Review Article ISSN 2835-6276

American Journal of Medical and Clinical Research & Reviews

Iron Deficiency Anemia in Infants

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Received: 02 Oct 2024; Accepted: 05 Oct 2024; Published: 10 Oct 2024

Citation: Fatma mohamed mahmoud. Iron Deficiency Anemia in Infants. AJMCRR 2024; 3(10): 1-6.

Abstract

Iron deficiency is the most common nutritional deficiency worldwide, with infants being particularly vulnerable. Iron deficiency anemia (IDA) in infancy can significantly impact growth, development, and overall health. This comprehensive review summarizes the current understanding of IDA in infants, including its etiological factors, clinical features, diagnostic approach, treatment strategies, and preventive measures. Risk factors for IDA in infants include inadequate dietary iron intake, increased physiological requirements during this period of rapid growth, prematurity, low birth weight, and chronic blood loss. IDA in infancy has been associated with impairments in cognitive development, motor function, and social-emotional wellbeing, with some effects persisting into later childhood. Prompt diagnosis involves assessment of hemoglobin, red cell indices, and iron status markers such as serum ferritin. Oral iron supplementation remains the mainstay of treatment, with parenteral iron therapy reserved for severe or refractory cases. Prevention strategies focus on optimizing maternal iron status, ensuring adequate iron intake through exclusive breastfeeding in the first 6 months and timely introduction of iron-rich complementary foods, iron supplementation in high-risk populations, and limiting excessive cow's milk intake. Routine screening for IDA in infants, especially in at-risk groups, coupled with appropriate interventions, is crucial to address this preventable condition. Continued research is needed to explore innovative strategies for effective prevention and treatment of IDA in infancy, as well as to elucidate the long-term impact on child health outcomes. A coordinated effort from healthcare providers, policymakers, and community stakeholders is essential to reduce the global burden of IDA in infants and ensure optimal child growth, development, and well-being.

Keywords: Anemia, iron deficiency, infants, cognitive development, motor development, growth.

Introduction:

Iron deficiency anemia (IDA) is a global health concern of immense proportions, disproportionately affecting infants and young children. The World Health Organization estimates that approximately 43% of children under 5 years of age worldwide are anemic, with iron deficiency being the predominant cause (World Health Organization, 2008). Infants are particularly susceptible to IDA due to their rapid growth and increased iron requirements, which often exceed the dietary iron supply (Özdemir, 2015).

The consequences of IDA in infancy extend beyond the hematological parameters. Iron plays a critical role in neurodevelopment, and IDA during this crucial period has been linked to long-term deficits in cognitive function, motor skills, and behavior, some of which may persist despite iron repletion (Jáuregui-Lobera, 2014). This underscores the importance of early prevention, diagnosis, and treatment of IDA in infancy to optimize child health and development.

While the burden of IDA is higher in low- and middle-income countries, it remains a significant concern in developed nations, particularly among disadvantaged populations and those with suboptimal infant feeding practices. Addressing IDA in infancy requires a comprehensive approach that includes promoting optimal maternal iron status, supporting exclusive breastfeeding, ensuring timely introduction of iron-rich complementary foods, targeted supplementation, and routine screening (Baker et al., 2010).

Etiology and Risk Factors

The etiology of IDA in infants is multifactorial, involving an interplay of nutritional, physiological, and pathological factors (Powers & Buchanan, 2019). The most common cause is inadequate dietary iron intake relative to the increased requirements during this period of rapid growth and development (Dewey, 2001). Infants are born with a finite amount of iron stores, which are gradually depleted over the first few months of life. Exclusively breastfed infants are at risk of developing IDA after 4-6 months of age, as breast milk, although highly bioavailable, has a low iron content (Dewey & Chaparro, 2007). Delayed introduction or inadequate intake of iron-rich complementary foods further exacerbates this risk.

Excessive intake of cow's milk, especially before 12 months of age, is another significant contributor to IDA in infancy. In addition to its low iron content, cow's milk can interfere with iron absorption from other dietary sources and may lead to occult gastrointestinal blood loss in some infants (Agostoni & Turck, 2011).

Other risk factors for IDA in infants include prematurity, low birth weight, maternal iron deficiency, chronic blood loss (e.g., cow's milk protein-induced colitis, gastrointestinal malformations), and certain genetic disorders affecting iron metabolism (Powers & Buchanan, 2019; Camaschella, 2015). Socioeconomic disadvantage, food insecurity, and cultural dietary practices that limit iron intake also play a role in the development of IDA in this age group (Pivina, 2019).

Clinical Features and Consequences

The clinical presentation of IDA in infants can be subtle and nonspecific, often leading to delayed recognition. Common signs and symptoms include pallor, irritability, lethargy, poor feeding, and failure to thrive (Mattiello et al., 2020). Some infants may exhibit pica, a craving for non-food items such as dirt or paint chips. In severe cases, IDA can lead to tachycardia, cardiomegaly, and rarely, heart failure (Kato et al., 2022).

The most significant impact of IDA in infancy pertains to its effect on neurodevelopment. Numerous studies have demonstrated that IDA during this critical period is associated with impairments in cognitive function, motor development, and social-emotional wellbeing, some of which may persist into later childhood and adolescence despite iron therapy (Jáuregui-Lobera, 2014). Specific deficits have been noted in language development,

memory, processing speed, and overall intellectual performance (Pivina et al., 2019). While the exact mechanisms are not fully elucidated, it is believed that iron deficiency alters neurotransmitter metabolism, myelination, and neuronal energy metabolism, thereby affecting brain development and function (Bakthavatchalam et al., 2022).

Diagnosis

The diagnosis of IDA in infants involves a combination of clinical assessment, hematological parameters, and iron status markers. The World Health Organization defines anemia in infants aged 6-59 months as a hemoglobin concentration below 11 g/dL (Hoffbrand et al., 2019). However, hemoglobin alone is not sufficient to diagnose IDA, as it can be affected by various factors such as prematurity, infection, inflammation, and other nutrient deficiencies (World Health Organization, 2020).

Additional red cell indices that suggest IDA include microcytosis (low mean corpuscular volume), hypochromia (low mean corpuscular hemoglobin), and elevated red cell distribution width (Powers & O'Brien, 2019). Serum ferritin is the most specific biochemical marker of iron status, reflecting total body iron stores. In infants, a serum ferritin level <12 µg/L is indicative of iron deficiency (World Health Organization, 2020). However, ferritin is an acute-phase reactant and can be falsely elevated in the context of infection or inflammation, potentially masking underlying iron deficiency (Nemeth et al., 2003). In such cases, additional markers like transferrin saturation or soluble transferrin receptor may provide further diagnostic clarity (Powers et al., 2020).

It is important to consider other causes of microcytic anemia in infants, such as thalassemia traits, lead poisoning, or chronic diseases, based on the clinical presentation and laboratory findings (Stoffel et al., 2017). In refractory cases or those with atypical features, further evaluation for gastrointestinal blood loss, malabsorption, or other underlying pathologies may be warranted (Mantadakis, 2016).

Management

The management of IDA in infants primarily involves oral iron supplementation, along with dietary modifications and treatment of any underlying causes, if identified (Aksu & Ünal, 2023). Oral iron is the first-line therapy due to its effectiveness, safety, and low cost. The recommended daily elemental iron dose for infants is 3-6 mg/kg, administered in divided doses on an empty stomach to optimize absorption (Baker & Greer, 2010). Liquid iron preparations are preferred for this age group, with ferrous sulfate being the most commonly used formulation. However, newer preparations with lower elemental iron content, such as iron polysaccharide complex or ferrous bisglycinate, may have better gastrointestinal tolerability (Jullien, 2021).

Recent studies have explored alternative dosing regimens to improve adherence and minimize side effects, such as intermittent dosing or alternate-day dosing (Lennox et al., 2013). Co-administration of vitamin C can enhance iron absorption, while iron intake should be spaced apart from meals containing calcium, phytates, or tannins, which can interfere with absorption (Lukowski et al., 2010). The duration of iron therapy depends on the severity of anemia and the replenishment of iron stores, typically ranging from 3 to 6 months (Wang et al., 2013).

In severe cases of IDA (hemoglobin <5 g/dL) or those with signs of cardiac compromise, parenteral

iron therapy or blood transfusion may be necessary (Wong, 2017). Intravenous iron preparations, such as ferric carboxymaltose or iron sucrose, have been increasingly used in infants due to their favorable safety and efficacy profile (Mantadakis, 2016). However, the decision to use parenteral iron should be individualized based on the clinical scenario and potential risks.

Dietary counseling is an essential component of IDA management in infants. Parents should be educated about age-appropriate iron-rich food sources (e.g., iron-fortified infant cereals, pureed meats, legumes, green leafy vegetables), optimal feeding practices, and strategies to enhance iron absorption (Baker et al., 2010). In older infants and toddlers, excessive cow's milk intake (>500 mL/day) should be discouraged to prevent its interference with iron absorption from other foods (Baker et al., 2010).

Prevention

Preventing IDA in infants requires a life-course approach that begins prenatally and extends through early childhood. Key strategies include ensuring adequate maternal iron status during pregnancy, promoting delayed cord clamping, supporting exclusive breastfeeding for the first 6 months of life, timely introduction of iron-rich complementary foods, and targeted iron supplementation in high-risk populations (Baker et al., 2010).

Delayed cord clamping (waiting at least 60 seconds after birth) has been shown to improve iron stores and reduce the risk of IDA in infants, particularly in settings with a high prevalence of maternal anemia (Wang et al., 2013). Routine iron supplementation is recommended for exclusively breastfed infants starting at 4 months of age, preterm infants, and those with low birth weight (Baker et al., 2010). In areas with a high burden of IDA, universal iron supplementation may be considered for all infants (Wang et al., 2013).

Food fortification is another effective strategy to increase iron intake at the population level. Iron-fortified infant cereals and formulas have been widely used in many countries (Lennox et al., 2013). Micronutrient powders containing iron can be added to complementary foods to improve iron status in infants and young children (Özdemir, 2015).

Regular screening for anemia and iron deficiency is crucial for early detection and intervention, especially in high-risk infants. The American Academy of Pediatrics recommends universal screening for anemia at 12 months of age, with additional screening at other time points based on individual risk factors (Baker et al., 2010). Infants diagnosed with IDA should undergo follow-up testing to ensure resolution of anemia and replenishment of iron stores (Wong, 2017).

Conclusion

Iron deficiency anemia is a widespread and preventable condition that disproportionately affects infants worldwide. Its impact extends beyond hematological parameters, with significant consequences on neurodevelopment, growth, and overall health. Healthcare providers play a crucial role in identifying and treating IDA in infants promptly, particularly in high-risk populations.

Public health interventions, such as maternal iron supplementation, delayed cord clamping, exclusive breastfeeding, timely introduction of iron-rich

complementary foods, and targeted fortification strategies, are essential in reducing the global burden of IDA in infancy. Collaboration between healthcare professionals, policymakers, and community stakeholders is necessary to ensure the successful implementation and sustainability of these preventive measures.

Future research should focus on developing innovative diagnostic tools and therapeutic strategies to improve the detection and management of IDA in infants. This includes exploring the role of hepcidin as a biomarker of iron status, investigating the potential of iron-responsive microRNAs in the pathogenesis of IDA, and evaluating the efficacy and safety of newer oral iron formulations with enhanced bioavailability and tolerability.

Addressing IDA in infancy is a global health imperative, as it has far-reaching implications for child health, development, and future potential. A concerted effort from all stakeholders is needed to prevent, detect, and treat this condition effectively, thereby ensuring that every infant has the opportunity to thrive and reach their full potential.

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