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Review Article

Beneficial Impacts of Iron Fortification Versus Iron Supplementation During Pregnancy in Anaemia Prevention for Both Mother and Newborn in Developing Country

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Abstract: Iron deficiency is the most common micronutrient shortfall globally, and it disproportionately affects young children and expecting mothers. An iron deficit impacts children's neurodevelopment, adults' immune responses, and women's pregnancy outcomes. Iron supplementation and fortification programs have been successful in reducing this health burden. But for those who already have adequate iron in their bodies, iron fortification and supplements are probably not necessary, and they may even be harmful to some populations of individuals who do not have enough iron. In order to help decision-makers weigh the benefits and drawbacks of fortifying and supplementing with iron in pregnant women who are iron-deficient, iron-sufficient, or iron-overloaded, this research looks at the physiology of iron as a nutrient. The World Health Organization (WHO) states that iron deficiency accounts for approximately 50% of anemia cases worldwide, making iron deficiency anemia (IDA) the most common micronutrient disease. Even while it affects both developed and developing nations equally, developing nations nevertheless have a larger prevalence of it. The WHO reported that 65.5% of preschool-age children in South-East Asia suffer from anemia, making that region the world with the highest prevalence of anemia. The disorder was also present in 48.2% and 45.7% of non-pregnant and pregnant women, respectively. The most common nutritional shortfall worldwide, especially during pregnancy, is iron insufficiency. Anemia, especially severe anemia, has been linked in the literature to a higher risk of maternal death. Additionally, it exposes moms to a variety of perinatal risks. The effects of iron and iron-folate supplementation have been the subject of several research in the past, but information on the effectiveness and caliber of evidence supporting these therapies is few. With and without folate supplementation, the effects of iron fortification and iron supplementation on maternal anemia are discussed in this article, which also offers outcome-specific quality. For people who need supplementary or fortified iron during pregnancy, a moderate iron dose plan would probably be most beneficial. However, there may not be a single technique that is now widely accepted.

Keywords: Iron Deficiency, Iron Deficiency Anemia, Pregnancy, Anemia in Children, Iron Supplementation, Iron Fortification, Infancy

1. Introduction

Iron sufficiency must be maintained during pregnancy in order to reduce maternal morbidity, enhance fetal health, and give the newborn enough nutritional reserves for the early phases of postnatal life. Data are increasingly supporting the theory that the postnatal iron status at nine months of life is determined by the adequate fetal iron loading during pregnancy [1, 2]. Postnatal iron deficiency in newborns is less likely when neonatal iron stores are normal throughout gestation, delayed cord clamping is performed, and postnatal growth rate is not excessive [3]. It's also likely that proper loading of the infant via the maternal-fetal route reduces the requirement for too early postnatal iron supplementation in certain iron-sufficient cultures.

There is little question that women who are iron deficient are more likely to experience unfavorable pregnancy outcomes—those that impact the mother, the fetus, or the kids as a result. Because hemoglobin is a widely available test and because iron insufficiency is the most prevalent cause of anemia in most populations, hemoglobin is typically used as the biomarker for iron status in research. However, it might be challenging to interpret the results of these research since anemia and iron deficiency are not the same thing. Preterm birth [4-12], birth weight <2,500 grams [8, 13-15], and low birth weight for gestational age [3] are all linked to anemia at different stages of pregnancy. The majority of research indicates that providing anemic pregnant women with iron supplements lowers the incidence of both nonanemic iron deficiency and iron-deficiency anemia at term, as well as the risk of unfavorable outcomes. These findings support the benefits of fortification in this group [16, 17].

2. Iron Deficiency and Iron Deficiency Anemia

2.1. What Refers to Iron Deficiency and Anemia

The Greek term "anaimia," which means "without blood," is where the word "anemia" originates [18]. A shortage of red blood cells and/or hemoglobin causes anemia, which lowers the blood's ability to transport oxygen [19]. An individual is deemed to be anemic if their circulating hemoglobin level is less than 120 g/L, however this varies by age and sex depending on iron requirements and hemoglobin thresholds [18-20]. A chronic iron deficiency that eventually causes the body's iron reserves to be depleted is the cause of anemia [18-21]. Because iron is essential for the synthesis of red blood cells, low iron levels reduce the formation of hemoglobin, which in turn reduces the creation of red blood cells [18, 21, 22]. This chapter focuses on IDA, which is usually caused by insufficient food intake but can also occur from other illnesses such parasite infections, malaria, and hereditary hemoglobin abnormalities, as well as significant blood loss from trauma or postpartum hemorrhage [21, 22]. A number of risk factors for IDA have led to an uneven prevalence distribution worldwide, with developing nations in Asia and Africa having the largest proportion of cases [20]. The most frequently mentioned risk factors for IDA are poverty [20, 23], local dietary staples like rice, which have low bioavailability of iron [24], genetic hemoglobinopathies [25], drinking untreated water [26], sex [26, 27], low parental educational attainment [26-28], maternal anemia, and food insecurity [29]. Females are typically more likely than males to experience IDA. The information presented above makes it quite clear that the complicated causes of IDA encompass a number of different social, ecological, biological, and economic factors. However, poverty is the most noteworthy predictor in all of the studies. A chronic iron deficiency that eventually causes the body's iron reserves to be depleted is the cause of anemia [18, 21]. Because iron is essential for the synthesis of red blood cells, low iron levels reduce the formation of hemoglobin, which in turn reduces the creation of red blood cells [18, 21, 22]. This chapter focuses on iron deficiency anemia (IDA) during pregnancy. IDA is mostly brought on by insufficient food consumption, however parasite diseases, malaria, significant blood loss from trauma or postpartum hemorrhage, and hereditary hemoglobin abnormalities are other potential causes [22, 23].

Prevalence of IDA during pregnancy has been unevenly distributed globally due to a number of risk factors, with developing nations in Asia and Africa having the largest proportion of cases [20]. The most frequently mentioned risk factors for IDA are poverty [20, 23], local dietary staples like rice, which have low bioavailability of iron [24], genetic hemoglobinopathies [25], drinking untreated water [26], sex [26, 27], low parental educational attainment [26-28], maternal anemia, and food insecurity [29]. Females are typically more likely than males to experience IDA. The information presented above makes it quite clear that the complicated causes of IDA encompass a number of different social, ecological, biological, and economic factors. However, poverty is the most noteworthy predictor in all of the studies.

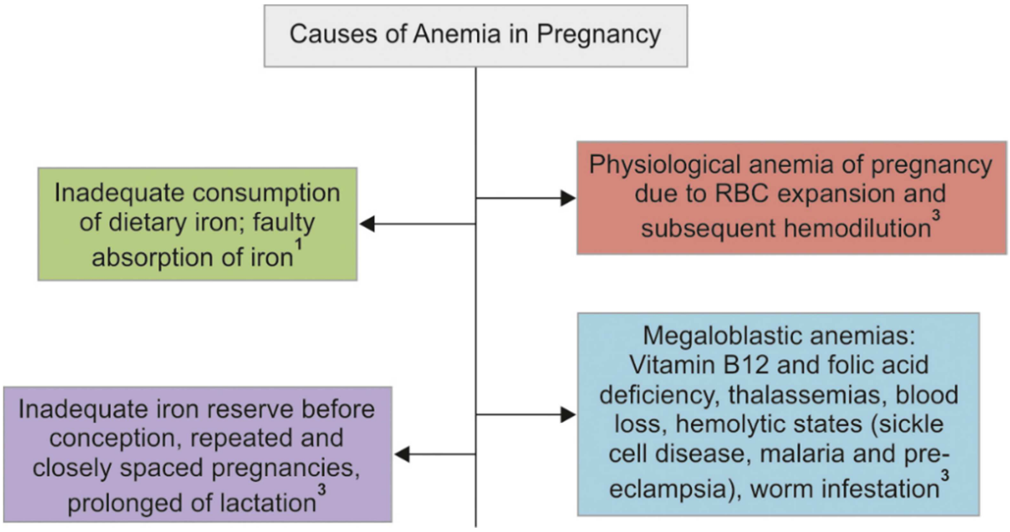

Figure 1. *Causes of Anemia During Pregnancy [70].*

2.2. Signs and Symptoms and Outcomes of Iron Deficiency Anemia During Pregnancy

Although each person's signs and symptoms are unique, IDA always has negative side effects. Due to the increased iron requirements associated with growth and pregnancy, postpartum and pregnant women are more vulnerable to iron deficiency, as are children and those with IDA [30]. Some of the most severe symptoms are also experienced by these populations [30]. Reduced labor capacity, immunological system malfunction, cognition impairment, weariness, pallor, and dizziness are some of the symptoms of IDA [18, 22, 23]. Because of bleeding during and after labor, severe anemia can drastically lower a woman's chances of surviving childbirth [30, 31]. Furthermore, anemia increases the chance of premature birth in pregnant women [24]. These factors lead to the conclusion that anemia has a significant role in maternal mortality in underdeveloped nations. Anemia is a contributing cause in 20% of maternal fatalities, according to the WHO [32]. 176 Public Health Topics Children are more vulnerable to the negative consequences of IDA, and if treatment is not received, they may exhibit extra signs and symptoms. Children who are anemic may face challenges related to height and weight, delayed learning and behavior development, and disruptions in their physical or mental development [28]. Children with IDA may have diminished psychomotor and cognitive abilities as a result of IDA's impact on neurocognitive development [18, 33]. These are most frequently assessed using psychomotor scales, cognitive function tests, educational achievement assessments, and standardized measures of mental development [34].

Pregnancy-related anemia affects both developed and developing countries equally and is a major source of co-morbidities and growing mortality rates. Bangladesh boasts one of the highest global rates of stunting and deficits in micronutrients. Reduced cell-mediated immunity, a diminished capacity to tolerate bleeding or postpartum hemorrhage, the stress of even a simple labor may result in heart failure, a susceptibility to preterm labor and PIH because of the associated malnutrition, a diminished capacity to enjoy pregnancy and motherhood because of exhaustion, and a potential or actual threat to life are all consequences of anemia on the mother. Effects on the fetus and newborn include growth retardation and intrauterine hypoxia, preterm, low birth weight (LBW), anemia many months after delivery from low blood reserves, increased risk of perinatal illness, and a higher mortality rate [35].

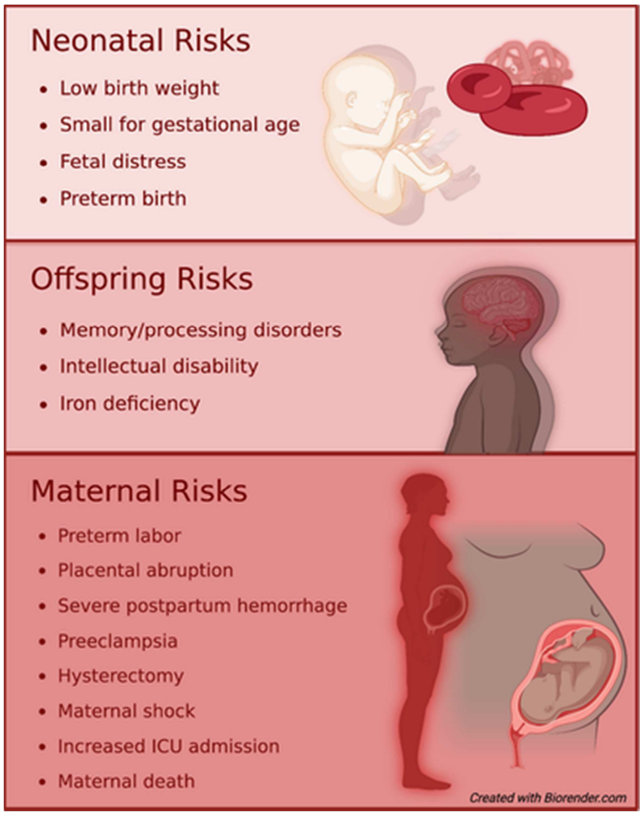

Figure 2. *Maternal and offspring complications imparted by iron deficiency anemia [36].*

3. Dietary iron for Iron Deficiency Anemia

There are two types of dietary iron: heme and non-heme. Meat, chicken, and fish are good sources of heme iron, which is more readily absorbed. Because it is supplied as the stable porphyrin complex and is unaffected by other dietary ingredients, this form of iron is readily absorbed [37]. On the other hand, non-heme iron, which is found in grains, legumes, and some vegetables, is more difficult to absorb [37]. The elemental iron is reliant on the many chemical forms of non-heme iron found in food as well as the body's capacity to identify and absorb it. For instance, compared to ferrous ($Fe2+$) iron, the chemistry of ferric ($Fe3+$) iron is significantly more sensitive to stomach pH levels; ferric iron must be absorbed in a more acidic environment [37]. In order to absorb as much elemental iron as possible, it might be crucial to combine vitamin C with dietary iron or iron supplements [21, 38]. The absorption of non-heme iron is known to be inhibited by tannins (found in tea, for example) and phytate (found in whole grains), which further complicates the situation with non-heme iron [21, 37].

4. Managing Iron Deficiency Anemia During Pregnancy

4.1. Iron Fortification and Iron Fortified Food in Pregnant Mother to Treat IDA

Governments, non-governmental organizations, and foreign assistance agencies alike must continue to prioritize treating iron deficiency and iron deficiency anemia during pregnancy. The best way to treat iron deficiency during pregnancy is to eat a healthy, balanced diet that naturally provides enough iron. But in a large portion of the poor world, where grains with low iron bioavailability are the primary source of sustenance, this is not the case. This creates a need for a simple, affordable, and manageable remedy, which might be found in fortification and supplementation. Although food fortification is generally regarded as the most economical method of treating IDA, there are several drawbacks to this strategy [24]. While government restrictions frequently enforce the fortification of basic food items (such as milk, breakfast cereals, and salt) and fortified goods are widely available in industrialized nations, this tactic may not be as successful in underdeveloped nations. In poor nations, even a slight price rise for basic goods might discourage people from using and buying them [24]. Thus, iron supplementation may be an additional effective strategy for treating IDA in expectant mothers. The possibility that households may buy foods that have been fortified in this situation might make the intervention more challenging to carry out.

There are currently a number of fortification strategies in use. Three of these tactics are described in reference [39]: One way to improve nutrition is to add fortified goods (like wheat flour) during food processing; another way is to add fortification at home during food preparation (like multiple micronutrient powders); and a third way is to use genetically modified foods (like genetically modified cereals) to improve nutrition. Iron fortification has been shown to be usually highly beneficial; a meta-analysis of randomized controlled trials for the treatment of iron deficiency reviewed 13 papers on iron fortification for women and 41 on iron fortification for children [40]. The fortification techniques employed in these studies included ferrous sulfate, ferrous pyrophosphate, sodium iron ethylenediaminetetraacetic acid (NaFeEDTA), fortified chocolates, and fortified curry powder [40]. These investigations showed that iron fortificants were useful in increasing hemoglobin concentration and reducing anemia in the research groups [40]. A separate meta-analysis of 60 trials found that iron-fortified meals are beneficial in decreasing IDA and increasing hemoglobin concentrations in studied populations [41].

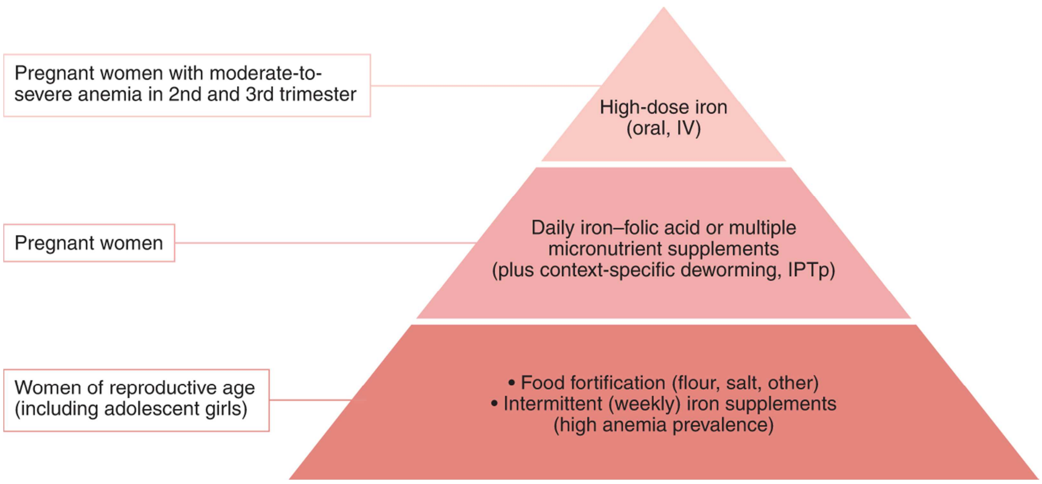

Figure 3. *Anemia Management of Pregnant Women [71].*

In order to provide more iron during eating, some foods can be cultivated and genetically engineered to contain more iron, while others can simply be fortified after harvesting. Globally, there has been a push for food fortification as a means of addressing micronutrient shortages. For instance, adding vitamins A, C, and D to milk during processing is mandated by law in both Canada and the US [43, 44]. It is believed that universal food fortification is a practical and affordable way to combat IDA [45].

Using rice as an example, certain strains of the grain have undergone genetic modification to increase their iron content, although this field of study is still in its infancy [46]. This can be done by breeding rice breeds with additional genes that enhance iron accumulation on polished white rice [47]. This can be accomplished, for example, by introducing a gene from soybeans into rice, which results in the addition of the protein ferritin. Research has indicated that this iron supply is bioavailable [47]. Rice loses a lot of its natural iron content when it is polished; thus, rice may be strengthened by adding an edible coating, which increases the amount of iron that is accessible in the rice [48]. A third way to fortify rice is to use a product called Ultra Rice, which is a high-iron simulated rice grain that can be mixed with regular rice and is well-accepted with no complaints of bad texture or flavor [45, 49].

In a randomized controlled research carried out in the Philippines, iron-fortified rice was proportionately mixed with regular rice to improve the amount of available iron in a serving of rice. For six months, Mexican industrial workers received five days a week of fortified rice; during that period, their iron status significantly improved, and the prevalence of anemia was reduced by 80% [45]. Nonetheless, a Brazilian investigation discovered that equivalent outcomes were obtained when fortified rice was used in child care facilities just once a week [49]. Apart from the enhanced iron status, a study conducted in Brazil discovered that a significant number of study participants and their families were amenable to including fortified rice in their diet without experiencing any negative effects or unpleasant flavor, color, or odor [50]. Given its high product acceptance and shown potential to improve iron status, iron-fortified rice might play a significant role in national nutrition policies.

It is possible to fortify wheat flour and maize flour to increase their iron content, which might help populations where a lot of wheat flour and its derivatives are consumed address iron deficiency [51]. Although the WHO is in favor of fortifying wheat and maize flour, it believes that national legislation requiring fortification will be the most effective way to reduce iron deficiency [52].

Women who consistently ate the fortified flour had a decreased frequency of iron insufficiency, according to a trial that evaluated the effectiveness of fortified wheat flour [50]. In a research using iron-fortified whole wheat flour and Indian schoolchildren, the prevalence of iron insufficiency dropped sharply from 62% to 21% after seven months [53].

Another strategy being investigated to alleviate iron deficiency in developing country communities is iron-biofortified pearl millet. According to a research conducted in Benin, eating iron-fortified pearl millet can quadruple a woman's absorption of iron and may be a very successful strategy for addressing iron insufficiency in millet-eating populations [54].

Although the hemoglobin concentration in the trial communities improved, this strategy for treating iron deficiency and IDA has drawbacks. The biggest obstacle turned out to be the cost to households of making the move to fortified food. For instance, in the Philippines, when the government flooded the market with unfortified rice, people started buying the less priced, unfortified rice instead of the marginally more expensive, iron-fortified rice, even though it had an additional advantage [48]. It is unclear how selling fortified food at markets might operate in other nations because the other research we analyzed did not explore this potential. Lowering the price of foods enriched with iron is probably a good way to lessen a pregnant mother's chance of developing iron deficiency anemia.

Figure 4. *Iron Fortification in food [42].*

4.2. Iron Supplements During Pregnancy to Manage IDA

A 67% decrease in iron deficiency anemia was observed in pregnant women using iron supplements, according to a study published in the Lancet Series on Maternal and Child Nutrition [55]. Furthermore, a review of research revealed that intermittent iron supplementation was useful in lowering the incidence of anemia in non-pregnant women by 27% [55]. Additionally, according to this research, taking iron supplements on a regular basis decreased the risk of low birth weight by 19% [55]. Even though iron supplementation has a high success rate, distribution and cost become significant issues that make it challenging to maintain compliance with iron deficiency reduction measures. Although elemental iron is significantly more abundant in the body, treating iron deficiency and IDA with iron supplementation—typically in the form of a tablet or liquid—is a costly choice. [24]. In addition to the challenges associated with program implementation, a cost-effectiveness analysis comparing the costs of iron supplementation and fortification was carried out in four global subregions: the African, South American, European, and South-East Asian subregions. This study demonstrated that because industrialized countries already had established, well-functioning distribution networks, supplementing was more economical there [18]. Yet, fortification is more economical in rural and underdeveloped areas, even if iron supplementation has a greater overall health benefit on a population [34].

Based on the small research done in India and Indonesia, the use of fortified sweets should be looked into more and incorporated in national programs to combat iron deficiency. Children and caregivers rated the product as extremely satisfactory in every research [56-58]. If included into educational programs or other official measures, it might be very beneficial in reducing the prevalence of iron deficiency in low-income countries.

4.3. Micronutrient Powders (MNPs) with Iron to Control IDA in Pregnancy

Anemia during pregnancy can be effectively reduced by using micronutrient powders that have iron-fortified vitamins in their composition. The advantages of the micronutrients these powders contain are obtained when they are put to food that is being cooked at home and then eaten. Since micronutrient deficiencies are so common in both developed and developing nations, this fortification approach has drawn a lot of interest from the nutrition community. This is because it has the ability to address numerous deficiencies at once. A powder containing iron and other micronutrients was created for the MNP brand Sprinkles, which may be "sprinkled" on supplemental foods before being given to kids [59, 60]. This is an efficient way to treat iron deficiency anemia in children and raise hemoglobin concentration, according to several research [60-64]. When compared to a control group that received no intervention, two studies conducted in Cambodia revealed a significant decrease in iron deficiency anemia in groups of children receiving daily sprinkles [65, 66]. In a Kenyan trial, Sprinkles was evaluated in a more practical environment by being sold in neighborhood markets. The results showed that Sprinkles was still effective in lowering iron deficiency in this scenario [67]. After 24 weeks of therapy, children in India, where IDA is quite common, had much lower levels of IDA because to the use of MNPs [68]. Micronutrient powders were found to dramatically lower the prevalence of anemia by 34%, iron deficiency anemia by 57%, and enhance hemoglobin concentration in a meta-analysis involving 17 trials [69]. These findings came from research conducted across a variety of nations, which is representative of many parts of the world: Ghana, India, Bangladesh, Kenya, Pakistan, and Haiti [69]. Even though the randomized clinical studies carried out to evaluate different MNPs have had positive results, they have all taken place in extremely controlled environments. Improvements in indicators like hemoglobin concentration and a decline in the frequency of anemia have been repeatedly demonstrated by studies; nevertheless, program adherence may vary in less regulated settings. The success of these programs may be impacted by factors including distribution, cultural culinary customs, and perceptions of MNPs; nonetheless, in the case of MNPs, there is a chance that this intervention will continue to be beneficial. Because micronutrient powders may be included into routine feeding procedures, they have been approved by caregivers in many communities worldwide [62-66]. According to a research on sprinkle adherence done in Bangladesh [61], groups who were given more flexible instructions for using 60 Sprinkles packets—as opposed to being advised to use them every day—showed better adherence and bigger hematological changes. More adherence and acceptability study will be helpful in creating a robust implementation plan for pregnant mothers to prevent IDA in various parts of the world.

5. Conclusion

A deficiency of iron during pregnancy can pose risks, negatively impact the health of both the mother and the fetus and raise the risk of morbidity and fetal mortality. Mothers who are affected often have trouble breathing, fainting, fatigue, palpitations, and trouble falling asleep. When it comes to government engagement, economic viability, and health-improving efficacy, fortification and supplementation differ significantly. For many developing countries, fortification may work better and more affordably than supplementation as a treatment for iron deficiency and iron-deficiency anemia. A more all-encompassing plan should be created to effectively address this micronutrient shortfall, even if iron supplements should continue to play a significant role in a national strategy to lower anemia and iron insufficiency, particularly during high-iron periods like pregnancy. In order to adjacent the nutritional gap and to reduce the main causes of maternal and fetal adverse outcomes due to iron deficiency in pregnant women of Bangladesh, our present motto should be to increase awareness, proper diagnosis, and to yield appropriate management approaches for iron deficiency during pregnancy.

Conflicts of Interest

The authors declare no conflicts of interest related to any financial, commercial, or other affiliations.

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