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IRON DEFICIENCY ANEMIA IN PREGNANCY: AN OVERVIEW OF CAUSES, DIAGNOSIS, AND THERAPEUTIC APPROACHES

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ABSTRACT

Iron deficiency remains the leading cause of anemia globally and continues to pose a significant public health concern, particularly in developing countries. Despite its high prevalence, limited research has focused specifically on Iron Deficiency Anemia (IDA) as a distinct clinical and pathological entity, with most studies addressing anemia in general. This review explores the concept of IDA, highlighting its etiology, pathophysiology, diagnostic criteria, complications, and management strategies. The primary causes include insufficient dietary iron intake, impaired absorption, chronic blood loss, and increased physiological demands, especially during pregnancy. Diagnosis is established through laboratory indicators such as decreased hemoglobin, serum iron, ferritin, and transferrin saturation levels, accompanied by elevated total iron-binding capacity. Management typically involves iron supplementation, nutritional optimization, and, in severe cases, erythropoietin therapy. This review emphasizes the critical importance of early diagnosis and targeted intervention to minimize adverse maternal and fetal outcomes associated with IDA.

Keywords: Iron Deficiency Anemia, Anemia, Etiology, Pathophysiology, Diagnosis, Complications, Treatments

1.0 INTRODUCTION

Anemia during pregnancy is defined by a hemoglobin concentration below 11 g/dL and is predominantly caused by iron deficiency, accounting for over half of all cases globally (James, 2021). It is estimated that nearly 40% of pregnant women and approximately one-third of non-pregnant women of reproductive age worldwide are affected by anemia (Stevens *et al*., 2013).

Iron deficiency refers to a condition in which the body's iron stores are reduced, either before or without the development of noticeable anemia. In contrast, iron-deficiency anemia is a more advanced stage, where low iron levels cause anemia marked by small, pale (microcytic and hypochromic) red blood cells (Camaschella, 2015).

Iron is a vital micronutrient that plays a key role in numerous biochemical processes as a component of ferroproteins and enzymes. Although it is among the most abundant elements on Earth, the forms of iron commonly found in nature are often insoluble and have low bioavailability in many diets. The human body maintains iron balance efficiently, losing less than 0.1% of its total iron content daily, an amount typically replenished through dietary absorption. Most of the body's iron resides in the hemoglobin of red blood cells, which contain about 1 mg of iron per milliliter of cells, amounting to approximately 2–2.5 g in total. Globally, excessive blood loss exceeding dietary iron intake remains the primary cause of iron deficiency (Nemeth, 2023).

In developing countries, anemia affects over two-thirds of pregnant women, with iron deficiency accounting for approximately 95% of these cases (Raut, 2022). Maternal

mortality rates linked to anemia are estimated to range from 34 deaths per 100,000 live births in Nigeria to as high as 194 per 100,000 in Pakistan. These wide disparities are likely due to differences in the prevalence and severity of anemia between the two countries (Abioye *et al*., 2024).

According to the World Health Organization (WHO, 2023), the highest burden of anemia occurs in the African and South-East Asian regions. In Africa, an estimated 106 million women and 103 million children are affected, while South-East Asia records approximately 244 million women and 83 million children are living with the condition.

Iron deficiency continues to be the predominant cause of nutritional anemia worldwide and represents a significant public health concern, particularly in low- and middle-income countries (Qamar *et al*., 2019). It is estimated that iron deficiency anemia accounts for 70–85% of anemia cases during pregnancy, with the highest prevalence observed across Africa (Hassan *et al*., 2014). Key contributing factors include high parity, advanced gestational age, low socioeconomic and educational levels, unemployment, and inadequate living conditions (Ugwu and Uneke, 2020).

Iron deficiency remains the predominant cause of anemia globally and continues to be a major public health concern. Despite its significance, there is a paucity of literature that distinctly addresses Iron Deficiency Anemia (IDA) as a separate clinical and pathological entity, with most existing studies focusing broadly on anemia. Consequently, this review is warranted to elucidate the fundamental concepts of IDA, including its etiology, pathophysiology, diagnostic markers, associated complications, and current therapeutic approaches.

2.0 ETIOLOGY

Several underlying factors may contribute simultaneously to an individual case (Besarab and Hemmerich., 2018).

2.1 Inadequate Iron Intake

When the amount of iron consumed is insufficient to satisfy bodily needs or to replace losses resulting from physiological or pathological processes, the body's iron stores gradually diminish. Absolute iron deficiency develops when these reserves cannot meet the body's demands and is most observed in children under five years old and in premenopausal women, particularly during pregnancy (Pasricha *et al*., 2021).

Insufficient iron intake can result from long-term adherence to vegetarian diets, where the high phytate and fiber content reduces iron bioavailability, or from restrictive diets that are naturally low in iron. Adolescents are especially at risk due to limited nutrition knowledge, body image concerns, and the influence of dietary fads, all of which contribute to inadequate iron consumption and the onset of iron deficiency anemia. Moreover, both breast milk and unmodified cow's milk provide minimal amounts of elemental iron, containing less than 0.7 mg/L (Leung *et al*., 2024).

Although both breast milk and cow's milk contain limited amounts of iron, the absorption rate differs significantly by around 50% of the iron in breast milk is absorbed, whereas only about 10% is absorbed from cow's milk. Moreover, excessive intake of cow's milk can interfere with the absorption of other vital nutrients and iron supplements (Aksu and Ünal, 2023).

2.2 Malabsorption

Diets rich in cereals tend to lower iron absorption since phytates present in these foods bind to iron, forming insoluble complexes that the body cannot easily absorb (Besarab and Hemmerich, 2018).

2.3 Rapid Growth

Iron deficiency anemia can occur because of hemodilution. In full-term infants, it is rare before six months of age due to sufficient iron reserves acquired at birth. However, preterm infants and those from multiple pregnancies such as twins or triplets are born with lower iron stores. The likelihood of deficiency

increases further when the mother herself is iron deficient, resulting in reduced fetal iron reserves. Because of the rapid growth and expansion of blood volume in preterm and multifetal infants, their iron stores may become depleted within the first two to three months of life, leading to iron deficiency anemia. A similar vulnerability is observed during adolescence, when accelerated growth and increased blood volume substantially raise iron requirements; if dietary intake does not keep pace, iron deficiency anemia may develop (Leung *et al*., 2024).

2.4 Pregnancy

Iron requirements increase markedly during pregnancy compared to the non-pregnant state, even though menstrual blood loss temporarily ceases. This heightened demand results from the need to expand maternal plasma volume, enhance red blood cell production, support the developing fetus and placenta, and compensate for iron loss during delivery. For a woman weighing about 55 kg, the total iron requirement throughout pregnancy is estimated at 1000 –1200 mg comprising roughly 350 mg for fetal and placental development, 500 mg for red blood cell mass expansion, and about 250 mg to replace delivery-related blood loss. The demand for iron also fluctuates during pregnancy, being minimal in the first trimester (around 0.8 mg/day) and increasing substantially in the third trimester (3.0 –7.5 mg/day) (Garzon *et al*., 2020).

2.5 Blood loss

Kohr (2016) highlighted that blood loss can arise from several sources, including gastrointestinal bleeding or chronic illnesses such as tuberculosis, peptic ulcers, and intestinal diseases. Additional causes include excessive or frequent menstrual bleeding, childbirth, repeated blood donations, traumatic injuries, hemorrhage, surgical procedures, and the use of certain medications. Intravascular hemolysis where red blood cells rupture within the bloodstream and release iron that is then excreted in the urine can also contribute to blood loss. This condition is sometimes observed in individuals who engage in intense physical activities, especially jogging. Gastrointestinal (GI) bleeding is the leading cause of iron deficiency in men and in women who are not menstruating. Even minor daily blood loss of about 5–10 ml can accumulate to 200–250 ml per month, corresponding to roughly 100–125 mg of iron loss, and may lead to iron deficiency anemia within one to one and a half years. Common GI conditions associated with bleeding include erosive gastritis, hiatal hernia, ulcerated Meckel's diverticulum, ulcerative colitis, Crohn's disease, intestinal polyps, diverticulosis, and hemorrhoids. Additional causes include gastric or duodenal ulcers, gastrointestinal tumors, and parasitic infections such as hookworm each parasite consuming approximately 0.3 ml of blood. Therefore, patients presenting with gastrointestinal blood loss should be thoroughly evaluated by a gastroenterologist to identify or rule out underlying GI disorders (Kudratova *et al*., 2023).

3.0 PATHOPHYSIOLOGY

Iron is a fundamental micronutrient vital for several physiological functions, particularly in oxygen transportation and cellular energy metabolism (Charlebois and Pantopoulos, 2023). The regulation of iron balance within the body largely depends on dietary intake, intestinal absorption, and the recycling of iron from degraded red blood cells (Shah *et al*., 2021). Iron in the human diet exists in two major forms: heme and non-heme. Heme-iron, which the body absorbs efficiently, is derived from hemoglobin and myoglobin found in animal products such as meat, poultry, and fish. In contrast, non-heme iron, found mainly in plant-derived foods like grains, legumes, and nuts, is absorbed less readily (Papagiannaki, 2025).

Iron absorption is influenced by several dietary factors that either enhance or inhibit its uptake. Ascorbic acid (vitamin C),

commonly present in fruits, vegetables, and juices, promotes non-heme iron absorption. Similarly, fermentation and germination processes in foods like soy sauce and sauerkraut enhance iron bioavailability by reducing phytate levels. Conversely, phytates found in grains, legumes, and seeds, along with tannins present in tea and coffee, interfere with efficient iron absorption (Kapil, 2017).

Anemia leads to significant health and developmental consequences due to impaired oxygen delivery to body tissues, affecting the performance of multiple organ systems. These adverse effects are closely tied to the underlying causes of anemia, which are often multifactorial and challenging to differentiate (Nehar *et al*., 2024).

4.0 DIAGNOSIS of IDA

Laboratory evaluation remains the primary method for identifying iron deficiency anemia. Typical diagnostic markers include low levels of hemoglobin (Hb), serum iron, transferrin saturation, and ferritin, along with an increased total iron-binding capacity. In most situations, assessing a complete blood count (CBC) together with serum ferritin levels provides adequate diagnostic information. During pregnancy, iron deficiency anemia is diagnosed when serum ferritin is below 30 µg/L, accompanied by hemoglobin values less than 11 g/dL in the first trimester, under 10.5 g/dL in the second trimester, and below 11 g/dL in the third trimester (Api *et al*., 2015).

Among the available biomarkers, serum ferritin is considered the most accurate indicator of iron status when inflammation is absent. However, since ferritin behaves as an acute-phase reactant, its concentration can remain normal or elevated during inflammatory conditions, even in individuals with true iron deficiency. Therefore, additional laboratory tests may be required for confirmation in such cases (Api *et al*., 2015). Hepcidin, a regulatory hormone involved in maintaining iron balance, is also not a dependable standalone marker for diagnosing complex forms of iron deficiency because its levels fluctuate and may not clearly differentiate between deficient and normal iron status (Nehar *et al*., 2024).

5.0 COMPLICATIONS of IDA

Iron deficiency anemia (IDA) is closely associated with an elevated risk of maternal complications such as preterm delivery, cesarean section, postpartum hemorrhage, and, in severe cases, maternal death. It also poses significant risks to the fetus, including intrauterine growth restriction and low birth weight. The severity and prevalence of these outcomes are influenced by various social determinants, including ethnicity, socioeconomic background, nutritional habits, and access to quality healthcare (Benson *et al*., 2024).

The harmful effects of IDA primarily arise from the blood's reduced oxygen-carrying capacity and decreased circulating volume, both of which adversely affect maternal and fetal health. Hemoglobin, an iron-dependent protein essential for oxygen transport, becomes significantly reduced in IDA, leading to hypoxia or inadequate oxygen delivery to maternal and fetal tissues (Ohuma *et al*., 2023).

Restricted oxygen and nutrient flow to the fetus impedes normal development and growth. As a compensatory response to hypoxia, the maternal cardiovascular system increases cardiac workload and output, which may result in cardiac strain and increase the likelihood of hypertensive disorders such as preeclampsia and gestational hypertension (Hutter *et al*., 2010).

In addition, iron plays a vital biochemical role as a cofactor in numerous enzymatic and metabolic processes within the central nervous system. Deficiency during critical developmental periods can cause profound neurological effects. Early iron deprivation disrupts neuronal growth, impairs myelination and oligodendrocyte function, and interferes with neurotransmitter synthesis and signaling, potentially resulting in long-term cognitive and

neurodevelopmental deficits (Garzon *et al*., 2020).

6.0 TREATMENT of IDA

Iron supplements are commonly used to restore iron levels in the body. For optimal absorption, they are best taken on an empty stomach. However, if gastrointestinal side effects occur, such as nausea or discomfort, they can be taken after meals. It is important to continue taking the supplements for several months to fully replenish iron stores. Common side effects may include constipation and black-colored stools (Paul *et al*., 2021).

When iron deficiency anemia (IDA) is detected in pregnant women, the recommended initial management approach is oral iron replacement therapy (IRT), especially within the first 14 weeks of gestation. However, if IDA is identified in the second or third trimesters, intravenous IRT is typically recommended for more effective correction. It is advised to reassess serum ferritin levels about 4 to 6 weeks after initiating therapy to evaluate the response and guide further management (Iolascon *et al*., 2024).

Erythropoietin (EPO) therapy has been demonstrated to be highly beneficial in treating anemia during pregnancy, particularly in cases involving renal impairment or when blood transfusion is not an option. Its increasing use is supported by evidence of its safety and effectiveness. Due to its large molecular size, EPO is unable to cross the placental barrier, and current studies have found no associated risks to fetal or neonatal health (Obianel *et al*., 2024).

7.0 Conclusion

This review summarizes the etiology, pathophysiology, diagnosis, complications, and treatment of Iron Deficiency Anemia (IDA). IDA is the most common form of anemia, primarily caused by blood loss, malabsorption, inadequate iron intake, rapid growth, and pregnancy. It increases the risk of cesarean delivery, postpartum hemorrhage, and maternal mortality, and adversely affects the fetus by causing low birth weight and growth restriction. Diagnosis is based on laboratory parameters showing decreased hemoglobin, serum iron, ferritin, and transferrin saturation levels, accompanied by an increased total iron-binding capacity. Management includes iron supplementation, dietary improvement, and, in severe cases, erythropoietin therapy.

8.0 Recommendations

This review suggests the following studies in the future:

1. A comprehensive review on iron deficiency anemia should be carried out covering all the states in Nigeria.
2. A study on iron deficiency anemia: implications and maternity cases in Zamfara State should be carried out in the future.
3. A study on assessment of iron deficiency anemia among pregnant women in Zamfara State should be conducted.

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