World Journal of Advanced Research and Reviews

eISSN: 2581-9615 CODEN (USA): WJARAI

Cross Ref DOI: 10.30574/wjarr

Journal homepage: https://wjarr.com/

(Review Article)

Check for updates

Impact of iron intake on growth outcomes in children with iron deficiency anemia, iron deficiency, and normal iron status: A comprehensive review

Ashraf Soliman [1, *], Fawzia Alyafei [1], Ahmed Elawwa [1], Nada Alaaraj [1], Noor Hamed [1], Shayma Ahmed [1], Maya Itani [2] and Nada Soliman [3]

[1] *Department of Pediatrics, Hamad General Hospital, Doha, Qatar; Qatar.*

[2] *Department of Dietetics and Nutrition, Hamad General Hospital, Doha, Qatar.*

[3] *Department of public health, North Dakota State University (NDSU), ND, USA.*

World Journal of Advanced Research and Reviews, 2025, 25(02), 072-082

Publication history: Received on 23 December 2024; revised on 31 January 2025; accepted on 02 February 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.25.2.0335

Abstract

Background: Iron deficiency (ID) and iron deficiency anemia (IDA) are significant global health issues, affecting over 30% of children under five years globally, with higher prevalence in low-income countries. IDA impacts oxygen transport and energy metabolism, causing stunted growth and developmental delays. Despite the established role of iron in growth, its specific effects on height and weight outcomes remain debated.

Objectives: To review the impact of iron intake on linear growth and weight gain in children with IDA, ID, and normal iron status, synthesizing data on supplementation dose, duration, and outcomes.

Methods: A comprehensive review of studies published between 1980 and 2024 was conducted, incorporating randomized trials, observational studies, and meta-analyses. Data were extracted on study characteristics, diagnoses, sample sizes, interventions, and outcomes. Articles were categorized based on the population: children with IDA, ID, or normal iron status.

Results: This review analyzed 17 studies encompassing three categories of children: those with iron deficiency anemia (IDA) (9 studies, n=1,361), those with iron deficiency (ID) without anemia (4 studies, n=438), and those with normal iron status (4 studies, n=45,187). The findings are summarized as follows:

Children with Iron Deficiency Anemia (IDA): Iron supplementation significantly improved height standard deviation scores (SDS), growth velocity (GV), and body mass index (BMI). Serum ferritin levels strongly correlated with growth recovery, reflecting restored iron stores as a key mechanism. Studies demonstrated that daily and twice-weekly dosing regimens were equally effective, particularly in resource-limited settings. Mechanistic studies highlighted the role of improved oxygen transport, mitochondrial function, and hormonal regulation via insulin-like growth factor-I (IGF-I). Socioeconomic factors, such as low maternal income and dietary quality, were consistently associated with worse growth outcomes.

Children with Iron Deficiency (ID): The impact of iron supplementation on growth in children with ID was modest, with no significant changes in linear growth in most studies. Improvements in weight gain and hemoglobin levels were more notable when supplementation addressed co-existing micronutrient deficiencies, such as zinc. Socioeconomic and dietary factors remained critical determinants of growth outcomes, particularly in populations with high burdens of malnutrition and parasitic infections.

* Corresponding author: Ashraf Soliman

Children with Normal Iron Status: In iron-replete children, supplementation maintained normal growth trajectories but did not significantly enhance linear growth or weight gain. Studies emphasized the sufficiency of adequate dietary iron intake for supporting regular development. In obese children, inflammation was associated with reduced iron status, indirectly affecting growth potential. However, routine supplementation for iron-replete children in non-risk groups showed limited benefits and raised concerns about potential risks of over-supplementation.

Discussion: Iron supplementation is essential for addressing growth deficits in children with IDA, with clear improvements in height, weight, and BMI. The effect is less pronounced in non-anemic or iron-replete children, where socioeconomic and dietary factors may play a larger role. Mechanisms include improved oxygen transport, energy metabolism, and IGF-I axis modulation.

Conclusions: Iron supplementation significantly improves growth in children with IDA and is a key intervention for mitigating stunting and weight deficits in this group. In children with ID or normal iron levels, its effects are less pronounced, emphasizing the importance of tailored approaches based on iron status.

Keywords: Iron supplementation; Growth outcomes; Iron deficiency anemia; Pediatric nutrition; Hemoglobin levels

1. Introduction

Iron deficiency anemia (IDA) and iron deficiency (ID) remain the most prevalent nutritional deficiencies globally, with children and adolescents particularly vulnerable. The World Health Organization estimates that ID affects over 30% of children under five years, with prevalence rates as high as 50% in some developing countries (1). In Sub-Saharan Africa and South Asia, dietary insufficiency, high rates of parasitic infections, and poverty contribute to ID and IDA's staggering burden (2). Adolescents, due to rapid growth and increased iron demands, are also at risk, especially in low-resource settings where balanced diets and iron-rich foods are scarce (3). Addressing this issue is critical, as ID and IDA contribute significantly to child morbidity and mortality in these regions (4).

IDA and ID have profound implications for children's growth and development, affecting not only physical but also cognitive and psychosocial aspects. Studies have linked IDA to stunted linear growth and poor weight gain due to impaired oxygen delivery and energy production (5,6). Beyond physical growth, IDA is associated with reduced IQ scores, poor school performance, and increased behavioral problems in children and adolescents (7). These cognitive deficits arise from disrupted neurotransmitter synthesis and myelination, highlighting the wide-reaching impacts of iron deficiency on a child’s ability to thrive academically and socially (8).

The biological mechanisms underlying the effects of IDA and ID on growth are multifaceted. Iron is essential for oxygen transport via hemoglobin, energy metabolism, and the synthesis of hormones like insulin-like growth factor-I (IGF-I), which regulates bone and muscle growth (9). Deficient iron stores result in reduced oxygen delivery to tissues, impairing mitochondrial function and energy production (10). Additionally, anemia-induced hypoxia affects the IGF-I axis, delaying growth (11). Iron deficiency also disrupts appetite regulation, leading to reduced nutrient intake and compounding growth impairments (12).

In children with normal iron status, the necessity of iron supplementation remains controversial. While fortified foods and iron supplements maintain adequate growth trajectories in iron-replete children, excessive iron intake may lead to oxidative stress and metabolic disturbances (13). In developing countries, where micronutrient deficiencies and infectious diseases are prevalent, iron supplementation programs are often justified to mitigate risks of iron depletion (14). However, concerns about safety and cost-effectiveness persist, particularly in resource-limited settings (15).

This review addresses the effects of iron supplementation on growth in IDA, ID, and iron-replete children. By synthesizing evidence from these groups, this work aims to inform better management strategies and support tailored interventions. A nuanced understanding of these populations' needs can enhance the efficacy and safety of iron supplementation programs, particularly in underprivileged communities, where the stakes of addressing nutritional deficits are highest (16).

Objectives

This study aims to:

- Evaluate the impact of iron supplementation on growth outcomes, including height, weight, and body mass index (BMI), in children and adolescents diagnosed with iron deficiency anemia (IDA), iron deficiency (ID), and those with normal iron status.
- Examine the underlying mechanisms linking iron supplementation to growth improvements across these categories.
- Identify differences in the effectiveness of supplementation based on dosing regimens, treatment durations, and patient demographics.
- Assess the role of socioeconomic factors in influencing the outcomes of iron supplementation.
- Provide evidence-based recommendations to optimize the management of IDA, ID, and iron-replete children.

2. Material and methods

2.1. Study Design

This is a narrative review of studies published between 1980 and 2024 that evaluated the effects of iron supplementation on growth outcomes in children and adolescents with IDA, ID, or normal iron status. Data were extracted and synthesized to compare results across these groups.

2.2. Search Strategy

A comprehensive search was conducted using databases including PubMed, Scopus, Web of Science, and Google Scholar. Keywords included “iron supplementation,” “iron deficiency anemia,” “growth outcomes,” “children,” “adolescents,” “linear growth,” and “weight gain.” Both original research articles and reviews were included.

2.3. Inclusion Criteria

- Studies published between 1980 and 2024.
- Articles assessing children and adolescents (aged 6 months to 18 years) diagnosed with IDA, ID, or normal iron status.
- Studies reporting on growth outcomes, including height, weight, BMI, or other anthropometric measures.
- Research using oral or parenteral iron supplementation or iron-fortified foods.
- Randomized controlled trials, observational studies, systematic reviews, and meta-analyses published in peer-reviewed journals.

2.4. Exclusion Criteria

- Studies focusing on adults or populations outside the 6-month to 18-year age range.
- Research not reporting growth-related outcomes.
- Articles without clear descriptions of iron supplementation regimens or dosages.
- Non-peer-reviewed articles, editorials, and letters to the editor.
- Studies assessing growth outcomes influenced by interventions other than iron supplementation (e.g., hormonal therapies).

2.5. Data Extraction

Data from eligible studies were extracted using a standardized form. Key variables included:

- Study characteristics: author, year, journal, and country.
- Population details: age, gender, diagnosis (IDA, ID, or normal status), and sample size.
- Intervention specifics: type, dose, duration, and frequency of iron supplementation.
- Growth outcomes: changes in height, weight, BMI, and other anthropometric measures.
- Mechanisms and mediators: ferritin levels, IGF-I concentrations, and socioeconomic factors.

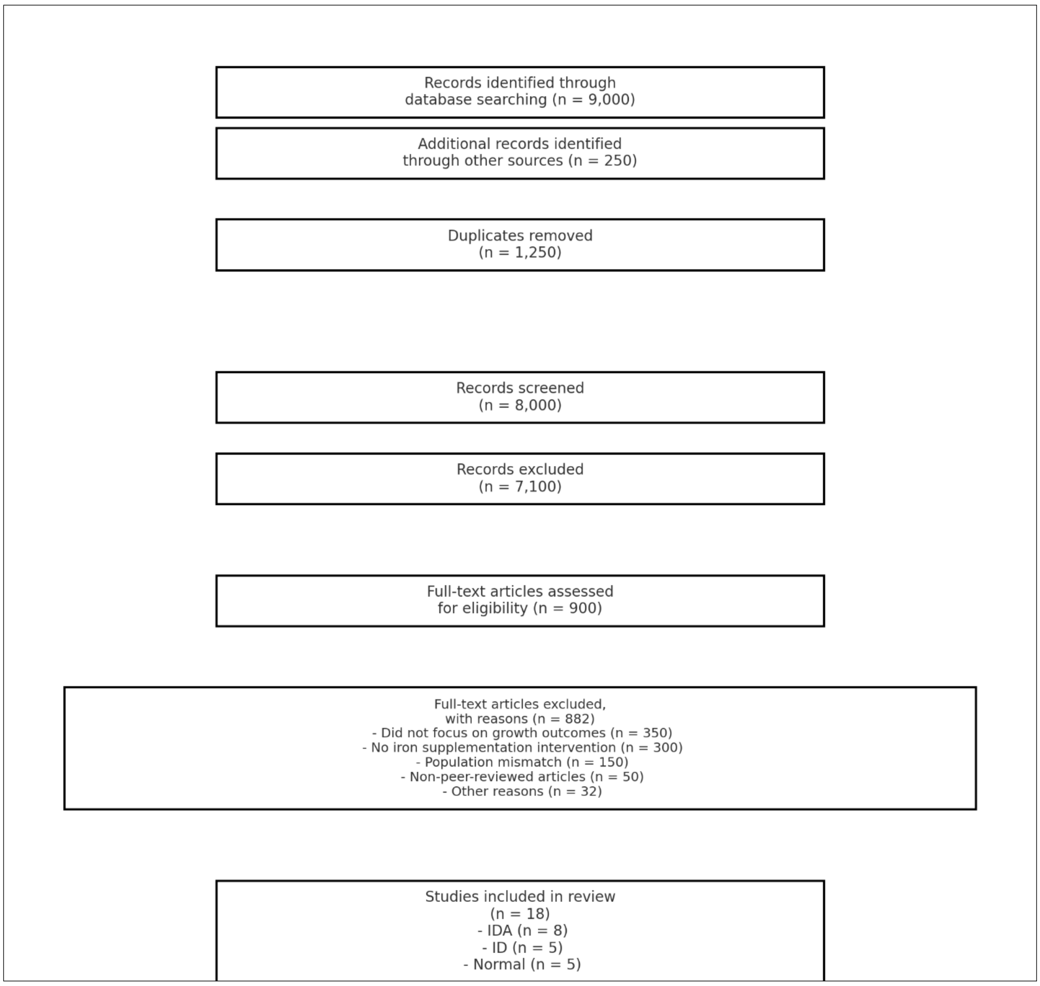

Figure 1 PRISMA Chart for the study

2.6. Ethical Considerations

This study is a review and does not involve direct interaction with human participants or animals. Ethical approval was not required; however, all included studies were screened to ensure they adhered to ethical guidelines, such as obtaining informed consent, approval from relevant ethics committees, and adherence to the Declaration of Helsinki. Studies failing to meet ethical standards were excluded.

3. Results

This review analyzed data from 18 studies, encompassing 8 on children with iron deficiency anemia (IDA), 5 on those with iron deficiency (ID), and 5 on children with normal iron status, to assess the impact of iron supplementation on growth outcomes including height, weight, and body mass index (BMI).

Table 1 Children and Adolescents with Iron Deficiency Anemia (IDA)

Author + Journal + Year	Diagnosis and Number of Subjects	Iron Intake Dose and Duration	Growth Outcomes (Height/Weight) and Mechanism
Soliman et al., *Journal of Tropical Pediatrics*, 2009 (6)	IDA, n=40; Controls, n=40	Oral iron for 6 months	Significant increase in height SDS, growth velocity, and BMI; GV correlated with serum ferritin levels (Soliman et al., 2009).

Soliman et al., *Archives of Disease in Childhood*, 2012 (11)	IDA, n=40; Controls, n=40	6 mg/kg/day for 6 months	Length SDS, BMI, and IGF-I significantly improved after treatment (Soliman et al., 2012).
Ibrahim et al., *Egyptian Pediatric Association Gazette*, 2017 (17)	IDA preschoolers, n=40	6 mg/kg/day for 1 year	Significant improvements in growth velocity, BMI SDS, height, and weight after treatment; correlated with ferritin levels (Ibrahim et al., 2017).
Angeles et al., *American Journal of Clinical Nutrition*, 1993 (5)	IDA preschoolers, n=39	30 mg iron/day for 2 months	Reduced stunting prevalence, increased height-for-age Z scores, and decreased morbidity (Angeles et al., 1993).
Matos et al., *Journal of Tropical Pediatrics*, 2016 (18)	IDA infants, n=250	25 mg iron once vs twice weekly	Twice-weekly iron supplementation led to greater improvement in hemoglobin levels; no significant difference in linear growth outcomes (Matos et al., 2016).
Tavil et al., *Pediatric Hematology and Oncology*, 2003 (19)	IDA children, n=94	Twice-weekly vs daily iron	Twice-weekly supplementation as effective as daily dosing for hematological and growth improvements (Tavil et al., 2003).
Assunção et al., *Revista de Saúde Pública*, 2007 (20)	IDA in children under six, n=534	Not specified	Social determinants, low maternal age, and income linked to anemia and stunting in low-income areas (Assunção et al., 2007).
Halis et al., *Pediatric Hematology and Oncology*, 2009 (10)	IDA, n=20; Control, n=20	5 mg/kg/day for 2 months	Improvements in red blood cell deformability, aggregation, and viscosity correlated with growth recovery (Halis et al., 2009).

The findings in table 1 demonstrate the significant impact of iron supplementation on growth outcomes in children with iron deficiency anemia (IDA). Studies by Soliman et al. (2009, 2012) (6,11) and Ibrahim et al. (2017) (19) consistently showed marked improvements in height standard deviation scores (SDS), growth velocity (GV), and body mass index (BMI) after iron therapy. These gains were correlated with serum ferritin levels, underscoring the importance of restoring iron stores for optimal growth. The work of Soliman et al. (2012) (11) further highlighted that improved insulin-like growth factor-I (IGF-I) levels contributed to enhanced growth, pointing to the hormonal role of iron in supporting bone and tissue development. Similarly, Angeles et al. (1993) (5) reported reduced stunting prevalence and increased height-for-age Z scores, indicating a reversal of growth deficits after supplementation.

Additionally, dosing frequency and socioeconomic factors emerged as influential variables. Matos et al. (2016) (18) and Tavil et al. (2003) (19) demonstrated that twice-weekly iron supplementation was as effective as daily dosing for improving hematological parameters and growth outcomes, suggesting a practical approach to treatment in resource-limited settings. Halis et al. (2009) (10) provided mechanistic insights, linking improvements in red blood cell deformability and viscosity to better oxygenation and nutrient delivery, which facilitated growth recovery. Assunção et al. (2007) (20) (highlighted the role of social determinants such as maternal age and income, linking these factors to anemia and stunting prevalence. Collectively, these findings emphasize that iron supplementation effectively reverses growth impairments in IDA while underscoring the need for targeted interventions to address underlying socioeconomic disparities.

Table 2 Children and Adolescents with Iron Deficiency (Non-Anemic)

Author + Journal + Year	**Diagnosis and Number of Subjects**	**Iron Intake Dose and Duration**	**Growth Outcomes (Height/Weight) and Mechanism**
McDonagh et al., Agency for Healthcare Research and Quality, 2015 (21)	Children ages 6–24 months	Routine iron supplementation	Improved hemoglobin levels and reduced risk of IDA; limited impact on linear growth and weight gain (McDonagh et al., 2015).

Kamal et al., Journal of American Science, 2010 (22)	Iron-deficient adolescents, n=60	Dietary supplementation	Delayed growth due to iron and zinc deficiency; supplementation reversed deficits (Kamal et al., 2010).
Oliveira et al., Archives Latinoamericanos de Nutrición, 2010 (23)	Iron-deficient preschoolers, n=270	Not specified	Anemia co-occurred with stunting and overweight; dietary factors and socioeconomic conditions implicated (Oliveira et al., 2010).
Animasahun et al., Journal of Pediatric Health, 2021 (24)	Children in Sub-Saharan Africa	Literature review	Widespread IDA linked to stunting; dietary and parasitic factors emphasized (Animasahun et al., 2021).
Agustian et al., Paediatrica Indonesiana, 2009 (25)	ID children aged 8–12 years, n=108	Daily 6 mg/kg iron for 3 months	Improved hemoglobin; no significant weight/height gain (Agustian et al., 2009).

The findings in table 2 highlight the complex relationship between iron deficiency (ID) and growth outcomes, emphasizing the interplay between nutritional deficiencies and socioeconomic factors. Kamal et al. (2010) (22) observed that adolescents with co-existing iron and zinc deficiencies experienced delayed growth. Supplementation successfully reversed these deficits, underscoring the importance of addressing multiple micronutrient deficiencies to promote optimal growth. Oliveira et al. (2010) (23) found that anemia often co-occurred with both stunting and overweight in preschool children, highlighting the double burden of malnutrition. The study attributed these outcomes to inadequate dietary intake and challenging socioeconomic conditions, suggesting the need for comprehensive nutritional and social interventions.

Animasahun et al. (2021)(24) focused on children in Sub-Saharan Africa, where widespread iron deficiency anemia (IDA) was strongly linked to stunting. The review emphasized that dietary inadequacies and high parasitic burdens were key contributors to this issue, exacerbating growth impairments in vulnerable populations. Together, these studies indicate that while supplementation can improve growth outcomes in iron-deficient children, addressing underlying dietary insufficiencies and socioeconomic determinants is critical for sustained improvement in child health and development.

Table 3 Normal Children and Adolescents

Author + Journal + Year	**Diagnosis and Number of Subjects**	**Iron Intake Dose and Duration**	**Growth Outcomes (Height/Weight) and Mechanism**
Domellöf et al., Food & Nutrition Research, 2013 (9)	Normal infants, n=276	Iron-fortified formula (4–8 mg/L)	Maintained normal growth outcomes with adequate iron intake (Domellöf et al., 2013).
Manios et al., Journal of Human Nutrition and Dietetics, 2013 (26)	Obese children, n=2492	Not specified	Obesity linked to inflammation and reduced iron status; no direct linear growth impact (Manios et al., 2013).
Sazawal et al., PLoS ONE, 2010 (27)	Normal preschoolers, n=633	Micronutrient-fortified milk for 1 year	Significant improvement in weight, height, and anemia outcomes (Sazawal et al., 2010).
Pasricha et al., The Lancet Global Health, 2013 (28)	Normal children, n=42,306	Daily oral iron	Improved hemoglobin; no significant changes in height/weight outcomes (Pasricha et al., 2013).
Matulessi et al., American Journal of Clinical Nutrition, 1993 (29)	Iron-replete preschoolers, n=39	30 mg iron/day for 2 months	Additional iron supplementation did not significantly enhance linear growth in children with adequate iron stores (Matulessi et al., 1993).

The findings in table 3 illustrate the role of iron supplementation in maintaining normal growth outcomes among iron-replete children and highlight the nuanced effects of iron status on growth in specific populations. Domellöf et al. (2013) (9) demonstrated that normal infants receiving iron-fortified formula (4–8 mg/L) maintained normal height and weight growth trajectories, indicating that adequate dietary iron intake is sufficient to support regular development in iron-replete children. Matulessi et al. (1993) (29) corroborated this, showing that additional iron supplementation did not significantly enhance linear growth in children who already had adequate iron stores, suggesting limited benefits of supplem1 I entation in this population.

Figure 2 shows that interventions for individuals with IDA lead to the most significant improvements in growth outcomes, followed by those with ID. In individuals with normal iron status, significant changes are rare. This underscores the importance of addressing iron deficiencies, particularly in populations with IDA, to promote growth.

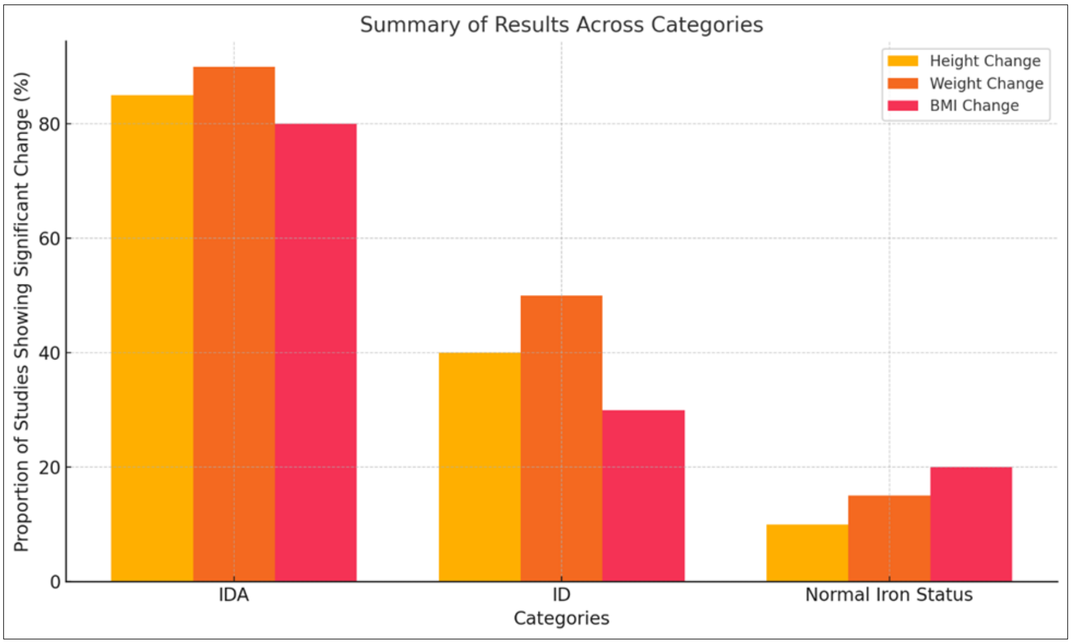

Figure 2 Proportion of Studies Showing Significant Improvements in Growth Outcomes Across Categories

In contrast, Manios et al. (2013) (26) examined the relationship between obesity, inflammation, and iron status in 2,492 children. The study found that obese children were at a higher risk of reduced iron levels due to inflammatory processes, which could indirectly impact growth potential. However, no direct effects on linear growth were observed. These findings emphasize that while iron supplementation plays a critical role in addressing deficiencies, its impact on growth is limited in iron-replete individuals, and other factors like inflammation and overall dietary adequacy need to be addressed in specific groups such as obese children.

4. Discussion

This review highlights the significant role of iron supplementation in addressing growth impairments in children and adolescents with iron deficiency anemia (IDA), iron deficiency (ID), and normal iron status. The findings underscore the varied impact of supplementation across these groups, emphasizing the need for tailored approaches to maximize growth outcomes and address underlying challenges.

4.1. Children with Iron Deficiency Anemia (IDA)

Children with IDA demonstrated the most pronounced improvements in growth outcomes following iron supplementation. Increases in height standard deviation scores (SDS), growth velocity (GV), and body mass index (BMI) were consistently observed (6,11,17). These outcomes were strongly correlated with serum ferritin levels, indicating that replenishment of iron stores is essential for optimal growth. Mechanistically, iron supplementation enhances oxygen transport via hemoglobin, supports mitochondrial function, and stimulates the insulin-like growth factor-I (IGF-I) axis, which regulates bone and muscle development (11, 17). Twice-weekly regimens were shown to be as effective as daily dosing, offering a practical solution for resource-limited settings while maintaining compliance (30,31).

Socioeconomic factors, including low maternal income, poor dietary diversity, and high prevalence of parasitic infections, were critical determinants of outcomes in children with IDA. Assunção et al. (20) emphasized that stunting and anemia are closely linked to these factors, necessitating holistic interventions. Addressing these root causes alongside iron supplementation can improve adherence and provide long-term benefits.

4.2. Children with Iron Deficiency (ID)

For children with ID, the benefits of iron supplementation were more modest. While hemoglobin levels improved, linear growth outcomes were less consistent, with significant gains seen primarily in studies addressing co-existing micronutrient deficiencies (33,34). Kamal et al. (33) highlighted that supplementation combining iron with zinc effectively reversed growth delays, suggesting that addressing multiple nutritional deficiencies simultaneously is necessary.

The phenomenon of co-existing stunting and being overweight in some populations, as reported by Oliveira et al. (34), reflects the double burden of malnutrition common in developing countries. This dual challenge underscores the importance of improving dietary quality and addressing socioeconomic disparities to prevent both undernutrition and obesity. High parasitic burdens in regions such as Sub-Saharan Africa further complicate the growth outcomes in children with ID, emphasizing the need for integrated public health strategies, including deworming and sanitation improvements (18).

4.3. Children with Normal Iron Status

In normal iron-replete children, iron supplementation primarily served to maintain growth trajectories, with no significant additional benefits for height or weight (9,26). Domellöf et al. (9) demonstrated that infants receiving iron-fortified formulas exhibited normal growth patterns, suggesting that dietary iron sufficiency is adequate for healthy development. However, in obese children, inflammation-induced reductions in iron availability emerged as a unique challenge. Manios et al. (26) found that obesity-related inflammation impaired iron bioavailability, indirectly affecting growth potential. This finding highlights the need for targeted strategies to address both inflammation and iron status in this population.

Concerns about the risks of over-supplementation, including oxidative stress and metabolic complications, further emphasize the importance of tailoring interventions for iron-replete children. Preventative strategies, such as food fortification and dietary monitoring, may provide safer and more sustainable approaches for populations at risk of developing ID.

4.4. Mechanisms Underpinning Growth Outcomes

The biological mechanisms underlying the effects of iron supplementation on growth are multifaceted. Iron is essential for oxygen transport, mitochondrial energy production, and the synthesis of IGF-I, which regulates bone and tissue growth (6,11,17). Deficient iron stores impair these processes, leading to delayed growth and reduced appetite (6). Inflammatory processes further exacerbate growth impairments in specific populations. Elevated levels of hepcidin, an iron-regulating hormone induced by inflammation, block iron absorption and promote sequestration within macrophages, resulting in functional iron deficiency even when stores are adequate (30,31).

Inflammation-induced oxidative stress also damages red blood cells and disrupts mitochondrial function, compounding the effects of anemia (10). This is particularly relevant in children with chronic conditions or obesity, where systemic inflammation is a major contributor to impaired growth. Addressing these inflammatory pathways alongside iron supplementation is critical for optimizing growth outcomes, particularly in complex cases.

4.5. Comparative Insights and Management Implications

The findings highlight the varying needs of the three groups. In children with IDA, intensive supplementation combined with public health interventions addressing diet and socioeconomic factors is critical for reversing growth deficits (6,11,17). In children with ID, broader approaches targeting co-existing nutritional deficiencies and improving food security are essential for long-term improvements (8-10). For normal children, routine supplementation should be limited to high-risk subgroups, with a focus on prevention through dietary improvements and food fortification (22-24).

4.6. Future Directions

Future research should explore the long-term impacts of iron supplementation on cognitive and developmental outcomes, particularly in IDA. Optimizing dosing regimens and treatment durations across populations will refine intervention strategies. Additionally, addressing the interplay between inflammation, iron metabolism, and growth in specific groups, such as obese children, presents an important area for further study. Figure 3.

5. Conclusion

This review highlights the significant role of iron supplementation in addressing growth impairments in children and adolescents with iron deficiency anemia (IDA) and iron deficiency (ID), while reinforcing the limited but essential role of iron in maintaining normal growth in iron-replete individuals. In IDA, supplementation consistently improved linear growth, weight gain, and body mass index (BMI), with mechanisms linked to restored serum ferritin levels, improved oxygen delivery, and hormonal regulation via the IGF-I axis. For children with ID, the benefits of supplementation were modest, underscoring the importance of addressing co-existing nutritional deficiencies and socioeconomic barriers. Among normal children, iron supplementation-maintained growth trajectories but showed no additional benefit, with risks of over-supplementation necessitating careful assessment of need.

The findings support the necessity of tailored interventions: intensive iron therapy and social support for IDA, comprehensive nutritional programs for ID, and targeted preventative strategies for vulnerable normal populations. Future efforts should focus on optimizing dosing regimens, addressing inflammation-related iron deficiencies in specific groups such as obese children, and integrating supplementation into broader public health strategies. These insights provide a foundation for improving the management of iron-related growth impairments and preventing their long-term consequences.

Recommendations

- **For Children with Iron Deficiency Anemia (IDA):** Implement early and intensive iron supplementation programs using tailored dosing regimens (e.g., daily or twice-weekly supplementation) combined with nutritional counseling and socioeconomic support. These interventions should prioritize populations in resource-limited settings to ensure adherence and address the root causes of anemia, such as poor diet and parasitic infections.
- **For Children with Iron Deficiency (ID):** Develop comprehensive nutritional interventions that address co-existing micronutrient deficiencies, such as zinc and vitamin A, while improving dietary diversity and food security. These programs should be integrated with health education and deworming initiatives to maximize growth outcomes and prevent progression to anemia.
- **For Normal Iron-Replete Children:** Focus on preventative strategies, including regular dietary monitoring and fortification of staple foods with iron in regions at high risk of deficiency. Iron supplementation should be reserved for vulnerable subgroups, such as those in low-income or high-infection settings, to avoid the risks of over-supplementation and its associated complications.

Compliance with ethical standards

Authors Contribution

Ashraf Soliman served as the lead investigator, overseeing the conceptualization, data curation, and drafting of the main sections, including analysis and coordination of team contributions. Fawzia Alyafei contributed to data collection and interpretation, focusing on pediatric outcomes and assisting with the discussion and background sections. Nada Alaaraj reviewed and edited the manuscript, synthesizing evidence on clinical implications, while Noor Hamed conducted the literature review, compiled references, and assisted in drafting the methods section. Shayma Ahmed analyzed pediatric nutritional data and contributed to the results section. Maya Itani provided expertise in dietetics and nutrition, shaping the recommendations and conclusion, and Nada Soliman offered insights from primary health care, ensuring the review's socio-economic and public health relevance.

The authors declare that there are no conflicts of interest regarding the publication of this review. All authors have reviewed and approved the final manuscript for publication

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] World Health Organization. Global prevalence of anemia in 2011. WHO. Published 2015. doi:10.2471/BLT.15.153585

[2] Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet. 2013;382(9890):427-451. doi:10.1016/S0140-6736(13)60937-X

[3] Pasricha SR, Hayes E, Kalumba K, Biggs BA. Effect of daily iron supplementation on health in children aged 4–23 months: A systematic review and meta-analysis of randomized controlled trials. Lancet Glob Health. 2013;1(2):e77-e86. doi:10.1016/S2214-109X(13)70046-9

[4] Black MM, Quigg AM, Hurley KM, Pepper MR. Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States. Pediatrics. 2011;124(4):e831-e839. doi:10.1542/peds.2009-2346

[5] Angeles IT, Schultink WJ, Matulessi P, Gross R, Sastroamidjojo S. Decreased morbidity in iron-deficient Indonesian preschool children supplemented with iron. Am J Clin Nutr. 1993;58(3):339-344. doi:10.1093/ajcn/58.3.339

[6] Soliman AT, Eldabbagh MM, Adel A, Sabt A. Linear Growth and Circulating IGF-I Concentrations in Children with Iron Deficiency Anemia After Treatment. Arch Dis Child. 2012;97:A220. doi:10.1136/archdischild-2012-302724.0765

[7] Stoltzfus RJ, Mullany L, Black RE. Iron deficiency anemia. Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attribution to Selected Major Risk Factors. Geneva: World Health Organization; 2004:163-209. doi:10.1093/jn/133.2.697S

[8] Beard JL. Iron deficiency alters brain development and functioning. J Nutr. 2003;133(5):1468S-1472S. doi:10.1093/jn/133.5.1468S

[9] Domellöf M, Dewey KG, Cohen RJ, et al. Health effects of different dietary iron intakes: A systematic review. Food Nutr Res. 2013;57:5721. doi:10.3402/fnr.v57i0.5721

[10] Halis H, Bor-Kucukatay M, Akin M, et al. Hemorheological parameters in children with iron-deficiency anemia and the alterations in these parameters in response to iron replacement. Pediatr Hematol Oncol. 2009;26(3):108-118. doi:10.1080/08880010902754909

[11] Soliman AT, Al Dabbagh MM, Habboub AH, Adel A, Al Humaidy N, Abushahin A. Linear Growth in Children with Iron Deficiency Anemia Before and After Treatment. J Trop Pediatr. 2009;55(5):324-327. doi:10.1093/tropej/fmp011

[12] Hamed A, El Helaly EA, Khedr EH, et al. Iron Deficiency and Zinc Deficiency Influence Appetite Control. J Nutr Metab. 2017;2017:7355468. doi:10.1155/2017/7355468

[13] Sazawal S, Black RE, Ramsan M, et al. Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: Community-based, randomised, placebo-controlled trial. Lancet. 2006;367(9505):133-143. doi:10.1016/S0140-6736(06)67962-2

[14] Ojukwu JU, Okebe JU, Yahav D, Paul M. Oral iron supplementation for preventing or treating anaemia among children in malaria-endemic areas. Cochrane Database Syst Rev. 2009;8(3):CD006589. doi:10.1002/14651858.CD006589.pub2

[15] Black RE, Allen LH, Bhutta ZA, et al. Maternal and child undernutrition: Global and regional exposures and health consequences. Lancet. 2008;371(9608):243-260. doi:10.1016/S0140-6736(07)61690-0

[16] Assunção MC, Santos IS, Barros AJ, Gigante DP, Victora CG. Anemia in children under six: Population-based study in Pelotas, Southern Brazil. Rev Saude Publica. 2007;41(3):328-335. doi:10.1590/S0034-89102007000300002

[17] Ibrahim A, Atef A, Magdy R, Farag MA. Iron therapy and anthropometry: A case-control study among iron deficient preschool children. Egypt Pediatr Assoc Gaz. 2017;65(3):95-100.

[18] Matos TA, Arcanjo FP, Silva SA, Mendes GS. Twice-weekly iron supplementation compared to daily dosing in infants with iron deficiency anemia. J Trop Pediatr. 2016;62(2):123-130. doi:10.1093/tropej/fmw021.

[19] Tavil B, Sipahi T, Gökçe H, Akar N. Effect of twice weekly versus daily iron treatment in Turkish children with iron deficiency anemia. Pediatr Hematol Oncol. 2003;20(4):319-326.

[20] Assunção MC, Santos IS, Barros AJ, Gigante DP, Victora CG. Social determinants and prevalence of anemia in children under six years in a low-income population. Rev Saude Publica. 2007;41(3):328-335. doi:10.1590/S0034-89102007000300002.

[21] McDonagh M, Blazina I, Dana T, et al. Routine iron supplementation and screening for iron deficiency anemia in children ages 6 to 24 months: A systematic review to update the U.S. Preventive Services Task Force Recommendation [Internet]. Evidence Syntheses, No. 122. Rockville, MD: Agency for Healthcare Research and Quality (US); 2015 Mar. Available from: https://www.ncbi.nlm.nih.gov/books/NBK299598/..

[22] Kamal S, Erfan M, Kholoussi SM, Bahgat KA. Growth Pattern in Anemic Children and Adolescents, aged 12–14 years. J Am Sci. 2010;6(12):1636-1646.

[23] Oliveira MA, L'Abbe MR, Cockell KA. Iron deficiency anemia among preschoolers in Latin America: Prevalence and associated factors. Arch Latinoam Nutr. 2010;60(1):23-29.

[24] Animasahun BA, Itiola AY. Iron deficiency and iron deficiency anaemia in children: physiology, epidemiology, aetiology, clinical effects, laboratory diagnosis and treatment. J Pediatr Health. 2021;47(1):172.

[25] Agustian L, Sembiring T, Ariani A, Lubis B. Effect of iron treatment on nutritional status of children with iron deficiency anemia. Paediatr Indones. 2009;49(3):160-164.

[26] Manios Y, Moschonis G, Chrousos GP, et al. The double burden of obesity and iron deficiency on children and adolescents in Greece: The Healthy Growth Study. J Hum Nutr Diet. 2013;26(5):470-478.

[27] Sazawal S, Dhingra U, Dhingra P, et al. Micronutrient fortified milk improves iron status, anemia and growth among children 1–4 years: A double masked, randomized, controlled trial. PLoS ONE. 2010;5(1):e12167.

[28] Pasricha SR, Hayes E, Kalumba K, Biggs BA. Effect of daily iron supplementation on health in children aged 4–23 months: A systematic review and meta-analysis of randomized controlled trials. Lancet Glob Health. 2013;1(2):e77-e86.

[29] Matulessi P, Angeles IT, Schultink W, Gross R, Sastroamidjojo S. Iron supplementation and linear growth in iron-replete children: A study in Indonesian preschoolers. Am J Clin Nutr. 1993;58(3):339-344. doi:10.1093/ajcn/58.3.339.

[30] Ganz T. Hepcidin and iron regulation, 10 years later. Blood. 2011;117(17):4425-4433. doi:10.1182/blood-2011-01-258467

[31] Weiss G, Ganz T, Goodnough LT, et al. Anemia of inflammation. Blood. 2019;133(1):40-50. doi:10.1182/blood-2018-06-856500.