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LITERATURE REVIEW

The role of iron adequacy for maternal and fetal health

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Abstract

Nearly half of pregnant women in the world are reported to suffer anemia. And most of them are caused by iron deficiency, while the others by folate, vitamin B_{12} or vitamin A deficiency, chronic inflammation, parasite infections and hereditary disorders. Anemia in pregnant women is characterized when <11 g/dL or any time during pregnancy. And when followed by low iron, it's called iron deficiency anemia.

Iron plays an important role in many metabolic processes by transporting oxygen and allowing cells to generate energy. Low iron levels during pregnancy leading to anemia, related to an heightened risk of mother and fetus disease. Iron deficiency anemia can affect fetal development and persist long-term, while mild and serious pregnancy anemia can lead to premature birth, maternal and child mortality, bleeding, and infectious disease. The iron requirement during pregnancy exceeds 1000 mg for red cell expansion, 300 mg – 350 mg for developing fetus and placenta, and 250 mg for variable blood loss at delivery. Iron adequacy during pregnancy can be assured by proper nutrition, iron supplementation and fortification, and intravenous iron or blood transfusion. Iron supplementation is only enough to cover the prenatal iron requirements.

Summary: Iron deficiency leading to anemia, rising risk of negative pregnancy outcomes. To meet increasing iron requirements during pregnancy including iron supplementation, fortification of staple iron foods, and intravenous iron or blood transfusion if required.

Keywords iron, maternal, fetal, health

Introduction

Macro-elements and micro-elements are important for the proper functioning of living organisms. Iron, which is mostly inorganic, is an essential micronutrient and plays a major part in many of the human body's metabolic processes, including oxygen transport, oxidative metabolism, and cell growth.[1-3]

Approximately 3-5 g iron is present in the adult human body (44-55 mg per kg body weight in adult men & women), with hemoglobin incorporating more than 2/3, a four-unit molecule, one heme group and one protein chain that can be fully oxidized into the lungs and can be carried out by the lungs via the arteries to all cells across the body.[2,4,5] The erythrocytes contain many of the iron in the body, such as hemoglobin, whilst ferritine and hemosiderin contain many enzymes in the liver, spleen, bone marrow and myoglobin, including catalase, peroxidase and cytochrome.[3,5]

The intake of iron is present in both iron to heme (10%) and those without heme (90%). Heme iron includes any type of iron from animal products in which the iron is chemically bonded within the porphyrin ring structure as shown in both myoglobin

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and hemoglobin. Iron that is not heme iron is called non-heme iron.[3,5,6]

Iron absorption occurs in the small intestine specifically in the duodenum and the upper portion of the jejunum.[1,6,7] Heme irons are soluble and are easily absorbed by a less unknown process of heme oxygenase 1 (HO-1) through the brush boundary of the enterocyte. Non-heme iron occurs in the intestinal lumen as an oxidized form of $Fe3^{+}$ (ferric) and transformed to Fe^{2+} (ferrous) form either via a brush boundary membrane ferric reductase, probably a duodenal cytochrome b (Dcytb), or by a dietary reducing agent before it can be transported via the intestinal epithelium by a transporter called the divalent metal transporter 1 (DMT1) together with zinc, copper.[1]

It is important to ensure the balance of iron homeostasis in the body as iron plays an integral role in several metabolic processes. Iron homeostasis is also required to prevent iron toxicity, non-protein bound iron (NPBI) reacts with oxygen and produces reactive oxygen species (ROS) with the ability to damage DNA, proteins, lipids, other cellular molecules and stem cells.[1,7,8] Iron homeostasis is controlled by a hepatocyte-producing hormone receptor and binds to ferroprotein named hepcidin (hepatic bactericidal protein) by control of intestinal and tissue release of iron. When iron storage and availability are limited, the amount of hepcidin is limited so that any excess absorbed in the gut or deposited in tissues is released. The contrary is true when storage and bioavailability are high. Then, the amount of hepcidin increases and controls the release of iron from the body through the plasma.[4,7-11]

The role of iron in maternal and fetal health

Iron has been discovered to be necessary for vital physiological body functions, e.g. oxygen transport, hemoglobin and myoglobin synthesis, and cell growth and differentiation.[1]

The average adult body contains around 3–5 g of iron (45–55 mg/kg adult men's body weight).[2] Iron requirements increase dramatically during pregnancy to support an increasing volume of red cells, growing fetuses and placenta plus any expected or unforeseen blood loss at delivery, particularly with caesarean delivery.[5,12] The need for iron for pregnancy is more than 1000 mg, 500 for red cell enlargement, 300-350 for fetal and placental development, and 250 for variable blood loss when delivered.[7,13]

Iron is vital for the production of hemoglobin and is required during pregnancy for the development of the fetal brain. Throughout pregnancy., it is necessary to maintain an adequate maternal diet only enough to provide the critical nutrient for fetal development and birth outcomes. The disparity in maternal nutrition contributes to a rise in the risk of chronic post-life disease.[14]

Maternal health related to iron

The iron requirement increases during pregnancy, the maternal hematological system undergoes physiological changes to accommodate the growth of the fetus and placenta throughout pregnancy. Plasma volume increases and the red cell mas duplicates to ensure proper circulation and oxygen supply to the maternal organs including to the placenta for fetal development and to promote the impact of blood loss during supply.[12,14-16]

Iron deficiency is a major micronutrient deficiency in the world. The prevalence of iron deficiency between expectant mothers, babies and young children may be due to high iron requirements during periods of rapid development.[8,14,17] Pregnancy anemia is the result of nutritional deficiency due to the lack of iron and folate in the diet, but other factors can additionally cause anemia including decreased absorption, chronic blood loss, increased demand, concomitant medical disorder, and malaria.[18] That describes gestational anemia as a hematocrit <33 % and/or hemoglobin < 11 g/dL or at any time during pregnancy. The Centers for Disease Control and Prevention (CDC) describes anemia as hemoglobin < 11 g/dL and/or hematocrit less than 32 % in the first and third quarters and hemoglobin < 10.5 g/dL and/or hematocrit less than 32 % in the second.[7,13,19]

Women who are pregnant are identified to have adverse maternal and newborn health effects and make a greater threat of death during pregnancy and during the post-natal period. The potential negative health consequences for the mother include fatigue, weakened immune function, reduced tolerance to blood loss during delivery, an increased risk of infection, and a shortened lifespan due to heart failure. Postpartum depression and behavioral problems exist in some cases of childbirth. Anemia during pregnancy is linked to several health risks including preterm birth or low birth weight. Preterm and Low Birth Weight are still the leading causes of neonatal death in some of the countries, often associated with an increased risk of intrauterine death, a low APGAR score of 5 minutes, and an intrauterine growth restriction.[10,19-23] The A study confirms a connection between low hemoglobin levels in women during pregnancy and possible increased risk for postpartum hemorrhage and includes evidence of a connection between extreme anemia and uterine atony requiring emergency hysterectomy.[18]

Fetal health related to iron

Restricting fetal growth is significant for determining a child's health in the immediate future. Infants who do not grow to their maximum size are at higher risk of dying in their first year and of developing chronic diseases later in life, including coronary heart disease and type 2 diabetes. The infant is dependent on certain nutrients passed from mother to child. However, maternal nutrition plays a vital role in fetal development, and it is during the first trimester when fetal growth is most vulnerable. Iron deficiency is by far the greatest micronutrient deficiency. Data indicates that early pregnancy iron deficiency has an adverse effect on fetal development. Maternal anemia frequently exhibits a risk of low birth weight, either due to premature birth or reduced fetal growth linked to IDA, or due to delayed neurocognitive development.[10,14,24] Iron is essential for enzymes involved in specific cerebral functions including serotonin and dopamine, a precursor to epinephrine and norepinephrine, myelination and production of neurotransmitters.[14]

There is evidence that iron deficiency during pregnancy and/or anemia later in pregnancy affects learning, motor and emotional development, and children who experience perinatal iron deficiency are at greater risk of failing to meet educational goals. In addition, children who also undergo iron deficiency are more likely to bear as adults. As a result, a shortage of iron in one generation will lead to a shortage of iron in the next. Given the possible neurological effects, such as stunted motor development, lower IQ, learning disabilities, and memory deficits.[25,26]

An alteration in the gut microbiome through an increase in intestinal iron results in the growth of potentially pathogenic bacteria. By at least one week of life, elevated intraluminal iron is most likely to occur in elevated dietary iron intake, inflammation, or both. Both are states characterized by low iron absorption as well as high levels of non-absorbed iron that remain intraluminal. Whether changing the microbiome increases the incidence of infectious diseases is a significant issue. These findings will likely affect future policy decisions.[8] The main nutritional function of iron is to promote post-birth erythropoiesis, with insufficient preterm infant iron stores unable to support post-natal erythropoiesis and post-birth development.[13]

Risk factors for iron deficiency in maternal, infancy, and toddlerhood

Iron is typically in low amounts in diets. If iron is not being absorbed from the diet the person may have a nutritional iron deficiency.[1] Iron deficiency anemia is the highly typical form of anemia that occurs in adolescents and has several risk factors ranging from low iron intake, menstrual status and pattern, obesity, socio-economic and malnutrition as risk factors for IDA, especially in developing countries.[27] Maternal pregnancy smoking and pregestational or gestational diabetes mellitus are major risk factors for low fetal iron status.[14] Iron deficiency in pregnancy is one of the most commonly diagnosed causes of pregnant women's health issues and the poor health of newborns. The factors of primary food shortages, parasites, and parasitic disease during pregnancy are major causes of anemia.[28]

Iron accretion occurs during the third quarter of pregnancy. Infants have enough iron at birth to cover their iron needs during the first four to six months. Iron transfer from mothers to children in conditions like diabetes is reduced, but in children less than 5 years of age, iron is not impaired by maternal anemia or factors leading to decreased iron transport during pregnancy.[29]

Management of iron deficiency during pregnancy and lactation

Iron and anemia are important health indicators in mothers and in children. Iron deficiency is a significant health issue for pregnant women before, during, and after pregnancy and this deficiency directly associates with negative pregnancy outcomes. Effective management is crucial to minimize the need for red cell transfusion, and especially the need for transfusions for a pregnant woman. The purpose of encouraging iron fortification during pregnancy is to reduce maternal morbidity, to provide sustenance for the fetus, and to prepare a newborn for early postnatal life. The growing evidence supports the notion that prenatal iron status affects iron status in the children.[8]

During pregnancy, a mother takes in an average of 1,000 mg of iron. The baby's dosage rose from 6 mg/day in the first trimester to 19 mg/day in the second trimester to 22 mg/day in the third. Unlike the recommendation for non-pregnant, non-lactating women, the recommendation for lactating women is based on only the presumption of lactation-induced amenorrhea and does not take into account that some women enter or end iron insufficiency or deficiency during pregnancy.[7,13,30]

UK guidelines recommend that pregnant women be advised of iron-rich food sources and any factors that may inhibit or promote iron absorption, as well as why fulfilling iron requirements during pregnancy is beneficial. The recommended daily intake of iron as a function of age is approximately 27 mg in the UK and 30-60 mg in most other countries.[7,16,31,32] The estimated population requirement or average population requirement (AR) ranges from 7 mg/day to 22 mg/day and the recommended daily dietary allowance (RDA) or population nutrient intake (PNI) or recommended dietary intake (RNI) ranges from 11.5 mg/day to 27 mg/day for 97.5 mg/day in the population.[9]

During pregnancy, iron absorption triples, with the woman's iron requirement rising from 1-2 mg to 6 mg per day. The foods with the highest levels of dietary heme iron are red meat, poultry, and fish. Heme or non-heme iron absorb 2-3 times faster. The food as a whole has many other organic compounds. that enhance the bioavailability of non-heme iron in other sources. Vitamin C (ascorbic acid) aids in the absorption of iron by non-heme foods, thus increasing vitamin C in the meal. Fermentation and germination increase the bioavailability of non-heme iron by reducing the phytate content, an inhibitor for iron absorption. Coffee and tea tannins hinder the absorption of iron in the body. If a woman becomes iron-deficient in pregnancy, she must be supplemented through diet or by taking oral formulas. The minimum daily dosage of iron for iron deficiency is 100-200 mg. High doses of these nutrients should be avoided, as high doses cause increased oxidative stress and an increased risk of infection.[33,34] For better purposes, it is advised to take iron supplements on an empty stomach because it is absorbed less efficiently when taken on a full stomach.[30,31] The increase in hemoglobin levels in the blood indicates a positive response to the treatment and supports the diagnosis. The maximum rate of iron absorption is 20 to 25 % among individuals who are iron deficient when taking oral iron supplements. The effectiveness of oral iron supplementation is reduced when intestinal absorption is compromised (e.g., in celiac disease, autoimmune gastritis, ACD, or post-gastric or duodenal resection,) or the iron loss is significant and/or persistent. Adherence to oral iron therapy can be an obstacle to treatment since a patient may experience GI adverse reactions such as nausea, epigastric pain, diarrhea and constipation.[35,36]

Intake of intravenous iron helps treat the symptoms of iron-deficiency anemia. Parenteral therapy can be used in patients unable to consume or tolerate oral therapy, such as those who have undergone gastrointestinal surgery or pregnant women who have experienced inadequate oral therapy. In patients with confirmed iron deficiency anaemia and Hb <100 g/L after 34-week gestation, IV iron should be considered. Blood transfusion is recommended for pregnant women with hemoglobin levels less than 8 g/dL unless reassuring fetal cardiac tracing and normal amniotic fluid volume is present.[35,37] Two units of packed red blood cells should be administered if transfusion is performed, and the condition of the patient should be re-evaluated to guide future care.[35] Transfusion is simply a short-term solution for a problem, and proper care must include the diagnosis and treatment of the underlying condition. In addition, intravenous iron (as well as erythropoiesis-stimulating agents, if necessary) tends to maintain Hb levels and iron stores, and avoids transfusions in the future.[36]

Conclusion

Iron deficiency during pregnancy provides women and their babies with better outcomes. The usefulness of iron supplementation more than counterbalances any dangers to pregnant women that lack iron. During pregnancy, the mother's body requires an increased amount of iron to support the growth of red blood cells, fetus, and placenta and blood loss at delivery. During pregnancy, meeting the iron requirement is vital to preventing adverse health outcomes for the mother, child, and fetus. The most prevalent nutrient deficiency worldwide is iron deficiency, and it is most prevalent in pregnant women because the additional iron critical for fetal development is not readily received by the mother's body. WHO recommends universal oral iron supplements for pregnant women. The recommendation to take iron or iron-folic acid supplements to reduce the risk of adverse pregnancy outcomes and increase offspring iron stores. Provision of low doses of iron and folic acid when stores are nearly depleted is the most effective and safest way to achieve iron status.

Conflict of Interest

The authors declared no conflict of interest regarding this article.

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