# Iron's Contribution to Children's Cognitive Development throughout the First 1000 Days of Life : A Literature Review

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**ABSTRACT**
Iron is an essential micronutrient that plays a critical role in brain development through processes such as myelination, neurotransmitter synthesis, energy metabolism, and synaptogenesis. Iron deficiency during the first 1000 days of life can disrupt neural network formation and lead to long-term cognitive impairments that are often irreversible. This literature review aims to analyze the contribution of iron during the first 1000 days of life to children's cognitive development and to emphasize the importance of nutritional interventions starting from pregnancy. This literature review was conducted using primary research articles published in English or Indonesian between 2020 and 2025. Relevant studies were identified through systematic searches in PubMed, ScienceDirect, Google Scholar, and ResearchGate, employing the PICO framework and appropriate keywords. Adequate iron status from pregnancy through early childhood is crucial for optimal cognitive development. Sufficient iron supports myelination, neurotransmitter synthesis, and the development of memory, language, and learning abilities. Conversely, iron deficiency during the first 1000 days of life is associated with reduced cognitive function, developmental delays, and an increased risk of long-term neurocognitive disorders. Optimal iron intake during the first 1000 days of life is essential to support maximal brain development, prevent long-term cognitive impairments, and enhance children's future intellectual potential.
**Keyword :** Iron, first 1000 days, cognitive development, iron supplementation, child

## Introduction

Iron plays a critical role in fetal growth and child development, particularly during the first 1,000 days of life (pregnancy up to 2 years of age). One of its primary functions is the formation of hemoglobin, the protein responsible for binding and transporting oxygen throughout the body. Beyond hematopoiesis, iron is essential for energy metabolism, immune function, digestion, and thermoregulation[1].

The first 1,000 days of life represent a critical window of opportunity, often referred to as the "golden period," during which events profoundly influence a child's future health, intelligence, development, and productivity[2,3]. During this period, the brain undergoes extraordinarily rapid development, forming approximately 1,000 new neural connections per second at an activity rate nearly twice that of an adult brain[4]. These neural connections establish the foundational architecture for cognitive and behavioral development, while also underpinning future mental health and learning capacity[4].

Iron is an essential micronutrient required to support this rapid brain development. Iron deficiency, particularly during the fetal and infancy stages, can lead to irreversible neurocognitive impairments, even after iron status has been corrected[5]. This occurs because iron is directly involved in fundamental brain processes, including myelination, neurotransmitter synthesis, and energy metabolism[6,7]. Biologically, iron performs several pivotal functions within the central nervous system. First, it serves as a cofactor for enzymes critical to myelination, the process of forming the myelin sheath that insulates nerve fibers in the brain and spinal cord. Iron deficiency impairs myelin formation, thereby slowing neural signal transmission. Second, iron is required for the synthesis of key neurotransmitters such as dopamine, serotonin, and norepinephrine, which regulate emotion, attention, and behavior. Third, iron supports cerebral energy metabolism by facilitating the production of fatty acids and ketones, the primary energy substrates for neurons. Fourth, iron contributes to dendritic arborization and synaptogenesis, thereby enhancing neuronal connectivity and the efficiency of neural networks[8].

Adequate nutrition, including sufficient iron intake, during the first 1,000 days of life is therefore directly linked to a child's capacity to grow, learn, and thrive. Recommended strategies include iron supplementation for pregnant women, optimal nutrition during lactation, and the provision of iron-rich complementary foods from six months to two years of age[2,9]. Iron deficiency during this critical period can result in reduced brain cell proliferation, impaired myelination, and incomplete neuronal maturation, ultimately affecting cognitive function[5,8]. Both animal studies and human observational research demonstrate that prenatal and early postnatal iron deficiency can induce permanent alterations in brain structure and chemistry particularly in the hippocampus, a region crucial for learning and memory[11,12].

Thus, iron makes an indispensable contribution to optimal brain growth and development during the first 1,000 days of life. Iron deficiency during this window can exert long-lasting adverse effects on cognitive function, even if iron status is later restored. This literature review aims to examine the role of iron during the first 1,000 days of life in supporting children's cognitive development and to underscore the importance of early nutritional interventions and supplementation.

**Material and Methods**

This study is a narrative literature review designed to examine the relationship between iron status and cognitive development in children during the first 1,000 days of life (from conception through the age of two years) and to highlight the critical importance of early nutritional interventions, particularly the provision of adequate iron beginning in pregnancy, as a cornerstone of optimal cognitive development. The review was structured using the PICO framework, defined as follows:

1. Population (P): Pregnant women, infants, and children aged 0–24 months within the first 1,000 days of life.
2. Intervention (I): Achievement of adequate iron status through dietary intake, iron supplementation, or optimal maternal iron status during pregnancy and lactation.
3. Comparison (C): Individuals with iron deficiency or those who did not receive iron supplementation or specific iron-targeted intervention.
4. Outcome (O): Cognitive and neurodevelopmental outcomes measured with validated, standardized instruments such as the Bayley Scales of Infant and Toddler Development (BSID), Mullen Scales of Early Learning (MSEL), Ages and Stages Questionnaire (ASQ), or equivalent tools.

A comprehensive literature search was conducted across four electronic databases: PubMed, ScienceDirect, Google Scholar, and ResearchGate. The following keywords and their combinations were used: “iron”, “iron deficiency”, “iron supplementation”, “cognitive development”, “neurodevelopment”, “infants”, “pregnancy”, and “first 1000 days”. Boolean operators (AND, OR) and truncation were applied as appropriate to maximize retrieval. Only articles published between 2021 and 2025 were considered. Selection of studies was performed in two stages (title/abstract screening followed by full-text review) based on predefined inclusion and exclusion criteria.

Inclusion and exclusion criteria were defined as follows: Studies were included if they were primary research articles published in national or international peer-reviewed journals between 2020 and 2025, written in Indonesian or English, and directly examined the relationship between iron status or iron supplementation and cognitive or neurodevelopmental indicators in children during the first 1,000 days of life. Studies were excluded if they were systematic reviews, meta-analyses, case reports, or did not directly assess cognitive outcomes.

The search strategy, guided by the PICO framework and relevant keywords, initially identified 54 scientific articles. During the identification stage, duplicates were removed and irrelevant records were excluded based on title and abstract screening, leaving 14 potentially eligible articles. These 14 articles underwent full-text review to assess their relevance to the first 1,000 days of life period and conformity with the predefined inclusion criteria, including suitability of study design. Ultimately, nine articles met all criteria and were included in the final analysis. Of these, seven were published in international peer-reviewed journals and two in Indonesian national journals. The selected studies employed a variety of designs, including randomized controlled trials (RCTs), prospective cohort studies, cross-sectional studies, and longitudinal studies.

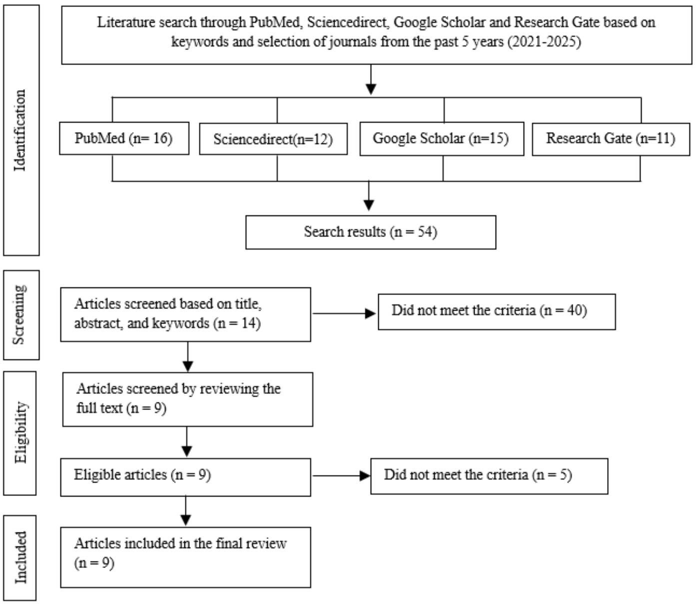


**Figure 1.** Flow diagram of the literature search strategy and screening process.

**Result**

Following the literature search and selection process, nine primary research articles that fully met the inclusion criteria were identified. A summary of the main characteristics and findings from these studies is presented in Table 1.

**Table 1.** Summary of Primary Research Studies on the Relationship Between Iron Status and Children's Cognitive Development (2021–2025)

| Study Title | Author(s); Year | Study Design | Sample | Key Findings | Conclusion |
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| Enteral Iron Supplementation in Infants Born Extremely Preterm and its Positive Correlation with Neurodevelopment; Post | German et al., 2021 | Post-hoc RCT | 692 preterm infants (gestational age 24–28 weeks) | Higher enteral iron doses were positively associated with Bayley-III cognitive scores at 2 years of age; each additional 50 | Iron contributes to enhanced cognitive development in preterm infants by supporting myelination and brain |

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| Hoc Analysis of the Preterm Erythropoietin Neuroprotection Trial Randomized Controlled Trial | | | | mg/kg of cumulative iron was associated with a 0.77-point increase in cognitive score. | synaptogenesis. |
| Iron status in early infancy is associated with trajectories of cognitive development up to pre-school age in rural Gambia | McCann et al., 2023 | Prospective cohort study | 179 infants aged 5–12 months (Gambia) | Higher ferritin levels from 5 months of age were associated with better cognitive and attention scores persisting into the preschool years. | Iron status established early in life contributes to sustaining long-term cognitive developmental trajectories through myelin formation and optimal neuronal function. |
| Importance of Maternal Iron Status on the Improvement of Cognitive Function in Children After Prenatal Iron Supplementation | Iglesias-Vázquez et al., 2023 | Prospective cohort study | 729 pregnant women and their children (Spain) | Iron supplementation during pregnancy in mothers with low iron stores was associated with higher IQ scores in their children at 4 years of age. | Prenatal iron plays a critical role in fetal brain development,particularly in synaptogenesis and myelination, which underpin later intelligence. |

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| Neurological Development and Iron Supplementation in Healthy Late-Preterm Neonates | Luciano et al., 2021 | Double-blind RCT | 102 healthy late-preterm infants | Iron supplementation at 1 mg/kg/day for 6 months significantly improved motor and cognitive scores (assessed by GMDS-II) compared to the control group. | Iron supplementation contributes to accelerated maturation of the nervous system and improved cognitive function in infants born late-preterm. |
| Chronic Iron Deficiency and Cognitive Function in Early Childhood | Luo et al., 2022 | Multi-country longitudinal cohort study | 400 children aged 6–24 months | Chronic iron deficiency from infancy was associated with a 6–9 point lower IQ score in preschool-aged children. | Iron deficiency impairs brain oxygenation and dopamine metabolism, resulting in adverse long-term effects on memory and attention functions. |
| Iron Status and Developmental Delay Among Children Aged 24–36 Months | Ferdi, Bardosono & Medise, 2022 (Indonesia) | Cross-sectional | 80 children aged 24–36 months (Jakarta, Indonesia) | Children with iron deficiency had a 6.9-fold higher risk of cognitive delay, particularly in | Iron deficiency leaves long-term adverse effects on cognitive development even after the |

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| | | | | the language and fine motor domains. | first 1,000 days of life have passed. |
| Impact of Iron Deficiency on Cognition in School Age Children | Sitorus & Salsabila, 2023 (Indonesia) | Cross-sectional | 120 children aged 6–12 years (West Java, Indonesia) | Children with iron deficiency exhibited significantly lower scores in memory, attention, and learning ability compared to their non-deficient peers. | The effects of early-life iron deficiency can persist into school age, underscoring the critical importance of adequate iron status during the first 1,000 days of life. |
| Associations of Maternal Dietary Iron Intake During Pregnancy with Infant Neurodevelopment | Qin et al., 2025 | Prospective cohort study | 483 pregnant women and their infants at 12 months of age (Tiongkok) | Higher maternal iron intake (particularly heme-iron) during the third trimester was associated with a reduced risk of neurodevelopmental impairment in infants at 12 months of age. | Adequate maternal iron intake directly contributes to optimal brain and cognitive development in infants during the first year of life. |
| Early Iron Supplementation of | Bah et al., 2023 | RCT (preprint) | 100 exclusively breastfed | Iron supplementation | Early iron supplementation |

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| Exclusively Breastfed African Infants: Randomized Double-Blind Efficacy Trial | infants aged 6–10 weeks (The Gambia) | significantly increased ferritin and hemoglobin levels, although cognitive outcomes were not assessed in this study. | significantly improves hematological status in infants; its potential long-term cognitive effects are currently under further evaluation. |

**Discussion**

**Relationship Between Iron Status and Children's Cognitive Development**

Synthesis of the nine primary studies summarized in Table 1 reveals a consistent and robust association between iron status and cognitive development during the first 1,000 days of life. Collectively, these studies confirm that adequate iron availability during this critical period plays an essential role in supporting key neurodevelopmental processes, including myelination, neurotransmitter regulation, and cerebral energy metabolism processes that form the foundational basis for learning, attention, and memory functions[13,15].

Studies by Luo et al. (2022), McCann et al. (2023), and Ferdi et al. (2022) consistently demonstrated that children with low ferritin levels or iron deficiency anemia exhibited significant cognitive delays. In contrast, McCann et al. (2023) further reported that higher ferritin concentrations from as early as five months of age were associated with superior cognitive developmental trajectories persisting into the preschool years, thereby reinforcing the critical importance of achieving adequate iron status early in life.

**Benefits of Iron Supplementation in Preterm and High-Risk Infants**

In preterm infants, iron supplementation has been consistently shown to improve cognitive, motor, and language outcomes. Among studies focusing on this vulnerable population, German et al. (2021) demonstrated that higher cumulative enteral iron doses were associated with significantly better Bayley-III cognitive scores at two years of age[13]. Similarly, Luciano et al. (2021) reported that daily supplementation of 1 mg/kg for six months markedly enhanced both motor and cognitive scores (assessed by GMDS-II) in healthy late-preterm infants[16]. These findings align with the characteristically low iron stores observed in preterm infants, underscoring the necessity of early and targeted iron intervention to support optimal brain maturation and neurodevelopmental outcomes.

**Maternal Iron Status During Pregnancy and Its Influence on Child Development**

Prenatal studies, including those by Iglesias-Vázquez et al. (2023) and Qin et al. (2025), underscore the pivotal role of adequate maternal iron status in supporting offspring neurodevelopment. Specifically, Iglesias-Vázquez et al. (2023) reported that iron supplementation tailored to mothers with low iron reserves during pregnancy was associated with enhanced IQ scores in children at four years of age[15]. Similarly, Qin et al. (2025) found that higher maternal iron intake particularly heme iron during the third trimester correlated with a reduced risk of neurodevelopmental impairments in infants[20]. These observations highlight the essential contribution of sufficient iron during gestation to fetal myelin formation and neuronal differentiation.

**Long-Term Impact of Iron Deficiency**

Longitudinal evidence strongly reinforces that the consequences of iron deficiency extend far beyond the immediate period of deficiency. Luo et al. (2022) demonstrated that chronic iron deficiency originating in infancy was associated with a reduction of up to 9 IQ points by preschool age[17]. Conversely, McCann et al. (2023) observed that higher ferritin levels established as early as five months of age were linked to more favorable cognitive trajectories persisting into the preschool years[14]. Taken together, these findings indicate that the adverse effects of early iron deficiency are not merely transient but may persist into later childhood, even after iron status has been subsequently corrected.

**Early Iron Intervention in Healthy Infants**

Early iron intervention also demonstrates promising benefits even in apparently healthy populations. Bah et al. (2023) reported that iron supplementation initiated as early as 6–10 weeks of age in exclusively breastfed infants significantly improved ferritin and hemoglobin levels, although cognitive outcomes were not assessed in that study[21]. These results suggest potential long-term neurodevelopmental advantages; however, further research incorporating validated neurocognitive endpoints is warranted to confirm such benefits.

**Iron Deficiency Patterns and Study Findings in Indonesian Children**

Research conducted in Indonesia aligns closely with international evidence. Ferdi, Bardosono, and Medise (2022) reported that children aged 24–36 months with iron deficiency faced an almost seven-fold higher risk of cognitive delay, particularly in language and fine motor domains[18]. Similarly, Sitorus & Salsabila (2023) demonstrated that the adverse effects of iron deficiency during the first 1,000 days of life can persist into school age, manifesting as reduced memory, attention, and learning abilities[19]. These findings underscore that iron deficiency anemia remains a major public health nutrition problem in Indonesia, with serious long-term implications for human capital development and national productivity.

**Factors Contributing to Heterogeneity Across Studies**

The heterogeneity observed across studies can be largely explained by several key factors. First, the timing of iron intervention is critical; supplementation initiated within the first 6 months of life consistently demonstrated stronger cognitive benefits than interventions begun after 12 months of age[13,17]. Second, baseline iron status significantly influenced outcomes, with clear benefits of supplementation observed primarily in children who were iron-deficient or had low iron stores at the outset, whereas iron-replete children showed minimal or no additional gain[17,18]. Third, differences in the sensitivity and domains assessed by various cognitive measurement tools (e.g., Bayley-III, GMDS-II, MSEL, ASQ) contributed to variations in reported effect sizes[18,20]. Finally, the presence of concurrent deficiencies of other micronutrients known to affect brain development such as zinc, folate, and vitamin B12 may have modified or confounded the isolated effects of iron in some studies[5,9].

**Biological Mechanisms Underlying the Effects of Iron on Cognitive Development**

The observation that iron supplementation yields the most pronounced benefits in preterm infants and pregnant women with low iron reserves is fully consistent with the established biological roles of iron. Iron deficiency during critical developmental windows disrupts key neurobiological processes, including myelination, neuronal energy metabolism, and the synthesis of neurotransmitters such as dopamine and serotonin neurochemicals that are essential for memory, attention, and executive function[6,8,10,11]. Consequently, vulnerable populations with compromised iron status derive the greatest neurodevelopmental advantage from timely supplementation.

In conclusion, this review firmly establishes iron as an indispensable and non-substitutable factor for optimal cognitive development in children. Ensuring adequate iron status throughout the first 1,000 days of life whether through targeted supplementation in high-risk groups or balanced dietary intake represents a cornerstone public health strategy to prevent deficiency and enable every child to reach his or her full developmental potential. Optimal iron provision during this critical period not only maximizes cognitive outcomes but also prevents irreversible long-term deficits.

## Conclusion

Iron plays an irreplaceable role in supporting optimal cognitive development during the first 1,000 days of life. Iron deficiency during this critical window disrupts fundamental neurodevelopmental processes including myelination, neurotransmitter synthesis, and cerebral energy metabolism leading to long-term cognitive and motor deficits that are often difficult or impossible to fully reverse. The beneficial effects of iron supplementation are most pronounced in populations with established deficiency or at high risk of deficiency. Consequently, targeted early interventions comprising iron supplementation for pregnant women and high-risk infants, routine monitoring of iron status, and comprehensive nutritional education represent strategic and evidence-based measures to ensure every child can achieve his or her maximum brain developmental potential.

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