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A COMPREHENSIVE REVIEW OF IRON FOLIC ACID THERAPY IN MANAGING GESTATIONAL ANEMIA

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Abstract : Gestational anaemia is still a significant global public health issue, especially in low- and middle-income nations. Globally, gestational anaemia—which is mostly brought on by iron deficiency continues to be a major cause of maternal and neonatal morbidity. Pregnancy-related physiological alterations, such as an unequal expansion of plasma volume in relation to red blood cell mass, cause physiological (dilutional) anaemia. Nevertheless, when maternal iron stores are insufficient to satisfy the heightened needs of foetal growth, placental development, and enhanced maternal erythropoiesis, pathological anaemia, most frequently iron deficiency anaemia, or IDA develops. In order to meet the increased physiological iron demands necessary for the growth of the foetus, placental development, and maternal red cell mass expansion, the World Health Organization advises regular iron-folic acid (IFA) supplementation throughout pregnancy. Prophylactic supplementing for all pregnant women and therapeutic dose for those with anaemia based on hemoglobin and iron status markers are both essential components of effective IFA prescribing in gestational anaemia. To replenish iron reserves, increase haemoglobin concentration, and avoid folate deficiency-related problems such megaloblastic anaemia and neural tube abnormalities; standard regimens usually contain daily elemental iron and folic acid. Nevertheless, proper dosage and organised patient counseling are both necessary for the best results. Improving adherence, reducing discontinuation owing to gastrointestinal side effects, and dispelling myths about iron therapy are all made possible by counselling. Treatment effectiveness is greatly increased by providing information on appropriate dosage timing, dietary enhancers and inhibitors of iron absorption, anticipated side effects, and the significance of continuing medication even after hemoglobin normalisation. In situations of intolerance, malabsorption, or severe anaemia, rapid transfer to parenteral medication is made possible by routine monitoring and follow-up. Maternal tiredness, infection risk, obstetric problems, and blood transfusion requirements are decreased when comprehensive IFA prescription is paired with patient-centered counseling. Furthermore, it enhances foetal outcomes by decreasing the prevalence of low birth weight, preterm delivery, and poor neonatal iron reserves. Improving long-term mother and child health outcomes and lowering the burden of gestational anaemia require bolstering prenatal care services, guaranteeing a continuous supply of IFA, and incorporating organised counselling procedures into daily practice.

IndexTerms **– Anaemina, Hemoglobin, IFA, Pregnancy, Maternal, Iron deficiency, folate.**

INTRODUCTION

Women undergo several physiological changes during pregnancy. Among these physiological changes, the changes that occur in the blood circulatory system are most prominent, allowing for the normal growth of the foetus. Even in normal pregnant women, the haemoglobin level decreases due to dilution as a result of the increase in the volume of blood. Since iron and folic acid, in quantities required by the fetus, are preferentially transported to the fetus, the mother would likely develop iron-deficiency anaemia and folic acid-deficiency anemia. Approximately 20% of pregnant women develop anaemia, and most of these are due to iron deficiency, folic acid deficiency, or both. The use of iron and folic acid supplements in pregnant women is a matter of controversy, and the policy regarding this treatment differs from country to country. [1]

Classification of anaemia

Anemia can be classified into:

1- Microcytic& Hypochromic anaemia:
mean corpuscular volume (MCV) <80 FL, mean corpuscular hemoglobin (MCH) < 27 pg which occur in iron deficiency anemia, thalassemia, anemia of chronic disease (some cases), lead poisoning, and sideroblastic anaemia (some cases).

2- 2-Normocytic & Normochromic anemia:
MCV 80-95 fL MCH ≥ 27 pg, which occur in in hemolytic anaemia, anemia of chronic disease (some cases), after acute blood loss, renal disease, mixed deficiencies, bone marrow failure (e.g. post chemotherapy, infiltration by carcinoma, etc.).

3- Macrocytic anemia
MCV> 95fL occur in megaloblastic: vitamin B12 of folate deficiency, nonmegaloblastic: alcohol, liver disease

Hemoglobin concentration for diagnosing anemia [2]

Classification of anemia in pregnancy
Grossly classified into two types:
(A) Pathological anemia in pregnancy.
(B) Physiological anemia in pregnancy.

(A) Pathological anemia in pregnancy.
It is further subclassified into
1. Deficiency Anemia, e. g.
-Iron deficiency
-Folic acid deficiency
-B12 deficiency
-Protein deficiency
2. Hemorrigic:
Acute hemorrhagic: Following bleeding in early month of pregnancy or APH
Chronic hemorrhagic: as by hookworm infestation, GI (gastrointestinal) bleeding.
1. Hereditary: Thalassemias –Haemolobinopathies.
Hereditary hemolytic anemia – RBCs defects.
2. Bone Marrow insufficiency: as by radiation, marrow suppressant drugs.
3. Anemia of infection – as by malaria tuberculosis
4. Chronic diseases: as in nephropathies & neoplastic disorders.
It is noteworthy that obstetricians are concerned with two common types of anemia. They are:
5. Deficiency anemia,
6. Hemorrhagic anemia
It has been found that there is increased prevalence of anemia in pregnancy in tropical countries.
This is due to
a. Faulty dietary habit,
b. Faulty absorption mechanism,
c. More iron loss due to sweating and repeated pregnancy at short interval; prolonged period of lactation,
d. Infection: Chronic malaria, tuberculosis,
e. Excess demand of iron: pregnancy is an iron deficit state.

(B) Physiological Anemia
During pregnancy there is a disproportionate increase in plasma volume upto 50%, RBC 33% and Hb 18- 20% mass. In addition, there is marked demand of extra iron during pregnancy, especially in the second half of pregnancy. So, physiological anaemia results from the combined effects of hemodibalance. [3]

CRITERIA OF ANEMIA
The severity of anemia was determined based on the world health organization (WHO) criteria and was categorized as mild, moderate, severe anemia based on the hemoglobin concentration. For pregnant women, the criteria for non-anemia was hemoglobin concentration of 110 g/l or higher (11g/dl or higher), mild anemia was hemoglobin concentration of 100-109 g/l (10-10.9g/dl), moderate anemia was hemoglobin concentration of 70-99 g/l (7- 9.9 g/dl), and severe anemia was hemoglobin concentration lower than 70 g/l (<7g/dl) [2]

Maternal outcome in anemia
Mild anemia
The work capacity of women with mild anemia during pregnancy is reduced. They will not be able to earn their livelihood if the work requires manual labour. Women with chronic mild anemia will have pregnancy and delivery without any untoward consequences, since they are well compensated.
Moderate anemia
Women with moderate anemia have marked reduction in work capacity and will find it difficult to manage their domestic chores and childcare. The available data from India and abroad suggest that maternal morbidity is increased in women with Hb levels below 8gm/dl. They are prone to infections and recovery from infections takes longer. Premature births are more in women with moderate anaemia. They give birth to babies with low birth weight. Prenatal mortality is increased in these babies. They will not be able to tolerate blood loss before or during delivery. They will succumb to infections easily. Maternal deaths due to antepartum and post-partum haemorrhage, pregnancy induced hypertension and sepsis are high in women with moderate anemia.
Severe anemia
Three stages of severe anemia have been identified - compensated, decompensated, and associated with cardiac failure. Cardiac decompensation typically occurs when the Hb level is below 5.0 g/dl. The cardiac output is increased even at rest. The stroke volume is increased and the heart rate is increased. Palpitations and dyspnea even at rest are manifestations of these changes.[1]

Epidemiology:
As per the WHO report, the prevalence of anaemia in pregnant women is 55.9% globally. In India, the prevalence of anaemia has been estimated to be 33.0% to 89.0% [10]. The current descriptive case series study aims to find the prevalence and identify the

epidemiological factors of anaemia in pregnant women from the urban field practice area of the department of Community Medicine, Belgaum Institute of Medical Sciences, Belgaum, Karnataka, India.[4]

ETIOLOGY:

- Nutrient deficiencies:

Iron deficiency, Vitamin B12 deficiency, Folate deficiency

- Other contributing factors:

Multiple pregnancies, Frequent pregnancies, Heavy blood loss from menstruation, Chronic diseases like kidney diseases

- Malabsorption issues:

Crohn's disease, Celiac disease

- Genetic disorder

The most common types of anaemia affecting pregnant women are:
Iron deficiency anaemia, Folate deficiency anaemia, Vitamin B12 deficiency anaemia [4]

Risk Factors:

excessive menstrual bleeding prior to the index pregnancy, intestinal parasitic infection, gastritis with bleeding due to duodenal ulcer, and family illiteracy played the leading role with respect to the incidence of anemia.[5]

Pathophysiology

• Increased iron requirement: Total additional iron requirement across pregnancy is approximately 800–1000 mg (rough estimate): ~300 mg for foetal/placental development, ~500–700 mg for expansion of maternal red cell mass and losses. Highest demands occur in the second and third trimesters. (Georgieff 2020 [7]; Benson 2021 [10]).

• Physiologic haemodilution: Plasma volume increases more than red cell mass (peak plasma expansion ~40%); this relative dilution lowers measured Hb (physiological anaemia) and must be distinguished from pathological iron deficiency. (Peña-Rosas 2015 [09]; Georgieff 2020 [7]).

• Hepcidin regulation and iron absorption: Hepcidin, the liver-derived iron regulatory hormone, is normally suppressed in pregnancy to increase intestinal iron absorption and mobilize stores for the fetus. Low hepcidin favours maternal iron absorption and increased placental transfer, whereas inflammation or infection can raise hepcidin and blunt oral iron uptake. Measurement of hepcidin is an area of active research for personalised IFA strategies. (Koenig 2014[8]; Nemeth 2023[14]; Rosson recent review).

• Maternal–fetal iron transfer: The placenta actively transports iron to the fetus even when maternal iron stores are low; fetal iron priority can deplete maternal reserves. Cord blood ferritin correlates with maternal iron status. (Georgieff 2020[7]).

• Other contributors: Poor dietary intake (low bioavailable iron), parasitic infections (hookworm), heavy menstrual bleeding prior to conception, short interpregnancy intervals, multiple gestation, and socioeconomic factors increase IDA risk. Genetic haemoglobinopathies (thalassemia trait) complicate interpretation of iron indices. (Benson 2021[10]; Obianeli 2024[15]).

Impact of IFA (Iron–Folic Acid) pathophysiology

• Repletion of iron stores: Oral IFA provides elemental iron and folic acid, replenishing iron stores and supporting erythropoiesis. Regular supplementation prevents depletion caused by physiologic demands and improves maternal Hb when absorbed and adhered to. (Peña-Rosas 2015[9]; Duarte 2021[12]).

• Correcting anemia vs prevention: In iron-deficient pregnant women, therapeutic doses of oral iron (often higher elemental iron doses) raise Hb and reduce maternal morbidity. In iron-replete pregnant women, routine daily IFA reduces risk of developing anaemia at term and may reduce low birth weight risk in some settings. Effect sizes vary by baseline prevalence and adherence. (Cochrane reviews; Hansen 2023[11]).

• Limitations to oral IFA: Gastric intolerance, poor adherence, and conditions raising hepcidin (inflammation, infection) can limit effectiveness. In moderate–severe IDA or oral intolerance/poor response, intravenous iron preparations reliably restore iron stores faster and are increasingly recommended in guidelines. (Duarte 2021; recent systematic reviews).

• Role of folic acid: Folic acid (400 µg daily) is included to prevent folate deficiency and neural tube defects; it also supports erythropoiesis. Megaloblastic anaemia due to folate deficiency requires folate treatment and is separate from pure iron-deficiency states.

Complications:

Maternal complications

• Increased maternal morbidity and mortality: Severe anaemia (e.g., Hb <7 g/dL) substantially increases risk of maternal death, particularly in low-resource settings where obstetric haemorrhage and infections are common. (Benson 2021[10]; Georgieff 2020[7]).

• Cardiac strain and decompensation: Anaemia raises cardiac output and may precipitate heart failure in severely anaemic patients, especially with coexisting conditions or peripartum blood loss. Signs include tachycardia, dyspnoea and peripheral oedema in advanced cases.

• Increased susceptibility to infection: Iron deficiency alters immune responses; anaemic women may have higher susceptibility to infections and poorer recovery.

• Obstetric complications: Associations exist between maternal anaemia and increased risk of preterm labour, prolonged labour, increased need for cesarean delivery, postpartum haemorrhage, and transfusion. The magnitude varies with anaemia severity and timing (early pregnancy deficits often more consequential). (Peña-Rosas 2015[9]; Benson 2021[10]).

Fetal and neonatal complications:

• Preterm birth & low birth weight: Maternal IDA is associated with higher risk of preterm birth and low birth weight; systematic reviews support a link especially when anaemia is moderate–severe and present early in pregnancy. (Georgieff 2020[7]; Peña-Rosas 2015[9]).
• Impaired neonatal iron stores and infant iron deficiency: Low maternal iron leads to lower cord ferritin and neonatal iron stores, increasing risk of infant iron deficiency during infancy. This may affect growth and neurodevelopment. (Georgieff 2020[7]; Moyle 2024[13]).
• Neurodevelopmental outcomes: Observational evidence and preclinical models link fetal/neonatal iron deficiency with impaired myelination, neurotransmitter synthesis, and longer-term cognitive and behavioral deficits. RCT evidence is limited, but the biological plausibility is strong. (Georgieff 2020[7]; reviews).
• Perinatal mortality and stillbirth: Some studies show higher perinatal mortality with severe maternal anaemia, though confounding by socioeconomic and obstetric factors exists.

Signs and Symptoms:
• Fatigue, decreased stamina, and easy fatigability: Most common and often the earliest symptom, reflecting reduced oxygen-carrying capacity and decreased functional capacity.
• Pallor: Conjunctival and palmar pallor are clinical clues but are less sensitive than Hb measurement.
• Tachycardia and palpitations: Compensatory increase in heart rate for reduced oxygen delivery; may be more evident on exertion.
• Exertional dyspnoea: Breathlessness on mild exertion related to reduced oxygen delivery and increased cardiac output demands during pregnancy.
• Dizziness, lightheadedness, headaches: Especially when standing postural symptoms or with more severe anaemia.
• Pica: Craving and ingestion of non-food items (ice/soil/starch) associated with iron deficiency in many populations and may be an important clinical clue.
• Restless legs syndrome: Commonly reported in pregnancy and associated with iron deficiency in some women.
• Glossitis, angular cheilosis, brittle nails: Mucocutaneous signs of more advanced iron deficiency.
• Gastrointestinal intolerance to iron therapy: Oral iron commonly causes nausea, constipation, abdominal discomfort and dark stools counselling and management help adherence.
• Syncope, marked dyspnoea at rest, evidence of cardiac failure (raised JVP, pulmonary oedema), and markedly reduced exercise tolerance. These require urgent evaluation and often parenteral therapy or transfusion depending on severity and obstetric context.

Diagnosis and IFA Prescribing in Gestational Anemia
During pregnancy, maternal blood volume increases by approximately 40–60%, while red blood cell mass rises by only 20–50%. This disproportionate expansion results in physiological (dilutional) anaemia. A hematocrit of 30–32% is therefore considered normal during pregnancy. However, haemoglobin levels below 10 g/dL suggest pathological anemia rather than normal hemodilution.
The prevalence of anaemia increases as pregnancy advances. Mild anemia is observed in nearly 8% of women in early pregnancy, rising to about 12% in the second trimester and up to 34% near term. Severe anemia (haemoglobin <8 g/dL) has been associated with adverse fetal outcomes, including intrauterine growth restriction. Timely diagnosis and appropriate iron–folic acid (IFA) supplementation are therefore critical.

Iron Deficiency Anemia
Iron deficiency anemia (IDA) accounts for nearly 75% of anemia cases in pregnancy and affects approximately 40% of pregnant women worldwide. It is characterized by microcytic, hypochromic red blood cells.
Diagnostic findings include:
• Decreased hemoglobin and hematocrit
• Reduced RBC count
• Low mean corpuscular volume (MCV)
• Low serum ferritin and serum iron
• Increased total iron binding capacity (TIBC) and transferrin
• Reduced transferrin saturation
Peripheral smear typically shows microcytosis, hypochromia, anisocytosis, and pencil-shaped cells.

IFA Prescribing in IDA
All pregnant women should receive prophylactic iron and folic acid supplementation. Therapeutic dosing is indicated when hemoglobin is below recommended levels.
Recommended regimen:
• Prophylaxis: 60 mg elemental iron + 400 µg folic acid daily
• Treatment: 100–200 mg elemental iron daily in divided doses
Parenteral iron is considered when oral therapy is ineffective, poorly tolerated, or when rapid correction is required.

Megaloblastic Anemia
Megaloblastic anemia in pregnancy is primarily due to folate deficiency, while vitamin B12 deficiency is less common. It is characterized by macrocytic anemia.
Diagnostic findings include:
• Increased MCV

• Hypersegmented neutrophils
• Low serum folate or vitamin B12 levels
• Elevated homocysteine (folate deficiency)
• Elevated methylmalonic acid (B12 deficiency)
Pregnant women require at least 400 µg of folic acid daily to prevent neural tube defects. Higher doses may be required in deficiency states.

Microangiopathic Hemolytic Anemia (MAHA)
MAHA results from mechanical destruction of red blood cells within small blood vessels. It is associated with conditions such as HELLP syndrome, preeclampsia, thrombotic thrombocytopenic purpura (TTP), and hemolytic uremic syndrome (HUS).
Diagnostic findings include:

- Schistocytes on peripheral smear
- Elevated LDH
- Increased indirect bilirubin
- Reduced haptoglobiN
- Thrombocytopenia
- Management depends on the underlying cause. Delivery is definitive for HELLP and severe preeclampsia, while plasma exchange is indicated in TTP.

Aplastic Anemia
Aplastic anemia is a rare condition characterized by bone marrow failure leading to pancytopenia. It may coexist with pregnancy or rarely be triggered during pregnancy.
Management includes supportive care with transfusions to maintain hemoglobin between 7–8 g/dL and platelet counts above 10,000/µL. Hematopoietic stem cell transplantation is generally deferred until after delivery.

Sickle Cell Anemia
Sickle cell anemia is caused by a mutation in the beta-globin gene, resulting in hemoglobin S formation. Under low oxygen conditions, red cells assume a sickle shape, leading to hemolysis and vaso-occlusion.
Diagnosis is confirmed by hemoglobin electrophoresis demonstrating HbS. Pregnancy increases maternal and fetal risks, including vaso-occlusive crises, acute chest syndrome, and preeclampsia.
Routine prophylactic transfusions are not universally recommended. Transfusion is considered when hemoglobin falls below 7 g/dL or in severe complications.[19]

Diagnosis of Iron Deficiency Anemia (IDA)
A complete blood count (CBC) in iron deficiency anemia typically demonstrates reduced hemoglobin, decreased mean corpuscular volume (MCV), reduced mean corpuscular hemoglobin concentration (MCHC), and occasionally mild thrombocytosis. In early stages, peripheral smear findings may be subtle; however, as deficiency progresses, microcytosis, anisocytosis, and poikilocytosis become evident.
Serum ferritin is the most specific laboratory marker for iron deficiency. A ferritin level below 30 ng/mL is considered diagnostic in pregnancy. However, ferritin is an acute-phase reactant and may appear normal or elevated in inflammatory states, even in the presence of iron deficiency. Therefore, borderline values require further evaluation.
When ferritin results are inconclusive, a complete iron profile should be performed, including serum iron, total iron-binding capacity (TIBC), and transferrin saturation (calculated as serum iron divided by TIBC). Iron deficiency is suggested by low serum iron, elevated TIBC, and reduced transferrin saturation.
Emerging biomarkers such as soluble transferrin receptor levels, reticulocyte hemoglobin content (CHr or Ret-He), and serum hepcidin provide earlier insight into bone marrow iron availability and erythropoietic activity. Reticulocyte hemoglobin parameters are particularly useful in inflammatory states where ferritin and transferrin saturation may be unreliable. However, these advanced tests are not universally standardized and may not be readily available in public health settings. Furthermore, they do not reliably distinguish iron deficiency anemia from microcytic anemia caused by thalassemia or other hemoglobinopathies.[19]

Role of IFA Prescribing in Gestational Anemia
Gestational anemia, predominantly caused by iron deficiency, remains a major public health concern worldwide, particularly in developing countries. Increased iron requirements during pregnancy are necessary to support expanded maternal blood volume, placental growth, and fetal development. When these physiological demands are not met, iron stores become depleted, leading to reduced hemoglobin synthesis and impaired oxygen delivery to maternal and fetal tissues.
The prevalence of gestational anemia is especially high in low-resource settings due to poor dietary intake, repeated pregnancies, short interpregnancy intervals, parasitic infections, and limited access to antenatal care. If left untreated, anemia during pregnancy contributes significantly to maternal morbidity, preterm delivery, low birth weight, and increased perinatal mortality.
During pregnancy, plasma volume increases disproportionately compared to red blood cell mass, resulting in physiological hemodilution. However, when iron reserves are insufficient, pathological anemia develops. Iron is essential for hemoglobin synthesis, oxygen transport, enzymatic reactions, immune function, and cellular metabolism. Folic acid is equally important for DNA synthesis, cell division, and prevention of neural tube defects.
IFA supplementation addresses both iron deficiency and folate deficiency simultaneously, making it a comprehensive strategy in antenatal care. Prescribing IFA ensures restoration of iron stores, improvement in hemoglobin concentration, and prevention of megaloblastic changes due to folate deficiency.

Clinical Role of IFA in Preventing Maternal Complications

Appropriate IFA prescribing significantly reduces maternal complications associated with anemia. Correction of anemia improves physical capacity, reduces fatigue, enhances immunity, and lowers the risk of infections. Adequate hemoglobin levels are critical in preventing complications such as postpartum hemorrhage, cardiac stress, and poor wound healing.

Severe anemia increases the likelihood of blood transfusion during delivery, which carries additional risks. Regular IFA supplementation during antenatal visits reduces the progression from mild to severe anemia, thereby minimizing obstetric emergencies and maternal mortality.

Impact of IFA on Fetal and Neonatal Outcomes

Maternal iron status directly influences fetal growth and development. Inadequate iron supply impairs placental oxygen transfer, leading to intrauterine growth restriction and low birth weight. Studies have demonstrated that untreated maternal anemia is associated with preterm birth, reduced neonatal survival, and impaired cognitive development.

Iron plays a critical role in fetal brain development, particularly in myelination, neurotransmitter synthesis, and synaptogenesis. Timely IFA supplementation improves fetal iron stores, enhances birth weight, and supports optimal neurodevelopmental outcomes. Therefore, IFA prescribing contributes not only to safe delivery but also to long-term child health.

Prophylactic IFA Supplementation

Universal prophylactic IFA supplementation is recommended for all pregnant women, regardless of anemia status, particularly in high-prevalence regions. Prophylactic doses prevent depletion of maternal iron stores and reduce the risk of developing anemia later in pregnancy.

Routine supplementation should ideally begin in the early second trimester and continue throughout pregnancy and the postpartum period. Counseling regarding adherence, dietary advice, and management of minor gastrointestinal side effects improves compliance and therapeutic success.

Therapeutic IFA Prescribing in Diagnosed Cases

In women diagnosed with gestational anemia, therapeutic doses of IFA are prescribed based on severity. Hemoglobin levels and serum ferritin should be monitored periodically to assess response. Adequate duration of therapy is essential to replenish iron stores even after hemoglobin normalization.Selection of iron preparation depends on availability, affordability, and tolerability. Ferrous salts are commonly used due to cost-effectiveness, while newer iron complexes may offer better gastrointestinal tolerance. In cases of moderate to severe anemia or intolerance to oral therapy, parenteral iron administration may be required under medical supervision.

Challenges in IFA Implementation

Despite clear benefits, several barriers affect effective IFA prescribing. Poor compliance due to gastrointestinal side effects such as nausea, constipation, and metallic taste remains a common issue. Lack of awareness, myths regarding iron supplementation, and irregular antenatal visits further reduce adherence. Healthcare providers play a crucial role in counseling patients, addressing misconceptions, ensuring early diagnosis, and reinforcing the importance of regular supplementation. Strengthening public health programs and ensuring uninterrupted supply of IFA tablets are essential to improve outcomes.

Public Health and Intergenerational Impact

IFA supplementation is not merely an individual treatment strategy but a public health intervention with intergenerational benefits. Correction of maternal anemia reduces maternal mortality rates, enhances productivity, and improves neonatal survival. Children born to mothers with adequate iron status are more likely to achieve better cognitive development and academic performance.Thus, rational and consistent IFA prescribing contributes to breaking the cycle of malnutrition and anemia across generations. Integration of IFA supplementation into routine antenatal care services remains one of the most cost-effective maternal health interventions.[20]

Adverse Effects of Iron Deficiency Anemia in Pregnancy

Iron deficiency anemia (IDA) during pregnancy is associated with significant maternal, fetal, and neonatal morbidity. Due to increased iron requirements for expanding maternal blood volume, placental development, and fetal growth, pregnant women are particularly vulnerable to iron depletion. When iron deficiency progresses to anemia, systemic physiological compromise occurs.

1. Maternal Adverse Effects

Maternal complications include chronic fatigue, reduced exercise tolerance, dizziness, palpitations, and reduced work capacity. Impaired oxygen delivery to tissues may result in decreased cognitive function and poor concentration. Severe anemia increases cardiac workload, potentially leading to tachycardia, cardiac failure, and increased maternal mortality in extreme cases.

Iron deficiency also disrupts immune competence. Altered neutrophil–lymphocyte ratios and increased inflammatory markers have been observed in anemic mothers, predisposing them to infections and delayed recovery during the antenatal and postpartum periods.Obstetric risks include preterm labor, premature rupture of membranes, placental insufficiency, postpartum hemorrhage, and increased need for blood transfusion. Severe anemia may compromise uterine contractility, increasing the risk of prolonged labor and postpartum complications.

2. Fetal and Neonatal Adverse Effects

Maternal iron deficiency directly affects placental iron transport, leading to reduced fetal iron stores. Consequences include low birth weight, small-for-gestational-age infants, intrauterine growth restriction, and increased perinatal mortality.

Iron is essential for fetal brain development, particularly for myelination, synaptogenesis, and neurotransmitter synthesis. Deficiency during critical periods of gestation may lead to delayed motor milestones, impaired learning ability, memory deficits, and behavioral disturbances. Emerging evidence suggests that early iron deficiency may cause persistent neurodevelopmental alterations extending into childhood.Neonates born to anemic mothers often exhibit lower hemoglobin levels and depleted iron reserves, increasing their risk of early infant anemia. Delayed physical growth, reduced weight gain, and impaired immune response are additional concerns.

3. Long-Term Intergenerational Impact

The impact of gestational anemia extends beyond delivery. Chronic iron deficiency during fetal life may influence cognitive performance, academic achievement, and overall productivity later in life. Therefore, gestational IDA represents not only a clinical issue but also a broader public health challenge with socioeconomic implications.

II. Management Strategies to Overcome Gestational Iron Deficiency Anemia

1. Early Screening and Diagnosis

Routine antenatal screening through complete blood count and iron studies is essential for early identification. Hemoglobin estimation in each trimester allows timely detection and intervention. Serum ferritin measurement helps confirm iron deficiency.

2. Iron–Folic Acid (IFA) Supplementation

IFA supplementation remains the primary preventive and therapeutic strategy. Universal prophylaxis is recommended for all pregnant women due to increased physiological demand. Therapeutic dosing is required when anemia is diagnosed.

Oral iron preparations such as ferrous sulfate, iron polysaccharide complex, and iron protein succinylate have demonstrated comparable efficacy in improving hemoglobin and replenishing iron stores. Choice of preparation should consider tolerability, patient adherence, cost, and availability. Common side effects of oral iron include nausea, constipation, metallic taste, and epigastric discomfort. Proper counseling—such as taking iron after meals, dividing doses, or switching formulations—can enhance compliance.

3. Parenteral Therapy and Severe Cases

Parenteral iron is indicated in cases of severe anemia, intolerance to oral therapy, malabsorption, or late gestational presentation requiring rapid correction. Intravenous iron preparations effectively restore iron stores with fewer gastrointestinal effects.

Blood transfusion is reserved for life-threatening anemia or when there is hemodynamic instability, especially near term.

4. Nutritional and Public Health Measures

Dietary modification is a supportive strategy. Pregnant women should consume iron-rich foods such as green leafy vegetables, legumes, fortified cereals, red meat, and poultry. Vitamin C enhances iron absorption, while tea, coffee, and calcium-rich foods inhibit absorption and should be avoided around supplementation time.

Public health interventions including routine antenatal care, health education, deworming programs where indicated, and strengthening supply chains for IFA tablets play a crucial role in reducing anemia prevalence.

5. Monitoring and Follow-Up

Regular follow-up is necessary to assess hemoglobin response and treatment adherence. Hemoglobin should typically rise within 3–4 weeks of adequate therapy. Continuation of supplementation throughout pregnancy and postpartum period ensures replenishment of iron stores.[21]

Adverse Effects of Iron Folic Acid Supplements in Pregnancy:

Side Effect	Percentage Reported (%)	Pathophysiological Mechanism	Organ-System Impact	Impact on Supplement Duration
Constipation	28.5%	Slowing of intestinal peristalsis and increased water reabsorption in colon	Hard stools, abdominal distension, discomfort	Significant reduction in supplementation days
Diarrhoea	11.6%	Osmotic effect of unabsorbed iron altering intestinal flora	Loose stools, dehydration risk	Significant reduction in duration
Nausea	7.6%	Gastric mucosal irritation and vagal nerve stimulation	Reduced appetite, upper abdominal discomfort	Strong negative association with 90+ day compliance
Vomiting	5.1%	Activation of central emetic pathways due to gastric irritation	Fluid loss, weakness, electrolyte imbalance	Moderate reduction in duration

Heartburn	7.2%	Increased gastric acidity and esophageal irritation	Burning retrosternal sensation	Significant reduction in supplementation days
Severe Abdominal Pain	11.6%	Local inflammatory response within intestinal mucosa	Cramping and functional discomfort	Variable influence on compliance
Black Stools	4.7%	Oxidation of unabsorbed iron in colon	Harmless stool discoloration	Associated with shorter duration in some cases

Gastrointestinal symptoms arise primarily from the presence of free iron within the intestinal lumen. Iron can generate reactive oxygen species, leading to mucosal irritation and mild inflammatory changes. Altered gut motility and changes in microbiota composition further contribute to bowel disturbances.

Table 2: Systemic/Non-Gastrointestinal Side Effects – Prevalence, Mechanism and Duration Impact

Side Effect	Percentage Reported (%)	Underlying Mechanism	Organ-System Impact	Impact on Supplement Duration
Chest Pain	31.8%	Likely reflux-induced esophageal irritation rather than cardiac origin	Thoracic discomfort and anxiety	Minimal overall effect on duration
Bluish Lips/Nails	5.4%	Perceived circulatory changes or anxiety-related symptoms	Cosmetic concern	Minimal effect on compliance
Skin Reactions	2.5%	Mild hypersensitivity response	Localized rash or itching	Minimal impact on supplementation days

ORGAN-SYSTEM IMPACT AND NUTRITIONAL CONSEQUENCES

Persistent gastrointestinal symptoms may significantly influence maternal physiology. Repeated vomiting or diarrhoea can lead to dehydration and electrolyte imbalances, particularly sodium and potassium depletion. Electrolyte disturbances may manifest as fatigue, dizziness, muscle cramps, and in difficult situations, cardiovascular instability.

Reduced appetite secondary to nausea can compromise total caloric intake and diminish consumption of essential nutrients. Inadequate protein, vitamin, and mineral intake during pregnancy may negatively affect maternal energy balance and fetal growth. If supplementation is discontinued due to intolerance, iron deficiency anaemia may persist, reducing haemoglobin concentration and impairing oxygen delivery to maternal and fetal tissues.

EXPANDED CLINICAL INTERPRETATION

Although most IFA-related side effects are mild and dose-dependent, perception of discomfort significantly influences adherence. Symptoms such as black stools or mild nausea, though clinically harmless, may be misinterpreted as serious complications if not explained properly. [22]

Interactions

Food and drug interactions:

Food interactions: Inhibitors: Phytates (cereals/legumes), polyphenols/tannins (tea, coffee), calcium-rich foods/supplements reduce nonheme iron absorption. Avoid tea/coffee and calcium around dosing (1–2 hours separation recommended).

Enhancers: Vitamin C (ascorbic acid), organic acids, and meat (heme iron) increase iron absorption.

Drug - Drug interactions

Drug interactions: Iron chelates with several drugs reducing their absorption: tetracyclines, fluoroquinolones, levothyroxine, levodopa, some integrase inhibitors (dolutegravir) separate dosing by 2–4 hours when possible. Iron may also interfere with absorption of bisphosphonates and penicillamine.

Folate interactions: Antifolates (methotrexate, trimethoprim, pyrimethamine) antagonize folate metabolism; folic acid reduces methotrexate toxicity in low-dose regimens where indicated but may interact in high-dose oncology settings (use leucovorin rescue appropriately). Antiepileptic drugs (phenytoin, carbamazepine, phenobarbital) reduce folate levels via enzyme induction.

Implementation counseling should emphasize timing (empty stomach if tolerated; otherwise with small amount of food), separation from interacting drugs, and use of vitamin C co-administration if tolerated.[23,24,25,26]
Drugs to Steer Clear of During Pregnancy NSAIDs (Ibuprofen, Naproxen) for Pain Management
(Aleve) and Ibuprofen (Advil, Motrin): If taken during the third trimester, these medications may result in problems such as decreased amniotic fluid and heart problems in the foetus. Alternatives like acetaminophen (Tylenol) are safer.
Tetracyclines
Tetracycline antibiotics: These can have an impact on the baby's tooth and bone development, resulting in irreversible tooth discolouration and stunted bone growth. Cephalosporins and penicillin are safer substitutes.
Additional Drugs
Some Acne Drugs (Isotretinoin, for example)
Pregnant women should avoid isotretinoin (Accutane), a potent acne drug that has a significant risk of serious birth abnormalities.
A Few Herbal Supplements
During pregnancy, herbal supplements such as ephedra, ginkgo biloba, and St. John's Wort can be dangerous and increase the risk of miscarriage and early labour. Before using any herbal supplements, always get medical advice.
Using illegal substances and alcohol when pregnant
Alcohol use and illicit drug use during pregnancy carry serious dangers for the mother and unborn child, including miscarriage, developmental delays, and birth abnormalities. Pregnant women should abstain from these substances and get treatment if they are abusing them.
Hazards Associated with Illegal Substances
Cocaine, heroin, methamphetamine, and marijuana are a few examples of drug abuse. These chemicals can have serious consequences on pregnancy:

- **Cocaine:**
  Premature Birth: Preterm labour and birth are two consequences of cocaine usage.Low Birth Weight and Growth Issues: Infants who are exposed to cocaine during pregnancy frequently have smaller heads and lower birth weights, which may be signs of delayed brain development. Placental Abruption: Using cocaine can cause the placenta to prematurely detach from the uterus, a serious condition. This may cause serious bleeding in both the mother and the foetus, as well as, in certain situations, death in either scenario.Use of cocaine during pregnancy can result in severely elevated blood pressure, raising the risk of difficulties for both the mother and the unborn child. Cognitive and Developmental Issues: Prolonged cocaine exposure during pregnancy may cause behavioural issues, learning impairments, and problems with the child's cognitive development.
- **Heroin:**
  Neonatal Abstinence Syndrome (NAS): Babies born to heroin-using mothers frequently suffer from withdrawal symptoms after delivery, necessitating specialist treatment to control them.Low Birth Weight and Premature Birth: Heroin dramatically raises the chance of low birth weight and preterm birth, which can cause problems for the infant's early development. Developmental and Physical Delays: Prolonged heroin exposure during pregnancy might result in behavioural problems, smaller heads in infants, and developmental delays. The child's physical and cognitive development may suffer long-term consequences from these delays.
- **marijuana:**
  Low Birth Weight and Growth Issues: Regular use of marijuana during pregnancy may cause neonates to be shorter and have smaller heads. It is also linked to lower birth weights. Numerous postpartum health issues may be exacerbated by these developmental limitations.
  Preterm Birth and Stillbirth: Frequent marijuana usage may raise the chance of preterm birth and stillbirth, which puts the baby's growth and life at grave danger.
  Developmental Problems: Pregnancy-related marijuana exposure may have an impact on the growing baby's brain, resulting in long-term problems with memory, concentration, and problem-solving abilities. In fact, several studies even link prenatal marijuana use to a higher risk of autism in offspring.
  Alcohol:
  Foetal Alcohol Spectrum abnormalities (FASDs): Pregnancy-related alcohol use can result in a variety of abnormalities that include behavioural, learning, and physical issues.
  Alcohol raises the chance of miscarriage and stillbirth.
  Development Defects: Alcohol exposure during pregnancy may result in facial deformities and developmental limitations.[27]
  Anticonvulsants:
  Such as carbamazepine, sodium valproate, and phenytoin.
  Those on anticonvulsants had reduced blood levels of folate, vitamin B6, and vitamin B12. Regular blood tests should be performed to keep an eye out for this. It might also be helpful to take these nutrients as supplements.
- **Levothyroxine:**
  Iron: Levothyroxine's absorption might be decreased and its effectiveness diminished if taken concurrently with iron supplements. Levothyroxine and iron supplements should be taken at least two hours apart.

Iron-acid-reducing medications can have a detrimental effect on iron absorption, as can proton-pump inhibitors (like omeprazole and lansoprazole) and histamine-receptor antagonists (like ranitidine). When using the medicine for more than a year, this is very concerning. Iron supplements and this medicine should be taken at least two hours apart.

- **The trimethoprim:**

Folate's active form is produced by an enzyme that is inhibited by trimethoprim. Long-term high trimethoprim dosages can raise the risk of folate insufficiency. Frequent blood tests are necessary. [28]
Counselling to maximize adherence:

Counselling is central to converting prescriptions into clinical benefit. Studies and systematic reviews show that counselling and health education significantly improve adherence to IFA and hemoglobin outcomes, particularly when counseling is structured and integrated with routine ANC visits. Digital interventions (SMS reminders, apps) and community health-worker engagement also show benefit.

Counselling:

Explain why IFA matters: Briefly explain the role of iron and folic acid — for mother's strength, reducing bleeding risk, preventing low birth weight and improving baby's health. Use simple language and local metaphors where helpful.

Describe the regimen clearly: Name the tablet, the dose, when to take it (time of day), and duration (e.g., "one tablet daily from now until delivery and for X weeks postpartum"). Use teach-back: ask the woman to repeat the plan in her own words.

Discuss common side effects and management: e.g., "Some women get stomach upset or constipation — take with food, try at bedtime, eat more fiber, and tell us if it's severe." Anticipatory guidance reduces dropouts.

Set adherence strategies: link pill-taking to daily routines (after brushing teeth or with a specific meal), provide a calendar or pillbox, or use mobile reminders. Offer family engagement (ask spouse/partner to remind) where culturally appropriate.

Address beliefs and myths: Explore any traditional beliefs that discourage tablet use and respectfully address them.

Plan follow-up and monitoring: Arrange next ANC visit, specify Hb recheck timing, and provide contact information for side-effect concerns.

Use visual aids and simple leaflets: Pictorial leaflets increase retention in low-literacy settings.

Involve community health workers: For home visits, counselling reinforcement, and tracking missed doses.[29,30,31]

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