



Good clinical practice advice: Iron deficiency anemia in pregnancy[☆]

FIGO Working Group on Good Clinical Practice in Maternal–Fetal Medicine^{*,a}

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PREMISE

Anemia is one of the most prevalent health problems in the world, affecting almost half a billion women of reproductive age. Approximately 40% of fertile non-pregnant women have low iron reserves.¹ This condition can affect more than 10% of pregnancies in high-income countries, but its impact is much bigger (20%–70%) in low-income countries. Iron deficiency anemia is the most prevalent and also the most neglected nutrient deficiency in the world, particularly among pregnant women and children, and especially in low-income countries.²

WHO defines anemia in pregnancy as a hemoglobin concentration of less than 11 g/dL at any stage of pregnancy³; UK antenatal guidance⁴ and Centers for Disease Control and Prevention guidance define anemia as less than 110 g/L in the first trimester and less than 105 g/L in the second or third trimester.⁵

During pregnancy, increased maternal iron is needed as a result of the demands of the growing fetus and placenta, increased erythrocyte mass and, in the third trimester, expanded maternal blood volume.^{6,7} However, during pregnancy there are many risk factors for iron deficiency or iron deficiency anemia, including an iron-deficient diet, gastrointestinal issues affecting absorption, or a short interpregnancy interval.⁸ Other causes of anemia include parasitic diseases, micronutrient deficiencies, and genetically inherited hemoglobinopathies.⁹

The developing fetus is entirely dependent on its mother for nutritional requirements. All iron delivered to the baby comes from either maternal iron stores, absorption of iron from the maternal diet, or possibly turnover of maternal erythrocytes. Estimates vary, but each pregnancy requires at least 300 mg of iron taken from the mother's liver stores,¹⁰ and others have proposed that the value is even higher—up to 500 mg.

Late in pregnancy, an average of 5.6 mg of iron per day from dietary or endogenous maternal sources is transported across the placenta to cover fetal demands.¹¹ The quantity of iron absorption during

the second half of gestation, and principally in the third trimester, is around six times higher than the quantity of iron typically absorbed from dietary sources in non-pregnant women. That represents 30% of the 20 mg of iron that is catabolized daily from senescent red blood cells.¹¹

A strong association has been found between moderate to severe anemia at 28 weeks of gestation and the severity of intra- and postpartum hemorrhage,⁷ which cause 23% of maternal deaths.¹² Nevertheless, some papers reported no significant association between anemia and preterm delivery, low birth weight infants, or maternal morbidity, except in cases of severe anemia.¹³ Traditionally, maternal anemia was frequently thought to be associated with a suboptimal fetal outcome; however, data supporting this concept are not clear.^{14,15}

Fetal iron needs will be compromised when maternal iron stores are suboptimal.^{16,17} There is insufficient information about what proportion of early-life anemia is caused by maternal iron deficiency during pregnancy, or if there is any trimester-associated risk that is more highly associated with neonatal iron deficiency.^{16,17} Growing information suggests that altered or limited iron supply in utero, during key windows of development, may lead to adaptive responses that permanently impact metabolic or developmental programming and the developing brain.^{18,19}

The conclusions of several studies are controversial regarding the association of mild anemia and adverse maternal and fetal outcomes, resulting in the fact that a chronic mild anemia can lead to a normal course of pregnancy and to a labor without any adverse consequences.²⁰ The relationship between anemia and perinatal mortality is still unclear. Delaying the time at which the umbilical cord is clamped after delivery has a significant impact on the net amount of blood and, hence, iron stores transferred to the neonate at birth.²¹

Although iron deficiency in pregnancy is, in principle, identifiable, treatable, and possibly preventable, there is uncertainty about its

significance as a clinical and public health problem, and whether systematic screening and treatment for iron deficiency and iron deficiency anemia in pregnancy would improve maternal and infant outcomes.

Routine screening for iron deficiency anemia in asymptomatic women may or may not be conducted since there is still a lack of sufficient evidence to develop a recommendation for this procedure.²² However, the most important institutions include in their guidelines that screening should be done in every trimester, using WHO definitions, or at least at 28 weeks, and also when clinical signs suggest the presence of anemia, but this depends on the facilities and the health organization.²³

There is a variety of treatment options for iron deficiency and iron deficiency anemia in early pregnancy. These include oral iron and parenteral iron (intravenous and intramuscular preparations). A systematic review and meta-analysis has reported that prenatal iron in the context of maternal anemia increases maternal hemoglobin, reduces iron deficiency, and reduces low birth weight.²⁴ Intravenous iron use is recommended only in the second trimester for safety reasons. Women with established iron deficiency anemia should be given 100–200 mg elemental iron daily and should be advised on correct administration to optimize absorption.

Referral to secondary care should be considered if there are significant symptoms and/or severe anemia (hemoglobin <7.0 g/dL), late gestation (>34 weeks), or a failure to respond to a trial of oral iron. Women with anemia may require additional precautions for delivery, including delivery in a hospital setting, available intravenous access, active management of the third stage of labor, and preparation for excess bleeding.

Previous studies have provided sufficient evidence to show that iron supplementation with or without folic acid results in a significant reduction in the incidence of anemia during pregnancy.^{25,26} Newer evidence is consistent with the same results; iron supplementation is often effective in improving maternal hematologic indices and may result in a lower incidence of women with iron deficiency and iron deficiency anemia during pregnancy and at delivery. However, evidence is insufficient to demonstrate a substantial effect on clinical outcomes for women and infants. No study has directly compared clinical outcomes or harms of screening or not screening pregnant women for iron-deficiency anemia.²³ One important condition for treatment is that adequate staffing and facilities for testing, diagnosis, treatment, and program management before commencement of the screening program should be available.^{27,28}

Rigorous studies are needed to fully understand the short- and long-term effect of routine iron supplementation and screening during pregnancy on women and infants. Until then, the evidence on routine iron supplementation and screening in prenatal care will remain unclear at best.

FIGO recommends the following:

1. Anemia is defined as hemoglobin less than 11.0 g/dL during pregnancy and postpartum.
2. Full blood count should be assessed at least at booking and at 28 weeks.

3. All women should be given dietary information to maximize iron intake and absorption.
4. Routine iron supplementation for all women in pregnancy is recommended, according to the health policies of the countries, especially in areas with a high prevalence of anemia. The minimum dosage should be 30 mg of elemental iron a day.
5. Unselected screening with routine use of serum ferritin is generally not recommended although individual centers with a particularly high prevalence of at-risk women may find this useful.
6. Women with iron deficiency anemia should be given 100–200 mg elemental iron daily. They should be advised on correct administration to optimize absorption.
7. Referral to secondary care should be considered if there are significant symptoms and/or severe anemia (hemoglobin <7.0 g/dL), late gestation (>34 weeks), or if there is failure to respond to a trial of oral iron.
8. Once hemoglobin is in the normal range, supplementation should continue for 3 months and at least until 6 weeks postpartum to replenish iron stores.
9. Pregnant women with anemia may require additional precautions for delivery, including delivery in a hospital setting, available intravenous access, active management of the third stage of labor, and preparation for excess bleeding. Suggested hemoglobin cutoffs are less than 10.0 g/dL for delivery in hospital and less than 9.5 g/dL for delivery in an obstetrician-led unit. Women with hemoglobin less than 10.0 g/dL in the postpartum period should be given 100–200 mg elemental iron for 3 months.
10. Parenteral iron should be considered from the second trimester onward and during the postpartum period for women with confirmed iron deficiency who fail to respond or who are intolerant to oral iron.
11. Blood transfusion should be reserved for those with risk of further bleeding, imminent cardiac compromise, or symptoms requiring immediate attention.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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