



## IRON CORNER

### Overview of Iron Deficiency Anemia in Women

Anemia is an extremely common condition, affecting many persons across the life span, in both developed and developing countries. Data from the WHO Vitamin and Mineral Nutrition Information System for 1993-2005<sup>1</sup> estimated the global anemia prevalence as 24.8 %, affecting 1.62 billion people. Of those affected, 41.8 % occurred in pregnant women and 30.2 % in non-pregnant women. This equates to 677 million pregnant women and 489 million non-pregnant women worldwide.

The consequences of anemia have been shown to significantly affect morbidity and mortality, serving as an independent risk factor in many reports.<sup>2</sup> Iron deficiency anemia accounts for the greatest proportion of cases with an estimated 50% of all causes of anemia. The most common etiologies of iron deficiency anemia in premenopausal women is related to menstrual blood loss while in post-menopausal women, blood loss from the gastrointestinal tract is the most common etiology.

The consequences of anemia are related to a wide varying clinical spectrum irrespective of gender, or age. In all women, it may be associated with decreased cognitive function, concentration and attention<sup>3</sup>. Pregnant women have an increased risk of preterm delivery, intrauterine growth restriction, and disturbed post-partum maternal –infant interaction, with potential for subsequent developmental deficits in childhood. Congdon et al<sup>4</sup>, in a study to determine the long-term effects of iron deficiency on the neural correlates of recognition memory in children concluded that not only do iron deficient neonates have delayed growth and development but a statistically significant increase in the number of cognitive and behavioral abnormalities up to ten years after iron repletion.

Anemia has a significant impact on overall quality of life, including such symptoms of easy fatigability, decreased functional capacity and exercise tolerance, depression and cold intolerance. Restless leg syndrome and pica, especially for ice, have also been associated with iron deficiency and iron deficiency anemia. Most times women fail to recognize pica as a problem, leading to

missed opportunities to detect iron deficiency earlier. In severe cases of anemia, congestive heart failure and arrhythmias may also be precipitated.

During pregnancy, several physiologic changes occur that lead to hemodilution as a result of plasma volume expansion, estimated to be approximately 40-50% until the 30<sup>th</sup> week of gestation, in addition to a 20-30% increase in red blood cell mass. Iron deficiency anemia may also occur in pregnancy due to a combination of increased maternal and fetal erythropoiesis. There is preferential transfer of maternal iron to the fetus to meet red blood cell synthesis requirements, leading to the further depletion of iron stores. During delivery blood loss, which may range from 250 mls to > 1000 mls may worsen anemia and iron deficiency.

In the postpartum period, reversal of the physiologic changes of pregnancy may lead to the correction of anemia. However, in some patients anemia may persist, frequently due to iron deficiency with the following risk factors:<sup>5,6</sup> multiparity, obesity, anemia during pregnancy, age < 20yrs and unmarried status. Additionally, socioeconomic factors have a complex interplay in the development of post-partum anemia as demonstrated in the Special Supplemental Nutrition program for women, infants and children's study.<sup>5</sup> Of the nearly 60,000 participants, 27% overall, 40% of Hispanic, and 48% of African Americans were found to be anemic between 4-26 weeks postpartum, despite these women having normal hemoglobin levels during pregnancy. The impact of anemia may be two fold affecting both maternal and fetal cognition leading to childhood developmental delay, due to the negative impact of maternal cognition, mood and behavior on maternal –fetal interactions.

In premenopausal women, blood loss secondary to menstruation is a common cause of iron deficiency anemia. This becomes problematic when menstrual blood loss exceeds 80 milliliters per cycle or lasts for greater than 7 days. In postmenopausal women, anemia prevalence varies widely, due to a combination of multiple factors that include nutritional deficiencies, such as iron, folate or vitamin B12, gastrointestinal losses and anemia due to chronic inflammation. The prevalence of post-menopausal anemia increases with increasing age.



## IRON CORNER

Irrespective of etiology, the recognition of anemia and prompt attempts at correction are key to improving overall quality of life and symptoms associated with this condition. Treatment should be tailored to the clinical scenario and underlying etiology. Iron supplementation should be given to all patients except those with iron overload syndromes, with a goal of replenishing iron stores and correcting hemoglobin and red cell indices to normal.

Oral iron is an acceptable route of administration in those patients who tolerate enteric iron supplementation and when slow correction is clinically acceptable. However in the presence of intolerance or non-responsiveness to an oral regime, or when more rapid correction is needed, parenteral iron may be required. Oral iron should be continued for 3 months following the correction of iron deficiency anemia to ensure adequate repletion of all iron stores.

In pregnancy, parenteral iron may be required due to failure to meet the increased body demands and depleted iron stores preceding pregnancy despite adequate oral therapy. The side effect profile associated with oral therapy may preclude continued oral iron therapy. Side effects that may be unacceptable include nausea, vomiting, colicky abdominal pain, diarrhea and constipation. There are currently five parenteral iron preparations approved for use in the USA these are: low molecular weight iron dextran, sodium ferric gluconate, iron sucrose, ferumoxytol and ferric carboxymaltose.<sup>7</sup> Ayub et al in a study of a group of 100 pregnant women with gestational age greater than 12 weeks and confirmed diagnosis of iron deficiency anemia concluded that total parenteral iron replacement with low molecular weight iron dextran is an effective and safe method for the treatment of iron deficiency anemia in a selected group of pregnant women.<sup>8</sup> Auerbach et al supported this in a study that evaluated the safety and efficacy of the rapid administration of 1 gram of low molecular weight iron dextran. In this study a subgroup analysis of 31 infusions in 43 women with pregnancy-related anemia (second and third trimester, or postpartum), revealed four adverse reactions which were easily managed. This finding supported that of the entire study population that at a dose of 1 gram Intravenous

iron dextran may be safe and efficacious in the management of iron deficiency anemia.

Breyman and Auerbach<sup>9</sup> in a review of treatment of iron deficiency in gynecology and obstetrics stated that, in a meta-analysis of more than 10,000 patients who received parenteral iron, minor infusion reactions were observed but serious adverse events were not increased compared with any comparator including placebo. Studies comparing intravenous iron formulations with oral iron in pregnancy show advantages to intravenous iron in terms of hemoglobin and ferritin increase during pregnancy and after birth.

Breyman and Auerbach conclude: "Later complications, such as preterm labor and peripartum bleeding, can be prevented by proactive intervention. Such intervention is especially important given the known delay in growth and development and statistically significant increments in cognitive and behavioral abnormalities, which persist after treatment, in infants born iron deficient. The administration of allogeneic blood should be a last resort in pregnant women and those in the puerperium."<sup>9</sup> Anemia, and in particular iron deficiency anemia, affects a tremendous number of women across an entire life span, with multiple factors contributing to its development. The consequences of anemia have a significant impact on the quality of life and morbidity and mortality of women and their infants. Therefore, its early recognition and treatment is important to improve quality of life and decrease serious morbidity for women globally.

**December 2018**

### References

1. McLean E, Cogswell M, Egli I, Wojdyla D, de Benoist B. Worldwide prevalence of anemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005. *Public Health Nutr.* 2009 Apr;12(4):444-54. doi: 10.1017/S1368980008002401. Epub 2008 May 23. PubMed PMID: 18498676.
2. Iron Deficiency Anemia Assessment, Prevention, and Control: A guide for program managers WHO/NHD/01.3, United Nations Children's Fund, United Nations University World Health Organization.
3. Friedman AJ, Chen Z, Ford P, Johnson CA, Lopez AM, Shander A, Waters JH, van Wyck D. Iron deficiency anemia in women across the life span. *J Womens Health (Larchmt).* 2012 Dec;21(12):1282-9. doi: 10.1089/jwh.2012.3713. PubMed PMID: 23210492.



# IRON CORNER

4. Congdon EL, Westerlund A, Algarin CR, Peirano PD, Gregas M, Lozoff B, Nelson CA. Iron deficiency in infancy is associated with altered neural correlates of recognition memory at 10 years. *J Pediatr*. 2012 Jun;160(6):1027-33. doi: 10.1016/j.jpeds.2011.12.011. Epub 2012 Jan 11. PubMed PMID: 22244466; PubMed Central PMCID: PMC3360801
5. Bodnar LM, Scanlon KS, Freedman DS, Siega-Riz AM, Cogswell ME. High prevalence of postpartum anemia among low-income women in the United States. *Am J Obstet Gynecol*. 2001 Aug; 185(2):438-43. PubMed PMID: 11518906.
6. Bodnar LM, Siega-Riz AM, Miller WC, Cogswell ME, McDonald T. Who should be screened for postpartum anemia? An evaluation of current recommendations. *Am J Epidemiol*. 2002 Nov 15;156(10):903-12. PubMed PMID: 12419762.
7. Ayub R, Tariq N, Adil MM, Iqbal M, Junaid A, Jafery T. Efficacy and safety of total dose infusion of low molecular weight iron dextran in the treatment of iron deficiency anemia during pregnancy. *J Coll Physicians Surg Pak*. 2008 Jul;18(7):424-7. doi: 07.2008/JCPSP.424427. PubMed PMID: 18760066.
8. Auerbach M, Pappadakis JA, Bahrain H, Auerbach SA, Ballard H, Dahl NV. Safety and efficacy of rapidly administered (one hour) one gram of low molecular weight iron dextran (INFeD) for the treatment of iron deficient anemia. *Am J Hematol*. 2011 Oct;86(10):860-2. doi: 10.1002/ajh.22153. Epub 2011 Aug 29. PubMed PMID: 21922526.
9. Breymann C and Auerbach M. Iron Deficiency in gynecology and obstetrics: clinical implications and management. *American Society of Hematology. Hematology* 2017. 152-159.

### **Disclaimer**

*This content is covered by an important disclaimer that can be found at [www.iron.sabm.org](http://www.iron.sabm.org). Please read this disclaimer carefully before reviewing this content.*