

Review Article

# The Beneficial Impact of Iron-Fortified Complementary Feeding in the Burden of Iron Deficiency Anaemia (IDA) in Children of Bangladesh

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## Abstract

Fortifying food with iron is the most cost-effective way to avoid iron deficiency anemia, a global public health crisis. In addition to choosing the appropriate dietary context for ingestion, it is critical to choose the appropriate iron form and food carrier. Among the increased hazards include low birth weight and preterm delivery. Children with IDA have slower development, worse cognitive performance, and lower levels of physical activity. In women, it also raises the risk of morbidity and death. The amount of iron required in the diet, one's socioeconomic status, and overall health are all crucial factors to take into account. To combat IDA, a variety of dietary approaches, iron-fortified foods, supplements, and disease management techniques have all been employed. Nowadays, food fortification with iron is seen to be a long-term, sustainable solution. To be effective, the iron fortification program's food transporters and fortificants must be deemed safe, pleasant, and acceptable by the target population. It also shouldn't have a detrimental effect on the stability and acceptance of the finished product. This article provides a thorough summary of the current state of iron deficiency in women and children in Bangladesh. This study addresses current issues as well as the efficacy of current therapeutic strategies. Prevention-focused treatments ought to take precedence over treatment-focused ones in high-risk populations. Unknown are the long-term benefits, and unfavorable outcomes are possible. Despite the tremendous progress made, several plans and initiatives are still being supported. These issues are to coverage, quality, and compliance. The findings suggest that iron deficiency and anemia are still major problems in Bangladesh, despite the fact that certain severe deficiencies have been addressed by current intervention efforts. There is a need for more integrated solutions to assist current intervention efforts. Furthermore, new approaches to the management of certain types of iron deficiency anemia are proposed.

## Keywords

Iron Deficiency Anemia, Fortified Infant Cereals, Iron-Fortified Complementary Feeding, Infants and Young Children, Health Economics Bangladesh

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**Received:** 26 January 2024; **Accepted:** 5 February 2024; **Published:** 20 February 2024



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## 1. Introduction

Almost half of the two billion cases of anemia that occur globally are caused by iron deficiency. It is the most prevalent deficiency in micronutrients. Because of their fast development, infants and children are especially vulnerable to iron deficiency anemia (IDA). This is significant since iron is necessary for neurodevelopment and a deficit may affect brain growth. Iron deficiency is recognized to be linked to decreased cognitive function in newborns and early children, and chronic damage is suspected, at least when IDA initially manifests in infancy [1-3]. Because it necessitates large sample numbers and extended follow-up periods, this link has been difficult to verify in randomized controlled experiments. The ability to translate findings into recommendations has been hampered by the fact that much past and present intervention research has focused on rapid laboratory outcomes. Over the last ten years, research in this field has expanded our understanding of the potential dangers associated with iron supplements, emphasizing the need of using evidence-based treatment when balancing benefits and downsides [4].

Iron deficiency anemia (IDA) is common in both industrialized and developing nations, particularly in young children, teenagers, and women who are about to become parents. 1. This nutritional condition affects 3.5 billion people in underdeveloped countries, accounting for thirty to sixty percent of cases in women and children [5]. Anemia affects 52% of pregnant women worldwide and 76% of pregnant women in South Asia. 94 Anemia affects almost all pregnant and breastfeeding women in Pakistan, as well as almost two-thirds of young children, half of all women in reproductive age, and more than 30% of adult males. According to multicenter studies, iron deficiency accounts for 78–85% of anemia in children under five. 42 Sixty-seven percent of five-year-old economically disadvantaged children in Karachi were anemic, meaning their hemoglobin level was less than 11 g/dL. 27 Another research by Paracha and Jamil 67 on children in the Northwest Frontier Province between the ages of 6 months and 5 years revealed a 50.1 percent prevalence of anemia.

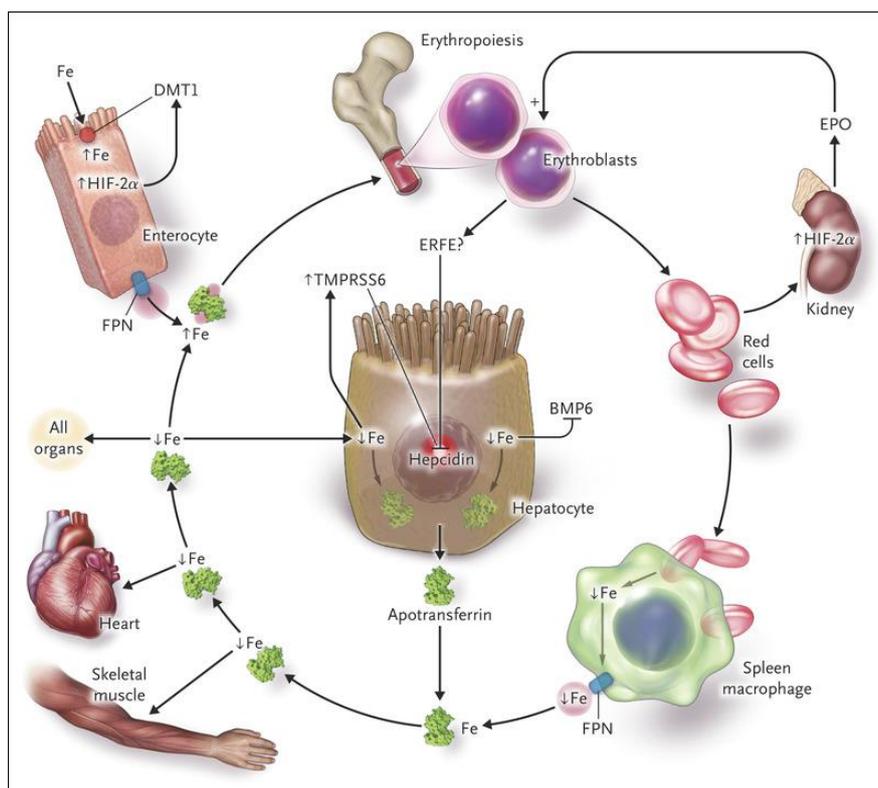
Since mothers' iron insufficiency during pregnancy has been related to anemia in children, a few surveys on iron deficiency in women have been out in Pakistan. Anemia affects 82.9 percent of toddlers, 83 percent of pregnant women, 78 percent of nursing women, and 85 percent of teenage females, according to Khan and Jalil 43. Even if the expected changes in hemoglobin concentration distributions from 1995 to 2011 indicate a decline in the prevalence of anemia worldwide, the numbers are nonetheless shocking. According

to estimates from the World Health Organization (WHO), iron deficiency causes anemia in 800 million women and children.

Anemia and iron deficiency limit an individual's ability to work, which can have detrimental effects on the economy and inhibit the nation's progress. Because of all of this, it is widely acknowledged that one of the top priorities in public health nutrition is reducing the worldwide incidence of iron deficiency and iron deficiency anemia. The World Health Organization (2012) [5] stated that a "Comprehensive implementation plan on maternal, infant, and young child nutrition" was approved by the World Health Assembly in Resolution 65.6 of that year. The plan established six Global Nutrition Targets for 2025, the second of which was to "achieve a 50% reduction in anemia in women of reproductive age." Many iron delivery strategies are used in public health initiatives today to treat and prevent anemia; nevertheless, dietary fortification with iron seems to provide the optimum risk-benefit ratio.

## 2. Condition of Anemia and Iron Deficiency in Bangladesh

As per the NMS 2011-2012, anemia was diagnosed in 26% of NPWL women and 33% of children aged 6-59 months. Anemia was defined as a Hb concentration of 110 g/l in children and 120 g/l in NPWL women [6]. The prevalence reported in 1997–1998 (47 percent in children aged 6-59 months and 45 percent in NPWL women) and 2003 (557% in children aged 6-59 months and 329 percent in NPWL women) is significantly lower than these figures [6, 7]. The NMS 2011-2012 findings indicate that the national prevalence of Fe deficiency (serum ferritin concentration 120 g/l in preschool-age children and 150 g/l in NPWL women) is only 107% in preschool-age children and 71% in NPWL women, contrary to earlier small-scale studies that suggested Fe deficiency is a major cause of anemia [7-9]. Moreover, only 48% of NPWL mothers and 72% of children reported having Fe-deficiency anemia (IDA). To establish IDA, serum ferritin concentrations of 120 g/l and Hb concentrations of 120 g/l were employed in preschool-aged children, and serum ferritin concentrations of 150 g/l in NPWL women [10]. Given that IDA is far less common in school-age children, it is possible that Fe deficiency is not the main cause of anemia among Bangladeshi people [10]. Despite this, Fe only provides 41–82% of the RDA for different population groups. Some parts of Bangladesh appear to have significant groundwater concentrations of Fe, primarily in the ferrous (Fe<sup>2+</sup>) form, which is more bioavailable than the ferric form [11].



**Figure 1.** Iron Deficiency Anemia [31].

The low frequency of Fe insufficiency in the NMS 2011–2012 was linked to the high Fe concentration in drinking water from tube wells [12]. A small-scale study conducted in rural northern Bangladesh on women revealed a connection between daily intake of Fe from drinking water and levels of plasma ferritin and total body Fe [13]. However, a recent study using NMS 2011–2012 data discovered that Bangladeshi NPWL women living in high and low Fe groundwater locations had different frequencies of anemia and Fe deficiency [14]. However, IDA can only explain about 10% of the anemia because women's and children's anemia levels are still high. A number of other factors should be taken into account, such as deficiencies in vitamin B6, vitamin B12, vitamin A, vitamin C, folic acid, and riboflavin. These points highlight the significance of other hematopoietic micronutrients in managing and preventing 90–95 percent of anemia cases [15]. Non-nutritional causes of anemia include worm infestation, malaria, chronic infections, and genetic abnormalities (e.g., hemoglobinopathies) [8, 11, 12]. Although there are no national statistics on the incidence of thalassemia, it is believed to be a factor; one study found that thalassemia prevalence was 28%, which is associated with an increased risk of anemia [7].

### 3. Requirements for Iron in Infants from the Age of Six Months

Despite the fact that between the ages of 6 and 12 months,

the demand for iron rises (per kg), well-nourished populations usually do not need iron supplements at this stage of life. Instead, it is advised to take supplementary meals that include a significant quantity of iron [16–18]. Several recent investigations have found a correlation between these enhanced recommendations and a lower incidence of iron deficiency and IDA [3]. The iron status of two cohorts of infants was examined before and after improved Icelandic dietary requirements were implemented in an epidemiological research conducted in Iceland. Comparable investigations done between 1995 and 1997 discovered that the frequency of iron deficiency was lower (1.4%) and that out of 141 babies, none of them were anemic at 12 months. In addition, there was a 2.7% IDA and a 20% iron deficit in these kids. The drop in prevalence was attributed to the switch in the baby diet of Iceland from cow's milk to iron-fortified formulas and cereals [19, 20]. Iron-fortified milk or cereals can effectively reduce the incidence of anemia in newborns and early children who are at risk of iron deficiency, according a recent meta-analysis [21]. The quantity of iron in the food has an impact on iron needs as well. Recently, a randomized study was carried out in the US to evaluate weaning newborns from pureed beef to cereals with iron supplements. The meat intervention resulted in a drop in iron consumption (3.3 mg/day vs. 7–12 mg/day), but the iron status remained constant at 9 months of age, suggesting that the increased bioavailability of heme-bound iron re-lowers the needs. Nonetheless, it was shown that both groups had a considerably higher prevalence of mild anemia and low ferritin levels [22, 23].

## 4. Iron-Based Interventions for Toddlers and School-Aged Children

Iron supplements administered to preschoolers and school-age children were the subject of two recent meta-analyses. The effects on iron deficiency, iron-deficiency anemia (IDA), and specifically on cognitive development are little understood. Thompson et al. found evidence of better iron status after finding 15 research including kids between the ages of 2 and 5 [24]. Low et al. looked at 32 studies, 31 of which assessed kids from low- and middle-income countries who were between the ages of 5 and 12 [25]. Iron supplementation, according to the researchers, enhanced long-term development and decreased the frequency of iron insufficiency and IDA in high-risk contexts. Additionally, they discovered that youngsters who took supplements performed much better on attention and focus tests and had significantly higher global cognitive scores (0.50 points). In subsamples of children who were anemic, the effect on the intelligence quotient was 4.55 points [24].

## 5. Iron Fortification's Impact in Complementary Feeding Practice

The World Health Organization (WHO) and the US Institute of Medicine suggest daily iron intakes of 9.3 mg and 11 mg for children aged 6 to 12 months, respectively, due to the high pace of growth during this period [11]. For children between the ages of 12 and 24 months, the recommended daily iron intake is 5.8 mg to 7 mg, as opposed to 6 to 12 months [1, 2]. Given that breastfeeding only provides around 0.2 mg of iron per day, by the time a baby is 6 or 8 months old, a net daily need of 9 to 10 mg and 5 to 7 mg of iron from other sources, respectively, is required until the child is 24 months old. By the time they are six months old, most newborns require an external source of iron; if they are at high risk of iron deficiency, they may require it sooner. Nonetheless, some babies (if they were born with normal birth weight, to moms who were iron-depleted, and if they got peripheral blood transfer by delayed umbilical cord clamping) had enough iron reserves at birth to endure until eight or nine months of age.



Figure 2. Iron Fortified Feeding Components [26].

Since the quantity required from supplemental meals is significant in comparison to the iron content of these foods, iron is frequently the most restrictive nutrient at this age [3-5].

In Bangladesh, infants consuming supplemental foods were consuming 0.5 mg/day of iron at 6 to 8 months and 0.7 mg/day at 9 to 12 months [27]. After taking into account the amount obtained from breastfeeding (0.2 mg/day), the total iron intake (0.7 to 0.9 mg/day) was only 8 to 9 percent of the amount recommended by the WHO (9.3 mg/day). The aver-

age amount of iron consumed in Malawi from supplemented meals was 2.8 milligrams daily at 9 to 11 months, 3.5 milligrams daily from 12 to 23 months, and 1.2 milligrams daily at 6 to 8 months [27]. Iron's estimated bioavailability ranged from 5.5% to 7.4%, so at 6 to 8 months, supplemented meals only met 6% of the expected iron needs; at 9 to 11 months, they provided 13%; and at 12 to 23 months, 30%. Meat, chicken, and fish accounted for only 0–4% of the total iron in the diet. While the average daily consumption of iron was

only 2.9 mg, 31% of infants aged 6 to 12 months in a rural South African dietary survey ingested baby cereals fortified with iron on the day of the food recall. The average iron intake (5.3 mg/day) fell well short of the necessary intakes, even among infants who had iron-fortified cereal, because of the relatively small portion size (20 g/day dry cereal) and low amount of fortification (15 mg of iron per 100 g of dry product) [28]. As such, most populations in underdeveloped countries have a large gap between their consumption and demands of iron.

## 6. Home Iron Fortification in Children with Anemia in Bangladesh

An effective way to prevent anemia and iron deficiency in newborns and early children is by home fortification with multiple micronutrient powder (MNP), which includes iron, according to a recent Cochrane meta-analysis [23]. The previously reported link between IDA in babies and long-term cognitive impairment has been validated by case-control research from Bangladesh. The purpose of the study was to evaluate the impact of a nine-month training program on an infant's motor development. Even after receiving treatment for their IDA, cases with IDA who were diagnosed at six months of age responded to the intervention less favorably than controls, suggesting ongoing impairment [29].

A recent meta-analysis examining the effects of iron supplementation on neurodevelopment in children with non-anemic iron deficiency found insufficient evidence since just two studies including children between the ages of one and five could be discovered [30]. Ferritin remained unchanged in the Bangladesh trial, while supplemented children had a comparable increased height growth pace [11]. The potential for interactions with other micronutrients is one problem with these multiple micronutrient experiments. Children who received multiple micronutrients showed significantly greater weight-for-height and hemoglobin levels than children who received iron alone, suggesting that micronutrients have synergistic effects [32]. Another Chinese RCT that used a two-by-two factorial design found that children aged 3-6 who were at high risk of malnutrition benefited similarly from iron and vitamin A supplementation. They discovered that while taking iron and vitamin A supplements separately had neither beneficial or harmful effects, doing so for six months reduced the incidence of respiratory tract infections and diarrhea-related illnesses [7]. Researchers discovered that children who received supplements reported anxiety less frequently in the aforementioned Chinese MNP experiment. The trial's shortcomings were a skewed baseline percentage of anemia, a lack of participant blinding to the intervention, and the possibility of confounding effects from other micronutrients [25].

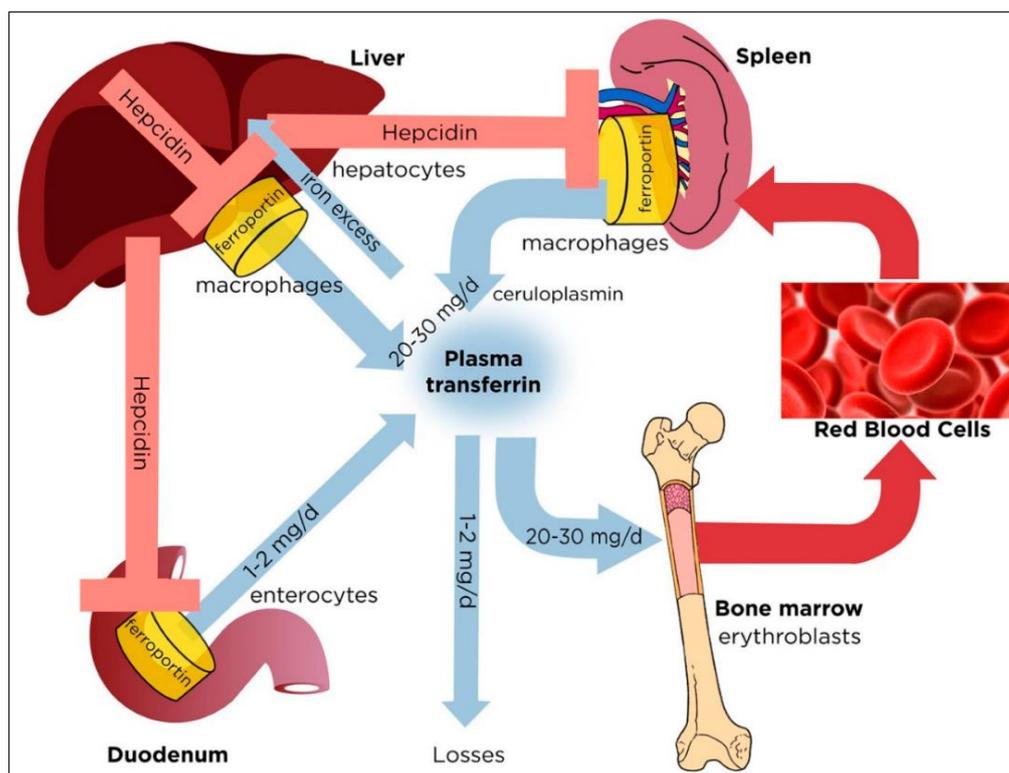
## 7. The Stability and Bioavailability of Iron Fortificants

Minerals are more resistant to processing than vitamins are. They do, however, change when they are exposed to heat, air, or light. Minerals like copper, iron, and zinc are impacted by moisture and can react with foods high in proteins and carbs. Numerous fortifiers can be used to fortify iron. Finding an iron compound that is stable, well-absorbed, and doesn't alter the food vehicle's flavor or appearance is the most challenging assignment.

Failure of iron-fortification programs has been attributed to discoloration, unappealing flavor, and consumer rejection of iron-fortified foods. Ferrous iron is more readily available than ferric iron because ferric iron is less soluble in the stomach. However, in the stomach, the action of reducing agents such as ascorbic acid and gastric hydrochloric acid may change ferric iron into more soluble ferrous iron [25].

The phrase "bioavailability of dietary components" originated in pharmacology due to the phenomenon of oral medications appearing in plasma. When it comes to mineral bioavailability, particularly in the case of iron, bioavailability—which was determined by *in vitro* solubility—was formerly thought to be the same as absorption. Better potential absorption and, hence, better bioavailability make an iron complex more soluble. This solubility technique deals with the concept of iron availability, or dialysability, in the event that transit over a semipermeable membrane is used to simulate the digestive process. The amount of ingested iron that is absorbed by the intestines and utilized through typical metabolic pathways or stored is referred to as iron bioavailability. It is expressed as a percentage of total consumption and is influenced by environmental and dietary factors [30]. This more comprehensive approach to iron bioavailability includes the following processes: release from its matrix, absorption into the systemic circulation, distribution to tissues, metabolic utilization, or storage in the body. When it comes to food science and technology, the first two are the most crucial to consider.

Non-heme sources that have been commonly employed in fortification include iron-EDTA, ferrous sulfate, elemental iron (reduced iron), ferric orthophosphate, ferrous fumarate, sodium ferric pyrophosphate, and other compounds [30]. Every fortifier has advantages and disadvantages. Ferric orthophosphate is the most stable form of iron, although it's not easily obtained. Ferrous fumarate is also a stable substance, however it gives wheat flour a different hue. For maize flour, it works better. Ferric phosphate increases iron absorption, however it is costly and unstable. Therefore, the most feasible options for fortifying wheat are iron-EDTA, ferrous sulfate, and elemental iron [34]. Ascorbic acid has a direct correlation with the absorption of ferric iron during meals because it activates the duodenal ferric reductase [35].



**Figure 3.** Iron Bioavailability [33].

The amount of iron in a single fortified product shouldn't exceed what's necessary. Twenty to forty percent of the daily requirements should be met by a single food item for fortification. Fortification with iron at a level of 60 ppm elemental iron and 1.5 ppm folic acid has been recommended by numerous international organizations [36]. This can be stored for up to three months at ambient temperatures of 35 °C and humidity of 90% without affecting the sensory characteristics of the flour or foods made from fortified wheat flour. Wheat flour and wheat-based products stored for up to three months below 30 °C may be supplemented with up to 40 ppm ferrous sulfate and up to 15 ppm iron EDTA in hot, humid regions without causing any negative effects. Of all the iron fortifiers, ferrous sulfate has the highest relative bioavailability and is a water-soluble iron fortifier [29, 37]. However, it is highly unstable and may have an impact on the vehicle-food quality and shelf life due to likely oxidized off-tastes, color changes, and metallic flavors [38]. Elemental iron is more stable and half as bioavailable as ferrous sulfate [23]. If elemental iron is used as the fortifier, higher doses (two or three times those needed for ferrous sulfate) could be needed to make up for the decreased bioavailability. As a result, fortification with ferrous sulfate is less costly than fortification with elemental iron. Due to variations in preparation and baking techniques, there is some overlap between studies, although elemental iron

fortification at a higher rate also had a detrimental effect on chapatti quality [39, 40].

The age of an individual determines the quantity of iron that their body needs. The mineral helps establish a reserve of iron in babies, kids, and teenagers by promoting increased hemoglobin mass, tissue synthesis, and iron storage. All demographic groups have modest losses in urine and sweat, as well as exfoliation of skin cells and physiologically regulated iron loss in feces. Women of reproductive age may lose a substantial quantity of iron due to menstrual blood loss. The distribution is believed to be skewed and challenging to evaluate, even though several research have demonstrated a connection between the duration of the menstrual cycle, the volume of menstrual losses, and serum ferritin. It is well recognized that a person's physiological state and iron status have a significant impact on their ability to absorb iron. Serum ferritin levels, particularly those below 60 g/L, are adversely correlated with dietary iron absorption in healthy individuals. Furthermore, it has been discovered that pregnant women's higher iron requirements are satisfied by improved iron absorption efficiency. There is disagreement over the Recommended Dietary Allowance (RDA) for iron due to the several factors involved in iron homeostasis being so complicated and unpredictable, as Table 1 illustrates.

**Table 1.** Recommended Dietary Intake of iron (mg/day) by age and gender among different agencies and countries selected.

	Spain (2015) a	United Kingdom (1991)	Nordic CM (2014)	Brazil (2005) d	IOM (2001)	FAO/WHO (2004)	EFSA (2015)
0-12 months	7	7.8	8	0.27	0.27	6-19	11
1-3 years	7	6.9	8	9	11	4-12	7
4-6 years	9	6.1	8	6	7	4-13	7
7-9 years	9	8.7	9	9	10	4-18	11

In conclusion, the FAO/WHO emphasizes the importance of dietary iron bioavailability and states that women of reproductive age (except from those in Brazil) and pregnant women should consume the highest recommended amounts of iron.

For iron fortification, a variety of fortificants are available. The most difficult task is to find an iron compound that is well-absorbed, stable, and doesn't change the flavor or look of the food vehicle. It is important to consider other aspects of solubility, such as desired bioavailability and practicality in real-world situations. In this case, it could be better to use a material that is less bioavailable for iron but that can be put to food at higher concentrations without affecting organoleptic processes. Higher temperatures and moisture contents cause ferrous sulfate, the most bioavailable iron component, to rust when fortified items are kept. The ferrous form turns into the ferric form during oxidation [37]. Brown precipitates might result from the food product becoming brown due to ferric complexes. Because of their insoluble nature, the resultant ferric complexes are poorly absorbed in the intestinal lumen [41]. To make ferrous sulfate more stable, EDTA might be added [18, 42]. When bread rolls enriched with FeSO<sub>4</sub> are combined with Na<sub>2</sub>EDTA, the amount of iron absorbed increases by 1.9–3.9 times. On the other hand, as excessive haem consumption has been linked to prostate and colorectal cancer, questions have been raised over the safety of using haem iron. The only non-haeme form of iron that is resistant to phytates' inhibitory effects is sodium iron EDTA (NaFeEDTA), which is also two to three times more bioavailable than ferrous salts [43, 44]. According to recent research, NaEDTA improved the native and extra iron's bioavailability in fortified chapattis in vitro. On the other hand, studies using Caco-2 cells showed that EDTA did not increase iron absorption. 34. Cereal meals are popular choices for fortification since they are staples in many cultures throughout the world and may be processed in solid form to create cereal-based diets fortified with iron. This applies to both weaning and maturity. The WHO recommends using ferrous sulfate, ferrous fumarate, ferric pyrophosphate, and electrolytic iron as iron compounds to fortify cereals. Since cooking and industrial heat processing may change the fortifier or the surrounding dietary components, they should also be taken

into consideration since they may decrease the bioavailability of iron.

## 8. Currently Operating Public Health Initiatives Designed to Protect Toddlers from Iron Deficiency Anemia

Delaying the cutting of the cord, using a bed net when sleeping, nursing exclusively, spacing out births, and washing your hands all lower the incidence of anemia in babies, young children, and mothers in Bangladesh. Iron-folic acid (IFA) supplements, a more varied diet, sleeping beneath a bed net, intermittent preventive treatment (IPTp) for malaria, frequent hand washing, and deworming medications are some ways to avoid anemia during pregnancy. Anemia can be avoided and healthy growth can be encouraged in young infants by continuing nursing, providing enough supplemental food (containing micronutrients), treating and avoiding malaria, washing hands often, and taking deworming medications. IFA supplements, deworming medication, and hand washing all help avoid anemia in adolescents. Family planning helps to postpone childbirth.

There are new iron fortifiers in development. Nanotechnology engineering is used to generate iron that is easily absorbed through physiological channels and is nano-sized. However, since too much free iron in biological systems may be dangerous, industrial manufacture must be done under the strictest safety regulations. Fe (III) oxide nanoparticles were shown to be absorbed by the ferric route in an animal model, and they had no detrimental effects on organ or hemato-logical processes. This implies that tailored iron fractions and forms might be developed with the goal of lowering iron absorption and solubility. Biofortification, which involves breeding and genetic modification of plants to create a final plant meal with a greater iron content, is an additional alternative that has high promises. There have been attempts at micronutrient biofortification in staple foods, but the ultimate aims are still far off, and before implementation, all safety, cost-benefit, and low environmental effect requirements must be satisfied.

## 9. Conclusions

In poor nations, improper supplemental feeding practices are a prevalent issue. The fact that typical local foods don't usually contain enough of important micronutrients is another cause for concern. In developing nations like South Asia, where iron deficiency is common, it is imperative to promote optimal weaning practices and the intake of inexpensive, nutritionally adequate supplemental meals for infants and young children. By lowering the incidence of iron deficiency and IDA in young children, healthy weaning practices like using Sprinkles can help accomplish at least four of the eight Millennium Development Goals. Several nutritional studies have demonstrated that, particularly for children between the ages of 6 and 12, the amount of iron consumed from typical supplemented meals in developing nations is frequently insufficient. Conventional food processing methods such as soaking, fermentation, and germination may increase iron intake somewhat, but they don't seem to increase iron bioavailability to the same degree. Dietary diversity and enrichment of additional meals (e.g., with fish powder) are good for the child's total nutritional intake, but they frequently don't close the iron deficiency. Due to these factors, the majority of individuals will require iron supplementation in one form or another, whether through home-made fortification products or commercially available supplemental meals. Iron deficiency and anemia rates may be decreased by commercially supplemented complementary meals, provided that the iron amount and chemical type are both appropriate. On the other hand, a baby formulation designed for older children will give older children more iron than they need, and a child formulation meant for younger children—ages 6 to 12 months—will give younger children less iron than they need. Thus, even in the unlikely event that commercially fortified supplementary meals were widely available and reasonably priced, another method would very probably be needed to raise newborns' iron intake to the necessary level. Unlike the case of iron supplements, no study included in this review discovered any adverse consequences from fortifying supplemental meals at home or increasing iron consumption. However, large-scale studies involving a sizable number of children with iron deficiency are necessary. Studies contrasting the physiological effects of iron supplied with food with iron delivered in between meals may also be helpful. With iron-fortified foods, the quantity of iron consumed at each meal is probably going to be little; but, with home fortification, the daily dosage of iron may be absorbed in one meal. Therefore, it may be helpful to investigate the effects of consuming iron throughout a variety of meals.

## Conflicts of Interest

The authors declare no conflicts of interest.

## References

- [1] Abbasi, S., & Azari, S. (2011). The efficiency of novel iron microencapsulation techniques: Fortification of milk. *International Journal of Food Science and Technology*, 46(9), 1927-1933.
- [2] Aly, S. S., Fayed, H. M., Ismail, A. M., & Hakeem, G. L. A. (2018). Assessment of peripheral blood lymphocyte subsets in children with iron deficiency anemia. *BMC Pediatrics*, 18(1), 49.
- [3] Au, A. P., & Reddy, M. B. (2018). Caco-2 cells can Be used to assess human iron bioavailability from a semipurified meal. *Journal of Nutrition*, 130(5), 1329.
- [4] Balk, J., Connorton, J. M., Wan, Y., Lovegrove, A., Moore, K. L., Uauy, C., et al. (2019). Improving wheat as a source of iron and zinc for global nutrition. *Nutrition Bulletin*, 44(1), 53-59.
- [5] Blanco-Rojo, R., Pérez-Granados, A. M., Toxqui, L., González-Vizcayno, C., Delgado, M. A., & Vaquero, M. P. (2011). Efficacy of a microencapsulated iron pyrophosphate-fortified fruit juice: A randomised, double-blind, placebo-controlled study in Spanish iron-deficient women. *British Journal of Nutrition*, 105(11), 1652-1659.
- [6] World Health Organization, The United Nations Children's Fund (UNICEF), International Council for the Control of Iodine Deficiency Disorders (ICCIDD) (2007) Assessment of Iodine Deficiency Disorders and Monitoring their Elimination: A Guide for Programme Managers. Geneva: WHO.
- [7] Hallberg L (1991) Bioavailability of dietary iron in man. *Ann Rev Nutr* 1, 123-147.
- [8] Merrill RD, Shamim AA, Ali H, et al. (2011) Iron status of women is associated with the iron concentration of potable groundwater in rural Bangladesh. *J Nutr* 141, 944-949.
- [9] National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International (2015) Bangladesh Demographic and Health Survey Report 2014: Key Indicators. Dhaka, Bangladesh and Rockville, MD: NIPORT, Mitra and Associates, and ICF International.
- [10] Abdel Moety, G. A. F., A. M. Ali, R. Fouad, W. Ramadan, D. S. Belal, and H. M. Haggag. 2017. Amino acid chelated iron versus an iron salt in the treatment of iron deficiency anemia with pregnancy: A randomized controlled study. *European Journal of Obstetrics & Gynecology and Reproductive Biology* 210: 242-6.
- [11] Sharma DP, Maheshwari A, Chakrabarti C, Patel DJ. Assessment of Iodine Deficiency among School-Going Children of Age Group 6 to 12 Years in Kachchh District, Gujarat State: Cross-Sectional Hospital-Based Study. *J Lab Physicians*. 2021 Jul 6; 13(4): 332-337. <https://doi.org/10.1055/s-0041-1731138>. PMID: 34975252; PMCID: PMC8714303.
- [12] Cosmas Zyaambo, Olusegun Babaniyi, Peter Songolo, Adamson S. Muula, Emmanuel Rudatsikira, Seter Siziya: Prevalence and predictors of smoking in a mining town in Kitwe, Zambia: A 2011 population-based survey, *Health Vol. 5 No. 6*, June 11, 2013, <https://doi.org/10.4236/health.2013.56136>

- [13] Institute of Public Health Nutrition (IPHN), Helen Keller International (HKI) (1985) Bangladesh Nutritional Blindness Study 1982-83. Dhaka, Bangladesh: IPHN and HKI.
- [14] Eden AN, Sandoval C. Iron deficiency in infants and toddlers in the United States. *Pediatr Hematol Oncol* 2012; 29: 704-709.
- [15] United Nations Children's Fund, Micronutrient Initiative (2004) Vitamin and Mineral Deficiency: A Global Progress Report. Ottawa, Canada: Micronutrient Initiative.
- [16] Saha L, Pandhi P, Gopalan S, Malhotra S, Saha PK. Comparison of efficacy, tolerability, and cost of iron polymaltose complex with ferrous sulphate in the treatment of iron deficiency anemia in pregnant women. *MedGenMed*. 2007 Jan 2; 9(1): 1. PMID: 17435611; PMCID: PMC1924983.
- [17] Akhtar, S., T. Ismail, S. Atukorala, and N. Arlappa. 2013. Micronutrient deficiencies in South Asia - Current status and strategies. *Trends in Food Science & Technology* 31 (1): 55-6.
- [18] Bothwell, T. H., and Charlton, R. 1981. Iron deficiency in women. *Int. Nutr. Anemia Consultative Group (INACG)*, Washington DC.
- [19] Brooker, S., Peshu, N., Warn, P. A., Mosobo, M., Guyatt, H. L., Marsh, K., and Snow, R. W. 1999. The epidemiology of hookworm infection and its contribution to anemia among pre-school children on the Kenyan Coast. *Trans. Royal Soc. Trop. Med. Hygiene*, 93: 240-246.
- [20] Brune, M., Rossander-Hulten, L., Hallberg, L., Glerup, A., and Sandberg, E. 1992. Iron absorption from bread in humans: Inhibiting effects of Cereal fiber, phytate, and inositol phosphate with different numbers of phosphate groups. *J. Nutr.*, 122: 442-449.
- [21] Hurrell, R. F., and Cook, J. D. 1990. Strategies of iron fortification of foods. *Trends in Food Sci. Technol.*, 9: 56-61.
- [22] Hurrell, R. F. 2002. How to ensure adequate iron absorption from iron-fortified food. *Nutr. Rev.*, 60: 7S-15S.
- [23] Ioannou, G. N., Dominitz, J. A., Heagerty, P. J., and Kowdley, K. V. 2004. The effect of alcohol consumption on the prevalence of iron overload, iron deficiency, and iron deficiency anemia. *Gastroenterology*, 126: 1293-1301.
- [24] Thompson J, Biggs BA, Pasricha SR. Effects of daily iron supplementation in 2- to 5-year-old children: systematic review and meta-analysis. *Pediatrics* 2013; 131: 739-753.
- [25] Low M, Farrell A, Biggs BA, Pasricha SR. Effects of daily iron supplementation in primary-school-aged children: systematic review and meta-analysis of randomized controlled trials. *CMAJ* 2013; 185: E791-E802.
- [26] Liberal, Â.; Pinela, J.; V íar-Quintana, A. M.; Ferreira, I. C. F. R.; Barros, L. Fighting Iron-Deficiency Anemia: Innovations in Food Fortificants and Biofortification Strategies. *Foods* 2020, 9, 1871. <https://doi.org/10.3390/foods9121871>
- [27] Blanco-Rojo, R., & Vaquero, M. P. (2019). Iron bioavailability from food fortification to precision nutrition. A review. *Innovative Food Science & Emerging Technologies*, 51, 126-138.
- [28] Cengiz, A., Kahyaoglu, T., Schroen, K., & Berton-Carabin, C. (2019). Oxidative stability of emulsions fortified with iron: The role of liposomal phospholipids. *Journal of the Science of Food and Agriculture*.
- [29] Upadhyay A, Gothwal S, Parihar R. Effect of umbilical cord milking in term and near-term infants: randomized control trial. *Am J Obstet Gynecol* 2013; 208: 120; e121-126.
- [30] Taylor TA, Kennedy KA. Randomized trial of iron supplementation versus routine iron intake in VLBW iMiller SM. Iron supplementation in premature infants using the zinc protoporphyrin to heme ratio: short- and long-term outcomes. *J Perinatol* 2013; 33: 712-716 infants. *Pediatrics* 2013; 131: e433-e438.
- [31] *N Engl J Med* 2015; 372: 1832-1843, <https://doi.org/10.1056/NEJMra1401038>
- [32] Merrill RD, Labrique AB, Shamim AA, et al. (2010) Elevated and variable groundwater iron in rural northwestern Bangladesh. *J Water Health* 8, 818-825.
- [33] Holbein BE, Lehmann C. Dysregulated Iron Homeostasis as Common Disease Etiology and Promising Therapeutic Target. *Antioxidants*. 2023; 12(3): 671. <https://doi.org/10.3390/antiox12030671>
- [34] Domellof M, Braegger C, Campoy C. Iron requirements of infants and toddlers. *J Pediatr Gastroenterol Nutr* 2014; 58: 119-129.
- [35] Hurrell, R. F. 1997. Preventing iron deficiency through food fortification. *Nutr. Rev.*, 55: 210-222.
- [36] Anderson, G. J., and D. M. Frazer. 2017. Current understanding of iron homeostasis. *The American Journal of Clinical Nutrition* 106 (6): 1559S-66S.
- [37] Duley L, Batey N. Optimal timing of umbilical cord clamping for term and preterm babies. *Early Hum Dev* 2013; 89: 905-908.
- [38] Zhang L, Kleiman-Weiner M, Luo R, et al. Multiple micronutrient supplementation reduces anemia and anxiety in rural China's elementary school children. *J Nutr* 2013; 143: 640-647.
- [39] Pasricha SR, Drakesmith H, Black J, et al. Control of iron deficiency anemia in low- and middle-income countries. *Blood* 2013; 121: 2607-2617.
- [40] Glazer Y, Bilenko N. [Effect of iron deficiency and iron deficiency anemia in the first two years of life on cognitive and mental development during childhood]. *Harefuah*. 2010 May; 149(5): 309-14, 335. Hebrew. PMID: 20929071.
- [41] Radlowski EC, Johnson RW. Perinatal iron deficiency and neurocognitive development. *Front Hum Neurosci* 2013; 7: 585.
- [42] Hurrell, R. F., Juillerat, M. A., Reddy, M. B., Lynch, S. R., Dassenko, S. A., and Cook, J. D. 1992. Soy protein, phytate, and iron absorption in man. *Am. J. Clin. Nutr.* 56: 573-578.
- [43] Erickson-Owens DA, Mercer JS, Oh W. Umbilical cord milking in term infants delivered by cesarean section: a randomized controlled trial. *J Perinatol* 2012; 32: 580-584.
- [44] Abdullah K, Kendzerska T, Shah P, et al. Efficacy of oral iron therapy in improving the developmental outcome of preschool children with nonanaemic iron deficiency: a systematic review. *Public Health Nutr* 2013; 16: 1497-1506.