Association of Ontario Midwives
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IRON DEFICIENCY ANEMIA

in the childbearing year

Diagnosis and treatment

This document offers an overview of management approaches to iron deficiency anemia during pregnancy and postpartum.

It complements a plain-language resource for clients, *Iron deficiency anemia and you*, as well as the AOM's CPG on postpartum hemorrhage.

Despite the relatively high prevalence of iron deficiency anemia, there is little evidence-based guidance regarding management of iron deficiency during pregnancy and postpartum. Guidelines that address iron deficiency anemia in the childbearing year include:

IRON DEFICIENCY ANEMIA

- Defined as reduced capacity for transport of oxygen in the blood, as demonstrated by lower than normal values of hemoglobin or ferritin. (1,2)
- Iron deficiency anemia occurs when red blood cell production is inadequate due to insufficient dietary intake and absorption of iron. It can also be caused by excessive blood loss (e.g., following postpartum hemorrhage). Iron deficiency is the most common cause of anemia worldwide. (3,4) Iron deficiency anemia, by definition, responds to treatment with iron. (5,6)

Iron deficiency - investigation and management (7)
Guidelines and Protocols Committee of the British Columbia Medical Association, 2010
http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/iron-deficiency

UK guidelines on the management of iron deficiency in pregnancy (6)
British Committee for Standards in Haematology, 2011
http://www.bcshguidelines.com/documents/UK_Guidelines_iron_deficiency_in_pregnancy.pdf

Screening for iron deficiency anemia and iron supplementation in pregnant women to improve maternal health and birth outcomes: U.S. Preventative Services Task Force recommendation statement (8)
U.S. Preventative Services Task Force, 2015
http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/iron-deficiency-anemia-in-pregnant-women-screening-and-supplementation

DIAGNOSIS

DIAGNOSIS OF IRON DEFICIENCY ANEMIA		
Prenatal		
Lab Test	Value	Description
Hb	< 110 g/L	First and third trimester
	< 105 g/L	Second trimester
	Due to the wide range of individual differences in hemodilution, hemoglobin values alone may not be adequate for assessing iron deficiency anemia during pregnancy. (5)	
Ferritin	< 15 ug/L	Diagnostic of iron deficiency anemia. Provides information about the capacity of the body's iron reserves and is an important component of assessing iron deficiency anemia during pregnancy (6,9)
	< 30 ug/L	Consider oral iron supplementation of 65 mg daily at this value. This level indicates early iron depletion that is insufficient to meet the increased need for iron in pregnancy and unlikely to be resolved without treatment. (6)
	If serum ferritin levels are normal or elevated in the presence of low hemoglobin, further investigation into possible hemoglobinopathies (e.g. ß-thalassemia, sickle cell anemia, anemia of infection, hemorrhagic anemia, vitamin B12 or folic acid deficiency) may be warranted. Ferritin is an acute phase reactant and tends to be elevated in the presence of infection. For this reason, ferritin readings taken during illness may not be accurate. (5,9)	
Postpartum		
Lab Test	Value	Description
Hb	< 100 g/L	≥ 48 hours postpartum.
	< 80 g/L	< 48 hours postpartum
	Peripheral vasodilation, extracellular volume, glomerular filtration and cardiac output all decrease in the first week postpartum and hemodilution begins to resolve. (10) Hemoglobin concentration should thus be given an opportunity to stabilize before performing any postpartum assessment of iron deficiency anemia. Some researchers and guideline developers suggest waiting at least 48 hours following birth before sampling blood for hemoglobin. (6,9,10) One study suggests that if hemoglobin needs to be assessed in the 24- to 48-hour postpartum period, a lower diagnostic cut-off of < 80g/L may be appropriate given these hemodynamic changes. (11) Most of the circulatory changes taking place tend to reach a steady state by five to seven days postpartum and so this may be the most reliable time to assess hemoglobin after birth. (9,10)	
Ferritin	N/A	Ferritin is an unreliable marker for assessing iron in the immediate postpartum. (9,10,12)
	Because the immediate postpartum period is associated with systemic inflammation, ferritin levels are likely to be artificially elevated for one to six weeks following birth. (9,10,12)	

Differentiating iron deficiency anemia and B_{12} and folate deficiency

- Iron deficiency anemia is associated with smaller red cells (decreased mean corpuscular volume (MCV)).
- Vitamin B12 and folate deficiency are associated with large red cells (increased MCV).
- Mixed deficiency causes a mixture of small and large red cells.

HB LEVEL	MCV LEVEL	FERRITIN	TYPE OF ANEMIA
Low	Low	Low	Iron deficiency
Low	High	Low or normal	B12 or folate deficiency
Low	Normal	Low or normal	May indicate mixed anemia

TREATMENT OF IRON DEFICIENCY ANEMIA

The most recent Cochrane review examining treatment of iron deficiency anemia in pregnancy noted few high-quality trials assessing the effects of iron administration to treat anemia in pregnancy. (13) The review found that oral iron supplementation was associated with reduced risk of anemia and improved hematological indices (hemoglobin and/or ferritin) compared to placebo, along with negative gastrointestinal effects. (13) Treatment with parenteral iron (IV and IM) produced more immediate higher hemoglobin and/or ferritin values than oral iron, but the review's authors noted concerns about rare adverse effects like allergic reactions. (13)

Oral iron supplementation

- 100 to 200 mg of elemental iron taken daily as oral iron supplements is recommended as the first line of treatment for iron deficiency anemia in both pregnancy and postpartum. However, 50 to 80 mg per day of elemental iron may result in less gastrointestinal discomfort and may be adequate treatment. (5,6,14)
- A variety of oral iron preparations are currently available in Canada, including ferrous sulfate, ferrous gluconate, ferrous fumarate and iron-polysaccharide complexes. (15)
- The recommended dose of 100 to 200 mg per day is based on studies of anemic (cis) men and some evidence suggests that lower doses may be adequate to treat iron deficiency anemia during the childbearing year, especially given the high iron absorption capacity in pregnancy. (5)
- Side-effects of oral iron supplementation include nausea, vomiting, dyspepsia, constipation and diarrhea and are generally dose-dependent. Side-effects tend to subside with continued use though compliance is often a significant barrier to treatment. (15)

Instructions and reminders for clients who are taking oral iron supplements

- Iron is best absorbed on an empty stomach. If gastrointestinal upset is a concern, iron may be taken with or just after meals at doses < 100 mg and gradually increased after 4 to 5 days. (14)
- Administration of 200 mg of vitamin C for every 30 mg of iron may increase iron absorption by 10%. (14)
- U.K. guidelines recommend avoiding slow-release and enteric coated forms of oral iron as they may move undigested past the ideal site of absorption (duodenum and proximal jejunum). (6)
- Oral iron tablets can be toxic to children so storage safety is an important consideration for families with older children. (6,16)

Treatment follow-up

- Following completion of two weeks of oral iron therapy, some authors suggest reassessing hemoglobin levels to test therapeutic response with an expected increase in hemoglobin of ≥ 10 to 30g/L. (6,9,10) Iron therapy should be continued for three to six months even if symptoms of anemia are resolved. Both hemoglobin and ferritin levels may be tested following a three-month course of oral iron treatment to ensure iron stores are replete. (6,9,10)
- Oral iron is sometimes insufficient for replenishing severe deficiencies in overall iron stores, which may be seen in cases of iron deficiency anemia associated with significant postpartum hemorrhage. (15)

IV iron therapy

- If anemia persists after two weeks of oral iron treatment with good compliance, there are concerns about malabsorption of oral iron, or there is a requirement for fast iron repletion (e.g. anemia diagnosed late in pregnancy with a planned home birth), IV iron may be considered. (5,15)
- Some studies have shown IV iron therapy produces a greater and more immediate increase in hemoglobin levels compared to oral iron supplementation and without the side-effects of oral iron or the risks associated with blood transfusion. (15,17)
- Randomized controlled trails comparing IV iron to oral iron supplementation for treating anemia postpartum have shown similar hemoglobin concentrations in groups treated with oral iron and IV iron at six to eight weeks postpartum, though ferritin stores are higher in those treated with IV iron. These studies are small and generally of low quality. (15,17–20) The most recent Cochrane review of treatments for postpartum iron deficiency anemia noted that while intravenous iron was associated with fewer gastrointestinal side effects than oral iron, anaphylaxis and cardiac events occurred infrequently in participants receiving IV iron therapy and more data are needed to establish safety. (13,15,17,20) The review reported three cases of anaphylaxis or evidence of hypersensitivity and one case of a cardiac arrhythmia among 767 participants who received IV iron across eight small, low-quality trials. (20)
- To avoid iron toxicity, U.K. guidelines recommend that iron deficiency anemia should be confirmed with ferritin testing before IV iron is administered. (6)
- Currently, iron dextran, iron sucrose and sodium ferric acid gluconate are the most commonly used IV preparations in Canada. (15)
- The costs associated with hospital visits (including physician and hospital fees as well as travel, parking and childcare costs) may present a barrier to accessing IV iron for some midwifery clients.

Blood transfusion

Research increasingly suggests that risks of blood transfusion for obstetric patients may outweigh benefits except in extreme, life-saving circumstances. The risk of immunological reaction after red cell transfusion has been reported as about 1/1000. (15,17,21–23) Blood transfusion may also increase risk of blood-borne cancers. (15,21)

One trial evaluating outcomes in participants who had experienced postpartum hemorrhage and were randomized to transfusion or routine care found that improvements to fatigue scores associated with transfusion were "clinically negligible" and not associated with any cost savings. (21) Hemoglobin levels were comparable between groups at six weeks postpartum. (24) Many researchers call for conservative use of blood products due to risks to long term immunological health and the health of possible future pregnancies. (15,20,21,24–26)

CHEST OR BREASTFEEDING AND IRON DEFICIENCY ANEMIA

- One study has shown an association between postpartum anemia and shortened duration of chest/breastfeeding. (27) Given that iron deficiency anemia increases the risk of fatigue, and fatigue is a commonly-cited reason for early nursing cessation, appropriate treatment of postpartum iron deficiency anemia may help clients meet nursing goals. (27)
- Effective treatment of postpartum anemia is also important because studies have shown that lactoferrin levels in human milk are similar in anemic and non-anemic study participants, suggesting that the body will adjust lactoferrin levels as needed even in the presence of anemia. (28) Though not entirely understood, this mechanism promotes healthy iron intake in the nursing infant, but may have negative consequences for the long-term health of lactating clients if iron deficiency anemia goes untreated.
- Although the increased fatigue associated with iron deficiency anemia may make nursing particularly challenging, maintaining secondary amenorrhea as long as possible may be beneficial in terms of conserving overall blood supply and, by extension, iron stores. (1)
- There is no contraindication to chest or breastfeeding while taking iron supplements at therapeutic doses. (16)

IMPROVING ACCESS TO NUTRITION AND SUPPLEMENTS FOR CLIENTS ON SOCIAL ASSISTANCE

Anyone who is pregnant and/or breastfeeding and receiving Ontario Works is entitled to receive an additional $40 per month ($50 if lactose intolerant) through the Pregnancy/Breastfeeding Nutritional Allowance. Midwives can complete forms provided by Ontario Works caseworkers to obtain this funding for clients.

Writing prescriptions for over-the-counter medications like iron supplements and prenatal vitamins may ensure coverage for recipients of Ontario Works. This may make iron supplements accessible for clients who cannot otherwise afford them.

Ontario Works Special Diet Allowance

Midwives cannot currently authorize the Ontario Works Special Diet Allowance for clients during pregnancy. If a midwife believes a pregnant client should be receiving a Special Diet Allowance, referral should be made to a physician who can authorize access to this extra funding for conditions that may require a special diet, such as iron deficiency anemia.

Midwives can authorize the Special Diet Allowance for infants who require formula in cases where chest or breastfeeding is either contraindicated or there is inadequate lactation to sustain nursing. The Special Diet Allowance for infants is paid for the first 12 months of life.

SOCIO-CULTURAL CONSIDERATIONS

- Midwifery clients in Ontario bring a range of perspectives to their care, some of which may impact their understanding and acceptance of western biomedical approaches to the diagnosis and treatment of anemia. (29-31)
- Differing baseline hemoglobin levels prior to pregnancy may be related to issues like vegetarianism, veganism, poverty, food security, or prior hormone use (i.e., testosterone). (5,32)
- Population-specific hemoglobin reference ranges have not been established.
- Adequate treatment of iron deficiency anemia prenatally may be especially important for clients who may refuse blood transfusions. (1,5)

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