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Review Article

Anemia in Pregnancy: a Practical Review

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Abstract

Iron-deficiency is the most common cause of anemia during pregnancy. It is essential to identify the cause of the anemia for proper and effective management and treatment. However, the definition and parameters of anemia during pregnancy differ among regulatory bodies. If not diagnosed or managed adequately, anemia during pregnancy can severely affect the mother and fetus. Pregnant and lactating mothers have enhanced iron demand. A balanced diet and iron supplements help avoid iron depletion and iron-deficiency anemia. Most pregnant women are prescribed oral iron supplements; however, an iron deficit can occur even with iron supplementation. Also, iron supplement intake may be limited by poor compliance due to intolerance and gastrointestinal side effects. These limitations can be overcome by dose titration and prescribing alternative oral iron supplements with non-enteric-coated iron preparations. The prophylactic use of oral iron supplements is promoted in developing and many developed countries. Oral iron supplements are the standard of care for iron-deficiency anemia during pregnancy. In low tolerance, due to gastrointestinal side effects, parenteral iron therapy may be utilized. Blood transfusion is sometimes advised—with caution—for severe iron-deficiency in patients with a high risk of cardiac failure. In addition to iron-deficiency in severe anemia in pregnancy, folic acid and vitamin B12 deficiencies may occur. Hence, a prophylactic iron supplement with 0.4 mg/day of folic acid is recommended. Iron-deficiency anemia remains the leading cause of anemia in pregnancy. If untreated, it can result in several complications in the mother and fetus, including maternal mortality and preterm birth. Thus, the timely diagnosis and management of anemia in pregnancy are vital.

Keywords: *Celiac Disease; Folate Deficiency; Hair Loss; Hemoglobinopathies; Pregnant Women; Vegan; Vegetarianism; Vitamin B12 Deficiency*

Abbreviations

IDA: Iron-Deficiency Anemia; JPAC: Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee; LBW: Low-Birth-Weight; RBC: Red Blood Cell; WHO: World Health Organization

Introduction

Anemia is a manifestation of several pathological conditions. Distinct etiologies are bone marrow suppression, which leads to low red blood cell (RBC) production, and blood loss from external or internal bleeding (hemolysis) [1,2]. Although there are different types of anemia, depending on the underlying pathophysiology, iron-deficiency and congenital hemoglobinopathies are the most common types during pregnancy [3]. However, it is essential to identify the cause of anemia for appropriate and effective management [4].

Definition

The definition of anemia during pregnancy among regulatory bodies is not equivocal. The World Health Organization (WHO) defines it as antenatal hemoglobin levels < 110 g/L and postnatal hemoglobin levels < 100 g/L. The British Committee for Standards in Haematology guidelines defines pregnancy anemia as hemoglobin level < 110 g/L in the first trimester, < 105 g/L in the second trimester, and < 100 g/L during the postpartum period. This guideline follows physiological hemodilution (maximal in the second trimester) [5,6].

Prevalence

Worldwide, anemia affects approximately 1.62 billion individuals, corresponding to about 24.8% of the total global population [7–9]. The highest prevalence of anemia has been noted among pre-school children (47.4%) and pregnant women (41.8%) [7,10]. Even in developed countries, anemia's prevalence during pregnancy is considerably high (around 30–40%) [7,11,12].

Causes of anemia in pregnancy

Iron-deficiency is the most common cause of anemia during pregnancy [1,2]. The occurrence and progression of anemia depend on the iron store of individuals. Also, factors—such as age, nutritional status, iron absorption, and iron loss—influence an individual's ultimate iron status and the development of anemia [1,2].

Iron-deficiency anemia (IDA)

Iron-deficiency anemia (IDA) is caused by several factors, such as inadequate nutritional intake due to malnutrition, low socioeconomic status, vegetarianism, chronic illness; malabsorption due to celiac disease and atrophic gastritis; and chronic blood loss due to esophageal varices, hiatus hernia, bleeding peptic ulcer, inflammatory bowel disease, hookworm infestation, hemorrhoids, and menorrhagia. Moreover, certain pathological and physiological conditions, such as pregnancy and a growth spurt, can precipitate IDA [13,14].

Consequences of anemia during pregnancy

If not diagnosed correctly or managed appropriately, anemia during pregnancy has serious consequences. Both the mother and fetus are at risk of experiencing complications arising from the condition [1,2,5–7,13,14].

Maternal complications

Chronic IDA during pregnancy depreciates the general well–being of the woman, causing fatigue and decreasing the capacity to perform daily tasks and activities [15]. Common presenting signs and symptoms of anemia during pregnancy are pallor, difficulty in breathing, palpitation, headache, lightheadedness (and episodes of fainting), and irritability [16–18].

Such patients can develop pica in rare cases, characterized by a craving for non-food substances, such as clay and dirt [19]. Iron-deficiency alters the temperature-regulating capacity of affected pregnant women, making them feel cold [11]. Before the decrease in

blood hemoglobin due to iron-deficiency, the body tries to compensate for the iron deficit by utilizing its iron store (ferritin) [20]. Thus, in the initial stages, the hemoglobin level is maintained at the cost of depleting of the body's iron store. Hence, it is likely that in some patients, anemia symptoms, such as fatigability, irritability, lack of the concentration, and hair loss, could occur without a diagnosis of anemia [20,21]. In severe cases, cardiac failure might occur [22,23].

The rate of preterm births is twice higher in pregnant women with anemia than pregnant women without anemia [24]. Several studies have established anemia during pregnancy as an independent risk factor for preterm delivery. Other risk factors that independently contribute to preterm delivery are advanced age, parity, ethnic background, a history of low-birth-weight (LBW) or preterm delivery, smoking, body weight before pregnancy, and poor weight gain during pregnancy [25,26], which are more prevalent in pregnant women with anemia [27,28].

During labor, such as placental abruption and increased postpartum hemorrhage incidence, complications are also high in women with anemia [29]. According to Lewis (2008), about 600,000 post-partum maternal deaths occur globally due to numerous complications [30]. Anemia is a direct, contributory factor for about 8–16% of maternal deaths [31], especially in developing countries. In addition to preterm labor, anemia increases the risk for other complications, such as an increased likelihood of infection, bleeding, eclampsia, obstructed labor, and abortion [32]. Anemia could increase the risk of maternal death, especially in the postpartum period [33].

Fetal and neonatal complications

Several studies have suggested a significant correlation between anemia's severity in pregnant women and the risk of premature birth and LBW infants [26–28]. The maternal iron deficit can increase iron-deficiency risk among neonates, especially during the first three months of life [11,34–38].

Terefe., *et al.* (2015) compared the blood profiles and iron statuses of newborn babies of mothers with differing anemia degrees. The researchers found a correlation between the mothers' hematological status and iron stores and those of the neonates [36].

Powers and Buchanan (2014) reported that iron stores in children born of anemic mothers could persist for more than a year [37]. Several studies, that tracked the neonates of anemic mothers up to early infancy and pre-school, found that anemia in children led to low IQ scores, poor school performance, visual and motor coordination deficits, and subnormal language development, among others [37]. Hence, early diagnosis and relevant management are essential in preventing long-term complications in children with anemia.

Iron is an essential micronutrient for neuronal functioning and development [39,40]. Chronic IDA leads to faulty energy metabolism, resulting in impaired neuronal function and development (myelination) [41,42]. In children, chronic IDA adversely effects cognitive, social, emotional, and physical development [43,44].

Breastfeeding plays a protective role in IDA in children [45,46]. However, if the mother has IDA, this protection is lost [11,20], implying the importance of the early diagnosis and timely management of IDA.

Role of diet in IDA

Iron requirement during physiological conditions, such as pregnancy and puberty, as discussed earlier, increases [1,2,37]. Therefore, pregnant and lactating mothers have increased iron demand. Maintaining a balanced nutritional state is vital to prevent IDA [37,47]. A combination of a balanced diet and a prophylactic iron supplement helps avoid iron depletion [13,39,48] and, thus, IDA in pregnant women.

Nevertheless, an iron deficit can occur even with adequate iron supplementation [20,21]. In developed countries, including the United Kingdom (UK), about 50% of reproductive age women have poor dietary iron supply, making them susceptible to an increased risk of IDA during pregnancy [38].

Similar findings were documented in a study of UK women aged between 19 and 34 years. About 40% of the study population had iron levels less than the recommended level [1]. Vegans and vegetarians have a higher risk of developing IDA [49], especially during pregnancy [50]. Hence, pregnant vegans and vegetarians may require iron supplements.

Pregnant teenagers are another group at increased risk of developing IDA [51]. In addition to their own elevated physiological needs (due to pubertal growth spurts) [52], pregnancy demand greater nutritional support [53]. In most cases, teenage pregnancies are unplanned [54]. Without any prior nutritional supplements, the risk of IDA in this population further increases [55].

Management of IDA

Oral supplements

Most pregnant women are prescribed oral iron supplements [56]. The optimal dose of iron supplementation is based on the blood profile and preexisting iron–deficiency, although the typical daily dose comprises 100–200 mg of elemental iron [57]. Iron absorption is the highest when taken on an empty stomach and about 1 h before a meal and with a vitamin C supplement (or fruit juice rich in the vitamin) [1,2,58–60].

According to Tolkien., *et al*. (2015), the intake of iron supplements is limited by poor compliance due to intolerance and gastrointestinal side effects, such as gastric irritation, diarrhea, constipation, and nausea [61]. These limitations can be overcome by dose titration and prescribing alternative oral iron supplements [62]. Moreover, in this case, enteric-coated iron preparations are to be avoided since iron is released from these preparations beyond the duodenum (the leading iron absorption site), leading to inadequate absorption and the failure of oral iron therapy [63].

Considering the increased incidence of IDA, prophylactic use of oral iron supplements is promoted in developing and developed countries [64]. In the UK, iron supplements are prescribed based on blood workup results [65]. However, in developing countries, screening pregnant women may not be possible [64], and prophylactic daily oral supplements at 60 mg/day of elemental iron are prescribed to prevent and manage IDA [64].

Intravenous iron supplements

Oral iron supplements are the standard of care for IDA, including anemia during pregnancy. In low tolerance, due to gastrointestinal side effects, parenteral iron therapy may be advised as an alternative [60–63]. According to the Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC), parenteral iron therapy resullts in better response and compliance in severe IDA cases, especially during the late stage of pregnancy, in patients with inflammatory bowel disease, and those receiving dialysis [66].

Blood transfusion

Blood transfusion is sometimes advised for severe iron-deficiency in patients at a high risk of cardiac failure [67,68]. However, the transfusion also involves risks, such as circulatory overload, transfusion reaction, and increased fetal hemolytic disease risk [69]. Therefore, blood transfusion should only be performed after careful assessment of risks versus benefits [67–69].

In addition to iron-deficiency in severe anemia in pregnancy, folic acid and vitamin B12 deficiencies may occur [70]. Folate deficiency occurs due to an imbalance between host requirement and supply from the diet [71]. Hence, a prophylactic iron supplement with 0.4 mg/day of folic acid is suggested [72].

Conclusion

Worldwide, iron-deficiency anemia remains the leading cause of anemia in pregnancy. Left untreated, it can lead to complications both in the mother and fetus, including maternal mortality and preterm birth, respectively. Studies have revealed that persisting low iron-status IDA in children leads to poor neurological, physical, social, and emotional development. Thus, the timely diagnosis and effective management of anemia in pregnancy are essential. Maternal oral iron supplementation remains the mainstay of treatment; however, in those who cannot tolerate oral iron therapy, parenteral iron therapy is required. In certain severe cases, blood transfusion is indicated.

Conflict of Interest

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

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