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IRON DEFICIENCY ANAEMIA: ENEMICAL TO PREGNANCY

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ABSTRACT
Iron deficiency anaemia is a critical condition in pregnancy which may not easily be predicted. It has caused a lot of havocs to the mothers and the babies. A widespread health issue that primarily affects pregnant women is iron deficiency anemia. Pregnancy-related iron deficiency anemia is linked to higher rates of maternal and perinatal morbidity and mortality. Infant neurocognitive deficits may also be linked to maternal iron deficiency. Hepcidin, the principal regulator of iron homeostasis, influences the rise in iron requirements that occur during pregnancy. The persistent prevalence of maternal anemia worldwide suggests that current methods of iron supplementation are ineffective. The dose and frequency of oral iron administration may be changed to increase therapeutic effectiveness in light of recent advances in our understanding of systemic and placental iron homeostasis.

KEYWORDS: *Pregnancy, Iron, Iron deficiency anaemia, Anaemia, Maternal outcome, Hepcidin.*

INTRODUCTION
Worldwide, iron deficiency anemia (IDA) affects about 1.24 billion people.[1-3] It is one of the major global causes of years spent with a disability, disproportionately affecting women, low-middle socioeconomic groups, and populations in Asia and sub-Saharan Africa.[4-5] 32 million women are thought to be affected by maternal anemia worldwide. 46 percent of pregnant women were anemic at some point, according to a sizable UK cohort study.[6-8] The most frequent cause of maternal anemia is iron deficiency (ID), but other factors include haemoglobinopathies like sickle-cell anemia and thalassemia; a lack of folate or B12, or both; hookworm infection; schistosomiasis; and HIV infection.

It is now well established that anemia is linked to poor outcomes for pregnant women, fetuses, and newborns.[9-10] Anaemia is now more widely recognized as a potentially modifiable risk factor for postpartum hemorrhage, which is the main cause of maternal morbidity and mortality.[11-12] Preterm birth, growth restraint, and increased mortality are some of the negative fetal and neonatal outcomes.[13-14]

This review covers iron homeostasis, current definitions of IDA in pregnancy, harmful effects of anemia on mothers and babies, and the most recent recommendations for treating IDA during pregnancy and after delivery. The management of other anemia-causing conditions is outside the purview of this review and is covered elsewhere.[15-16]

Iron homeostasis during pregnancy
Iron requirements during pregnancy
Due to its crucial roles in processes like DNA synthesis, cell growth and differentiation, immunity, mitochondrial function, and responses to hypoxia, iron is an essential element needed by almost all organisms.[17-18] Pregnancy-related iron needs increase roughly ten-fold from 0.8 mg/day in the first trimester to 7.5 mg/day in the third trimester in order to support the growth of the placenta and fetus, accommodate blood loss during delivery, and support the increase in maternal red cell mass.[19] The placenta needs about 90 mg of iron on its own, and during a typical pregnancy, it transfers about 270 mg of iron to the fetus.[20]

The function of hepcidin

Hepcidin, a peptide hormone primarily produced in the liver and eliminated by the kidneys, regulates the body's iron homeostasis.[21] Ferroportin, the only iron transport protein found in mammals, is controlled by hepcidin's actions.[21] Ferroportin is expressed at all sites involved in iron-plasma exchange and transports dietary, stored, or recycled iron to blood plasma. These sites include the basolateral membrane of duodenal enterocytes, macrophages, hepatocytes, and the basal surface of placental syncytiotrophoblasts facing the fetal circulation.[22] Hepcidin inhibits iron export to blood plasma at each of these locations by causing ferroportin to degrade intracellularly. Rapid fluctuations in plasma iron concentrations can be caused by changes in hepcidin levels.

When there is inflammation, an infection, a cancer, or too much iron in the body, hepcidin expression rises.[18] Iron is trapped within macrophages and duodenal enterocytes and is therefore inaccessible to tissues that need it due to ferroportin's degradation by hepcidin. Oral iron may not be effective in inflammatory states because of a process called the "hepcidin block," which prevents iron from being absorbed in the duodenum. In states of ID, anemia, hypoxemia, and increased erythropoietic drive, hepcidin expression is decreased.[18]

Hepcidin rises during the first trimester of a healthy pregnancy in comparison to the non-pregnant state, but it falls during the second and third trimesters.[23] It is assumed that this pattern promotes increased dietary iron absorption and releases iron from stores. But as pregnancy progresses, maternal hepcidin is suppressed for an unknown reason. The emergence of ID may be the main factor, despite the fact that low hepcidin concentrations have been observed even in women who are iron-sufficient at delivery.[24]

Non-anaemic iron deficiency

The final symptom of ID is anemia because erythropoiesis is frequently preserved until the disease is advanced. Therefore, a significant portion of the burden of ID in pregnant women will go unnoticed if the absence of anemia is assumed to indicate adequate iron stores. Although non-anemic iron deficiency (NAID) is more widely acknowledged as a disease, its clinical significance in pregnancy is not clear. A recent study of 102 pregnant women who were not anemic discovered that 42% of them had evidence of ID, as indicated by a ferritin level less than 30 g/L or transferrin saturation below 20%, but there was a lack of information on the outcomes for the mother and the fetus.[25]

In a recent systematic review, participants who received iron had lower levels of subjective fatigue than those who did not receive it when they were healthy, non-pregnant women with NAID.[26] However, there were no improvements in objective tests of physical strength like time trials, tests to determine when a person will exhaust themselves, or measures of maximum oxygen consumption. Additionally, it was determined that the overall quality of the evidence ranged from low to moderate. There may be worse postoperative outcomes for patients with NAID compared to those with iron stores that are sufficient, according to small exploratory studies on patients having elective colorectal and cardiac surgery.[27-28]

Many pregnant women with ID may go unnoticed if the assessment of iron status is based solely on the presence of anemia. It is necessary to conduct more research on the diagnosis of NAID and its effects on maternal and fetal outcomes. Serum ferritin screening for pregnant women has been advocated, but there are cost concerns and a lack of well-designed prospective studies to back this method, so it is currently advised to take a more targeted approach to identifying and treating pregnant women who are at risk.[29]

Outcomes associated with maternal anaemia

Maternal outcomes

Fatigue, pallor, angular cheilitis, weakness, palpitations, shortness of breath, restless legs, pica syndrome, irritability, and poor concentration are some of the clinical indicators and symptoms of IDA. In NAID, these might also exist.

Observational studies47,48 have shown a link between maternal anemia and mortality, with one study showing a linear increase in maternal mortality of 29% for every 10 g/L decrease in maternal hemoglobin. A recent study found that severe anemia, defined as Hb 110 g/L. The advanced maternal age, ethnicity, body mass index, smoking status, and a variety of medical comorbidities were among the numerous confounders that the authors controlled for.[30]

The effects of maternal ID on the brain and cognitive development of the neonate are of growing interest. The first two years after birth are when the fetus's brain grows the fastest, reaching a total volume that is between 80 and 90 percent of that of an adult. Myelination, monoamine neurotransmission, and hippocampal development are among the iron-dependent processes taking place at this time. It has been demonstrated that ID alters the expression of genes important for hippocampal development and function. Evidence of ID in utero has been linked to infants who have abnormal neurological reflexes, poor memory, altered interactions with caregivers, and abnormal neural maturation. Low ferritin levels in utero have also been connected to IQ, language, and tractability deficits at up to 5 years of age[31] Studies examining the effects of iron supplementation have produced conflicting findings. In one study in Nepal, prenatal iron supplementation for women at high risk of developing ID led to improved intellectual and fine motor functioning in follow-up children aged 7-9 years.[32] However, in other studies, the effects of iron supplementation on children whose

mothers have established ID have been less clear, suggesting that timing of the intervention is crucial; earlier supplementation during the antenatal period may be necessary for a beneficial effect on the developing brain. Neurodevelopmental outcomes of offspring should be included in future maternal intervention studies.[33]

At the time of Delivery and After

In addition to having lower iron reserves to support compensatory erythropoiesis after significant blood loss, women who enter labor with IDA are at an increased risk of postpartum hemorrhage. Obstetric indications should be used to determine the delivery method, but other factors such as appropriate intravenous access, group and screen availability, delivery in a unit run by an obstetrician, and active management of the third stage of labor should also be taken into account.[29]

The risk of postpartum anemia is decreased by proper management of IDA during the antenatal period. Current recommendations advise measuring Hb within 48 hours of delivery in women with uncorrected anemia in the antenatal period, blood loss of more than 500 mL, or signs and symptoms suggestive of anemia. Women without active bleeding and anemia that is asymptomatic or barely symptomatic may be able to get by on oral iron. 40–80 mg of elemental iron per day for three months is the suggested dosage.[29]

Women who need immediate treatment for symptomatic anemia or who cannot tolerate oral iron should be offered intravenous iron. Recent research found that women who received intravenous iron as opposed to oral iron experienced a mean improvement of 9 g/L (95 percent CI: 4-13 g/L) at 6 weeks postpartum. The reported rate of anaphylaxis in women receiving intravenous iron was 0.6%. Intravenous iron may reduce fatigue and depression scores up to 12 weeks after delivery, according to low-quality research.[34] We require well-planned, sufficiently powered, randomised controlled trials.

Many women have died as a result of iron deficiency anaemia in pregnancy. Iron status should be monitored in pregnant women for improved maternal and child care. For women who have severe active bleeding, impending cardiac compromise, or anaemia symptoms that require immediate attention, allogeneic red blood cell transfusion should be avoided. Women should be fully informed of the potential risks of transfusion, including being unable to donate blood in the future, and any potential alternative treatments.

CONCLUSION

Worldwide, iron deficiency anaemia continues to be the most frequent factor contributing to maternal anemia, having harmful effects on both the mother and the fetus. Antenatal anemia is a risk factor for maternal and perinatal mortality, preterm labor, low birthweight babies, and postpartum hemorrhage, according to extensive epidemiological studies. Poor infant neurodevelopmental outcomes may also be correlated with maternal iron deficiency anaemia. Low maternal quality of life scores and postpartum anemia have been linked. Many women have died as a result of iron deficiency anaemia in pregnancy. Iron status should be monitored in pregnant women for improved maternal and child care.

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