FIGO COMMITTEE REPORT

Good clinical practice advice: Iron deficiency anemia in pregnancy

FIGO Working Group on Good Clinical Practice in Maternal–Fetal Medicine*

*Correspondence: Gian Carlo Di Renzo, Department of Obstetrics and Gynecology, University of Perugia, Santa Maria della Misericordia University Hospital, Perugia, Italy. Email: giancarlo.direnzo@unipg.it

Endorsed in March 2017 and April 2018 by the FIGO Executive Board. This advice should not be considered as standards of care or legal standards in clinical practice.

Working Group members and expert contributors are listed at the end of the paper.

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. 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.

WHO defines anemia in pregnancy as a hemoglobin concentration of less than 11 g/dL at any stage of pregnancy; UK antenatal guidance 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.

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. 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. Other causes of anemia include parasitic diseases, micronutrient deficiencies, and genetically inherited hemoglobinopathies.

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, 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. 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.

A strong association has been found between moderate to severe anemia at 28 weeks of gestation and the severity of intra- and postpartum hemorrhage, which cause 23% of maternal deaths. 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. Traditionally, maternal anemia was frequently thought to be associated with a suboptimal fetal outcome; however, data supporting this concept are not clear.

Fetal iron needs will be compromised when maternal iron stores are suboptimal. 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. 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.

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. 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.

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

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. 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 if there is 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. 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. 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.

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.
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.

FIGO WORKING GROUP ON GOOD CLINICAL PRACTICE IN MATERNAL–FETAL MEDICINE (2015-2018)

Gian Carlo Di Renzo, Italy (Chair); Eduardo Fonseca, Brazil; Eduardo Gratacos, Spain; Sonia Hassan, USA; Mark Kurtser, Russia; Fergal Malone, Ireland; Shilpa Nambiar, Malaysia; Kypros Nicolaides, UK; Nancy Sierra, Mexico; Huixia Yang, China (members). Carlos Fuchtnner, Bolivia (FIGO President Elect, Ex Officio); Vincenzo Berghella, USA (Society for Maternal–Fetal Medicine); Ernesto Castelazo Morales, Mexico (FIGO Committee for Capacity Building in Education and Training); Mark Hanson, UK (FIGO Working Group on Adolescent, Preconception and Maternal Nutrition); Moshe Hod, Israel (Committee on Pregnancy and NCD; Working Group on Hyperglycemia in Pregnancy); Yves Ville, France (International Society of Ultrasound in Obstetrics and Gynecology); Gerard Visser, Netherlands (FIGO Committee for Safe Motherhood and Newborn Health); Joe Leigh Simpson, USA (March of Dimes).
EXPERT CONTRIBUTORS

Abdallah Adra (Department of Obstetrics and Gynecology, American University of Beirut Medical Center, Lebanon); Roza Bataeva (Fetal Medicine Centre, Russian Medical Academy of Advanced Studies, Moscow, Russia); Luis Cabero Roua (Autonomous University of Barcelona, Hospital Materno-infantil Valle Hebron, Barcelona, Spain); Ramen H. Chmait (Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Keck School of Medicine, University of Southern California, USA); Yvonne Cheng (Department of Obstetrics and Gynaecology, Chinese University of Hong Kong); Irene Giardina (Centre of Perinatal and Reproductive Medicine, University of Perugia, Italy); Jon Hyett (Department of Women and Babies, Royal Prince Alfred Hospital, Australia); Asma Khalil (Fetal Medicine Unit, Department of Obstetrics and Gynaecology, St. George's University Hospitals NHS Foundation Trust, London, UK); Narendra Malhotra (Global Rainbow Healthcare, India); Pierpaolo Mastroiacovo (Alessandra Lisis International Centre on Birth Defects and Prematurity, International Clearinghouse for Birth Defects Surveillance and Research, Rome, Italy); John Morrison (Department of Obstetrics & Gynaecology, National University of Ireland); Amala Nazareth (Emirates Medical Association Ob Gyn, United Arab Emirates); Liana Chiu Yee Poon (Department of Obstetrics and Gynaecology, Chinese University of Hong Kong); Chittaranjan N. Purandare (International Federation of Gynaecology and Obstetrics [FIGO], St. Elizabeth Hospital, Walkeshwar and BSES Hospital Mumbai, India); Ruben Quintero (Plantation General Hospital and Wellington Regional Medical Center, Coral Gables, Florida, USA); Waldo Sepulveda (Maternal–Fetal Diagnostic Center, Santiago, Chile); Valentina Tosto (Centre of Perinatal and Reproductive Medicine, University of Perugia, Italy).

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

REFERENCES