Indian Council of Medical Research (ICMR)

In daily clinical practice, it is more useful to start with the analytical parameters of the haemogram. MCV allows us to classify anemia as microcytic (MCV < 82 fL), normocytic (MCV = 82-98 fL) and macrocytic (MCV > 98 fL)[6]

RDW is a rough indicator of anisocytosis and is an essential complement to MCV.[9]

## Classification of anaemia as RDW and MCV

| | ↓MCV | Normal MCV | ↑MCV |
|---|---|---|---|
| **Normal RDW** | **β-thalassemia** | **Normocytic** | **Bone marrow aplasia** |
| | α-thalassemia | | |
| Increased RDW | Iron deficiency | Inflammatory anemia<br>Hypothyroidism | Megaloblastic anemia |

- *Microcytic anemia (MCV < 82 fL)*

Iron deficiency anemia (IDA), thalassemia, and anemia of chronic diseases (ACD) are the three main diagnostic possibilities. A fourth

option, sideroblastic anemia, is so uncommon that it is rarely evaluated in the initial diagnosis unless there is a history of lead contamination.

- **Iron Deficiency Anemia (IDA)**
  - IDA is the most frequent cause of anemia in pregnancy on a global scale.[14] Most standards advocate screening for anemia during pregnancy in the first trimester (or at booking), then at 24-28 weeks, and finally at 36 weeks.[15] A deviation from the above parameters should often be treated as pathologic and warrant further testing for the etiology and appropriate management of anemia during pregnancy.[4]
  - Laboratory parameters to diagnose iron status includes Serum Iron, Tsat%, Ferritin (µg/dl), sTFR, sTFR/log ferritin, ZPP, Serum hepcidin.[16]

Laboratory parameters to diagnose iron status[16]

**Comparison of anaemia types — part 1 of 2**

| | ID | IDA | AOCD | ID and AOCD |
|---|---|---|---|---|
| **Serum Iron** | ↓ | ↓ | ↓ | ↓ |
| Tsat% | > 16 | < 16 | N/↓ | N/↓ |
| Ferritin (µg/dl) | < 30 | < 12 | > 100 | <100 |
| sTFR | ↑ | ↑ | N/↑ | Variable |
| sTFR/log ferritin | NA | > 2 | < 1 | > 2 |

| | | | | |
|---|---|---|---|---|
| **ZPP** | **N** | **↑** | **↑** | **↑** |
| Serum hepcidin | ↓ | ↓ | ↑ | N/↑ |

**Comparison of anaemia types — part 2 of 2**

| | **Normal value (adult female)** |
|---|---|
| **Serum Iron** | **10–30 µM/L** |
| Tsat% | >16 to <45 |
| Ferritin (µg/dl) | 20–200 |
| sTFR | ↑ |
| sTFR/log ferritin | |
| ZPP | ↑ |
| Serum hepcidin | ↑ |

ID iron deficiency; IDA iron deficiency anemia; AOCD anemia of chronic disease; N indicates normal; T sat transferrin saturation; sTFR soluble transferrin receptor ZPP, Zn Protoporphyrin

- The gold standard for diagnosing IDA is bone marrow stainable iron reserves, although the test is invasive and cannot be used during pregnancy.[17]

- In comparison to serum iron, transferrin saturation (Tsat), and erythrocyte protoporphyrin levels, serum ferritin is a more sensitive and focused diagnostic for ID.[18] The best test currently available for confirming iron insufficiency in pregnancy is low serum ferritin values.[19]
- When a woman has sufficient iron reserves, her serum ferritin rises early in the pregnancy, drops to roughly 50% of pre-pregnancy levels by 32 weeks (due to hemodilution), then slightly rises in the third trimester.[20]
- *Newer RBC Parameters*

Modern automated analysers can measure advanced red blood cell and reticulocyte indices, including percentage hypochromic reticulocytes (%HYPOr), reticulocyte hemoglobin content (CHr), and percentage circulating microcytes (%HYPOm), which are recognized indications of iron deficient erythropoiesis.

They can be easily used for diagnosing and monitoring therapy in IDA in pregnancy and have also been shown to be earlier markers of response to iron therapy than MCV.[21] To validate the use of these markers during pregnancy, additional research is necessary.[22]

Newer RBC parameters for IDA

| | Normal range | Clinical utility |
|---|---|---|
| **%HypoM** | **< 3.4%** | **Indicator of IDA** |
| %HypoR | < 3.7% | Indicator of IDA |
| CHr | < 25 pg | Measures functional iron available over 3–4 days, early indicator of IDA and response to iron therapy |
| M/H[23] | < 3.7 | Differentiating IDA from Beta Thalassemia trait |

%HypoM %Hypochromic microcytes; %HypoR %Hypochromic reticulocytes; CHr reticulocyte hemoglobin content; M/H Microcytic RBC%/Hypochromic RBC%

- *Anaemia of Chronic Disease (ADA)*

After IDA, ACD is the most common kind of anaemia in the general population. ACD is caused by a variety of factors, including acute and chronic infections (18%-95%), cancer (30%-77%), autoimmune illnesses (including chronic inflammatory bowel disease), 8%-71%, solid organ transplant rejection (8%-70%), and chronic renal disease (23%-50%). ACD affects 20% of older adults with anemia (30% excluding nutritional inadequacy), and 4.3% have ACD with kidney failure. As a result, we should remember that ACD is the most common diagnosis in the elderly and inpatients, and the second most common diagnosis in outpatients under the age of 65.[24]

- *Normocytic anaemia (MCV = 82-98 fL)*

In order to differentiate among regenerative (hemolysis and bleeding) or hypo-regenerative anemia (bone marrow aplasia, chronic disease, nutrition deficiency and hemopathy), it is necessary to determine the corrected RPI.

- *Hemolytic Anaemia*[25]

Red blood cells are prematurely destroyed in hemolytic anemia, which can be chronic or fatal. Hemolysis in the reticuloendothelial system can happen intravascularly, extravascularly, or both ways. The differential diagnosis has multiple items as follows

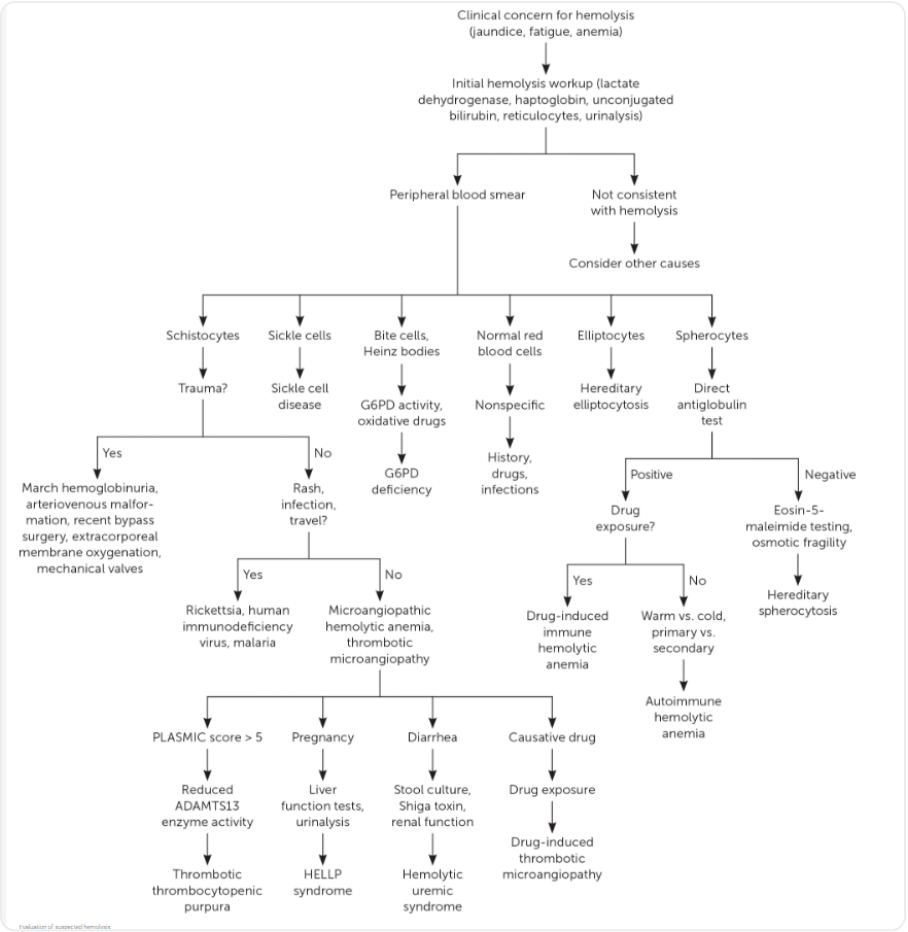
TABLE 1

**Differential Diagnosis of Hemolysis**

| Class/type | Diseases | Mechanism | Site | Laboratory tests | Treatment |
|---|---|---|---|---|---|
| Alloimmune | Transfusion reactions, hemolytic disease of the fetus and newborn | Trapping, phagocytosis, complement | Intravascular | Neonatal DAT | Halt transfusion, supportive |
| Autoimmune hemolytic anemia | Warm or cold autoimmune hemolytic anemia | Trapping, phagocytosis, complement | Extravascular or intravascular | DAT | Steroids, avoidance, treatment of other disease |
| Drug induced | Drug-induced thrombotic microangiopathy, drug-induced immune hemolytic anemia, oxidative hemolysis | Direct, toxin, phagocytosis, fragmentation | Extravascular or intravascular | Schistocytes, DAT, Heinz bodies | Drug withdrawal |
| Envenomation | Insects, cobra, brown recluse spider | Direct | Extravascular or intravascular | — | — |
| Enzymopathy | G6PD or pyruvate kinase deficiencies | Oxidative lysis | Intravascular | Enzyme activity measurement | Avoidance, splenectomy |
| Hemoglobinopathy | Sickle cell disease, thalassemias, hemoglobin defects | Trapping | Extravascular | Hemoglobin electrophoresis | Disease-specific treatment |
| Infection | Malaria, *Babesia, Bartonella, Clostridia, Rickettsia, Haemophilus influenzae,* human immunodeficiency virus | Direct, toxin, phagocytosis, fragmentation | Extravascular or intravascular | Pathogen-specific testing | Infection-specific treatment |
| Membranopathy | Hereditary spherocytosis, hereditary elliptocytosis, paroxysmal nocturnal hemoglobinuria | Trapping | Extravascular | Osmotic fragility test, eosin-5-maleimide binding | Splenectomy, eculizumab (Soliris; paroxysmal nocturnal hemoglobinuria) |
| Microangiopathic hemolytic anemia/thrombotic microangiopathy | Thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, disseminated intravascular coagulation, HELLP syndrome, drug-induced thrombotic microangiopathy | Fragmentation | Intravascular | Peripheral blood smear (showing schistocytes), assessment of ADAMTS13 activity, liver enzyme tests, coagulation study, culture | Plasma exchange, steroids, delivery, drug withdrawal |
| Osmotic | Freshwater drowning | Osmotic lysis | Intravascular | — | — |
| Systemic disease | Malignant hypertension, systemic lupus erythematosus, scleroderma, liver disease, vasculitides, hypersplenism | Trapping, fragmentation | Extravascular or intravascular | Disease-specific testing | Disease-specific treatment |
| Trauma | Endovascular devices, aortic stenosis, extracorporeal membrane oxygenation, arteriovenous malformation, march hemoglobinuria, burns | Fragmentation, direct | Intravascular | — | Stop trauma |

DAT = direct antiglobulin test; G6PD = glucose-6-phosphate dehydrogenase; HELLP = hemolysis, elevated liver enzymes, and low platelet count.

When hemolysis is suspected, the history should include known medical diagnoses, medications, personal or family history of hemolytic anemia, and a complete review of systems. The physical examination should focus on identifying associated conditions, such as infections or malignancies.




Lab parameters and cause:

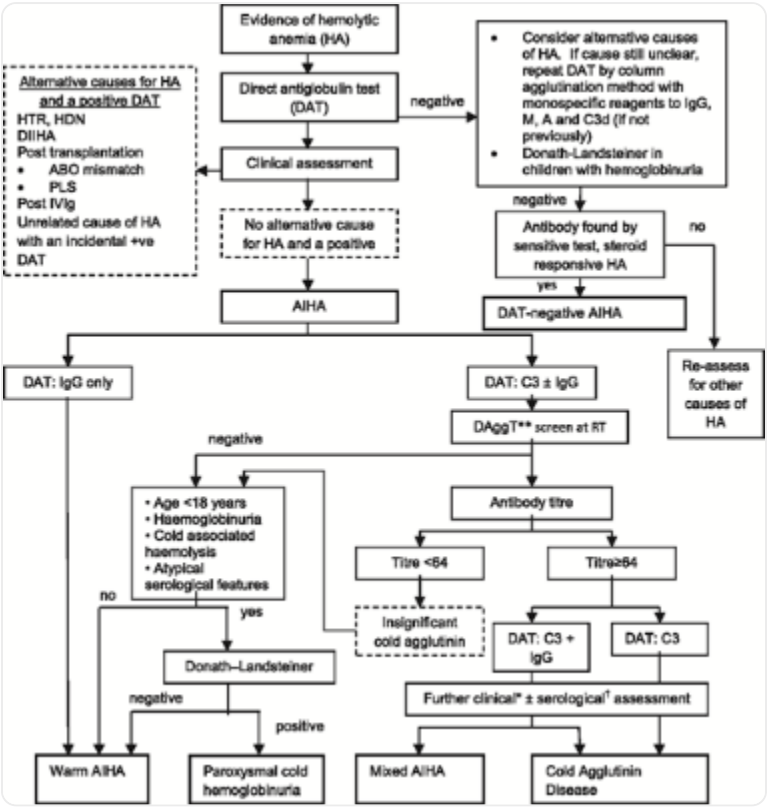
## Initial Laboratory Tests for Hemolysis

| Test | Finding in hemolysis | Cause |
|---|---|---|
| Haptoglobin | Decreased | Binds free hemoglobin |
| Lactate dehydrogenase | Elevated | Released from lysis of red blood cells |
| Peripheral blood smear | Abnormal red blood cells | Based on cause of anemia |
| Reticulocyte count | Increased | Marrow response to anemia |
| Unconjugated bilirubin | Increased | Increased hemo-globin breakdown |
| Urinalysis | Urobilinogen, positive for blood | Free hemoglobin and its metabolites |

## Autoimmune Hemolytic Anaemia's

- The incidence of AIHA in pregnancy is limited and is estimated to be around 1 in 50,000 pregnancies. AIHA may be primary (due to pregnancy per se, which is very rare) or secondary to autoimmune diseases like Systemic Lupus Erythematosus, malignancies, infections or immunodeficiency.[26]
- AIHA is characterized by the development of red cell autoantibodies and the destruction of erythrocytes. It is classified as warm (65%), cold (30%), and mixed (5%) type based on direct antiglobulin test (DAT).

- In warm AIHA, the antibodies are normally IgG type, which readily cross the placenta and up to 50% are accompanied by complement-mediated positive DAT. Conversely, more than 90% of the cold antibodies are IgM, which is a good activator of the complement system but without the ability to cross the placental barrier.[27]




## Macrocytic anemia

Megaloblastic anemia (vitamin B12 deficiency folic acid or both) is the most frequent kind of anemia after IDA and ACD. The diagnosis is suspected when MCV is elevated, and is confirmed by measuring serum vitamin B12 and serum and erythrocyte folate.[9]

The table below summarizes the investigations and their interpretations in each type of anemia.

**Comparison of anaemia types — part 1 of 2**

| Parameter | Iron Deficiency Anaemia | Megaloblastic Anaemia | Microangiopathic Haemolytic Anaemia (MAHA) | Aplastic Anaemia |
|---|---|---|---|---|
| **Haemoglobin** | ↓ | ↓ | ↓ | ↓ |
| **Haematocrit** | ↓ | ↓ | ↓ | ↓ |
| **RBC count** | ↓ | ↓ | ↓ | ↓ |
| **MCV** | ↓ | ↑ | Normal | Normal to ↑ |
| **MCHC** | ↓ | Normal | Normal | Normal |
| **RDW** | ↑ | ↑ | ↑ | Usually normal |
| **Reticulocyte count** | ↓ to normal | ↓ to normal | Markedly ↑ | ↓ |
| **Serum ferritin** | ↓ | Normal or ↑ | Normal | Normal or ↑ |
| **Serum transferrin** | ↑ | Normal | Normal | Normal |
| **Transferrin saturation** | ↓ | Normal | Normal | Normal |
| **TIBC** | ↑ | Normal | Normal | Normal |

| **Serum iron** | **↓** | **Normal** | **Normal to ↑** | **Normal** |
|---|---|---|---|---|
| **Serum vitamin B12** | Normal | ↓ (B12 deficiency) | Normal | Normal |
| **Serum folate** | Normal | ↓ (folate deficiency) | Normal | Normal |
| **Peripheral smear morphology** | Microcytic, hypochromic RBCs, anisopoikilocytosis, pencil cells | Macro-ovalocytes, hypersegmented neutrophils | Schistocytes, fragmented RBCs, helmet cells | Normocytic or macrocytic RBCs, paucity of cells |
| **WBC count** | Normal | ↓ or normal | Normal | ↓ |
| **Platelet count** | Normal or ↑ | ↓ or normal | ↓ (often severe) | ↓ |
| **LDH** | Normal | ↑ | Markedly ↑ | Normal |
| **Indirect bilirubin** | Normal | ↑ | ↑ | Normal |
| **Haptoglobin** | Normal | ↓ | Markedly ↓ | Normal |
| **Haemoglobin electrophoresis** | Normal | Normal | Normal | Normal |
| Modified from : Al-Khaffaf A, Frattini F, Gaiardoni R, Mindiola E, Sissa C, Franchini M. Diagnosis of anemia in pregnancy. J Lab Precis Med 2020;5:9 | | | | |

| | | | | |
|---|---|---|---|---|
| doi: 10.21037/jlpm.2019.12.03 | | | | |

**Comparison of anaemia types — part 2 of 2**

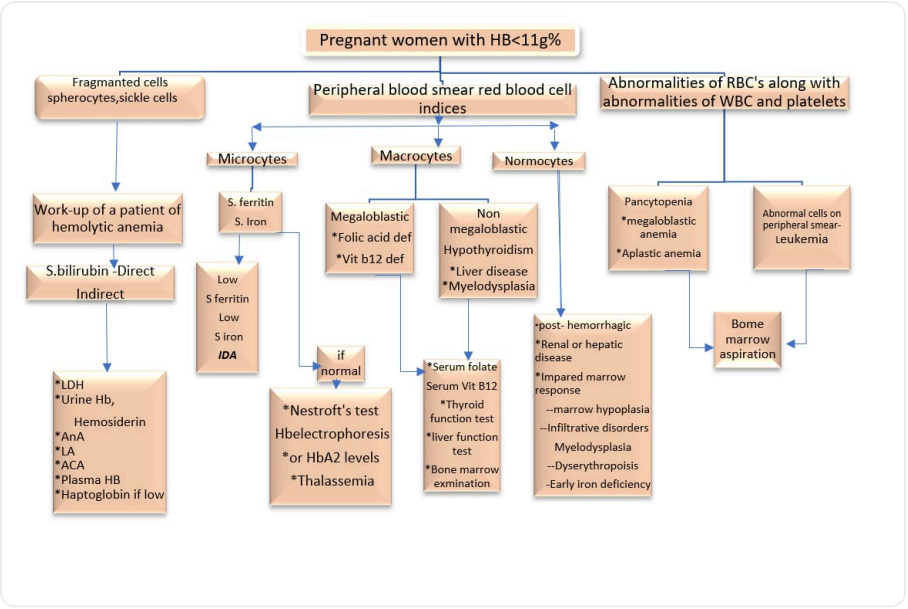
| Parameter | Sickle Cell Anaemia | Thalassaemia | Anaemia of Chronic Disease (ACD) |
|---|---|---|---|
| **Haemoglobin** | **Moderate to severe ↓** | **Moderate to severe ↓** | **↓** |
| **Haematocrit** | ↓ | ↓ | ↓ |
| **RBC count** | ↓ | Normal to ↑ (trait); ↓ (major) | ↓ |
| **MCV** | Normal to ↓ | Markedly ↓ | Normal to ↓ |
| **MCHC** | Normal to ↓ | Normal to ↓ | Normal |
| **RDW** | ↑ | Normal or slightly ↑ | Normal or mildly ↑ |
| **Reticulocyte count** | ↑ | ↑ | ↓ to normal |
| **Serum ferritin** | ↑ | Normal or ↑ | Normal to ↑ |
| **Serum transferrin** | Normal | Normal | ↓ |
| **Transferrin saturation** | Normal | Normal to ↑ | ↓ |

| TIBC | Normal | Normal | ↓ |
|---|---|---|---|
| **Serum iron** | Normal | Normal to ↑ | ↓ |
| **Serum vitamin B12** | Normal | Normal | Normal |
| **Serum folate** | Normal | Normal | Normal |
| **Peripheral smear morphology** | Sickled cells, target cells, Howell–Jolly bodies, polychromasia | Marked microcytosis, hypochromia, target cells, basophilic stippling | Normocytic or mildly microcytic RBCs |
| **WBC count** | Normal or ↑ | Normal | Normal |
| **Platelet count** | Normal or ↑ | Normal | Normal or ↑ |
| **LDH** | ↑ | Mildly ↑ | Normal |
| **Indirect bilirubin** | ↑ | Mildly ↑ | Normal |
| **Haptoglobin** | ↓ | Mildly ↓ | Normal |
| **Haemoglobin electrophoresis** | HbS present (± HbF) | Diagnostic pattern (↑$HbA_2$, ↑HbF depending on type) | Normal |
| Modified from : Al-Khaffaf A, Frattini F, Gaiardoni R, Mindiola E, Sissa C, Franchini M. Diagnosis of anemia in pregnancy. J Lab | | | |

**Precis Med 2020;5:9 doi: 10.21037/jlpm.2019.12.03**

## Conclusion

Multidisciplinary approach involving Obstetricians, Haematologists and other specialists is key to successful and timely diagnosis.

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CHAPTER 02

# Prevention of Anemia in Pregnancy

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IN THIS CHAPTER

Why Prevention Matters | Life-Cycle Approach | Antenatal Strategies | Nutrition & IFA | Government Initiatives | Implementation

## Introduction

Anaemia in pregnancy remains one of the most common nutritional disorders worldwide and is a major cause of maternal and perinatal morbidity, particularly in low- and middle-income countries. The **World Health Organization (WHO)** defines anaemia during pregnancy as a haemoglobin concentration below **11.0 g/dL**, although physiological haemodilution in the second trimester should be considered during clinical interpretation (1). Iron deficiency accounts for nearly two-thirds of cases and is the leading nutritional cause of anaemia in pregnancy.

India continues to bear a disproportionately high burden of maternal anaemia. According to the **National Family Health Survey-5 (NFHS-5), 52.2% of pregnant women** aged 15–49 years are anaemic (2). Maternal anaemia is associated with increased risks of postpartum haemorrhage, maternal infections, preterm birth, fetal growth

restriction, low birth weight, and adverse neonatal outcomes (4,5). Despite effective preventive interventions, many women enter pregnancy with depleted iron stores because of poor nutrition, adolescent pregnancy, closely spaced births, and chronic infections.

Prevention is therefore more effective than treatment alone. A **life-course approach**, beginning in adolescence and continuing through the preconception, antenatal, intrapartum, and postpartum periods, is essential for reducing the burden of maternal anaemia. This chapter reviews evidence-based preventive strategies relevant to Indian obstetric practice, integrating current recommendations from the **WHO**, **Government of India**, and **FOGSI**.

## Why Prevention Matters

Pregnancy increases iron requirements by approximately 1000 mg to support maternal erythropoiesis, placental growth, fetal development, and blood loss during delivery (6). As dietary intake alone cannot meet this demand, women with inadequate iron stores are at high risk of iron deficiency anaemia. In India, poor dietary iron intake, low iron bioavailability, adolescent pregnancy, repeated pregnancies, short interpregnancy intervals, and chronic infections contribute to depleted iron reserves. Effective prevention therefore requires a life-course approach integrating nutritional improvement, iron supplementation, infection control, reproductive health, and health education rather than antenatal supplementation alone (3,7,8).

## Clinical Pearl

**The most effective strategy for preventing anaemia in pregnancy is to ensure that women enter pregnancy with adequate iron stores rather than attempting to correct severe anaemia during late gestation.**

## Prevention Across the Reproductive Life Cycle

Maternal anaemia prevention requires a **continuum-of-care approach**, with interventions before conception, throughout pregnancy, during childbirth, and postpartum. This life-course strategy integrates nutrition, reproductive health, and primary healthcare in line with the **Anaemia Mukt Bharat** programme.

## 1. Adolescence: The First Window of Opportunity

Adolescence is a critical window for preventing maternal anaemia, as rapid growth, menstruation, and inadequate nutrition often deplete iron stores before pregnancy. Weekly Iron and Folic Acid Supplementation (WIFS), nutrition education, deworming, menstrual hygiene promotion, and delayed marriage and first pregnancy help improve iron reserves and reduce anaemia (9-12).

## 2. Preconception Care: Optimising Maternal Iron Stores

Preconception care is fundamental to preventing maternal anaemia, as many women enter pregnancy with depleted iron stores. Women planning pregnancy should undergo haemoglobin estimation, nutritional assessment, and evaluation for iron, folate, vitamin B12deficien cy, or haemoglobinopathies when indicated (3,6,8). Anaemia should be corrected before conception, particularly in women with previous severe anaemia or chronic medical disorders. Counselling should emphasise a balanced iron-rich diet, folic acid supplementation, healthy lifestyle, and an interpregnancy interval of at least 24 months to restore iron stores and reduce recurrent anaemia (3,6,8,17).

## 3. Prevention During Early Pregnancy

The first antenatal visit is crucial for preventing maternal anaemia. Early registration (<12 weeks) enables timely haemoglobin estimation, risk assessment, nutritional counselling, and initiation of iron–folic acid supplementation (3,7). Evaluation should include dietary history, obstetric and medical risk factors, and previous anaemia or postpartum haemorrhage. Women with moderate or severe anaemia require evaluation for the underlying cause. Counselling should reinforce adherence to supplementation, an iron-rich diet, and regular antenatal follow-up.

## 4. Antenatal Preventive Strategies

### Nutritional Interventions

Dietary diversification remains the foundation of anaemia prevention. Pregnant women should consume diets that provide adequate energy, protein, iron, folate, vitamin B12, and other micronutrients. Iron-rich foods include lean meat, fish, poultry, eggs, legumes, pulses, green leafy vegetables, millets, soybean, jaggery, nuts, and seeds (3,7,15).

The bioavailability of dietary iron is equally important. Vitamin C-rich foods such as amla, guava, citrus fruits, tomatoes, and lemon enhance absorption of non-haem iron, whereas tea, coffee, and excessive calcium consumed with meals reduce iron absorption (3,7,15). Traditional food preparation methods—including germination, fermentation, sprouting, and soaking—reduce phytate content and improve iron bioavailability.

Nutritional counselling should therefore focus not only on **what to eat**, but also on **how to maximise iron absorption**.

## Universal Iron–Folic Acid Supplementation

Universal iron–folic acid supplementation remains the most effective intervention for preventing iron deficiency during pregnancy because dietary intake alone cannot meet the increased physiological demand (3,6,7).

The Government of India recommends that every pregnant woman receive **60 mg elemental iron and 500 µg folic acid daily for at least 180 days during pregnancy, followed by another 180 days during the postpartum period** (3,7). Women with diagnosed anaemia require therapeutic iron according to severity and gestational age.

Poor adherence remains one of the greatest barriers to programme success. Gastrointestinal adverse effects, misconceptions regarding iron tablets, forgetfulness, and irregular drug supply frequently reduce compliance. Effective counselling, reassurance regarding transient side effects, advice to take tablets after meals or at bedtime, and involvement of family members significantly improve adherence (3,7,8).

Intravenous iron should be considered when oral iron is poorly tolerated, ineffective, or when rapid correction of iron deficiency is required, in accordance with national guidelines (6-8).

## Practice Point

Every antenatal visit should assess **adherence to iron supplementation**, not merely prescribe additional tablets.

## Food Fortification

Food fortification is a complementary public health strategy that improves population iron intake without requiring behavioural change. In India, the **Food Safety and Standards Authority of India (FSSAI)**

recommends fortification of staple foods including rice, wheat flour, edible oil, milk, and double-fortified salt (7,18). Fortified rice distributed through the Public Distribution System, Integrated Child Development Services, and school feeding programmes contributes to improved iron intake among vulnerable populations.

Although fortification cannot replace therapeutic supplementation during pregnancy, it helps improve iron stores before conception and reduces the overall burden of micronutrient deficiency.

## Prevention of Infection-Related Anaemia

Control of infections is an integral component of anaemia prevention. **Hookworm infestation** causes chronic blood loss, **malaria** leads to haemolysis and impaired erythropoiesis, while t**uberculosi**s and **HIV** contribute to anaemia of chronic disease (3,7).

A **single dose of albendazole (400 mg) after the first trimester** is recommended in **hookworm-endemic areas** (3,7). Prevention of malaria through insecticide-treated bed nets, vector control, early diagnosis, and prompt treatment remains essential in endemic regions. Screening and treatment of **urinary tract infections**, **tuberculosis, and HIV** should be integrated into routine antenatal care. Improvements in sanitation, **safe drinking water, and hygiene practices** further reduce recurrent infections and enhance nutritional status.(3,7)

## Monitoring During Pregnancy

Prevention does not end with initiation of iron supplementation. Haemoglobin should be reassessed during pregnancy according to national recommendations to evaluate response and identify women requiring further investigation or referral (3,7,8). Lack of improvement despite adequate compliance should prompt evaluation for vitamin B12

or folate deficiency, haemoglobinopathies, chronic kidney disease, inflammatory disorders, or ongoing blood loss (6,8).

Timely referral of women with severe anaemia to higher centres allows appropriate management before labour and reduces maternal and neonatal complications (4,7,8).

## Clinical Pearl

**Failure of haemoglobin to improve despite good adherence to oral iron should prompt evaluation for alternative causes of anaemia rather than simply increasing the iron dose.**

## 5. Prevention During Labour and the Postpartum Period

Preventive strategies should continue during childbirth and the puerperium. Women with anaemia are at increased risk of postpartum haemorrhage (PPH), heart failure, puerperal sepsis, delayed wound healing, and poor lactation (4,5). Therefore, intrapartum care should focus on minimising blood loss through **active management of the third stage of labour (AMTSL)**, prompt recognition and treatment of PPH, avoidance of unnecessary episiotomy, and judicious use of blood transfusion when clinically indicated (8).

Postpartum care offers an important opportunity to replenish maternal iron stores before subsequent pregnancies. The Government of India recommends continuation of **60 mg elemental iron with 500 µg folic acid daily for 180 days after delivery**, irrespective of the mode of birth (7). Nutritional counselling should continue during lactation, emphasising diets rich in iron, protein, folate, vitamin B12, and vitamin C. Effective postpartum contraception and an interpregnancy interval of at least **24 months** reduce recurrence of maternal anaemia and improve subsequent pregnancy outcomes (13,17).

## 6. Government of India Initiatives

India has adopted a comprehensive **life-cycle approach** to anaemia prevention through integrated national programmes targeting nutrition, maternal health, and reproductive care.

## National Iron Plus Initiative (NIPI)

The **National Iron Plus Initiative (NIPI)** provides prophylactic iron–folic acid (IFA) supplementation across the life cycle. For pregnant women, it recommends **daily IFA supplementation, deworming after the first trimester, nutrition counselling, periodic haemoglobin estimation, and referral of women with moderate or severe anaemia**. The programme also emphasises uninterrupted IFA supply, healthcare worker training, and community participation to improve adherence (7).

## Anaemia Mukt Bharat (AMB)

Launched in 2018, **Anaemia Mukt Bharat (AMB)** strengthens NIPI through the **6×6×6 strategy**, aiming to reduce anaemia prevalence by **3% annually**. Key interventions include **IFA supplementation, deworming, behaviour change communication, point-of-care haemoglobin testing, food fortification, and management of non-nutritional causes such as malaria and haemoglobinopathies**. The programme also focuses on digital monitoring, supply-chain strengthening, capacity building, and intersectoral convergence (7,14).

## POSHAN Abhiyaan

**POSHAN Abhiyaan** promotes maternal nutrition through dietary diversification, nutrition education, growth monitoring, and community mobilisation, complementing anaemia prevention efforts (15).

## Pradhan Mantri Surakshit Matritva Abhiyan (PMSMA)

**PMSMA** provides comprehensive antenatal care on the **9th of every month**, facilitating early detection of anaemia, risk stratification, counselling, and timely referral of high-risk women (16).

## 7. Implementation Challenges and Practical Solutions

Despite comprehensive national programmes, maternal anaemia remains highly prevalent because of poor adherence to iron supplementation, delayed antenatal registration, inadequate dietary intake, interrupted drug supplies, and failure to identify non-iron deficiency anaemia. Improving outcomes requires uninterrupted iron availability, effective counselling, point-of-care haemoglobin testing, timely referral of refractory cases, and sustained community engagement through behaviour change and nutrition education (3,7,8).

## Clinical Pearls

- Prevention of maternal anaemia begins **before conception**, not at the first antenatal visit.
- Early registration (**before 12 weeks**) is the single most important opportunity for preventive intervention.
- Every antenatal visit should assess **adherence to iron supplementation**, not merely prescribe additional tablets.
- Failure to respond to oral iron should prompt evaluation for alternative causes of anaemia.
- Continue iron supplementation for **180 days after delivery** to restore maternal iron stores.

**Table 1. Evidence-based Preventive Strategies Across the Reproductive Life Cycle**

| Stage | Priority preventive interventions |
|---|---|
| **Adolescence** | **Weekly iron–folic acid supplementation, dietary improvement, deworming, menstrual hygiene, delayed marriage** |
| **Preconception** | Haemoglobin screening, correction of nutritional deficiencies, nutrition counselling, family planning, birth spacing |
| **Early pregnancy** | Early antenatal registration, haemoglobin estimation, risk assessment, dietary counselling, initiation of IFA |
| **Antenatal care** | Daily IFA supplementation, dietary diversification, food fortification, deworming, infection prevention, repeat Hb monitoring |
| **Labour** | Active management of third stage of labour, prevention of postpartum haemorrhage, appropriate referral |
| **Postpartum** | Continue IFA for 180 days, nutritional rehabilitation, breastfeeding support, contraception, adequate birth spacing |

## Conclusion

Anaemia in pregnancy remains a major public health challenge in India but is largely preventable. A life-course approach, beginning before conception and continuing through pregnancy and the postpartum period, is essential. Universal iron–folic acid supplementation, nutritional optimisation, infection control, early antenatal care, and postpartum iron replacement form the cornerstone of prevention. National programmes provide a strong policy framework, but their success depends on effective implementation, uninterrupted supply,

and sustained behaviour change. Integrating clinical care with public health strategies is crucial to reducing maternal anaemia and improving pregnancy outcomes.

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CHAPTER 03

# Haemoglobinopathies: Diagnosis & Preconceptional Counselling

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IN THIS CHAPTER

Diagnosis | Iron Deficiency vs Trait | Diagnosis in Pregnancy | Special Considerations | Preconception Counselling | Summary

## Introduction

Hemoglobinopathies comprise a heterogeneous group of inherited disorders resulting from quantitative defects in globin chain synthesis (thalassemias) or qualitative abnormalities caused by structural variants of haemoglobin, such as sickle haemoglobin (HbS), haemoglobin C (HbC), haemoglobin D (HbD), and haemoglobin E (HbE). The ideal time for diagnosis is before conception, allowing complete evaluation, partner testing, reproductive counselling, and informed decision-making.

## Diagnosis

Diagnosis follows a stepwise approach beginning with simple haematological investigations and progressing to specialised molecular techniques. (1) A detailed history remains fundamental. Important points include:

- Family history of anaemia, transfusion dependence, splenectomy or unexplained childhood deaths
- Previous diagnosis of anaemia unresponsive to iron
- Ethnic origin from high-prevalence populations
- Consanguinity
- Previous pregnancy affected by hydrops fetalis or hemoglobinopathy
- History of recurrent blood transfusions
- Personal history of jaundice, gallstones or splenomegaly

On physical examination, patients with hemoglobinopathies may show pallor, mild enlargement of the spleen, frontal bossing in more severe disease, maxillary hypertrophy, skeletal deformities, and growth retardation. In contrast, carriers are typically asymptomatic and do not display these clinical features.

Complete blood count (CBC) is the first-line laboratory investigation (Table 1). (2) It is simple, widely available, even in low-resource settings, and provides baseline haemoglobin and haematocrit values that are essential for further evaluation.

**Table 1. CBC Findings in Common Hemoglobinopathies** (1)

Comparison of anaemia types — part 1 of 2

| Parameter | β-thalassemia trait | α-thalassemia trait | Iron deficiency | Sickle trait |
|---|---|---|---|---|
| **Haemoglobin (Hb)** | **Mildly reduced** | **Normal/mildly low** | **Reduced** | **Normal** |
| **RBC count** | Increased | Increased | Low | Normal |

| Mean corpuscular Volume (MCV) | <80 fL | <80 fL | <80 fL | Normal |
|---|---|---|---|---|
| **Mean Corpuscular Haemoglobin (MCH)** | <27 pg | <27 pg | Low | Normal |
| **Red Cell Distribution Width (RDW)** | Normal | Normal | Increased | Normal |
| **Reticulocytes** | Normal | Normal | Low | Normal |

**Comparison of anaemia types — part 2 of 2**

| Parameter | Sickle disease |
|---|---|
| **Haemoglobin (Hb)** | **Markedly reduced** |
| **RBC count** | Variable |
| **Mean corpuscular Volume (MCV)** | Normal/slightly increased |
| **Mean Corpuscular Haemoglobin (MCH)** | Normal |
| **Red Cell Distribution Width (RDW)** | Increased |
| **Reticulocytes** | Increased |

A disproportionately low MCV with a normal or elevated RBC count strongly suggests thalassemia trait rather than iron-deficiency anaemia. An MCV <80 fL indicates microcytosis and warrants evaluation for iron deficiency, thalassemia syndromes, haemoglobin E trait, and anaemia of chronic disease. An MCH <27 pg is highly sensitive for identifying hemoglobinopathy carriers and, together with MCV, remains the cornerstone of initial screening recommended by international guidelines. (3) Before interpreting haemoglobin fractions, iron deficiency should be excluded by measuring serum ferritin, serum iron, total iron-binding capacity, and transferrin saturation (Table 2). Correction of iron deficiency before repeat $HbA_2$ estimation improves diagnostic accuracy, as iron deficiency may falsely lower $HbA_2$ levels and mask β-thalassemia trait.

**Table 2. Differentiating Iron Deficiency from Thalassemia Trait (4)**

| Feature | Iron deficiency | Thalassemia trait |
|---|---|---|
| **RBC count** | Low | Normal/high |
| **MCV** | Low | Very low |
| **RDW** | High | Usually normal |
| **Ferritin** | Low | Normal |
| **$HbA_2$** | Normal/low | Increased (β-thalassemia) |
| **Response to iron** | Present | Absent |

Confirmation of hemoglobinopathies is performed by haemoglobin analysis, which can be carried out using protein chemistry techniques, most commonly capillary electrophoresis or high-performance liquid chromatography (HPLC) (Table 3). Less frequently, methods such as isoelectric focusing or traditional haemoglobin electrophoresis are employed. HPLC is the gold-standard investigation for diagnosis, as it separates haemoglobin fractions based on ionic interactions and provides accurate quantification of HbA, $HbA_2$, HbF, and variant haemoglobins. It offers several advantages: it is automated, rapid, highly reproducible, and quantitative, and it simultaneously detects multiple variants, making it particularly suitable for antenatal screening. (1)

**Table 3: Characteristic HPLC Patterns** (1)

| Disorder | Typical HPLC Findings | Disorder |
|---|---|---|
| **β-thalassemia trait** | $HbA_2$ ≥3.5%; HbF mildly increased | β-thalassemia trait |
| **β-thalassemia major** | HbF markedly elevated; HbA absent or markedly reduced | β-thalassemia major |
| **HbE trait** | HbE/$A_2$ peak 25–35% | HbE trait |
| **HbE disease** | HbE >85% | HbE disease |
| **HbS trait** | HbS 35–45% | HbS trait |
| **Sickle cell disease** | HbS >80%, absent HbA | Sickle cell disease |
| **HbSC disease** | HbS and HbC are approximately equal | HbSC disease |
| **HbD Punjab** | Prominent HbD peak | HbD Punjab |

Overall, first-line haematological and protein chemistry tests can detect most common haemoglobinopathies, but the diagnosis of both alpha and beta variants remains presumptive without DNA analysis.(5) Conventional screening has several limitations: some rare cases of beta thalassemia trait show normal $HbA_2$ and HbF levels and may be missed; alpha thalassemia trait involving two gene deletions cannot be directly identified and requires DNA confirmation; silent carriers with a single alpha gene deletion often have normal CBC and protein chemistry

results yet can still transmit HbH disease if their partner carries an alpha$^0$ deletion; and non-deletional variants such as Constant Spring carrier state may present with normal indices but still contribute to risk when combined with other alpha gene defects.(1)

DNA-based confirmatory testing is indicated when first-line screening results are abnormal or inconclusive, when patients with normal results belong to high-risk groups based on family history or epidemiology, or when rapid diagnosis is required in advanced pregnancy. Identifying the exact genetic variant also helps predict the clinical phenotype and guide counselling. Suspected beta thalassemia is evaluated by sequencing, with multiplex ligation-dependent probe amplification (MLPA) used to detect rare deletions or the hereditary persistence of fetal haemoglobin when sequencing is nondiagnostic. Alpha thalassemia is evaluated using gap-PCR or MLPA to detect deletions or duplications. Laboratories use targeted, variant-specific assays alongside automated Sanger sequencing to ensure accurate diagnosis.(6)

## Diagnosis in pregnancy

Pregnancy offers an important opportunity for identifying previously undiagnosed carriers. Screening should ideally be performed at the first antenatal visit, preferably before 10 weeks' gestation, to allow adequate time for partner testing and prenatal diagnosis, if required.

Universal screening is recommended in regions with a high prevalence of hemoglobinopathies or ethnically diverse populations.(7) Targeted screening should be offered to women with:

- Family history of hemoglobinopathy or unexplained anaemia.
- Previous child with thalassemia or sickle cell disease.
- Persistent microcytosis (MCV <80 fL) or hypochromia (MCH <27 pg).

- High-risk ethnic ancestry (Mediterranean, Middle Eastern, African, South Asian, Southeast Asian).
- Consanguineous marriage.

Partner testing is the critical next step once a woman is identified as a carrier, as fetal risk depends on the combined parental genotype rather than maternal status alone.(8). The stepwise antenatal screening algorithm is mentioned in Table 4.

**Table 4: Stepwise Antenatal Screening Algorithm** (7)

**1. First antenatal visit**

- Perform CBC with RBC indices in all women.

1. **Microcytosis or hypochromia detected (MCV <80 fL and/or MCH <27 pg)**

- Measure serum ferritin to exclude iron deficiency.
- Simultaneously perform HPLC or capillary electrophoresis if available.

1. **Abnormal haemoglobin fraction or persistent microcytosis with normal ferritin**

- Suspect thalassemia or structural haemoglobin variant.

1. **Confirm diagnosis**

- Use HPLC/capillary electrophoresis and molecular testing when indicated.

1. **Initiate partner testing immediately** if the woman is identified as a carrier.

1. **If both partners are carriers of clinically significant variants**

- Refer for genetic counselling.
- Discuss prenatal diagnostic options (chorionic villus sampling from 10–13 weeks or amniocentesis after 15 weeks).
- Offer reproductive counselling regarding fetal risk and available options.

## Special Considerations in Pregnancy

- Physiological hemodilution lowers haemoglobin concentration but does not significantly alter $HbA_2$ or HbF, allowing reliable interpretation of HPLC.

- Iron deficiency is common in pregnancy and may falsely reduce $HbA_2$, potentially masking β-thalassemia trait. Ferritin assessment and correction of iron deficiency are therefore essential before excluding carrier status.
- A recent blood transfusion can invalidate haemoglobin fraction analysis for up to 3 months; molecular testing should be considered in such cases.
- Women with unexplained persistent microcytosis despite normal iron stores and normal HPLC should undergo DNA analysis for α-thalassemia, particularly in high-prevalence populations.

## Preconception Counselling in Hemoglobinopathies

Preconception counselling aims to optimise maternal health, reduce pregnancy-related complications, and provide appropriate reproductive options before conception. Ideally undertaken several months before pregnancy, it allows time for clinical assessment, partner testing, genetic evaluation, and optimisation of medical therapy. Counselling should include confirmation of the diagnosis and genotype, assessment of disease severity and organ function, review of medications, immunisation status, and folic acid supplementation.(9)

Genetic counselling should be offered to all carriers and affected individuals to facilitate informed reproductive decision-making. It should explain inheritance patterns, recurrence risks, disease severity, reproductive options, and prenatal diagnostic techniques. Counselling should be non-directive, individualised, and culturally sensitive, with multidisciplinary input whenever feasible.(10)

Most clinically significant hemoglobinopathies follow an autosomal recessive mode of inheritance. When both parents are carriers of the same pathogenic variant (Table 5):(11)

- 25% chance of an affected child.
- 50% chance of a carrier child.

- 25% chance of an unaffected non-carrier child.

This recurrence risk remains constant for every pregnancy.

**Table 5: Genetic Risk According to Parental Genotype** (11)

| Maternal Genotype | Paternal Genotype | Risk to Offspring | Clinical Significance / Counselling |
|---|---|---|---|
| Normal | Normal | 100% unaffected | No increased genetic risk. Routine antenatal care. |
| Carrier (β-thalassemia trait) | Normal | 50% carrier, 50% unaffected; 0% affected | No risk of β-thalassemia major. Inform offspring of possible carrier status in adulthood. |
| Carrier (α-thalassemia trait; single gene deletion) | Normal | Approximately 50% silent carrier; 0% severe disease | Usually, there is no clinically significant fetal disease. |
| β-thalassemia trait | β-thalassemia trait | 25% β-thalassemia major/intermedia, 50% carrier, 25% unaffected | High risk of transfusion-dependent thalassemia. Offer prenatal diagnosis or PGT-M. |
| HbS trait (AS) | HbS trait (AS) | 25% sickle cell disease (SS), 50% sickle trait, 25% normal (AA) | Significant risk of severe sickle cell disease. Prenatal diagnosis recommended. |
| HbC trait (AC) | HbC trait (AC) | 25% HbCC disease, 50% HbC trait, 25% normal | HbCC usually causes mild chronic haemolytic anaemia. Discuss prognosis. |

| HbD trait | HbD trait | 25% HbDD disease, 50% carrier, 25% unaffected | HbDD disease is generally mild but requires counselling. |
|---|---|---|---|
| HbE trait | HbE trait | 25% HbEE disease, 50% carrier, 25% unaffected | HbEE disease is usually mild with microcytosis; reassurance is appropriate. |
| HbE trait | β-thalassemia trait | Up to 25% HbE/β-thalassemia, 25% HbE trait, 25% β-thalassemia trait, 25% unaffected | HbE/β-thalassemia has highly variable severity, ranging from mild anaemia to transfusion dependence. Prenatal diagnosis is recommended. |
| HbS trait | β-thalassemia trait | Up to 25% HbS/β-thalassemia, 25% HbS trait, 25% β-thalassemia trait, 25% unaffected | HbS/β-thalassemia may resemble sickle cell disease and can be severe, particularly with $\beta^0$ mutations. |
| HbS trait | HbC trait | 25% HbSC disease, 25% HbS trait, 25% HbC trait, 25% unaffected | HbSC disease generally has a milder phenotype than HbSS but carries significant maternal and fetal risks during pregnancy. |
| HbS trait | HbD trait | 25% HbSD disease, 25% HbS trait, 25% HbD trait, 25% unaffected | HbSD disease may present with clinically significant sickling and requires specialist follow-up. |

| | | | |
|---|---|---|---|
| **$\alpha^0$-thalassemia trait (--/αα)** | **$\alpha^0$-thalassemia trait (--/αα)** | **25% Hb Bart's hydrops fetalis (--/--), 50% α-thalassemia trait, 25% normal** | **Hb Bart syndrome is usually lethal without fetal intervention and is associated with severe maternal complications (mirror syndrome, preeclampsia, postpartum haemorrhage). Early prenatal diagnosis is mandatory.** |
| $\alpha^0$-thalassemia trait (–/αα) | $\alpha^+$-thalassemia trait (-α/αα) | 25% HbH disease (–/-α), 25% $\alpha^0$ trait, 25% $\alpha^+$ trait, 25% normal | HbH disease results in chronic hemolytic anaemia with variable transfusion requirements. Prenatal diagnosis should be discussed. |
| Sickle cell disease (SS) | Normal | 100% sickle cell trait (AS) | No HbSS offspring, but all children are carriers. |
| Sickle cell disease (SS) | HbS trait (AS) | 50% HbSS disease, 50% HbS trait | Extremely high risk of affected offspring. Early reproductive counselling and prenatal diagnosis are recommended. |

Baseline investigations should include a complete blood count with reticulocyte count, hemolytic markers (bilirubin, lactate dehydrogenase), renal and liver function tests, serum ferritin, urinalysis with urine protein quantification, blood group and red cell antibody screening, and screening for hepatitis B, hepatitis C, HIV, and other clinically indicated infections.(12) Cardiovascular assessment with electrocardiography and echocardiography should evaluate ventricular function and pulmonary hypertension, while renal, hepatic, pulmonary, neurological, ophthalmological, and musculoskeletal complications, including sickle nephropathy, chronic liver disease, acute chest syndrome, prior stroke, proliferative retinopathy, and avascular necrosis, should be assessed. (13) A detailed

transfusion history, alloantibody profile, frequency of vaso-occlusive crises, previous intensive care admissions, and current medications should also be reviewed to facilitate risk stratification, optimisation of therapy, individualised pregnancy planning, and multidisciplinary care.

Women with sickle cell disease should be counselled on measures to prevent vaso-occlusive crises and recognise early complications. They should maintain adequate hydration (approximately 2–3 L/day unless contraindicated), avoid dehydration, prolonged fasting, smoking, and extreme temperatures, and adhere to folic acid supplementation, vaccinations, and prophylactic medications. (14) They should seek immediate medical attention for fever (≥38°C), chest pain, breathlessness, neurological symptoms, or reduced fetal movements during pregnancy, as these may indicate serious complications requiring urgent evaluation.(14)

## General Principles Applicable to All Women with Hemoglobinopathies

1. Review all medications before conception and discontinue drugs with potential teratogenicity.
2. Prescribe folic acid supplementation (5 mg/day), which should be initiated before conception and continued throughout pregnancy to prevent neural tube defects and replenish folate stores is commonly recommended for women with chronic hemolytic disorders such as sickle cell disease and transfusion-dependent thalassemias. (13)
3. Avoid empirical iron supplementation unless iron deficiency has been confirmed biochemically, particularly in thalassemia syndromes where iron overload is common. (15)
4. Iron chelators should be discontinued before conception because of limited pregnancy safety data and potential teratogenicity, particularly during the first trimester. Women with transfusional iron overload should undergo preconception assessment with cardiac and liver MRI, and iron overload should be adequately

treated before pregnancy. In rare cases of significant cardiac iron overload, deferoxamine may be considered during the third trimester under specialist supervision.(16)

5. Review ACE inhibitors, ARBs, and other teratogenic medications in women with associated renal or cardiac disease. Women with chronic kidney disease should discontinue ARBs before conception, while ACE inhibitors should be stopped or switched to pregnancy-compatible alternatives when pregnancy is planned. Renal function and proteinuria should be monitored regularly throughout pregnancy.(17)
6. Assess vaccination status and optimise management of chronic comorbidities before pregnancy. SCD patients are hyposplenic and susceptible to infection, especially from encapsulated bacteria such as Haemophilus influenzae, Neisseria meningitidis, and Streptococcus pneumoniae. Pregnant women with sickle cell disease (SCD) should continue or begin taking penicillin prophylaxis due to their hyposplenism and elevated risk of pneumonia. Pneumococcal and influenza vaccinations should be administered if they have not been administered in the preceding five years.
7. Optimise cardiac, hepatic, endocrine, and renal function in women with severe hemoglobinopathies before conception.
8. Individualise transfusion strategies for women with transfusion-dependent thalassemia, HbE/β-thalassemia, HbH disease requiring transfusion, or sickle cell disease.
9. Hydroxyurea in Sickle cell disease: If women do become pregnant whilst taking hydroxycarbamide, it should be stopped as soon as possible owing to its teratogenic effects.(18) Women with severe disease should be evaluated for regular prophylactic red-cell transfusion or erythrocytapheresis as an alternative therapy. In women with severe sickle cell disease, the maternal risks of discontinuing hydroxyurea (increased vaso-occlusive crises, acute chest syndrome, and worsening anaemia) may outweigh the potential fetal risks, particularly when blood transfusion is not

feasible because of multiple alloantibodies or previous severe delayed hemolytic transfusion reactions. In such cases, continuation may be considered after multidisciplinary counselling, with detailed fetal ultrasound surveillance during pregnancy.

10. Optimal analgesics to use during pregnancy should be discussed, especially in women with SCD, as part of their pain management plan. Paracetamol and codeine-containing analgesics can be offered during pregnancy as first-line agents.

## Summary

Preconception screening and accurate diagnosis of hemoglobinopathies are essential to identify at-risk couples and facilitate informed reproductive decision-making. A stepwise diagnostic approach using complete blood count, red cell indices, haemoglobin fraction analysis (HPLC or capillary electrophoresis), and molecular testing accurately characterises carrier and disease states. Comprehensive preconception counselling should include partner testing, genetic risk assessment, baseline evaluation for disease severity and end-organ complications, optimisation of medical therapy, and discontinuation of potentially teratogenic medications.

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CHAPTER 04

# Iron Deficiency Anemia in Pregnancy

Dr Dhruva Halani

IN THIS CHAPTER

Pathophysiology | Diagnosis | WHO / ICMR / FOGSI | Maternal & Fetal Effects | Management | Postpartum Anemia | Monitoring

## INTRODUCTION

Iron deficiency anemia (IDA) is the most common medical disorder complicating pregnancy worldwide and remains a major public health challenge in India. Increased maternal iron requirements, inadequate dietary intake, poor absorption, repeated pregnancies, and infections contribute to its high prevalence. Untreated IDA is associated with maternal fatigue, reduced work capacity, cardiac failure in severe disease, postpartum hemorrhage intolerance, blood transfusion, preterm birth, low birth weight, and impaired neonatal iron stores. Early diagnosis, universal screening, dietary counselling, prophylactic iron supplementation, and appropriate use of oral or intravenous iron substantially improve maternal and fetal outcomes. This chapter summarizes current evidence and practical management for obstetric clinicians.

Pregnancy increases iron requirements because of expansion of maternal red cell mass, placental development, fetal growth, and blood loss at delivery [1,2]. Approximately 1000 mg of additional iron is required during pregnancy. Dietary intake alone is rarely sufficient; therefore prophylactic supplementation is recommended for all pregnant women in India [3,4].

Anemia affects a large proportion of pregnant women globally, with iron deficiency accounting for nearly half of all cases. India continues to bear one of the highest burdens. Socioeconomic disadvantage, nutritional deficiency, adolescent pregnancy, short interpregnancy interval, parasitic infestation, and poor compliance with supplementation are major contributors [5,6].

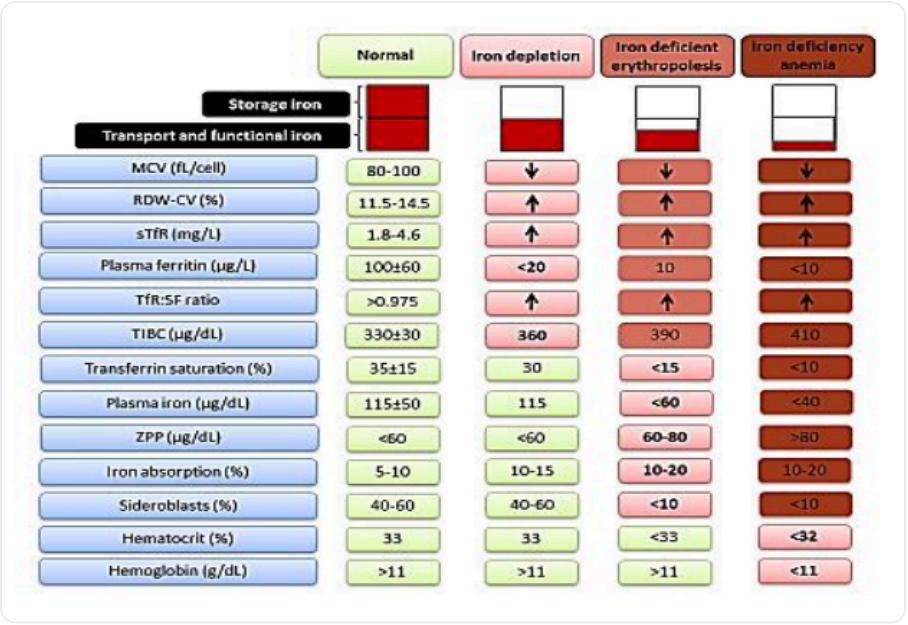


Figure 1: Various indicators of iron deficiency anemia

## Physiology and Pathophysiology

Iron demand rises progressively during pregnancy and peaks in the third trimester. Hepcidin levels decrease physiologically, facilitating intestinal iron absorption. When intake is inadequate, iron stores become depleted, serum ferritin falls, erythropoiesis becomes iron restricted, and microcytic hypochromic anemia develops [16,2,21].

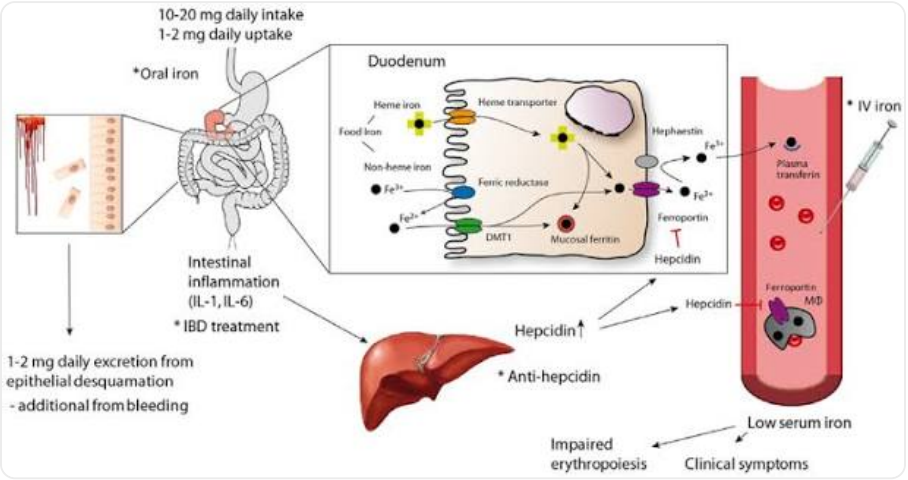


Figure 2: Showing pathophysiology of iron uptake and absorption leading to iron deficiency anemia

## Diagnosis

WHO defines anemia in pregnancy as hemoglobin below 11 g/dL. Complete blood count typically shows low hemoglobin, reduced mean corpuscular volume, and reduced mean corpuscular hemoglobin. Serum ferritin below 30 µg/L strongly supports iron deficiency in uncomplicated pregnancy. Additional investigations may include peripheral smear, reticulocyte count, C-reactive protein when inflammation is suspected, and hemoglobinopathy screening where indicated [7,8,9].

Early diagnosis of iron deficiency anemia (IDA) is essential to reduce maternal and fetal morbidity. Every pregnant woman should undergo routine screening during antenatal care. Diagnosis is based on **hemoglobin estimation**, followed by confirmation of iron deficiency using **serum ferritin** and other hematological indices whenever feasible.

## 1. WHO Recommendations [1,4]

Recent WHO/FIGO guidance recommends a uniform cutoff of **<11.0 g/dL in all trimesters** for programmatic use.

| Severity | Hemoglobin (g/dL) |
|---|---|
| Mild | 10.0–10.9 |
| Moderate | 7.0–9.9 |
| Severe | <7.0 |

## 2. ICMR/NHM (Government of India) Recommendations [5,6]

The National Health Mission under the **Anemia Mukt Bharat (AMB)** strategy recommends **hemoglobin estimation at every antenatal care (ANC) visit**, preferably using a validated digital hemoglobinometer or laboratory testing.

## Classification of Anemia (ICMR/NHM)

| Severity | Hemoglobin (g/dL) |
|---|---|
| Mild | 10.0–10.9 |
| Moderate | 7.0–9.9 |
| Severe | 4.0–6.9 |
| Very severe | <4.0 |

## 3. FOGSI Recommendations [7,10]

The Federation of Obstetric and Gynecological Societies of India recommends **screening all pregnant women at the booking visit** with:

- Complete blood count (CBC)
- Red cell indices (MCV, MCH, MCHC)
- Peripheral blood smear
- Serum ferritin (where available)

Additional investigations should be performed when the diagnosis is uncertain or there is poor response to iron therapy.

## Serum Ferritin [11,12]

Serum ferritin is the preferred laboratory marker of iron stores.

| Ferritin Level | Interpretation |
|---|---|
| <15 µg/L | Iron depletion |
| <30 µg/L | Diagnostic of iron deficiency in pregnancy (in the absence of inflammation) |
| >30 µg/L | Iron deficiency less likely; evaluate for other causes if anemia persists |

Figure 3: Indications for testing serum ferritin levels

1. Prior to starting iron therapy in therapeutic doses in patients with known haemoglobinopathy.
2. When an alternative aetiology of microcytic anaemia is being considered (chronic inflammation, lead toxicity, sideroblastic anaemia).
3. Suboptimal response to oral iron when compliance is doubtful.
4. In non-anaemic women at increased risk of iron depletion, such as those with previous anaemia, multiple pregnancy, teenage pregnancy, pregnancy with high risk of bleeding, or consecutive pregnancies with less than a year's interval.
5. After 8 weeks of therapeutic iron therapy when non-anaemic iron deficiency is being treated (i.e. serum ferritin < 30 µg/dL without anaemia).
6. Preferably prior to parenteral iron therapy to confirm iron deficiency.

## Additional Investigations [13,14]

When indicated, further evaluation may include:

- Serum iron
- Total iron-binding capacity (TIBC)
- Transferrin saturation

- Reticulocyte count
- C-reactive protein (CRP)
- Vitamin B12 and folate levels
- Bone marrow biopsy
- Hemoglobin electrophoresis or HPLC for suspected hemoglobinopathies
- Stool examination for helminths where clinically indicated

## Practical Clinical Approach

1. Screen all pregnant women at the booking visit.
2. Repeat hemoglobin estimation during the second and third trimesters according to national ANC schedules.
3. Confirm iron deficiency with serum ferritin whenever feasible.
4. Investigate alternative causes of anemia if ferritin is normal, anemia is severe, or there is inadequate response to therapy.
5. Initiate treatment promptly without delaying for extensive investigations in women with a high clinical suspicion of iron deficiency, particularly in high-prevalence settings.

Table 1: Summary of clinical significance and management in iron deficiency anemia

| Severity | Hemoglobin (g/dL) | Clinical Significance | Recommended Management |
|---|---|---|---|
| Normal | ≥11.0 | Adequate hemoglobin | Continue routine antenatal iron supplementation |
| Mild anemia | 10.0–10.9 | Usually asymptomatic | Oral iron therapy, dietary counselling, repeat Hb after 4 weeks |
| Moderate anemia | 7.0–9.9 | Fatigue, reduced exercise tolerance | Oral iron if early pregnancy; intravenous iron if late gestation, intolerance, or poor response |
| Severe anemia | <7.0 | High maternal and fetal risk | Hospitalization, intravenous iron or blood transfusion depending on clinical condition |
| Very severe anemia | <4.0 | Medical emergency | Immediate stabilization and blood transfusion |

## Signs and symptoms

Although Hbtest is recommended at first antenatal visit, examination for signs of pallor of the eyelids, tongue, nail beds, and palm should be regularly used. Some ID patients, with or without clinical signs of anemia may have alopecia, atrophy of tongue papillae, or dry mouth due to reduced salivation. The symptoms specific include; the syndromes of Plummer-Vinson or Paterson-Kelly (dysphagia with esophageal membrane and atrophic glossitis), gastric atrophy, stomatitis due to rapidly turning over of epithelial cells, spoon-shaped nails (koilonychia), and pallor.

These changes are caused by a reduction of iron-containing enzymes in the epithelia and gastrointestinal (GI)tract. The restless leg syndrome might be striking neurological sequelae prevalent in pregnancy. Pica, the eating disorder in which there is an appealing desire to lick or eat non-food items, such as gypsum, chalk, soil, ice (pagophagia) or paper, is prevalent in pregnant women. Pagophagia (intense desire to eat ice) is quite specific to ID and responds quickly to treatment (15,16).

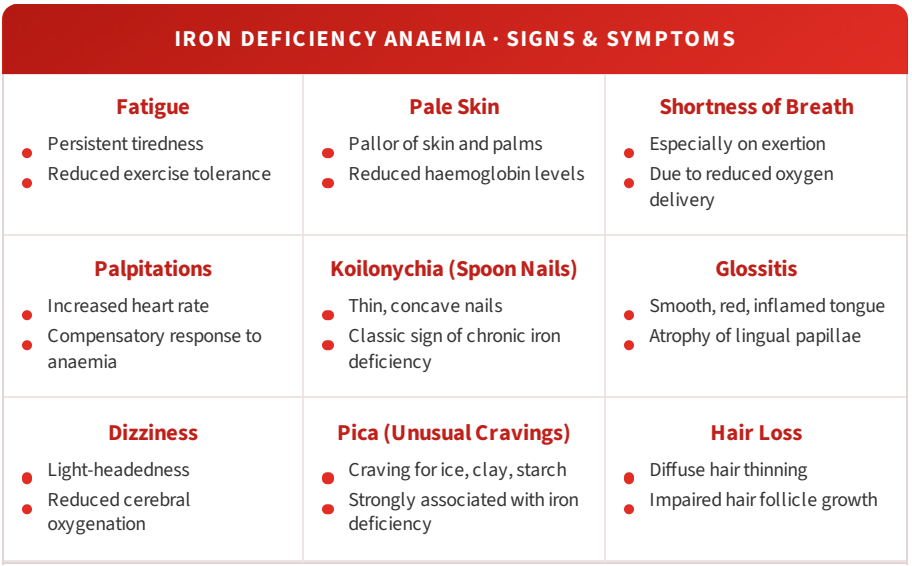


Figure 4: Showing signs and symptoms of iron deficiency anemia

## Maternal and Fetal Effects

Maternal consequences include fatigue, dizziness, reduced physical performance, susceptibility to infection, poor lactation, heart failure in severe anemia, and increased need for blood transfusion. Fetal consequences include fetal growth restriction, preterm birth, low birth weight, neonatal anemia, and reduced infant iron stores that may influence neurodevelopment.

Figure 5: Consequences of iron deficiency anemia (17)

| Antepartum complications | Intrapartum complications | Postpartum complications | Fetal outcome |
|---|---|---|---|
| **Increased risk of preterm delivery** | **Prolonged labour** | **Postpartum haemorrhage** | **Low birth weight** |
| Premature rupture of membranes | Increased rates of operative delivery and induced labour | Puerperal sepsis | Prematurity |
| Pre-eclampsia | Fetal distress | Lactation failure | Infections |
| Intrauterine death | Abruption | Pulmonary thromboembolism | Congenital malformation |
| Intercurrent infection | | Subinvolution of uterus | Neonatal anaemia |
| Antepartum haemorrhage | | Postpartum depression | Abnormal cognitive development |
| Congestive heart failure | | | Increased risk of schizophrenia |

## Prevention or dietary management

Routine antenatal care should include nutritional counselling emphasizing iron-rich foods such as green leafy vegetables, pulses, meat, fish, eggs, jaggery, and fortified cereals. Food fortification is combining commonly used food items with iron for cost effective and long term nutritional value (2,3). Vitamin C enhances absorption whereas tea and coffee inhibit absorption when taken with meals. National programs recommend daily iron and folic acid supplementation throughout pregnancy and the postpartum period. Deworming after the first trimester and treatment of malaria or other infections should be undertaken where appropriate (5,6).

Figure 6: Showing iron rich foods with iron in mg/100g

1. **Cereal grains and products**
   Whole wheat flour (4.9), Ragi (3.9), Jowar (4.1), Samai (9.3)
2. **Pulses and legumes**
   Bengal gram roasted (9.5), Bengal gram dhal (5.3), Cow pea (8.6), Green gram, whole (4.4), Horse gram, whole (6.77), Lentil (7.58), Dry peas (7.05), Soya bean (10.4)
3. **Leafy vegetables**
   Amaranth polygonoides (Ramdana or Rajgeera)(27.3), Amaranth tristis (38.5), Beet greens (16.2), Bengal gram leaves (23.8), Cauliflower greens (40.0), Mustard leaves (16.3), Radish leaves (18.0)
4. **Roots and tubers**
   Beet root (1.19), Carrot (1.03), Mango ginger (2.6), Onion small (1.2), Potato (0.48), Radish table (1.0)
5. **Other vegetables**
   Beans (2.6), Cowpea pods (2.5), Onion stalks (7.43)
6. **Nuts and oil seeds**
   Almond (5.09), Cashewnuts (5.81), Coconut dry (7.8), Garden cress seeds (100), Gingelly seeds (9.3), Groundnut (2.5), Niger seeds (56.7)
7. **Fruits**
   Ambada (3.9), Apricot dry (4.6), Currants, black (8.5), Dates dried (7.3), Watermelon (7.9), Peaches (2.4), Pineapple (2.42), Seethaphal (4.31)
8. **Meat and poultry**
   Beef meal (18.8), Egg, hen (2.1), Liver, sheep (6.3), Mutton, muscle (2.5)
9. **Milk and milk products**
   Cheese (2.1), khoa (5.8)

The average daily requirement of iron increases from 4-6 mg/day in the second and third trimesters to 10 mg/day during the last 6–8 weeks of pregnancy. These requirements are unlikely to be met by the diet alone because of poor accessibility, availability, and affordability of diversified food. Hence, regular iron supplementation is necessary for pregnant women to prevent IDA.

Table 2: Iron prophylaxis according to Anemia mukt bharat programme:

| S. no. | Age group | Dose | Regime | Service delivery |
|---|---|---|---|---|
| 1 | **6–60 months** | 1ml of IFA syrup containing<br>• 20 mg of elemental iron and<br>• 100 mcg of folic acid | • Biweekly throughout the period 6–60 months of age and<br>• De-worming for children 12 months and above. | Through ASHA<br>Inclusion in MCP card for entry by ASHA |
| 2 | **5–10 years** | Tablets<br>• 45 mg elemental iron and<br>• 400 mcg of folic acid | • Weekly throughout the period 5–10 years of age and<br>• Biannual de-worming | • In school through teachers<br>• For out-of-school children:- through Anganwadi centre (AWC) + Mobilization by ASHA |
| 3 | **10–19 years** | Tablets:<br>• 100 mg elemental iron and<br>• 500 mcg of folic acid | • Weekly throughout the period 10–19 years of age<br>• Biannual de-worming | • In school through teachers and<br>• For those out-of-school - through AWC and Mobilization by ASHA |
| 4 | **Preg. & lactating women** | Tablets:<br>• 100 mg elemental iron and<br>• 500 mcg of folic acid | • 1 tablet daily for 100 days, starting after the first trimester<br>• To be repeated for 100 days post-partum. | ANC/ ANM /ASHA Inclusion in MCP card |
| 5 | **Women rep. age (WRA)** | Tablets:<br>• 100 mg elemental iron and<br>• 500 mcg of folic acid | Weekly throughout the reproductive period | Through ASHA during house visit for contraceptive distribution |

Table 3: Iron prophylaxis according to WHO and MOHFW recommendations(18):

| | During pregnancy | | Postpartum |
|---|---|---|---|
| | Prophylaxis | Treatment | |
| WHO | Daily 60 mg iron+400 µg folic acid till term | Daily 120 mg iron+400 µg folic acid till term | Daily 60 mg iron and 400 µg folic acid- 3 months |
| MoHFW | Daily 100 mg iron+500 µg folic acid- for 100 days starting after thefirst trimester, at 14-16 weeks of gestation | • Mild anemia- 2 IFA tablets/day-100 days<br>• Moderate anemia- IM iron therapy+oral folic acid<br>• | Daily 100 mg iron+500 µg folic acid- 6 months |

## Management

Oral iron remains first-line therapy for mild to moderate IDA. Elemental iron 60–120 mg daily with folic acid is commonly prescribed. Alternate-day administration may improve gastrointestinal tolerance and absorption. Common adverse effects include nausea, constipation, metallic taste, and abdominal discomfort. Intravenous iron is preferred when oral therapy is not tolerated, absorption is impaired, hemoglobin response is inadequate, severe anemia is detected in late pregnancy, or rapid correction is required before delivery (19). Ferric carboxymaltose allows administration of larger single doses and improves convenience. Iron sucrose is effective but requires multiple infusions. Total iron requirement may be estimated using the Ganzoni formula or simplified dosing tables. Blood transfusion should be reserved for women with severe symptomatic anemia, hemodynamic instability, active bleeding, or those close to delivery in whom immediate correction is essential.

Table 4: Showing oral iron preparations and its pharmacological advantage (20,24)

| Preparation | Elemental Iron Content | Usual Dose | Advantages | Common Adverse Effects |
|---|---|---|---|---|
| Ferrous sulfate | ~60–65 mg/tablet | 1–2 tablets daily | Widely available, inexpensive | Nausea, constipation, metallic taste |
| Ferrous fumarate | ~100 mg/tablet | Once daily | High elemental iron content | Gastric irritation |
| Ferrous ascorbate | 100 mg/tablet | Once daily | Better absorption due to vitamin C | Mild gastrointestinal upset |
| Carbonyl iron | 100 mg/tablet | Once daily | Slower release, fewer gastrointestinal effects | Constipation (less frequent) |
| Iron polymaltose complex | Variable | Once daily | Better gastrointestinal tolerability | More expensive |

Table 5: Showing parenteral iron preparations and its pharmacological details (17,26):

| Characteristic | Ferric Carboxymaltose (FCM) | Iron Sucrose (IS) | Ferric Derisomaltose |
|---|---|---|---|
| Maximum dose/session | Up to 1000 mg | 200 mg | Up to 1000–1500 mg |
| Infusion time | 15–30 minutes | 30–60 minutes | 20–30 minutes |
| Number of visits | Usually one | Multiple (5–10) | Usually one |
| Test dose | Not required | Not required | Not required |
| Safety | Excellent | Excellent | Excellent |
| Cost | Higher | Lower | Higher |
| Preferred use | Late pregnancy requiring rapid correction | Cost-sensitive settings | Single high-dose replacement |

Table 6: Indications for blood transfusion in pregnant women with anemia (10,17)

| |
|---|
| **Antepartum Period** |
| **1.** Pregnancy <34 weeks |
| a. Hb <5 g/dL with or without signs of cardiac failure or hypoxia<br>b. Hb 5-7 g/dL – in presence of impending heart failure |
| **2.** Pregnancy >34 weeks |
| a. Hb <7 g/dL even without signs of cardiac failure or hypoxia<br>b. Severe anemia with decompensation |
| **3.** Anemia not due to hematinic deficiency |
| a. Hemoglobinopathy or bone marrow failure syndromes<br>b. Hematologist should always be consulted |
| **4.** Acute hemorrhage |
| a. Always indicated if Hb <6 g/dL<br>b. If the patient becomes hemodynamically unstable due to ongoing hemorrhage |
| **Intrapartum Period** |
| a. Hb <7 g/dL (in labor)<br>b. Decision of blood transfusion depends on medical history or symptoms |
| **Postpartum Period** |
| a. Anemia with signs of shock/acute hemorrhage with signs of hemodynamic instability.<br>b. Hb <7g% (postpartum ): Decision of blood transfusion depends on medical history or symptoms |

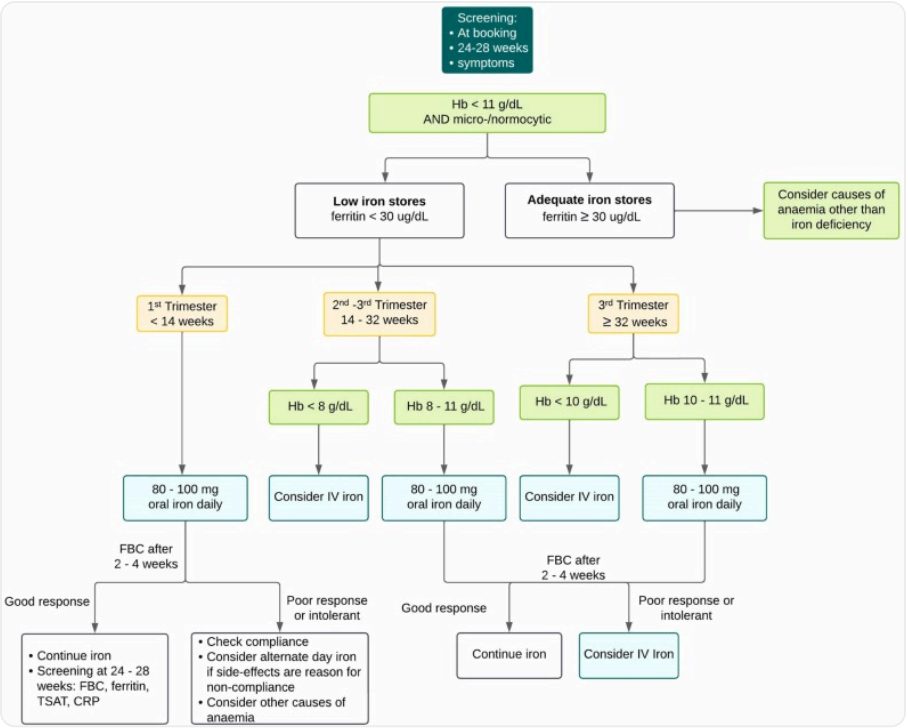


Figure 7: Showing algorithm for management of IDA trimester wise (21,22)

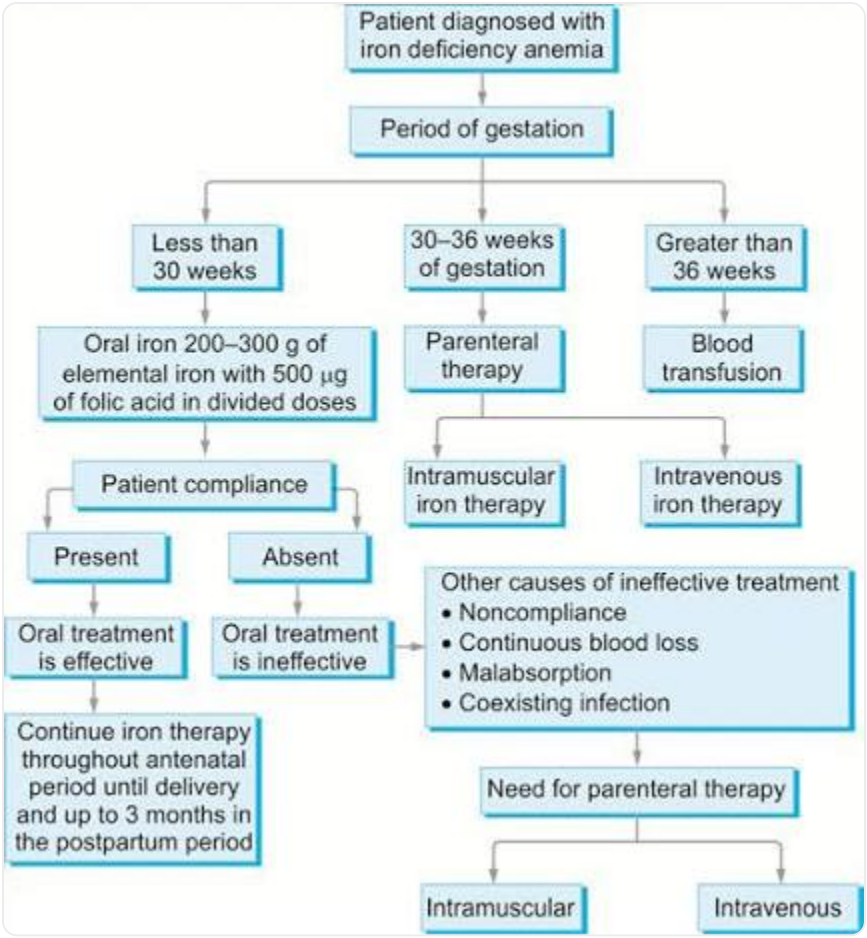


Figure 8: Showing algorithm for management of IDA in third trimester pregnancy

## Postpartum anemia

Postpartum anemia (PPA) is commonly defined as **hemoglobin (Hb) <10 g/dL within 48 hours after delivery**, although the World Health Organization defines anemia as **Hb <11 g/dL at 1 week postpartum and <12 g/dL during the first postpartum year**. Prompt recognition

and treatment are essential to improve maternal recovery, lactation, and quality of life (24,25).

## Management Principles

Management depends on the severity of anemia, hemodynamic status, ongoing blood loss, and patient symptoms.

Table 7: Showing management of postpartum anemia principles:

| Hemoglobin Level | Recommended Management |
|---|---|
| Hb 9–11 g/dL (mild to moderate, stable) | Oral elemental iron 80–100 mg daily for 3 months with dietary counseling. Reassess Hb after 2–4 weeks. |
| Hb <9 g/dL or intolerance/non-response to oral iron | Intravenous iron (preferably ferric carboxymaltose or iron sucrose) for rapid correction and replenishment of iron stores. |
| Hb <7 g/dL or symptomatic/hemodynamically unstable | Packed red blood cell transfusion followed by iron replacement to restore iron stores. |

## Oral Iron Therapy

- Elemental iron: **80–100 mg/day** for at least **3 months**.
- Advise intake on an empty stomach or with vitamin C-rich fluids.
- Avoid simultaneous intake with calcium, tea, coffee, or antacids.
- Continue treatment for **12 weeks after Hb normalization** to replenish iron stores.

## Intravenous Iron Therapy

IV iron is indicated in:

- Moderate to severe postpartum anemia.
- Intolerance or poor compliance with oral iron.
- Malabsorption syndromes.
- Need for rapid hemoglobin correction.

**Ferric carboxymaltose** allows administration of up to **1000 mg in a single infusion**, facilitating early recovery and reducing hospital visits. **Iron sucrose** remains a safe and effective alternative but requires multiple doses (26,27).

## Blood Transfusion (29)

Blood transfusion should be reserved for women with:

- Hemodynamic instability.
- Ongoing significant hemorrhage.
- Severe symptomatic anemia (usually Hb <7 g/dL).
- Cardiorespiratory compromise.

Transfusion should always be followed by iron therapy, as blood transfusion alone does not replenish iron stores.

## Follow-up (30)

- Repeat Hb after **2–4 weeks** to assess response.
- Continue iron supplementation for **3 months postpartum** or until iron stores are restored.
- Evaluate persistent anemia for ongoing blood loss, nutritional deficiencies (vitamin B12/folate), hemoglobinopathies, chronic disease, or infection.

### Clinical Pearls

- Correct postpartum anemia early to reduce fatigue, postpartum depression, impaired cognition, and breastfeeding difficulties.
- Intravenous iron should be considered the preferred option for women with Hb <9 g/dL who are hemodynamically stable.
- Restrictive transfusion practices should be followed, with individualized decisions based on symptoms and clinical status rather than hemoglobin alone.
- Counseling regarding iron-rich diet, adherence to therapy, and follow-up is an integral component of postpartum anemia management.

## Monitoring

Reticulocytosis appears within one week. Hemoglobin usually increases by 1–2 g/dL over the following 2–4 weeks with adequate treatment. Failure to respond should prompt reassessment of adherence, ongoing blood loss, incorrect diagnosis, infection, inflammation, or hemoglobinopathy. Iron therapy should continue for at least three months after normalization of hemoglobin and until six weeks postpartum.

## Conclusion

Iron deficiency anemia in pregnancy is preventable and treatable. Universal screening, dietary counselling, timely supplementation, accurate diagnosis, and evidence-based use of oral and intravenous iron improve maternal health and neonatal outcomes. Obstetricians should adopt standardized protocols aligned with national and international recommendations to reduce anemia-related morbidity.

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CHAPTER 05

# Sickle Cell Anaemia in Pregnancy

Dr Deepika Dewani

IN THIS CHAPTER

Genetics & Genotype | Pathophysiology | Preconception Counselling | Antenatal Management | Complications | Transfusion | Intrapartum Care

## 1. Introduction and burden

Sickle cell disease (SCD) is the commonest monogenic disorder of humankind and the first molecular disease to be characterised, yet it remains a disease of neglected populations. It is a chronic, inflammatory vasculopathy that begins with a single nucleotide substitution and ends, if unchecked, in cumulative end-organ damage. Pregnancy superimposes upon this fragile equilibrium an expanded but dilute circulation, a hypercoagulable milieu, increased oxygen consumption and a placenta that is itself a low-flow, high-resistance vascular bed — and thereby converts a chronic disease into an acute obstetric emergency in a substantial proportion of women.[2,3]

Some 300,000–400,000 affected infants are born each year; 75–80% of these births occur in sub-Saharan Africa, with India contributing the largest share in Asia. In the central Indian tribal belt — Madhya Pradesh, Chhattisgarh, Maharashtra, Gujarat, Odisha, Jharkhand and parts of southern India — carrier frequencies of 10–35% have been

documented.[1,8] Recognising this, the Government of India launched the National Sickle Cell Anaemia Elimination Mission in 2023, targeting screening of some seven crore people aged up to 40 years and elimination of the disease as a public health problem by 2047. Its second consequence is obstetric: increasing numbers of women now present already knowing their genotype, and the antenatal clinic becomes a principal point of case detection, partner testing and reproductive counselling.[7]

Even in high-income countries, pregnancies complicated by SCD carry a several-fold excess of maternal mortality and increased rates of pre-eclampsia, venous thromboembolism, acute chest syndrome, preterm birth, fetal growth restriction and perinatal death.[9,10,11,28]

## 2. Genetics, diagnosis and genotype

Haemoglobin S arises from a point mutation in the *HBB* gene on chromosome 11p15.4, in which adenine replaces thymine in the sixth codon (GAG → GTG): valine is substituted for glutamic acid at position 6 of the β-globin chain (β6 Glu→Val). When HbS gives up its oxygen, the resulting hydrophobic patch docks onto an adjacent tetramer; the molecules polymerise into long, rigid fibres that distort the erythrocyte into the characteristic sickle shape, damage its membrane and shorten its lifespan from 120 days to 10–20 days.[2,3]

Inheritance is autosomal recessive. Where both parents carry the trait, each pregnancy carries a 25% chance of an affected child (HbSS), a 50% chance of a carrier and a 25% chance of a child with normal haemoglobin (Figure 1). It is essential to explain to couples that these are independent probabilities applying afresh to every conception — a family that has already had one affected child does not thereby "use up" its risk.

**Figure 1. Inheritance of sickle cell disease — autosomal recessive transmission**

*HBB gene, chromosome 11p15.4 · Glu→Val substitution at codon 6 (β6 Glu>Val) · Every pregnancy carries the same independent risk*

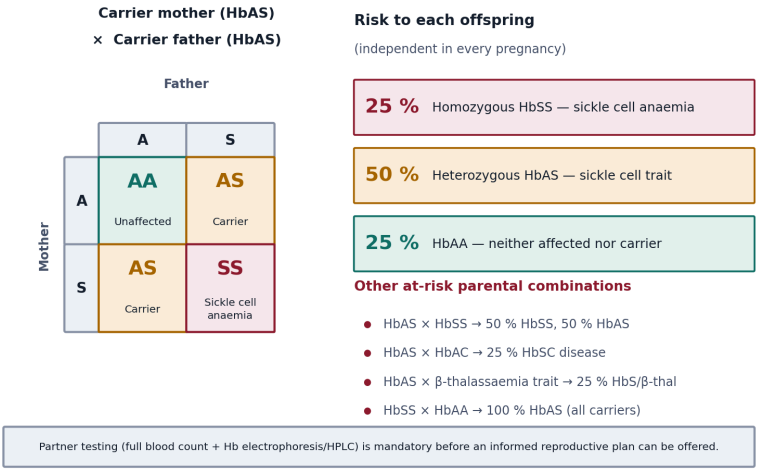


*Figure 1. Autosomal recessive inheritance of sickle cell disease, with other at-risk parental combinations.*

Severity is strongly modified by the co-inherited genotype and by the level of fetal haemoglobin (HbF), which inhibits HbS polymerisation; co-inheritance of α-thalassaemia is also protective (Table 1). Sickle cell trait (HbAS) is not a disease and does not alter obstetric management, but it identifies a woman whose partner must be tested.[2,4] Diagnosis is confirmed by high-performance liquid chromatography (HPLC) or capillary electrophoresis, supported by a full blood count, reticulocyte count and film. The solubility (sickling) test detects HbS but cannot distinguish trait from disease and must never be used alone; after recent transfusion, DNA-based genotyping may be required.[5,6]

**Table 1. Common sickle genotypes and their behaviour in pregnancy**

| Genotype | Haemoglobin composition | Typical Hb (g/dL) | Clinical behaviour in pregnancy |
|---|---|---|---|
| **HbSS (sickle cell anaemia)** | **HbS 80–95%, HbF 2–20%, no HbA** | **6–9** | **Most severe; frequent crises, acute chest syndrome, highest maternal and perinatal risk** |
| **HbSC disease** | HbS ~50%, HbC ~50% | 9–12 | Less anaemic, but retinopathy, avascular necrosis, chest syndrome and painful crises are common; risk is often underestimated |
| **HbS/$\beta^0$-thalassaemia** | HbS 80–90%, HbF raised, no HbA | 6–9 | Behaves like HbSS; splenomegaly more common |
| **HbS/$\beta^+$-thalassaemia** | HbS 55–75%, HbA 10–30% | 9–12 | Milder, but crises still occur; severity varies with residual HbA |
| **HbAS** (trait) | HbA ~60%, HbS ~40% | Normal | Not a disease; screen the partner. Rare risk of renal medullary events and papillary necrosis under extreme hypoxia or dehydration |

## 3. Pathophysiology

Two interlocking mechanisms explain the clinical phenotype (Figure 2). The **vaso-occlusive limb** begins with polymerisation of deoxygenated HbS; the rigid, dehydrated, adhesive erythrocyte binds to activated endothelium, to leucocytes and to platelets, obstructing the microcirculation and producing ischaemia–reperfusion injury. Repeated cycles generate the acute painful crisis, the acute chest

syndrome, stroke, avascular necrosis and — of particular obstetric relevance — infarction and thrombosis within the intervillous space. The **haemolytic–endothelial limb** arises from chronic intravascular haemolysis: free plasma haemoglobin and arginase scavenge nitric oxide, producing vasoconstriction, platelet activation and endothelial dysfunction. This limb underlies chronic anaemia, cholelithiasis, pulmonary hypertension, leg ulceration and, plausibly, the excess of pre-eclampsia observed in these pregnancies.[3,4]

Within the uteroplacental unit the consequences are structural and demonstrable: villous infarction, fibrinoid necrosis, decidual vasculopathy and reduced villous vascularity, with impaired trophoblastic invasion of the spiral arteries. The functional counterpart is uteroplacental insufficiency, expressed clinically as fetal growth restriction, oligohydramnios, abnormal umbilical artery Doppler indices, preterm birth and stillbirth.[11,12]

**Figure 2. Pathophysiology of sickle cell disease in pregnancy — the two limbs of injury**

*Polymerisation of deoxygenated HbS drives both a vaso-occlusive and a haemolysis–endothelial limb; pregnancy amplifies each*

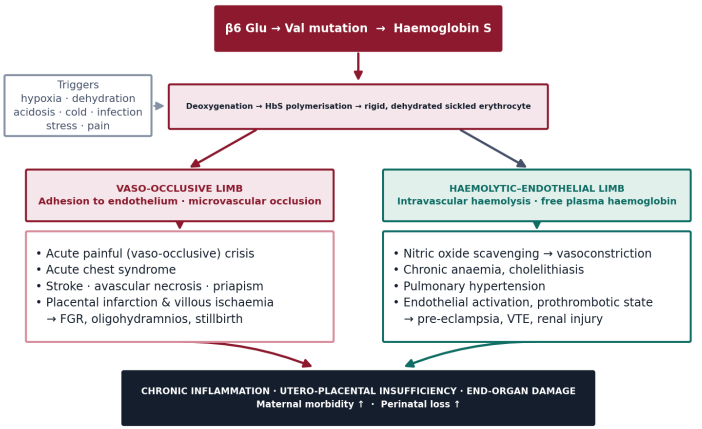


*Figure 2. The two limbs of sickle pathophysiology and their convergence on the uteroplacental unit.*

## 4. Physiological changes of pregnancy

Every adaptation of normal pregnancy is, for the woman with SCD, a hazard (Figure 3). Plasma volume rises by 40–50% while red-cell mass rises by only 20–30%, so a dilutional fall in haemoglobin is superimposed upon chronic haemolytic anaemia. Oxygen consumption rises by 20–30% and functional residual capacity falls, increasing the tendency to desaturation and thus the pool of deoxygenated HbS available to polymerise. Pregnancy is a hypercoagulable state — fibrinogen and factors VII, VIII and X rise, protein S falls — which compounds sickle-related endothelial activation and platelet adhesion. Venous stasis, aorto-caval compression and immobility in labour prolong red-cell transit through the microcirculation. Finally, the relative immunosuppression of pregnancy, superimposed upon the functional hyposplenism of SCD, leaves the woman poorly defended against encapsulated organisms.[12,25]

**Figure 3. Why pregnancy worsens sickle cell disease — physiological adaptation meets a fragile red cell**

*Normal maternal adaptations (left) collide with sickle pathophysiology (centre) to produce clinical risk (right)*

| Maternal physiological change | Interaction with sickle biology | Clinical consequence |
|---|---|---|
| Plasma volume ↑ 40–50 %, red-cell mass ↑ only 20–30 % | Dilutional fall in Hb superimposed on chronic haemolytic anaemia | Worsening anaemia · high-output state cardiac decompensation |
| Oxygen consumption ↑ 20–30 %; functional residual capacity ↓ | Greater tendency to desaturation; more deoxy-HbS available to polymerise | Vaso-occlusive crisis · acute chest syndrome, especially in third trimester |
| Hypercoagulable state: ↑ fibrinogen, ↑ factors VII/VIII/X, ↓ protein S | Added to sickle-related endothelial activation and platelet adhesion | Venous thromboembolism (up to 5-fold) placental thrombosis |
| Venous stasis, aorto-caval compression, immobility in labour | Sluggish microcirculatory flow prolongs red-cell transit and sickling | Painful crisis in labour · postpartum crisis and chest syndrome |
| Relative immunosuppression; urinary stasis and glycosuria | Functional hyposplenism → poor defence against encapsulated organisms | UTI/pyelonephritis · pneumonia sepsis-triggered crisis |

*Figure 3. How the physiological adaptations of pregnancy interact with sickle biology to produce clinical risk.*

## 5. Pre-conception evaluation and counselling

The pre-conception consultation is the single highest-yield intervention in this disease, because most of the risk is modifiable before the pregnancy begins. It has four elements: assessment of end-organ damage; review of medication; optimisation of prophylaxis; and genetic counselling with partner testing.[4,5]

Baseline assessment includes blood pressure, urinalysis with protein–creatinine ratio, renal and hepatic profiles, ferritin, retinal screening for proliferative sickle retinopathy, and echocardiography — a tricuspid regurgitant jet velocity of 2.5 m/s or more suggests pulmonary hypertension and carries a substantially increased maternal risk. Iron overload is assessed in the multiply transfused woman.[4,17,23]

## 6. Genetic counselling and prenatal diagnosis

Counselling must be non-directive, unhurried and delivered in the couple's own language. Where both partners carry a significant haemoglobinopathy allele, the options are: to accept the risk; prenatal diagnosis with the possibility of termination within the legal limit; pre-implantation genetic testing for monogenic disease (PGT-M); gamete donation; or adoption. The clinician's task is to explain the natural history accurately — including that with modern care many affected children survive into adult life — and then support whatever decision the couple reaches.[5,27]

Where the couple elects prenatal diagnosis, chorionic villus sampling at 11–14 weeks with DNA analysis of the *HBB* gene gives the earliest definitive answer; amniocentesis is available from 15 weeks. Non-invasive prenatal diagnosis using cell-free fetal DNA is becoming available but is not yet routine in most settings. In India, prenatal diagnosis must comply with the Pre-conception and Pre-natal Diagnostic Techniques Act — sex determination is prohibited — and

termination is governed by the Medical Termination of Pregnancy (Amendment) Act 2021, which permits termination up to 24 weeks for substantial fetal abnormality and beyond that limit only with the approval of a Medical Board.[6,7]

## 7. Antenatal management

Care is led by a multidisciplinary team — obstetrician, haematologist, anaesthetist, specialist midwife and neonatologist — and the woman should be seen before 10 weeks (Figure 4). Booking investigations are summarised in Table 2. Review is two- to four-weekly until 28 weeks, two-weekly thereafter and weekly from 34–36 weeks.[4,5]

**Table 2. Booking assessment**

| Domain | Investigations and actions |
|---|---|
| **Haematological** | **Confirm genotype; full blood count, reticulocytes, ferritin, LDH; extended red-cell phenotype or genotype (Rh C/D/E, Kell) and antibody screen** |
| Organ function | Urea, electrolytes, creatinine; liver function; urinalysis with protein–creatinine ratio; midstream urine culture; baseline oxygen saturation |
| Infection | Hepatitis B and C, HIV and syphilis serology; review immunisation status |
| Prophylaxis | Folic acid 5 mg; penicillin V; low-dose aspirin 75–150 mg from 12 weeks; VTE risk assessment for low-molecular-weight heparin |
| Counselling | Prenatal diagnosis; triggers to avoid; written crisis plan; when and where to seek urgent help |

Low-dose aspirin from 12 weeks is recommended for pre-eclampsia prophylaxis, and thromboprophylaxis with low-molecular-weight heparin is prescribed according to a formal risk assessment, with a low threshold for use during any admission.[21,22] Asymptomatic bacteriuria must be sought and treated at every visit, since urinary infection commonly precipitates crisis. Iron is given only when deficiency is proven — indiscriminate supplementation in a chronically transfused woman risks iron overload.[4]

The question of prophylactic transfusion remains unsettled. The randomised trial of Koshy and colleagues found that prophylactic transfusion reduced painful crises but did not improve perinatal outcome[14]; a later systematic review suggested possible reductions in maternal mortality and vaso-occlusive events, but the evidence was of low quality.[13] Current RCOG and ACOG guidance therefore does not recommend routine prophylactic transfusion; it is reserved for women with previous severe complications, multiple pregnancy or additional risk factors, decided case by case with haematology.[4,5]

**Figure 4. Care pathway for the pregnant woman with sickle cell disease**

*Multidisciplinary team: obstetrician · haematologist · anaesthetist · specialist midwife · neonatologist*

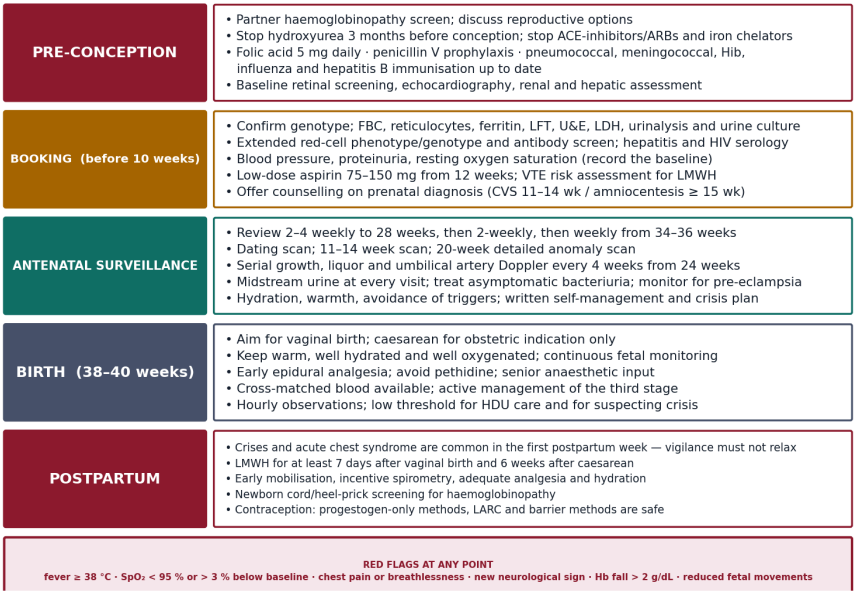


*Figure 4. Care pathway from pre-conception to the puerperium, with the red flags that apply at every stage.*

## Fetal surveillance

A dating scan is followed by the 11–14 week and 20-week anomaly scans, and thereafter by serial assessment of growth, liquor volume and umbilical artery Doppler every four weeks from 24 weeks. Reduced fetal movements must always be taken seriously. Birth is planned at 38–40 weeks: the placenta of a woman with SCD ages badly, and prolonging the pregnancy beyond term confers no benefit.[4,12]

## 8. Complications and their management

**Table 3. Principal complications and the essential response**

| Complication | Approximate risk | Key management point |
|---|---|---|
| **Acute painful (vaso-occlusive) crisis** | **Up to 50% of pregnancies** | **Analgesia within 30 minutes; hydration, warmth, oxygen; treat the trigger** |
| Acute chest syndrome | 7–20%; leading cause of sickle-related maternal death | Antibiotics, oxygen, analgesia, early transfusion or exchange; HDU care |
| Infection (urinary, pulmonary, puerperal) | 2–3 fold increase | Culture and treat every positive urine; low threshold for empirical antibiotics |
| Pre-eclampsia | 2–4 fold increase | Aspirin from 12 weeks; vigilant blood pressure and proteinuria surveillance |
| Venous thromboembolism | Several-fold increase | Risk-assess and prescribe LMWH; maintain a high index of suspicion |
| Fetal growth restriction | 2–4 fold increase | Serial growth scans and Doppler from 24 weeks |
| Preterm birth | ~2 fold increase | Anticipate; give steroids; avoid unnecessary iatrogenic prematurity |
| Stillbirth and perinatal death | Increased, particularly in HbSS | Surveillance and timely delivery at 38–40 weeks |

## 8.1 The acute painful crisis

Pain is the cardinal manifestation of SCD, the commonest reason for admission, a medical emergency — and chronically under-treated. The principles are: believe the patient; assess rapidly; give effective analgesia within 30 minutes of arrival; and reassess every 20–30 minutes until the pain is controlled (Figure 5).[16,19,24]

Assessment comprises a structured pain score, vital signs with oxygen saturation and temperature, and a search for the precipitant — infection, dehydration, cold, hypoxia, acidosis or stress. Investigations include a full blood count, reticulocytes, renal and liver profile, C-reactive protein, group-and-save, and blood cultures if febrile; a chest radiograph is obtained if there are any respiratory symptoms, and must never be withheld on account of the pregnancy. Analgesia is titrated on a ladder: paracetamol with or without a weak opioid for mild pain; non-steroidal anti-inflammatory drugs between 12 and 28 weeks only; and a strong opioid — morphine, orally, subcutaneously, intravenously or by patient-controlled analgesia — for moderate to severe pain. **Pethidine must be avoided**, because its metabolite normeperidine accumulates and lowers the seizure threshold. Adjuncts matter as much as the opioid: laxatives, antiemetics, antipruritics, thromboprophylaxis, two-hourly incentive spirometry and gentle rehydration, with oxygen if saturation falls below 95%.[19,24]

**Figure 5. Algorithm — acute painful (vaso-occlusive) crisis in pregnancy**

*Pain is an emergency: analgesia within 30 minutes of arrival, reassessed every 20–30 minutes until controlled*

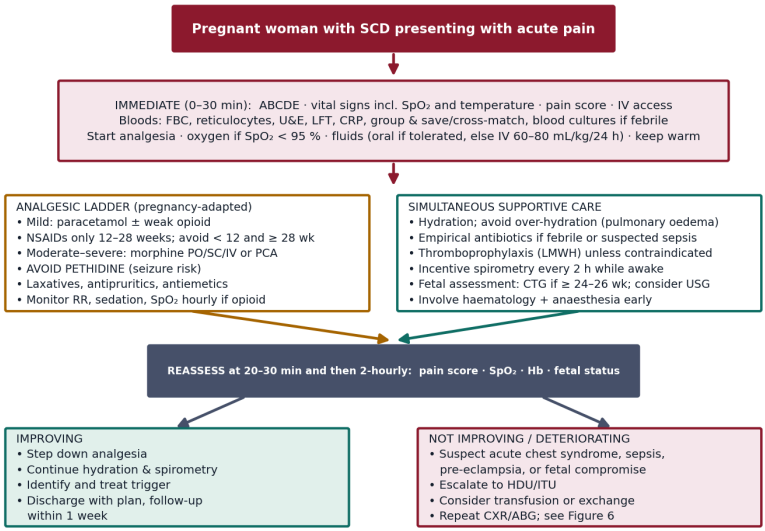


*Figure 5. Algorithm for the management of an acute painful crisis in pregnancy.*

## 8.2 Acute chest syndrome

Acute chest syndrome (ACS) is a new pulmonary infiltrate on chest radiography together with at least one of fever, chest pain, tachypnoea, cough, wheeze or hypoxaemia. It complicates up to a fifth of pregnancies in HbSS, frequently follows a painful crisis by two to three days, and is the leading cause of sickle-related maternal death.[15] Management (Figure 6) comprises transfer to a high-dependency area; oxygen titrated to a saturation of at least 95%; broad-spectrum antibiotics with a macrolide to cover atypical organisms; adequate analgesia, since under-treated pain causes splinting and hypoventilation; cautious fluids; bronchodilators where there is

wheeze; incentive spirometry; and thromboprophylaxis, with computed tomographic pulmonary angiography if pulmonary embolism is suspected. Simple top-up transfusion is indicated when the haemoglobin has fallen by 2 g/dL or more below baseline; urgent **exchange transfusion** is indicated for severe or progressive hypoxaemia, multilobar infiltrates, a rising HbS percentage or neurological involvement, aiming for HbS below 30% and haemoglobin around 10 g/dL. Delivery does not cure ACS and should be timed for maternal stability unless there is fetal compromise or the pregnancy is at or near term.[15,18]

**Figure 6. Algorithm — acute chest syndrome (ACS) in pregnancy**

*The commonest cause of sickle-related maternal death; suspect it in any breathless, hypoxic or febrile woman with SCD*

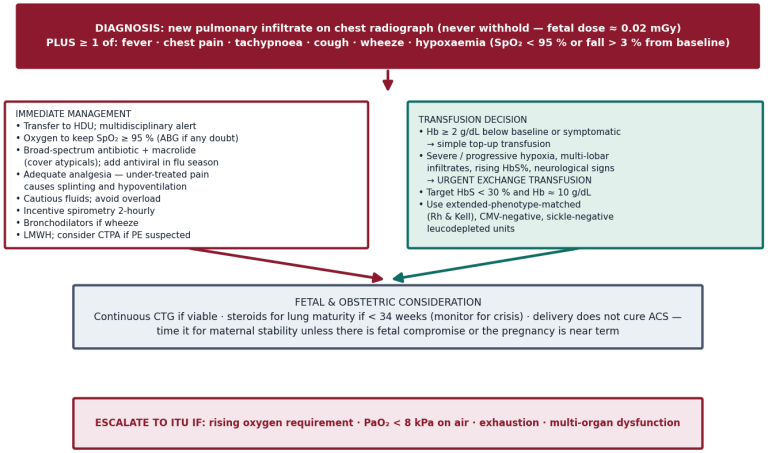


*Figure 6. Algorithm for the management of the acute chest syndrome in pregnancy.*

## 8.3 Other important complications

Infection is both a consequence of functional hyposplenism and a trigger of crisis; every positive urine culture is treated, and fever demands empirical antibiotics after cultures. A sudden fall in

haemoglobin with a low reticulocyte count suggests aplastic crisis (classically parvovirus B19, which also threatens the fetus with hydrops); a falling haemoglobin with a rising reticulocyte count and a tender enlarged spleen or liver suggests sequestration, which requires urgent transfusion. Hyperhaemolysis — a falling haemoglobin after transfusion, with reticulocytopenia — is treated with immunoglobulin and steroids, and further transfusion may worsen it.[17,18]

Any new neurological sign demands urgent imaging and consideration of exchange transfusion. Pre-eclampsia is two- to four-fold more common and may be hard to distinguish from a crisis with renal involvement; venous thromboembolism is several-fold more likely and remains a leading cause of maternal death. Pulmonary hypertension, proliferative retinopathy, avascular necrosis, chronic renal impairment and cholelithiasis become more prominent with cumulative disease burden.[9,20,21,28]

## 9. Transfusion therapy

Transfusion is life-saving but never trivial: alloimmunisation, delayed haemolytic reactions, hyperhaemolysis and iron overload are real and cumulative risks. Every unit must be extended-phenotype matched for Rh (C, D, E) and Kell, sickle-negative, leucodepleted and, where policy requires, cytomegalovirus-negative.[18] Simple top-up transfusion is indicated for symptomatic anaemia, a fall of 2 g/dL or more below baseline, acute chest syndrome, acute anaemic events and pre-operative optimisation. Exchange transfusion — manual or automated — is indicated for stroke, severe or progressive acute chest syndrome, multi-organ failure and severe sepsis, aiming for HbS below 30%. Routine prophylactic transfusion is not recommended (Section 7).[4,13,14,18]

## 10. Intrapartum and anaesthetic care

Labour concentrates every trigger of sickling — pain, dehydration, acidosis, hypoxia, stasis and cold — into a few hours. Vaginal birth is the aim; caesarean section is performed for obstetric indications only. The woman is kept warm, well hydrated and well oxygenated, with continuous pulse oximetry and continuous fetal monitoring; fluid balance is charted strictly, since over-hydration precipitates pulmonary oedema. Cross-matched, phenotype-matched blood should be available. Early epidural analgesia is preferred; pethidine is again avoided. Regional anaesthesia is preferred for caesarean section, general anaesthesia carrying the risks of hypoxia, hypothermia and atelectasis. The third stage is actively managed, with senior anaesthetic and haematological input available on the labour ward.[4,5,25]

## 11. Postpartum care, contraception and the newborn

Vigilance must not relax after delivery: painful crises and acute chest syndrome cluster in the first postpartum week, when attention has moved to the baby. Thromboprophylaxis with low-molecular-weight heparin is given for at least seven days after vaginal birth and for six weeks after caesarean section. Early mobilisation, incentive spirometry, analgesia and hydration matter as much as any drug. Breastfeeding is encouraged. Progestogen-only methods, intrauterine devices and barrier methods are all safe; combined hormonal contraception is used with caution where there are additional vascular risk factors. The newborn requires cord-blood or heel-prick haemoglobinopathy screening — every infant of a woman with HbSS is at least a carrier — because early diagnosis, penicillin prophylaxis and immunisation transform childhood survival.[4,6,17]

## 12. Conclusion

Sickle cell anaemia in pregnancy is a high-risk condition whose risk is, to a remarkable degree, modifiable. Almost every serious outcome is preceded by a missed opportunity: a partner not tested, a booking visit delayed, a urinary infection untreated, a pain score not acted upon, a transfusion given without matched blood, a puerperium in which vigilance relaxed. The obstetrician who understands the molecular lesion, anticipates the collision of pregnancy with a fragile red cell, and works within a disciplined multidisciplinary framework can offer these women what a generation ago was unattainable: the reasonable expectation of a safe pregnancy and a healthy child.

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CHAPTER 06

# Thalassaemia in Pregnancy

Dr Amrita Datta

IN THIS CHAPTER

Classification | Preconception Counselling | Maternal Complications | Antenatal Management | Iron Chelation | Intrapartum & Postpartum | Recent Advances

## Introduction

The Thalassaemia syndromes comprise a group of inherited haemoglobin disorders characterized by reduced or absent synthesis of one or more globin chains, causing chronic haemolytic anaemia of variable severity. They include a spectrum of disorders ranging from severe transfusion-dependent conditions such as alpha and beta thalassaemia major to more variable non-transfusion-dependent anaemia disorders such as alpha thalassaemia intermedia (Haemoglobin H and related compound alpha thalassaemia disorders) and beta thalassaemia intermedia syndromes. The global burden of thalassaemia is significant, with over 70 000 babies born with thalassaemia syndromes worldwide each year and more than 100 million individuals who are asymptomatic thalassaemia carriers. The challenges faced during pregnancy, due to iron overload and anaemia, are similar regardless of the genetic basis of the thalassaemia

syndrome, According to recent guidelines patients are considered based on clinical phenotype as transfusion-dependent thalassaemia (TDT) or non-transfusion-dependent thalassaemia (NTDT) which are dealt in this chapter.

Advances in transfusion practices, iron chelation along with other therapies and multidisciplinary care have enabled women with thalassaemia to achieve reproductive age and experience successful pregnancies. However such pregnancies are high risk due to increased maternal and fetal complications, necessitating coordinated management by obstetricians, haematologists, cardiologists, anaesthesiologists, and neonatologists.

India accounts for nearly 10% of the global burden of β-thalassaemia, with approximately 42 million carriers and an estimated 10,000–15,000 affected births annually. The prevalence varies geographically, reaching 3–17% in certain communities. Hence obstetricians must be familiar not only with the management of women affected by thalassaemia but also with carrier screening, genetic counselling, prenatal diagnosis, and prevention strategies.

## Classification

Clinically, thalassaemia is classified according to transfusion requirements rather than genotype.

1. Non-transfusion-dependent Thalassaemia (NTDT)

2. Transfusion-dependent Thalassaemia (TDT)

## Preconception Counselling

Preconception counselling represents remains pivotal to a successful pregnancy in thalassaemia. When both parents carry β-thalassaemia mutations, each pregnancy has a 25% chance of an affected or

unaffected fetus or a 50% chance of a carrier fetus which highlights the importance of a prenatal counselling. The primary objectives include:

- Optimization of haemoglobin stores
- Assessment of iron overload
- Identification of organ dysfunction
- Medication review
- Fertility assessment
- Genetic counselling

Initially, women should undergo the following investigations:

- Complete blood count
- Ferritin
- Liver function tests
- Renal function tests
- Thyroid profile
- HbA1c
- Vitamin D
- ECG
- Echocardiography
- Cardiac MRI T2
- Liver MRI for detecting iron overload
- Viral markers (HBV, HCV, HIV)
- Bone mineral density (if indicated)

Pregnancy should ideally be deferred until significant cardiac iron overload has been corrected. Universal haemoglobinopathy screening is increasingly advocated in high-prevalence regions as also mentioned in NHM guidelines. Partner testing is mandatory if the woman is identified as a carrier. Screening includes: CBC with RBC indices, a

peripheral Blood Smear, an Hb Electrophoresis or HPLC or a molecular testing where required.

## Pathophysiology in Pregnancy

Pregnancy causes physiological haemodilution with increased plasma volume and elevated erythropoietin levels. There is also enhanced iron absorption. But in women with thalassaemia, ineffective erythropoiesis and chronic haemolysis impair the ability to meet increased oxygen demands. Iron overload secondary to repeated transfusions results in cardiac dysfunction, hepatic disease, endocrine abnormalities, and diabetes mellitus, all of which influence outcomes in such pregnancies. Hypercoagulability of pregnancy is accentuated chronic haemolysis, endothelial dysfunction, and platelet activation in them increasing the risk of thromboembolism.

## Maternal Complications

Maternal risks depend largely on disease severity and pre-existing organ damage commonly affecting the following organs.

### Cardiovascular

Iron overload cardiomyopathy remains the leading cause of maternal morbidity and mortality. Pregnancy increases cardiac output by approximately 40–50%, which may precipitate heart failure in women with impaired ventricular function. Pulmonary hypertension worsens maternal prognosis and is generally considered a contraindication to pregnancy.

### Endocrine

Iron deposition within endocrine glands may result in:

- Diabetes mellitus
- Hypothyroidism

- Hypoparathyroidism
- Adrenal insufficiency
- Osteoporosis

### Hepatic

Repeated transfusions increase the risk of Hepatitis B, Hepatitis C, cirrhosis, and hepatic fibrosis. Liver dysfunction may worsen during pregnancy.

## Thromboembolism

Risk factors include:

- Splenectomy
- Platelet count >600×$10^9$/L
- Previous thrombotic history
- Immobility

Venous thromboembolism is quite common in postpartum period in such cases.

## Obstetric Complications

Thalassaemic pregnancies are at increased risk of:

- Abortion
- Pregnancy-induced hypertension
- Preeclampsia
- Gestational diabetes
- Caesarean delivery
- Postpartum haemorrhage
- Infection

## Fetal Complications

Chronic maternal anaemia and placental insufficiency in thalassaemia contribute to adverse fetal outcomes including:

- Fetal growth restriction
- Preterm birth
- Low birth weight
- Oligohydramnios
- Fetal distress
- Stillbirth (though rare with optimal care)

## Antenatal Management

Management of such pregnancies requires multidisciplinary care.

## Booking Visit

An initial assessment should include:

- Baseline haemoglobin
- Serum Ferritin
- Cardiac function
- Liver disease
- Endocrine evaluation
- Previous transfusion history
- Splenectomy status
- Chelation therapy

Preconceptual high-dose folic acid (5 mg daily) starting 3 months prior to conception reduces the risk of neural tube defect and should be continued throughout pregnancy. Recent guidelines recommend that splenectomised patients with thalassaemia syndromes require

penicillin prophylaxis as they are susceptible to infection by encapsulated bacteria. All patients should have vitamin D levels optimised and continue their routine supplementation during pregnancy. Aspirin prophylaxis with 75–150 mg daily in the evening is recommended from around 12 weeks of gestation until 36 week as risk of pregnancy induced hypertension is more in such pregnancies.

Iron supplementation should never be prescribed empirically and only be administered after laboratory confirmation of deficiency (low serum ferritin or transferrin saturation), as many women with thalassaemia have iron overload despite anaemia.

## Blood Transfusion

Goals in thalassaemic pregnancies differ according to disease phenotype.

## TDT

To maintain pre-transfusion haemoglobin around **10 g/dL** to ensure adequate fetal growth and suppress ineffective erythropoiesis.

## NTDT

Transfusions are individualized based on:

- Symptomatic anaemia
- Poor fetal growth
- Cardiac compromise
- Progressive fall in haemoglobin

Extended phenotype-matched packed red blood cells reduce alloimmunization. Below is a table for guiding transfusion practices in antenatal period.

**TABLE 4** Indications for transfusion during pregnancy.

| Indication | Recommendation |
|---|---|
| TDT | Continue with regular top up with pretransfusion Hb >100 g/L |
| NTDT + materno-fetal complication<br>Symptomatic anaemia<br>Evidence of fetal growth restriction | Top up transfusion, aim for post-transfusion Hb 120 g/L<br>Maintain pre transfusion Hb >100 g/L |
| NTDT untransfused<br>Hb >80 g/L at 36 weeks of gestation<br>Hb < 80 g/L at 36 weeks of gestation<br>Postnatal | Transfusion can be avoided before delivery<br>Consider 1–2 unit top up at 37–38 weeks<br>Cross-match 2 units on admission to labour ward<br>Transfuse as necessary |

*Source : Shah FT, Nicolle S, Garg M et al. Guideline for the management of conception and pregnancy in thalassaemia syndromes: A British Society for Haematology Guideline. Br J Haematol. 2024;00:1–16.*

## Iron Chelation Therapy

Iron chelators are generally discontinued once pregnancy is confirmed.

- Deferasirox – contraindicated
- Deferiprone – contraindicated
- Desferrioxamine – usually avoided during the first trimester; may be restarted in selected women after 20 weeks with severe cardiac iron overload after multidisciplinary consultation. A guideline can be found below

**TABLE 5** Recommendations for chelation therapy in pregnancy.

| Cardiac indications | Intensification therapy |
|---|---|
| Severe myocardial iron loading (cardiac T2* < 10 ms) | Low-dose subcutaneous DFO (20 mg/kg/day) on a minimum of 4–5 days a week by joint haematology–cardiology team from 20 to 24 weeks of gestation |
| Cardiac decompensation<br>LVEF fall >10% from baseline<br>Heart failure<br>Cardiac arrhythmia | Desferrioxamine IV 24 h infusion and consider optimal doses of 40–50 mg/kg/day |
| Severe hepatic iron loading | Consider low-dose chelation from 20 weeks of gestation based on MDT opinion on severity of iron burden and risk of developing endocrine complication or cardiac toxicity |

*Source : Shah FT, Nicolle S, Garg M et al. Guideline for the management of conception and pregnancy in thalassaemia syndromes: A British Society for*

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## Fetal Surveillance

Serial fetal surveillance is recommended. The following could be done:

- Dating scan
- First-trimester aneuploidy screening
- Detailed anomaly scan (18–22 weeks)
- Serial fetal growth assessment every 4 weeks from 24–28 weeks
- Doppler velocimetry when growth restriction is suspected
- Non-stress testing during the third trimester as indicated

Women with diabetes require fetal echocardiography in $2^{nd}$ trimester.

## Thromboprophylaxis

Thalassaemic pregnancies have predisposition to venous thromboembolism and thromboprophylaxis should be considered in them. Patients with thalassaemia who are splenectomised or have a platelet count above $600 \times 10^9$/L should be offered low-molecular-weight heparin (LMWH) thrombopro-phylaxis in addition to low- dose aspirin 75–150 mg daily. All pregnant patients with thalassaemia require LMWH during hospital admissions. Low-dose aspirin should be considered in women at increased risk of preeclampsia.

## Intrapartum Management

Delivery should occur in a tertiary care centre with senior consultants and multidisciplinary team around. Continuous maternal and fetal monitoring is recommended. Regional anaesthesia is preferred unless contraindicated. If red cell antibodies are present or haemoglobin <100 g/L,cross-matched blood should be ready after admission. Or else a bloodgroup and save sample are sufficient. In TDT patients, IV DFO 2 g

over 24 h should be administered throughout labour. Vaginal delivery is appropriate as thalassaemia is not an indication for caesarean section. Oxytocin should be actively administered during the third stage to reduce postpartum haemorrhage.

## Postpartum Care

Major priorities during this period include:

- Venous thromboembolism prevention. Postpartum thromboprophylaxis should continue for at least six weeks in high-risk women
- Restarting chelation therapy
- Optimizing transfusion schedule
- Contraceptive counselling
- Monitoring cardiac status

Breastfeeding is encouraged. Desferrioxamine is considered compatible with breastfeeding because oral absorption by the infant is negligible, whereas evidence for oral chelators remains limited. The entire range of contraceptive options is feasible and choice should be individualised

## Thalassaemia Trait in Pregnancy

Women with β-thalassaemia trait usually have mild microcytic anaemia and generally do not require transfusions. Important principles include avoiding unnecessary iron therapy and obstetric surveillance.

Below is a concise table showing management protocol of thalassaemic pregnancies:

**TABLE 3** Schedule of antenatal care.

| Appointment | Care for patients with thalassaemia in pregnancy |
|---|---|
| Booking appointment: see multidisciplinary team (MDT) | Information, education and advice about pregnancy in a patient with thalassaemia<br>Review partner results and discuss Prenatal Diagnosis if appropriate<br>Refer to diabetic antenatal team if diabetic<br>Assess endocrine, hepatic and cardiac status if this has not been done preconceptually.<br>Review TDT patients for cardiac and liver iron and LVEF. If not undertaken in 12 months prior to conception arrange Echo for Left ventricular ejection fraction (LVEF), MRI for cardiac T2* and liver iron burden. Abdominal ultrasound as baseline for NTDT to assess spleen, liver and gall stones.<br>Baseline full blood count, renal and liver function tests, urine protein/creatinine ratio, ferritin, B12, folate and blood group and antibody screen, red cell phenotype and extended genotype if not already done<br>Check thyroid function in each trimester if hypothyroid<br>VTE risk assessment—splenectomised higher risk<br>Prescribe 75–150 mg aspirin daily in evening and folic acid 5 mg daily if not already taking this.<br>Discuss vaccinations if splenectomised—Pneumovax, influenza, Sars-CoV 2, *Haemophilus influenzae type b* (Hib) and Meningitis C combined vaccination, Meningitis A, C Y,W and Meningitis B.<br>Discuss HPV vaccination if not immunised.<br>Penicillin prophylaxis—Penicillin V 250 mg bd (or erythromycin if allergic) |
| 7–9 weeks | Offer viability scan |
| 10–14 weeks | First trimester ultrasound scan |
| 16 weeks—MDT + midwife | Routine review as per NICE antenatal guideline<br>Glucose tolerance test (GTT) if high BMI or previous borderline GTT. If not available then fasting and random glucose at same time intervals |
| 20 weeks—MDT + midwife | Routine review as per NICE antenatal guideline NG201 |
| 20–24 weeks | Cardiac iron overload:<br>If T2* <10 ms: Commence low-dose desferrioxamine (20 mg/kg/d) on 4–5 days per week under haematology guidance<br>If T2* > 10 but <20 ms—assess individual risk and consider desferrioxamine<br>If T2* > 20 ms—not for desferrioxamine unless severe hepatic iron overload<br>Check thyroid function |
| 24 weeks—MDT + midwife | Routine review. Ultrasound for fetal growth and amniotic fluid volume |
| 26–28 weeks | Non-diabetic patients for GTT.<br>For diabetics, aim for monthly fructosamine <300 nmol/L |
| 28 weeks—MDT + midwife | Routine review. Ultrasound for fetal biometry<br>Specialist cardiology review. Formulate delivery plan based on cardiac function<br>Consider VTE thromboprophylaxis |
| 30 weeks—midwife | Routine review as per NICE antenatal guideline |
| 32 weeks—MDT + midwife | Routine review. Ultrasound for fetal growth/amniotic fluid volume |
| 34 weeks—midwife | Routine review |
| 36 weeks—MDT + midwife | Ultrasound for fetal growth and amniotic fluid volume<br>Review aspirin use and continuation.<br>Discuss timing and mode of delivery<br>Management of labour and delivery<br>Analgesia and anaesthesia<br>Care of baby after birth<br>Referral for Obstetric Anaesthetic review<br>Delivery care plan formulated and documented in the notes |
| 38 weeks—midwife and obstetrician | Routine review. Offer induction of labour if diabetic. Ensure desferrioxamine is available |
| 39 weeks—midwife | Routine review |
| 40 weeks—obstetrician | Routine review |
| 41 weeks—obstetrician | For a non-diabetic patient with a normally grown baby offer induction in accordance with the NICE guideline for induction of labour |

*Source : Shah FT, Nicolle S, Garg M et al. Guideline for the management of conception and pregnancy in thalassaemia syndromes: A British Society for Haematology Guideline. Br J Haematol. 2024;00:1–16.*

## Recent Advances

Recent developments as mentioned below have transformed reproductive outcomes:

- MRI T2* permits accurate quantification of myocardial iron before conception.
- Improved transfusion protocols have significantly reduced maternal mortality.
- Universal carrier screening is increasingly recommended in high-prevalence populations.
- Preimplantation genetic testing allows birth of unaffected offspring in carrier couples.
- Gene-editing therapies and lentiviral gene therapy (e.g., betibeglogene autotemcel) have shown promising long-term results in selected patients with transfusion-dependent β-thalassaemia, although their role in pregnancy continues to evolve.
- Multidisciplinary pregnancy clinics have markedly improved live birth rates

### Conclusion

Thalassaemia has evolved from a disorder associated with infertility and poor pregnancy outcomes to one in which successful motherhood is achievable with modern multidisciplinary care. Early preconception counselling, comprehensive assessment of iron overload and organ function, appropriate transfusion support, individualized thromboprophylaxis, and genetic counselling remain the pillars of management.

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CHAPTER 07

# Megaloblastic Anaemia in Pregnancy

Dr Neema Acharya

IN THIS CHAPTER

Etiology | Pathophysiology | Clinical Features | Maternal & Fetal Effects | Diagnosis | Management | Key Points

## Introduction

Megaloblastic anemia is a macrocytic anemia, where there is impaired DNA synthesis, leading to poor erythropoiesis and megaloblast formation within the bone marrow. In pregnancy, the common cause of megaloblastic anemia is folate deficiency, whereas vitamin B12 deficiency is rare. However, it should be noted that this condition causes nervous complications and adverse effects on the fetus. Pregnancy leads to increased needs of folate due to fetal growth, placenta formation, and increased maternal red blood cells mass.

## Epidemiology

- Megaloblastic anemia is relatively uncommon when compared to iron deficiency anemia during pregnancy.

- Deficiency of folate continues to be more common in developing and intermediate countries due to malnutrition, absence of food fortification, multiparity, and infections.
- Deficiency of vitamin B12 has come into recognition among vegetarians, women with malabsorption syndromes, postbariatric surgery, pernicious anemia, and long-term metformin use.

## Etiology

### Folate Deficiency

## Increased requirements

- Pregnancy
- Multiple gestation
- Lactation
- Hemolytic disorders

## Decreased intake

- Poor nutrition
- Alcoholism
- Overcooked vegetables

## Malabsorption

- Celiac disease
- Tropical sprue
- Inflammatory bowel disease

## Drug-induced

- Methotrexate

- Phenytoin
- Trimethoprim
- Sulfasalazine

### Vitamin B12 Deficiency

- Strict vegan diet
- Pernicious anemia
- Gastric surgery
- Ileal disease or resection
- Crohn disease
- Long-term metformin use
- Nitrous oxide exposure

## Pathophysiology

Folate and B12 vitamins are required as coenzymes for the synthesis of thymidine during DNA replication. When there is deficiency of these vitamins, the nuclei do not mature but the cytoplasm matures normally leading to nuclear-cytoplasmic asynchrony. This leads to:

• An ineffective erythropoiesis

• Macro-ovalocytes

• Hypersegmented neutrophils

• Hemolysis intramedullarly

• Pancytopenia in extreme cases

Deficiency of B12 vitamins causes accumulation of methyl. (BSH)

## Risk Factors

- Poor socioeconomic status
- Multiple pregnancy

- Closely spaced pregnancies
- Hyperemesis gravidarum
- Malnutrition
- Malabsorption disorders
- Vegetarian diet (B12 deficiency)
- Anticonvulsant therapy
- Previous bariatric surgery

## Clinical Features

### Symptoms

- Fatigue
- Weakness
- Dyspnea
- Palpitations
- Dizziness
- Loss of appetite

### Signs

- Pallor
- Mild jaundice
- Glossitis ("beefy red tongue")
- Angular cheilitis
- Hyperpigmentation (occasionally)

### Neurological manifestations (Vitamin B12 deficiency)

- Paresthesia
- Ataxia
- Peripheral neuropathy

- Loss of vibration sensation
- Cognitive impairment (advanced disease)

## Maternal Complications

- Severe anemia
- Cardiac failure (rare)
- Increased susceptibility to infections
- Postpartum hemorrhage due to poor uterine contractility associated with severe anemia
- Increased need for blood transfusion
- Neurological deficits (B12 deficiency)

## Fetal Complications

- Neural tube defects
- Intrauterine growth restriction
- Low birth weight
- Preterm birth
- Recurrent pregnancy loss
- Fetal vitamin B12 deficiency
- Developmental delay in offspring of severely deficient mothers

## Diagnosis

### Complete Blood Count

- Hemoglobin reduced
- MCV >100 fL
- Macrocytic anemia
- Low reticulocyte count

### Peripheral Blood Smear

- Macro-ovalocytes
- Hypersegmented neutrophils
- Anisopoikilocytosis

### Biochemical Tests

- Serum folate
- RBC folate (better indicator of tissue stores)
- Serum vitamin B12
- Serum methylmalonic acid (elevated in B12 deficiency)
- Homocysteine (elevated in both folate and B12 deficiency)

### Bone Marrow

Reserved for uncertain diagnosis.
Shows:

- Hypercellularity
- Megaloblastic erythropoiesis
- Giant metamyelocytes

## Differential Diagnosis

- Iron deficiency anemia
- Mixed nutritional anemia
- Liver disease
- Hypothyroidism
- Myelodysplastic syndrome
- Drug-induced macrocytosis

## Management

### General Measures

- Nutritional counseling
- Treatment of underlying cause
- Correction of associated iron deficiency if any.

### Folate Deficiency

## Folic acid

- 1 mg orally per day until resolution of anemia
- - Continue supplementation regularly
- - Severe malabsorption: intravenous administration of folate is required.

### Vitamin B12 Deficiency

Hydroxocobalamin or Cyanocobalamin

• 1000 µg IM weekly for 4-6 weeks

• Then monthly if deficiency is permanent

High dose vitamin B12 orally might work in selected individuals where absorption is intact.

Note: B12 deficiency must be treated prior to or concomitantly with folic acid since folic acid alone could lead to improvement in anemia while letting the neurological damage continue.

### Blood Transfusion

Indications include:

- Severe symptomatic anemia

- Cardiac failure
- Hemodynamic instability
- Parturient who requires rapid resolution of the problem

PREVENTION

- Folic acid supplementation to all pregnant women.
- Standard: 400 µg daily, started before conception and continued through the early stages of pregnancy. Pregnant women who have a high incidence of neural tube defects need 5 mg daily, starting before conception and up to the first trimester, after which normal doses should be taken. (OBGYN Online Library)
- Balanced diet containing: Green vegetables, Citrus fruits, Legumes, Liver, Eggs, Meat, Milk products

PROGNOSIS

The recovery process for the mother can be quite fast if the disease is detected early enough and she receives appropriate treatment. However, neurological effects associated with vitamin B12 deficiency can be partially irreversible.

The goal of this chapter is to provide a comprehensive review of **megaloblastic anemia in pregnancy**, including its etiology, pathophysiology, clinical features, diagnosis, prevention, and management. As the principles of **peripartum care of anemia** are common to all forms of anemia in pregnancy, they are discussed separately in the respective chapter and are not covered in detail here.

## Key Points

- The most common cause of megaloblastic anemia during pregnancy is folate deficiency.
- Macrocytosis with hypersegmented neutrophils highly indicates this condition.

- Vitamin B12 deficiency must always be ruled out before administering treatment for isolated folate deficiency.
- Folic acid supplementation is important in preventing neural tube defects as well as maternal folate deficiency.

**P.S.** Readers are advised to go through to the chapters related to Peripartum Care of Anemia for the overall management of anemia during labor, delivery, and the postpartum period as the protocol for management of anemia is common to all types of anemia.

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CHAPTER 08

# Transfusion in Pregnancy

Dr Nivedita Jha, Dr Vijitha MP

IN THIS CHAPTER

Indications | Pre-transfusion Assessment | Compatibility & Safety | Blood Components | Monitoring | Massive Transfusion | Complications

## 1.Introduction

Blood transfusion is one of the most important life-saving interventions in modern obstetric practice. Pregnancy is associated with profound increase in total blood volume along with other physiological changes in the hematological and cardiovascular system. The need for these adaptations are to support fetal growth and prepare the mother for delivery and to combat the loss during delivery.

Obstetric hemorrhage remains one of the leading causes of maternal morbidity and mortality worldwide, particularly in low- and middle-income countries. Blood transfusion plays a pivotal role in restoring oxygen-carrying capacity, correcting coagulopathy, and stabilizing women with severe anemia or acute blood loss. When used appropriately, it significantly improves maternal outcomes and can be life-saving for both the mother and the fetus.

## 2.When do we transfuse a pregnant women??

1.Pregnancy less than 34 weeks:

- Hb less than 5 g/dL (with/without signs of heart failure)
- Hb between 5–7 g/dL (with signs of heart failure)

2.Pregnancy more than 34 weeks:

- Hb less than 7 g/dL (without signs of heart failure)
- Severe anaemia with heart failure

3.Anaemia due to acute hemorrhage:

- Hb at or below 8 g/dL
- Ongoing hemorrhage with hemodynamic instability (Hb estimation not Needed)
- Common causes :

Placenta previa

Placental abruption

Uterine rupture

Ectopic pregnancy

4.Non-nutritional anaemia:

- Hemolytic anaemia – Thalassemia, sickle cell crisis
- Bone marrow deficiency (aplastic anaemia)

5.Coagulation Disorders:

- Disseminated intravascular coagulation (DIC).
- Liver disease with coagulopathy.
- Severe preeclampsia/HELLP syndrome with bleeding manifestations.
- Replacement of clotting factors using FFP or cryoprecipitate.
- 6.Thrombocytopenia:

Platelet transfusion when:

- Prophylactic Platelet count <10,000/μL even without bleeding manifestation.
- Platelet count <50,000/μL before cesarean section or neuraxial anaesthesia/analgesia.
- Severe thrombocytopenia associated with DIC or HELLP syndrome.

## 3.Pre transfusion Assessment

## General Principles of transfusion

• A valid, written and informed consent needs to be taken before blood transfusion Wherever feasible.

• In case of emergency situations, information on blood transfusion should be provided retrospectively.

• The justification for the transfusion and a record of the consent should be noted in the patient's case notes.

The following should be incorporated in the consent, to be provided in local language which the patient understands:

- Need for transfusion of blood and blood products
- Type of blood component used
- Advantages and disadvantages of transfusion
- Risks and adverse reactions of transfusion
- Cost and availability of blood components
- Alternative strategies if available
- Flip charts, infographics, pictorials if possible

## 4.Blood product compatibility and safety prior to transfusion in pregnancy

• ABO-, rhesus D- (Rh D-) and K- (Kell-) compatible red cell units should be transfused which are tested negative for virology screen (HIV, HBsAg, HCV).

• If clinically significant red cell antibodies are present, then blood negative for the relevant antigen should be cross-matched before transfusion.

• Cytomegalovirus- (CMV-) seronegative red cell and platelet components should be provided for elective transfusions during pregnancy.

Table 1 on FOGSI Recommendations:

| **Recipient should receive ABO type specific compatible blood or red blood cell components** | **Grade A** |
|---|---|
| Rh(D) negative recipient should receive Rh(D) negative blood or red blood cell components | Grade A |
| In the absence of ABO type specific blood, group O packed red cells can be transfused | CPP |
| In case clinically significant red cell antibodies are present, then blood negative for the relevant antigen should be cross-matched and transfused | Grade A |
| Red cell and component transfusion should be human immunodeficiency virus (HIV), hepatitis B surface antigen, hepatitis C virus (HCV), Venereal Disease Research Laboratory (VDRL), malarial parasite negative | Grade A |

*CPP – Clinical practice points.

## 5.Transfusion of blood and blood products

## Table 2 – Components of transfusion

| S.No | Components | Contents | Storage |
|---|---|---|---|
| 1. | Packed red cell | Hb rich erythrocytes | 2-8`c |
| 2. | Platelets | Platelet concentrate<br>(apheresis/pooled) | Room temperature |
| 3. | Fresh frozen plasma (FFP) | Coagulation factors<br>(including heat labile factors) | Less than -18`c |
| 4. | Cryoprecipitate | Vwf, factor 8,factor 13, fibrinogen(higher concentration), fibronectin | Less than -18`c |

**Equipment :** sterile, pyrogen free disposable set with filter. The filter helps in preventing the administration of particulate debris (170-260 microns)

## 6.Blood component transfused and Expected increase

- 1 unit Packed Red Blood Cells (PRBC) - Hemoglobin ↑ by ~1 g/dL (Hematocrit ↑ by ~3%) in a 70-kg adult
- 1 adult therapeutic dose of platelets (1 apheresis unit or 4–6 pooled random donor units) - Platelet count ↑ by 30,000–60,000/μL

- Cryoprecipitate One pool (≈10 units) increases fibrinogen by ~50–100 mg/dL (0.5–1 g/L) in an average adult
- Fresh Frozen Plasma (FFP) - Replaces clotting factors; does not significantly increase fibrinogen unless multiple units are given (typically 10–15 mL/kg is used to correct coagulopathy).

## 7.Monitoring during transfusion

## Clinical monitoring

Continuous pulse, BP, RR, $SpO_2$; temperature at least every 15 minutes in massive hemorrhage.

Watch for signs of acute transfusion reactions: fever, chills, rigors, urticaria, dyspnea, chest/back pain, hypotension, hemoglobinuria.

Monitor urine output (target ≥ 0.5 mL/kg/h) via Foley.

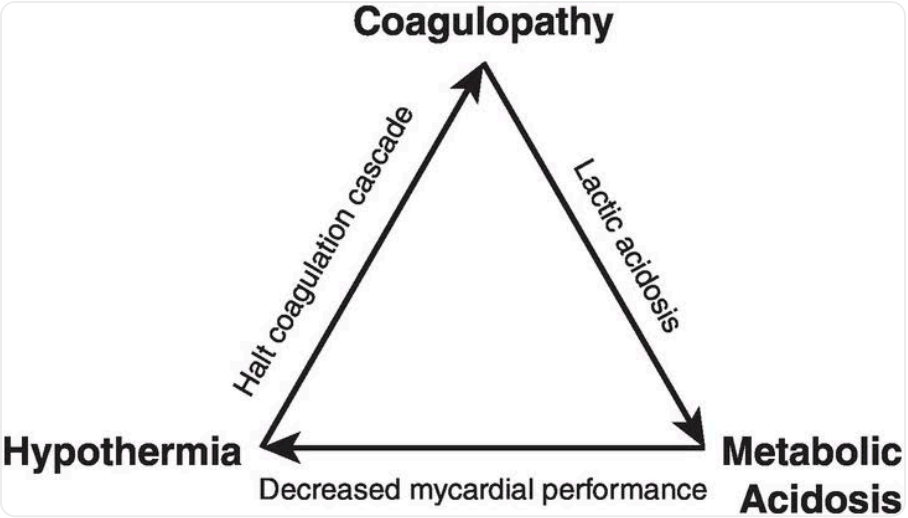
## Laboratory monitoring during ongoing bleeding

Repeat complete hemogram and coagulation profile including fibrinogen (if needed) at regular intervals (e.g., every 30–60 minutes in major obstetric hemorrhage) and after each set of components.

Use of viscoelastic testing (ROTEM/TEG) if available, guides in targeted transfusion therapy (e.g., FIBTEM for fibrinogen).

## 8.Massive transfusion protocol

A massive transfusion protocol (MTP) is a pre-activated, standardized system to rapidly deliver balanced blood components (RBCs, plasma, platelets, and often cryoprecipitate) in life threatening hemorrhage to avoid the lethal triad of death – metabolic acidosis, hypothermia and coagulopathy.




Ratio - 1:1 :1 (RBC: FFP: Platelet) for 6 rounds continues to remain the most widely used metric to guide MTPs worldwide as it closely resembles the whole blood.

Various definitions of massive blood transfusion (MBT) have been published in the medical literature, such as:

- Replacement of one entire blood volume within 24 hours
- Transfusion of >10 units of packed red blood cells (PRBCs) in 24 hours
- Transfusion of >4 units of PRBCs in 1 hour when ongoing need is foreseeable
- 50% of total blood volume (TBV) is replaced within 3 hours.

Criteria to trigger the activation of an MTP should be based on clinical judgement. However a score - Assessment of Blood Consumption), ABC score aids in the decision of activation of MTP. Parameters include

1.Penetrating mechanism of injury

2.Systolic Blood Pressure (SBP) ≤ 90 mm Hg

3.Heart Rate (HR) ≥ 120 beats per minute

4.Positive FAST (Focused Assessment with Sonography in Trauma) exam.

A score of two or more warrants MTP activation.

**9.When to stop MTP?**

The MTP should be stopped once hemorrhage is controlled and the patient is hemodynamically stable with acceptable laboratory targets, then transition to targeted, lab guided transfusion rather than following massive transfusion .

Lab targets includes

- Hb – more than 7g/dl
- INR ≤ 1.5–1.8, aPTT ≤ 1.5 × normal
- Platelets ≥ $50 \times 10^9$
- Fibrinogen ≥ 1.5 g/L
- Ionized Calcium ion > 1.15 mmol/L

## 10.Complications of blood transfusion

While generally safe and life-saving, blood transfusions carry risks. Common mild side effects include fever, chills, itching, and headache. Rare but serious complications include severe allergic reactions, acute breathing difficulties (TRALI), circulatory overload, and alloimmunization (developing antibodies that could complicate future pregnancies).

**Mild Side Effects (Common):**These reactions usually occur during or shortly after the transfusion and are typically mild.

- Fever and Chills: The most common reactions, easily treated with medication like paracetamol.

- Rash or Itchiness (Urticaria): Caused by mild allergic responses to proteins in the donor blood, which are often relieved with antihistamines.
- Headache: A temporary side effect that usually improves within a day.

**Severe Reactions (Rare):** These reactions are severe form, even life threatening requiring immediate cessation of transfusion.

- Transfusion-Related Acute Lung Injury (TRALI): A severe, potentially life threatening reaction characterized by **acute non cardiogenic pulmonary edema** that develops during or within 6 hours of transfusion . The possible mechanism being Immune-mediated (Donor anti- HLA antibodies react with recipient neutrophils). Treatment includes immediate cessation of transfusion and supportive measures.
- Transfusion-Associated Circulatory Overload (TACO): Occurs following volume overload during or after transfusion. This clinically manifests as acute pulmonary edema occurring during or within 12 hours of transfusion. Treatment includes immediate cessation of transfusion and supportive measures which includes diuretics.
- Hemolytic Reactions: A life-threatening event where the body's immune system acts against the transfused red blood cells due to a blood antigen mismatch. This can cause severe flank pain, breathing difficulty, and abrupt drops in blood pressure.

## Long-Term/Immune Complications

Alloimmunization: Pregnant women are more susceptible to developing antibodies against donor blood antigens. While this may not affect the current transfusion, it can create significant complications in future pregnancies (e.g., hemolytic disease of the fetus and newborn).

Infections: Although modern blood screening drastically reduces the risk, it does not completely eliminate the potential transmission of viruses like HIV or Hepatitis B and hepatitis C.

## 11.Special circumstances

- **Management of Inadvertent Rh-Positive Transfusion**

If an Rh-negative pregnant woman is accidentally transfused with Rh-positive blood – immediate action to be taken so as to prevent maternal alloimmunization which includes

1.Assessment of volume of Rh-positive blood transfused.

2.Consult a transfusion medicine specialist immediately.

3.Administer anti-D immunoglobulin (Rh Ig) as early as possible, ideally within 72 hours, if the woman is not already sensitized. Large doses of anti-D may be required depending on the volume of Rh-positive red cells transfused.

4.Monitor for evidence of alloimmunization with serial antibody screening.

Prevention:

Routine blood grouping and Rh typing at the first antenatal visit. Strict adherence to blood bank protocols to prevent Rh-incompatible transfusions.

- **Cell Salvage**

The main theoretical concerns are amniotic fluid contamination and feto-maternal red cell exposure .

Available guidance and patient information leaflets stated no evidence of amniotic fluid embolism caused by obstetric cell salvage in routine use.

Fetal red cells can enter the maternal circulation in pregnancy anyway, and studies have not shown a clear increase in clinically important antibody problems from cell salvage when standard precautions are used.

Rh-negative mothers

If the mother is Rh D -negative and the baby may be Rh D-positive, anti-D prophylaxis is still important after cell salvage.

Practice Recommendations -FOGSI CGPR:

- Cell salvage is an option for patients where the anticipated blood loss is great enough to induce anemia or expected to exceed 20% of estimated blood volume. (Grade C)
- Consent should be obtained for intraoperative cell salvage (IOCS) where possible and its use in obstetric patients should be done by a multidisciplinary team and subject to audit and monitoring. (Grade C)
- In case of Rh D - negative women (non sensitized) undergoing IOCS during cesarean section where cord blood group is confirmed as Rh D positive (or unknown), a minimum dose of 1,500 IU anti-D immunoglobulin should be administered following the reinfusion of salvaged red cells. (Grade C)

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CHAPTER 09

# Post-partum Care in Anaemic Women

Dr Sheela Mane

IN THIS CHAPTER

Definition | Etiology | Clinical Features | Diagnosis | Management | Prevention | NHM & RCOG

## Introduction

Postnatal anemia (PNA) refers to anemia occurring during the postpartum period, usually within the first six weeks after delivery. It commonly results from antenatal iron deficiency, blood loss during childbirth, or a combination of both. Early diagnosis and appropriate management improve maternal recovery, reduce fatigue, support successful breastfeeding, and decrease the risk of postpartum depression.

## Definition

There is no universal definition of postpartum anemia. According to various guidelines:

- World Health Organization (WHO):
  - Hemoglobin (Hb) <11 g/dL at 1 week postpartum.

- Hb <12 g/dL during the first postpartum year.
- RCOG and UK Guidelines:
  - Hb <10 g/dL within 48 hours after delivery is considered postpartum anemia.
- National Health Mission (India):
  - Hb <10 g/dL in the postpartum period requires treatment.

## Epidemiology

- Global prevalence ranges from 20–50%.
- In developing countries, prevalence may exceed 50–60%.
- In India, postpartum anemia is highly prevalent because of:
  - High rates of antenatal anemia
  - Nutritional deficiencies
  - Inadequate iron supplementation
  - Postpartum hemorrhage
  - Closely spaced pregnancies

## Etiology

### 1. Iron Deficiency

- Most common cause.
- Inadequate iron stores during pregnancy.
- Poor dietary intake.
- Increased iron requirements during pregnancy.

### 2. Blood Loss

- Normal vaginal delivery: approximately 500 mL.
- Cesarean section: approximately 1000 mL.
- Postpartum hemorrhage significantly increases risk.

### 3. Nutritional Deficiencies

- Folate deficiency.
- Vitamin B12 deficiency.

### 4. Hemoglobinopathies

- Thalassemia.
- Sickle cell disease.

### 5. Chronic Diseases

- Renal disease.
- Chronic infections.
- Autoimmune disorders.

## Risk Factors

- Antenatal anemia.
- Postpartum hemorrhage.
- Multiple pregnancy.
- Operative delivery.
- Prolonged labor.
- Instrumental delivery.
- Short interpregnancy interval.
- Poor nutrition.
- Low socioeconomic status.
- Teenage pregnancy.

## Clinical Features

### Symptoms

- Fatigue.

- Weakness.
- Dizziness.
- Palpitations.
- Dyspnea on exertion.
- Headache.
- Poor concentration.
- Reduced exercise tolerance.
- Depression and irritability.
- Difficulty breastfeeding.

### Signs

- Pallor.
- Tachycardia.
- Orthostatic hypotension.
- Flow murmur.
- Signs of heart failure (severe anemia).

## Complications

### Maternal

- Delayed recovery.
- Increased susceptibility to infections.
- Reduced milk production.
- Postpartum depression.
- Impaired cognition.
- Poor mother–infant interaction.
- Decreased physical performance.

### Neonatal

- Poor breastfeeding success.

- Delayed bonding.
- Possible impaired infant development secondary to reduced maternal care.

## Diagnosis

### History

- Antenatal Hb records.
- Blood loss during delivery.
- Symptoms of anemia.
- Dietary history.
- Previous anemia.

### Examination

- General physical examination.
- Hemodynamic stability.
- Pallor.
- Evidence of ongoing bleeding.

### Laboratory Investigations

- Complete blood count (CBC).
- Hemoglobin estimation.
- Peripheral smear.
- Serum ferritin (if infection is absent).
- Reticulocyte count (selected cases).
- Vitamin B12 and folate levels when indicated.

### Severity of Anemia

| Severity | Hemoglobin |
|---|---|
| Mild | 10–10.9 g/dL |
| Moderate | 7–9.9 g/dL |
| Severe | <7 g/dL |

## Management

Management depends on: severity, symptoms, hemodynamic status, and ongoing blood loss.

### 1. Oral Iron Therapy

**Indications:**

- Mild anemia.
- Hemodynamically stable women.

**Recommended dose:**

- 100–200 mg elemental iron daily.
- Continue for at least 3 months after normalization of Hb.

**Counseling:**

- Take on an empty stomach if tolerated.
- Vitamin C improves absorption.
- Avoid tea, coffee, and calcium near the time of iron intake.

**Common adverse effects:**

- Constipation.
- Nausea.
- Metallic taste.

- Black stools.

### 2. Intravenous Iron Therapy

**Preferred when:**

- Moderate to severe iron deficiency.
- Oral iron intolerance.
- Poor compliance.
- Malabsorption.
- Need for rapid correction.

**Common preparations:** Iron sucrose, ferric carboxymaltose.

**Advantages:**

- Faster Hb rise.
- Better replenishment of iron stores.
- Improved maternal fatigue.

### 3. Blood Transfusion

**Indications:**

- Severe anemia with symptoms.
- Hb <7 g/dL (individualized based on clinical status).
- Hemodynamic instability.
- Ongoing hemorrhage.

RCOG recommends that transfusion decisions should be individualized based on symptoms, ongoing blood loss, cardiovascular status, and patient preference rather than Hb concentration alone.

## Follow-up

- Repeat Hb after 2–4 weeks.

- Continue iron therapy for at least 3 months after Hb normalization.
- Assess treatment adherence.
- Nutritional counseling.
- Evaluate persistent anemia for alternative causes.

## Prevention

### Antenatal Measures

- Early screening.
- Iron and folic acid supplementation.
- Deworming where indicated.
- Nutritional counseling.
- Treatment of antenatal anemia.

### Intrapartum Measures

- Active management of the third stage of labor.
- Prevention and prompt management of postpartum hemorrhage.
- Judicious use of episiotomy.
- Careful surgical hemostasis.

### Postpartum Measures

- Early Hb assessment in high-risk women.
- Iron supplementation.
- Adequate nutrition.
- Follow-up after discharge.

## NHM (India) Recommendations

Under the National Health Mission:

- Screen all pregnant women for anemia during pregnancy and postpartum.
- Continue iron–folic acid supplementation for at least 3 months postpartum.
- Oral iron is recommended for mild anemia.
- Intravenous iron is recommended for moderate anemia when rapid correction is needed or oral therapy is not tolerated.
- Prompt identification and treatment of postpartum hemorrhage.
- Nutrition counseling and promotion of iron-rich foods.
- Follow-up Hb testing to assess response to treatment.

## RCOG Key Recommendations

- Measure Hb after significant peripartum blood loss (>500–1000 mL), uncorrected antenatal anemia, or symptoms suggestive of anemia.
- Oral iron is appropriate for stable women with mild anemia.
- Intravenous iron should be considered for women who cannot tolerate oral iron, have moderate to severe iron deficiency, or require rapid correction.
- Blood transfusion should be individualized and not based solely on Hb level.
- Investigate persistent anemia despite treatment.

## Key Points from Williams Obstetrics

- Iron deficiency is the leading cause of postpartum anemia.
- Blood loss during delivery is a major contributing factor.
- Prevention begins during antenatal care with adequate iron supplementation.
- Intravenous iron replenishes iron stores more rapidly than oral therapy.

- Correction of anemia improves maternal wellbeing and postpartum recovery.

## Conclusion

Postnatal anemia is a common and preventable condition with significant consequences for maternal health and infant care. Timely diagnosis, appropriate iron therapy, and structured postpartum follow-up remain the cornerstone of reducing the burden of postpartum anemia. Adherence to recommendations from Williams Obstetrics, RCOG, and the National Health Mission supports evidence-based management and improves maternal outcomes.

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