

# THE HIDDEN COGNITIVE BURDEN OF CHILDHOOD IRON DEFICIENCY ANEMIA: EVIDENCE FROM GLOBAL STUDIES

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## Abstract

**Introduction:** Iron Deficiency Anemia (IDA) remains one of the most significant public health problems worldwide. Prior studies have shown associations between low iron status/iron deficiency anemia and poor child development outcomes. Studies suggested IDA among younger children may cause permanent cognitive and/or developmental disabilities. **Methods:** Literature search was conducted across PubMed, Scopus, and Google Scholar for studies published between 2006 and 2025. Search terms included “anemia,” “children,” “pediatric,” “iron deficiency,” “cognitive,” “child development,” and “child nutrition.” Inclusion criteria of this review: pediatric populations (0–18 years), anemia-supplementation interventions, and outcomes related to nutrition, biochemical markers, or nutritional status. Fifteen core studies (RCTs, systematic reviews, meta-analyses, and narrative reviews) met all inclusion criteria. **Results:** The reviewed studies demonstrate that anemia in children, primarily due to iron deficiency, is associated with impaired cognitive and developmental outcomes. Iron deficiency affects brain development by disrupting oxygen delivery, myelination, and neurotransmitter function, particularly during early growth period in which it is critical. The biological effect is linked to deficits in attention, memory, learning performance, and school readiness. Based on the evidence, further suggests that these early impairments may persist into later educational and economic disadvantages, contributing to a profound long-term loss of human capital. **Conclusion:** Childhood anemia, especially IDA, is evidently associated with impaired cognitive and developmental outcomes. Early prevention, screening, and appropriate iron interventions are essential to protect neurodevelopment and support long-term human capital formation.

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**Keywords:** anemia, children, pediatric, iron deficiency, cognitive, child development, child nutrition

## Introduction

Anemia continues to be one of the most occurrence public health problems globally, from conception to the first 1,000 days. There are two types of anemia: nutritional and non-nutritional related. In nutritional anemia, there is insufficient intake of nutrients to meet the need for hemoglobin and erythrocyte synthesis.<sup>1</sup> Special attention needs to be given to the consumption of iron-rich or iron fortified foods because iron deficiency is the common cause of anemia among under-five year old children. More than 25% of the world's population has signs of anemia, and more than 50% of them, in particular women and children below 7 years of age, are especially vulnerable and suffer from iron deficiency anemia (IDA). IDA is a potentially serious, under-recognized nutritional problem that may adversely influence children's cognitive and behavioral development.<sup>2</sup>

Given IDA's leading role in anemia, prior studies have shown associations between low iron status or iron-deficiency anemia and poor child development outcomes. Iron participates in a variety of metabolic processes in the central nervous system. The role of iron in the synthesis of neural transmitters makes it very important for brain development both antenatally and postnatally. Iron supplementation may improve mental, psychomotor, and physical development in children, although evidence of such effects is relatively scarce.<sup>3</sup>

Early childhood factors can have persisting effects on children's growth and development. Severe iron deficit in young children in low-income countries is associated with substantial cognitive and motor impairments, which are complex to prevent. Early interventions and holistic systems are effective ways to improve iron status and reduce the prevalence of anemia,

as iron deficiency affects almost 2 billion people worldwide and is exacerbated by the poor bioavailability of iron in plant-based diets.<sup>1</sup>

A deficiency of iron among young children may cause permanent cognitive and developmental disabilities. Motor and social-emotional outcomes improve significantly with early iron supplementation, particularly when given before the manifestation of severe deficiency. Childhood iron deficiency can occur even in the absence of clinically evident anemia and has been linked to cognitive deficits in children, specifically in attention, intelligence, and behavior<sup>1</sup>, leading to both short-term cognitive impairment and long-term human capital loss. Although numerous studies have explored iron deficiency and cognition, evidence remains fragmented across mechanistic, epidemiological, and life-course perspectives. A synthesis integrating biological pathways and long-term human capital implications remains limited. This suggests that early iron deficiency may lead to permanent developmental consequences, which the supplement cannot completely rectify.<sup>2, 3</sup>

## Method

This narrative review was conducted through a comprehensive literature search across three major scholarly databases: PubMed, Scopus, and Google Scholar. The search covered studies published between 2006 to 2025, reflecting two decades of scientific advancement in probiotic research related to pediatric health and anemia from nutritional science point of view.

The primary search terms included: *“anemia,” “children,” “pediatric,” “iron deficiency,” “cognitive,” “child development,”* and *“child nutrition.”*

The inclusion criterias are as following:

1. Population: Pediatric subjects aged 0–18 years, across clinical, community, or experimental settings.
2. Intervention: Administration of anemia supplementation.
3. Outcomes: Reported effects on at least one of the following domains: Nutrition biochemical status (Hemoglobin, red blood cell); Physical indicators (pale, low energy); Development aspects (cognitive and other developmental aspect)

Titles, abstracts, and full-text articles were screened independently for relevance. A total of 15 studies met all inclusion criteria. These comprised randomized controlled trials (RCTs), systematic reviews and meta-analyses, and previous narrative reviews focusing on anemia and its correlation with cognitive aspect in children. These studies were synthesized narratively in the Results and Discussion sections, emphasizing mechanistic insights, clinical relevance, and consistency of findings across contexts.

## **Results and Discussions**

Of the included studies, the majority reported a significant association between iron deficiency anemia and impaired cognitive performance, particularly in domains of attention, memory, and executive function. Evidence from randomized controlled trials suggests modest improvements following iron supplementation, whereas observational studies consistently report lower cognitive scores among children with anemia. While most studies demonstrate an association, the strength of evidence varies by study design.

Randomized controlled trials provide stronger causal inference but often report modest

effect sizes. In contrast, cross-sectional studies frequently show larger associations, which may partly reflect residual confounding factors. Iron deficiencies often pairs with other individual, group (family/community), and/or environmental disadvantages which may affect cognitive development. Family socio-economic status (SES) should be considered, including economic circumstances, education, and occupation as study shows relationship between iron deficiency and SES, that later affecting cognitive test score.<sup>3</sup>

Further comparison done between children with IDA and good iron status in low SES families, the result shows that the average cognitive scores averaged 10 points lower in IDA children. The observed result study appears to make sense, the direct and indirect effects on early iron deficiencies can delay basic development process as in this kind of economically stressed environment, there are no resource nor capacity for compensation<sup>3</sup>. Whilst, in adolescence women, anemia status has no significant relationship with sleep quality and cognitive ability.<sup>4</sup>

Iron-deficiency anemia is perceived as the most common cause of nutritional anemia.<sup>5</sup> Micronutrients of known public health importance include the following: zinc, iodine, iron, selenium, copper, Vitamins A, E, C, D, B2, B6 and folate. Deficiency of these micronutrients has a significant impact on children health and cognitive development as well as on the economic development of communities and nations. The potential of the child for physical growth and mental development may become compromised due to deficiencies of micronutrients, which are commonly referred to as “hidden hunger”.<sup>6</sup>

Children with these micronutrient deficiencies are more vulnerable to develop frequent and a vicious cycle of under nutrition and recurrent infections. To emphasize on this, almost

two thirds of the deaths of children around the world are directly or indirectly related with nutritional deficiencies.<sup>7</sup> Micronutrient deficiencies, Iron in particular, can have long-term effect on cognition and behaviour in children. This is due to the impact on the rapidly brain development from early life stage to early childhood. Iron is vital, from hemoglobin synthesis to supporting neuroendocrine function. Therefore, it could affect cognition and behaviour in children.<sup>5</sup> UNICEF (1998) defined micronutrients as substances that are only needed by the body in minute amounts, which play leading roles in the production of enzymes, hormones and other substances, helping to regulate growth activity, cognitive development, functioning of the immune, reproductive systems.<sup>8</sup>

Early life determinants refer to critical windows of neurodevelopment, starting from preconception and pregnancy stage to infant and early childhood. Maternal anemia often occurs along with micronutrient deficit. This could happen due to inadequate antenatal care. In early childhood, anemia occurrence affected by breastfeeding and complementary feeding habit for early childhood as well as recurrent infections and inflammation, and poor sanitation and/or personal hygiene.<sup>9</sup> This childhood anemia circumstances could immediately cause upstream disadvantage such as reduced hemoglobin concentration, impaired iron bioavailability, chronic or recurrent anemia during sensitive developmental window. If ignored, a direct neurodevelopmental insult will occur.<sup>8</sup>

### **Neurodevelopmental Pathways Mechanism**

Anemia and IDA in children affects brain development during periods of rapid neurogenesis and synaptic organization. Nutrition insults occur during critical development

windows, it may induce brain anatomy and physiology alteration with possible long-term consequences.<sup>10</sup> The following mechanism explain how early anemia can lead to persistent cognitive impairment:

1. Oxygenation reduction

Hemoglobin is the primary component of red blood cells consists of four protein molecules known as globulin chains, with each chain containing a crucial structure called heme. This heme molecule contains iron, which is essential for oxygen and carbon dioxide transportation and contributes to the red coloration of blood.<sup>10</sup> Hemoglobin is essential for oxygen transportation throughout the body, therefore if its concentration is reduced could cause low oxygen delivery to brain regions that in charge for executive function (prefrontal cortex), memory function (hippocampus), and attention and motor control (basal ganglia). Low hemoglobin caused recurrent anemia that result in decreased energy production, impaired neuron maturation, and reduced dendritic growth.<sup>11, 12</sup>

2. Impaired myelination

Iron plays important role in formation and functioning of neural system, such as myelin synthesis and synapse formation. In the early life stages, myelination occurs rapidly, therefore iron deficiency may result thinner myelin sheaths, slower neural transmission, that impacting connectivity between regions.<sup>13</sup>

3. Altered neurotransmitter metabolism

Additionally, iron is the enzyme cofactor for neurotransmitter synthesis that covers dopamine, serotonin, and norepinephrine. In this stance, iron deficit can leads to

reduction and alteration of those enzymes that associated with poor concentration, reduced school engagement, and other behavioral difficulties in children.<sup>14</sup>

#### 4. Dysregulated stress & inflammatory pathways

Iron deficiency and anemia incident are accompanied by chronic inflammation and increased cytokine activity, which may affect neurological process. Furthermore, anemia-related physiological stress may increase cortisol exposure during developmental periods. If dysregulated could cause memory consolidation, emotional and executive function impairment.<sup>15</sup>

### **Cognitive and Functional Outcomes Throughout Life Stages**

The biological disruptions induced by childhood anemia particularly during sensitive periods of brain maturation, may translate into functional impairments that unfold progressively across the life span<sup>15</sup>. Within a life-course perspective, early neurodevelopmental compromise may initiate a trajectory of cognitive vulnerability that becomes increasingly visible as environmental demands intensify. Deficits in attention, memory, and executive functioning during early childhood can interfere with school readiness; these challenges may subsequently manifest as lower academic achievement and diminished educational attainment.<sup>16</sup>

Iron deficiency during the prenatal period and early infancy is associated with adverse behavioral and neurodevelopmental outcomes later in childhood and adolescence, particularly in areas such as attention, executive function, and emotional regulation<sup>17</sup>. Over time, such disadvantages may extend into reduced employment opportunities and earning potential, contributing to intergenerational cycles of socioeconomic vulnerability.

Framing childhood anemia within this continuum highlights its role not only as a clinical condition, but as a determinant of long-term human capital formation.<sup>18</sup>

### **The Outcomes**

Early neurodevelopmental disruptions associated with childhood anemia may initially manifest as intermediate functional impairments, including reduced attention span, deficits in memory and executive function, delayed language acquisition, slower information processing, and diminished school readiness. As cognitive demands increase with age, these early vulnerabilities may translate into measurable academic challenges, such as lower cognitive test scores, learning difficulties, behavioral problems, and reduced classroom engagement.<sup>19</sup>

Persistent educational disadvantages may contribute to poorer academic achievement, lower educational attainment, and ultimately reduced productivity and earning potential in adulthood. At a population level, these cumulative effects may reinforce intergenerational cycles of poverty and undernutrition, underscoring the broader socioeconomic implications of early-life anemia.<sup>20</sup> It is also important to be highlighted that the high IDA prevalence in developing countries, including Indonesia, is associated with stunting in children, suggesting a synergistic relationship.<sup>21</sup> There is not debatable that IDA is associated with the reduction of health status and quality of life of an individual, denoting that diagnosis and management of IDA are urgently required.<sup>22</sup> Nevertheless, experts agreed that a life course approach should be used as a framework to develop interventions in preventing IDA in every human life stages.<sup>23</sup>

## **Strength and Limitation**

This study offers a comprehensive synthesis of current evidence linking childhood anemia, particularly iron deficiency to cognitive and developmental outcomes across the life course. By integrating biological mechanisms with functional and socioeconomic consequences, the paper not only describing associations anemia within a broader neurodevelopmental and human capital framework, but also the inclusion of multiple study designs, ranging from randomized controlled trials to systematic reviews and longitudinal studies, strengthens the overall interpretation of findings.

Variations in diagnostic criteria for anemia/iron deficiency/IDA, differences in age groups, and inconsistencies in cognitive assessment tools limit direct comparability. Although associations are consistently observed, establishing causality remains challenging. Many studies are observational and not fully disentangle the independent effects of iron deficiency from confounding factors such as poverty, infection burden, caregiver stimulation, and overall nutritional status.

Taken together, while the evidence strongly suggests that childhood anemia poses meaningful risks to neurodevelopment, further well-designed longitudinal studies are needed to clarify the extent, timing, and reversibility of these effects.

## **Conclusion**

IDA among children still a major global health concern, especially in low- and middle-income settings. As iron deficiency remains the leading cause, its implications extend beyond low hemoglobin levels. The studies reviewed consistently show that inadequate iron during

critical periods of brain development can negatively influence attention, learning, behavior, and overall cognitive performance. Importantly, these effects may occur even before anemia becomes clinically apparent. The evidence suggests that childhood anemia affects development through a combination of biological vulnerability and environmental disadvantage, creating both immediate learning difficulties and potential long-term impacts on cognitive achievement and productivity.

These findings highlight that childhood anemia should be viewed not only as a nutritional disorder, but also as a condition with meaningful developmental and socioeconomic consequences. Early prevention such as screening, appropriate supplementation might be needed particularly during infancy and early childhood. Addressing IDA in children is therefore an investment in cognitive development and future human potential.

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### **Conflict of Interest**

Authors declare that there is no conflict of interests in this publication.

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