

CHAPTER VIII

IRON DEFICIENCY ANEMIA IN PREGNANCY

Erhan Huseyin Comert

*(MD), Gynecology and Obstetrics, Gole Government Hospital, Ardahan, Turkey
e-mail: erhan.comert@hotmail.com*

 ORCID 0000-0003-1431-2294

1. Description

Anemia is defined as low hemoglobin (Hb) concentration of blood. Iron deficiency continues to be a major problem for pregnant women around the world. It always has a place in current issues. Increasing red blood cell and hemoglobin production in the first trimester of pregnancy causes a physiological expansion in plasma volume (1).

It is necessary to distinguish between iron deficiency anemia and physiological anemia due to the negative effects that may occur on the mother and fetuses during pregnancy.

2. Causes of anemia in pregnancy

During pregnancy, iron consumption increases as the weeks progress during pregnancy due to the increase in blood volume and increased fetal requirements. Physiological anemia and iron deficiency anemia are the two most common causes of anemia in pregnant women. The blood volume increases by 30-50% due to the increase in plasma volume during pregnancy. The increase in erythrocyte volume is more than the increase in plasma volume. As a result of this situation, physiological anemia occurs. This situation is at their maximum levels during the 20-24 gestation week (2). Iron requirement is lowest in the first trimester. It is gradually increases and reaches the maximum level in the third trimester due to fetal growth and increasing fetal needs. A total of 1000mg of iron is required during pregnancy. If this value will be detailed, 1gr (1000mg) iron; 300mg for fetus, 50mg for placenta, 450mg for increased erythrocyte mass, 240mg for maternal essential basal iron use (3)(4). The general causes of anemia are summarized in table 1.

Table 1 Causes of Anemia

Insufficient intake with diet	Fe, Folic acid Vitamins A, C and B12
Erythrocyte diseases and hemoglobin disorders	Thalassemia Sickle cell anemia Malaria Glucose 6 Phosphate Dehydrogenase Enzyme Deficiency
Chronic diseases	Tuberculosis (TBC) Chronic kidney disease (CRF) Cancers Rheumatic diseases Sexually transmitted diseases (Syphilis, gonorrhea, HIV etc.)
Conditions that disrupt iron absorption, bleeding, infection	Parasitic diseases (Helminthiasis, Amebiasis, Giardiasis, Schistosomiasis) Iron metabolism disorder Bleeding hemorrhoids Antepartum bleeding Multiparity Gastric bypass Inflammatory bowel diseases

3. Causes of iron deficiency anemia during pregnancy

Iron deficiency anemia is the second most common anemia after physiological anemia during pregnancy. It is very common not only in pregnant women but also in women of reproductive age. Many factors can contribute to iron deficiency. One of the most common causes is insufficient iron intake with diet. Most women have iron deficiency anemia due to nutritional deficiency in developing countries. In women of reproductive age, additional iron support to daily iron intake is required during menstruation and this value is on average 0.8 mg/day (4).

Generally, during pregnancy respectively, for increased maternal blood volume, fetal blood cells and fetal growth, a total of 500mg, 300mg, 350mg iron is required. The need for iron gradually increases as the trimester of pregnancy progresses (figure 1) (4). Approximately 250 mg of iron is lost during labor.

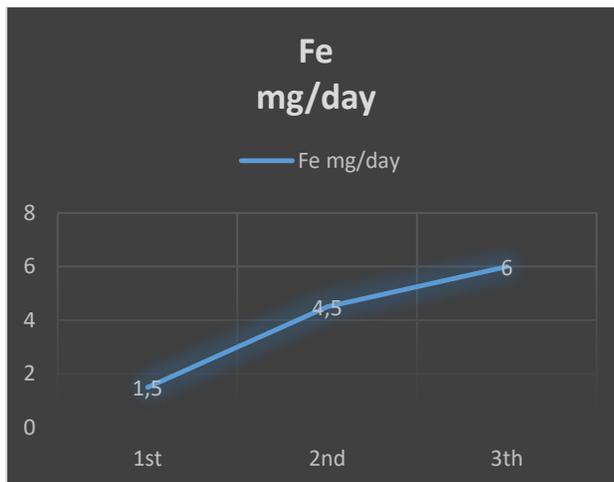


Figure 1. As the trimester of pregnancy progresses, the daily iron requirement increases. 1st trimester 1-2 mg/day, 2nd trimester 4-5mg/day, 3rd trimester 6mg/day.

In addition to all these needs, that affect iron absorption such as inflammatory bowel disease, bariatric surgery and not taking adequate iron supplements during pregnancy can cause anemia.

a) Increased iron requirement:

Iron consumption increases due to increased blood volume and increased fetus requirements during pregnancy. Although iron absorption increases during pregnancy, dietary iron intake is not sufficient to meet the need; therefore iron supplementation is required.

b) Insufficient iron stores:

- Insufficient intake with nutrition
- Multiparity (number of multiple births) -abortus
- Infections and especially parasitic diseases cause iron stores to empty or remain at low levels.
- Digestion / absorption disorder.

4. Signs and symptoms of iron deficiency anemia

Although some of the patients are asymptomatic, some patients may be accompanied by signs and symptoms on the table (Table 2). Although patients do not have anemia, symptoms may be observed due to low iron levels and ferritin.

Table 2 Iron deficiency symptoms and signs

Symptoms	Signs
●Fatigue	●Pallor
●Weakness	●Dry or rough skin
●Headache	●Blue sclera
●Irritability	●Atrophic glossitis with loss of tongue papillae accompanied by tongue pain or dry mouth
●Exercise intolerance	●Cheilosis (also known as angular cheilitis)
●Exercise dyspnea	●Koilonychia (spoon nails)
●Vertigo	●Chlorosis (pale, pale green skin; extremely rare)
●Angina pectoris	●Alopecia (rare) especially in severe cases

Table 3 Effects of anemia on mother and baby in pregnant women

Maternal	Fetal
Postpartum infection	Low birth weight
Infection during pregnancy	Preterm labor
Antepartum bleeding	Impaired motor development and coordination
Placental abruption	Growth and development restriction
Postpartum bleeding	Very low birth weight
Preeclampsia	Congenital anomaly
Premature rupture of membranes	Susceptibility to infections/lack of resistance
Need for transfusion	Lack of attention
Placental malaria	Neonatal death
Postpartum depression	Neurodevelopmental delay
Cessation of lactation	

5. Support dose, duration of treatment and time to start treatment

Different suggestions come up after the studies in literature. For example; providing iron support to all women and menstruating adolescents, iron supplementation during pregnancy and the postpartum period, and late clamping of the umbilical cord during delivery are on the agenda (5). In another study, it is recommended to use mebendazole and

albendazole for the treatment of parasites that reduce iron absorption during pregnancy (6).

Iron supplementation is recommended for 6 months from the second trimester and for 3 months after birth, taking into account the daily iron requirement of all pregnant women, within the iron support program published by the World Health Organization and the Ministry of Health in our country (40-60mg/day for 9 months)(7).

6. Treatment of anemia in pregnant women

Iron deficiency treatment in pregnant women is important in terms of providing adequate support during and after delivery. Oral iron preparations preferred in pregnant women with insufficient iron stores have gastrointestinal side effects. Oral iron preparations used daily accumulate in high concentrations in gastrointestinal mucosa cells and lumen and iron absorption gradually decreases. Intestinal mucosa cells renew themselves in 5-6 days. Therefore, it has been reported that weekly iron therapy instead of daily iron therapy improves gastrointestinal absorption and patient compliance (8).

A significant reductions maternal anemia and low birth weight risk (3%) was found with prenatal iron supplementation. For every 10 mg increase in daily iron intake rate;15 grams increase occurs in the baby's birth weight. 1 g/dl increase in hemoglobin concentration in the third trimester or birth causes an increase of 143 g in birth weight (4). In studies, there was no decrease in preterm delivery risk of pregnant women who received iron support.

a) Oral iron therapy

Most women with iron deficiency, especially those diagnosed in the first trimester, prefer oral iron treatment. Oral iron is safe, cheap and readily available. For many women, this is adequate therapy. Iron sulphate is the most commonly prescribed oral formulation.

Recommended oral iron doses range from 40 to 200 mg of elemental iron per day. Generally, 60mg of elemental iron is preferred. Absorption can be improved by taking vitamin C along with iron and also by avoiding coffee, tea and milk while taking iron supplements. The using oral iron preparations 3 times a week instead of daily intake increases the blood iron level in a shorter time.

b) Intravenous iron therapy

Intravenous iron form may be preferred in those who have severe anemia and whose iron level does not increase with oral treatment in the third trimester of pregnancy and/or cannot tolerate oral iron. It is not preferred because there are not enough safety data for first trimester use. It

is more effective than oral iron preparations and has less gastrointestinal side effects .

Indications

- Can not tolerate oral iron preparation
- Not increasing iron levels despite treatment
- Increasing iron level in a short time for pregnant women
- People who have had stomach and intestinal surgery, which has adverse effects on iron absorption

7. Evaluation of response to treatment

An increase in the number of reticulocytes is observed in the first week after iron replacement. An increase in hemoglobin level of at least 1g/dL is observed within about 2 to 3 weeks.

Hemoglobin level is checked within 2-3 weeks after oral iron therapy and oral iron tolerability is checked. If oral iron tolerance and increase in hemoglobin level are as expected, treatment continued throughout pregnancy and postpartum period. If the expected response and tolerance are not good, intravenous iron therapy should be considered.

8. Duration and frequency of follow-up

By the Ministry of Health in our country;

- For iron support; at least 3 follow-up during pregnancy, at least 1 follow-up postpartum
- Once a month for moderate anemia
- In severe anemia, the first follow-up is two weeks later, subsequent follow-ups once a month.

9. Iron use side effects

In order to increase tolerance, extending the time between doses, switching to a fluid that can be titrated more easily, or switching to intravenous iron (if in the second or third trimester) can be counted (9).

a) Side effects of intravenous iron therapy:

A meta-analysis on the safety of intravenous iron treatment revealed no increased risk for serious adverse effects, mortality and infection (10). Side effects such as fever, arthralgia, myalgia often heal spontaneously without intervention. It should be preferred as an alternative to erythrocyte transfusion in severe anemic cases, where there is no response to parenteral iron treatment or in cases where rapid correction is desired.

b) Drugs and foods that disrupt iron absorption:

- Anticonvulsants
- Sulfonamides
- Antacids
- Calcium-containing foods
- Tea, coffee, spinach, beets, soy products, phytat in bran and grains.

*Consumption with foods rich in vitamin C (orange juice) and acidic foods, and be consumed before eating increase the absorption of iron drugs.

References

1. Costantine MM. Physiologic and pharmacokinetic changes in pregnancy [Internet]. Vol. 5 APR, *Frontiers in Pharmacology*. Frontiers Media SA; 2014 [cited 2021 Jan 3]. Available from: [/pmc/articles/PMC3982119/?report=abstract](https://pubmed.ncbi.nlm.nih.gov/28034892/)
2. WHO | Archived: Iron deficiency anaemia: assessment, prevention and control. WHO [Internet]. 2018 [cited 2021 Jan 3]; Available from: http://www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/WHO_NHD_01.3/en/
3. Achebe MM, Gafter-Gvili A. How I treat anemia in pregnancy: Iron, cobalamin, and folate. *Blood* [Internet]. 2017 Feb 23 [cited 2021 Jan 3];129(8):940–9. Available from: <https://pubmed.ncbi.nlm.nih.gov/28034892/>
4. Bothwell TH. Iron requirements in pregnancy and strategies to meet them. In: *American Journal of Clinical Nutrition* [Internet]. American Society for Nutrition; 2000 [cited 2021 Jan 3]. Available from: <https://pubmed.ncbi.nlm.nih.gov/10871591/>
5. Goonewardene M, Shehata M, Hamad A. Anaemia in pregnancy [Internet]. Vol. 26, *Best Practice and Research: Clinical Obstetrics and Gynaecology*. *Best Pract Res Clin Obstet Gynaecol*; 2012 [cited 2021 Jan 3]. p. 3–24. Available from: <https://pubmed.ncbi.nlm.nih.gov/22138002/>
6. De Silva NR, Sirisena JLGJ, Gunasekera DPS, Ismail MM, De Silva HJ. Effect of mebendazole therapy during pregnancy on birth outcome. *Lancet* [Internet]. 1999 Apr 3 [cited 2021 Jan 3];353(9159):1145–9. Available from: <https://pubmed.ncbi.nlm.nih.gov/10209979/>
7. (No Title) [Internet]. [cited 2021 Jan 4]. Available from: https://www.who.int/nutrition/publications/en/ida_assessment_prevention_control.pdf
8. Peña-Rosas JP, Viteri FE. Effects and safety of preventive oral iron or iron+folic acid supplementation for women during pregnancy. In: *Cochrane Database of Systematic Reviews* [Internet]. John Wiley & Sons, Ltd; 2009 [cited 2021 Jan 3]. Available from: <https://pubmed.ncbi.nlm.nih.gov/19821332/>

9. Pavord S, Daru J, Prasannan N, Robinson S, Stanworth S, Girling J. UK guidelines on the management of iron deficiency in pregnancy. *Br J Haematol* [Internet]. 2020 Mar 1 [cited 2021 Jan 3];188(6):819–30. Available from: <https://pubmed.ncbi.nlm.nih.gov/31578718/>
10. Tomer A, Amir B, Alon G, Hefziba G, Leonard L, Anat GG. The safety of intravenous iron preparations: Systematic review and meta-analysis. *Mayo Clin Proc* [Internet]. 2015 Jan 1 [cited 2021 Jan 3];90(1):12–23. Available from: <https://pubmed.ncbi.nlm.nih.gov/25572192/>

