

The relationship between infant iron status and risk of neurological impairment

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Abstract

Background Iron deficiency (ID) is a commonly found nutritional disorder and a persistent problem, especially in Indonesia. Iron deficiency during the critical period in childhood brain development is estimated to cause irreversible damage that hinders infant development.

Objective To determine the relationship between infant iron status and neurological development.

Methods We conducted a cross-sectional study at the Growth and Development Outpatient Clinic, Prof. Dr. R. D. Kandou Hospital, Manado, from March to May 2015. By consecutive sampling, we obtained 44 healthy infants aged 7 to 10 months who fulfilled the inclusion criteria. Infants with a history of perinatal complications, such as head trauma, hypoglycemia, respiratory distress syndrome, infection, or malaria were excluded. Subjects' serum hemoglobin and ferritin were examined for iron status. Infants' risk of neurological impairment was assessed by the Bayley Infant Neurodevelopmental Screener (BINS). Results were analyzed by descriptive analysis for the characteristics and Spearman's rank correlation coefficient analysis for the relationship between iron status and neurological development.

Results From 14 infants with ID, 8 infants had a high risk of developmental impairment. Of the 30 non-ID subjects, 4 infants had a high risk of developmental impairment. Of the 30 non-ID infants, 16 infants had a low risk of impaired development, while 2 infants with ID had low risk of developmental impairment. Spearman's rho revealed that infant iron deficiency was significantly associated with high risk of neurological impairment. ($r = -0.547$; $P < 0.0001$).

Conclusion Lower serum ferritin levels (iron deficiency) is significantly associated with greater risk of impaired neurological development in infants aged 7-10 months. [Paediatr Indones. 2017;57:291-4 ; doi: <http://dx.doi.org/10.14238/pi57.6.2017.291-4>].

Keywords: iron deficiency; infant neurological development; Bayley Infant Neurodevelopmental

Nutrition has an important role for achieving optimal growth and development in childhood.¹ Iron deficiency is a common nutritional disorder and one of the main causes of nutritional anemia, especially in Indonesia.² Ringorongo reported that the incidence of iron deficiency (ID) in infants aged 0-12 months was 7.6%.³ In ID cases, not only tissue delivery of oxygen is compromised, but proliferation, growth, differentiation, myelinogenesis, immune function, energy metabolism, absorption, and biotransformation are also affected, leading to abnormal growth and behaviour.⁴ So far, there has been no consensus

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reported incidence of ID in Indonesian infants aged 0-6 months, because no gold standard cut-off point for ferritin levels are available for the determination of ID deficiency in such infants. Currently, in Manado, particularly in Prof. Dr. RD Kandou Hospital, there is limited data on the prevalence of ID and the relationship between iron status and neurological development in infants younger than 12 months.

The aim of this study was to assess for a potential relationship between infant iron status and impaired neurological development.

Methods

This cross-sectional study was performed from March to May 2015 and included all consecutive healthy infants aged 7 – 10 months at the Growth and Development Outpatient Clinic, Prof. Dr. R. D. Kandou Hospital, Manado. We estimated a required sample size of 32 subjects, based on $\alpha=0.05$ and power=80%. The inclusion criteria were infants who registered as patients at our hospital (either at the clinic or by birth), with clear childbirth medical records, good nutritional status, born full term with birth weight $\geq 2,500$ grams, Apgar score \geq eight at the 5th minute, and with parental consent. The exclusion criteria were history of perinatal complications, including head trauma, hypoglycemia, respiratory distress syndrome, infection, or malaria.

Iron deficiency was defined as serum ferritin < 12 $\mu\text{g/mL}$,⁵ with or without anemia. Anemia was defined as hemoglobin level < 11 g/dL.⁶ Infant neurological development status was assessed by BINS. This examination is a combination of neurological and

developmental evaluations of four conceptual areas of ability, i.e., basic neurological function, receptive function, expressive function, and cognitive processes. Results of the BINS examination were categorized as high, moderate, or low risk.⁷ History-taking and physical examinations were performed to assess for infection and inflammation, weight (kg), and length (cm). Based on Z-score, nutritional status was classified as well-nourished (weight-for-length index -2SD to 2SD). Venous blood specimens (5 mL) were drawn by laboratory staff and tested for serum hemoglobin (Hb) and ferritin levels. The Hb level was measured with cyanmethemoglobin assay and serum ferritin level was measured with immunochemiluminiscence (ICMA).

Descriptive data analysis was used for the subjects' characteristics and correlative data analysis with Spearman's rho was used to assess for a possible association between infant iron status and neurological development. This study was approved by the Ethics Committee of Sam Ratulangi University Medical School, Manado.

Results

Initially, 50 children were eligible for this study. However, six children were excluded due to parental refusal to have infants' blood drawn, leaving a total of 44 subjects.

The prevalence of ID in our subjects was 32%. These subjects comprised of eight males and six females. The highest prevalence was found in the 10-month age group (8/14) (Table 1).

Table 1. Baseline characteristics of subjects

Characteristics	Iron deficient (n=14)	Non-iron deficient (n=30)	Overall (N=44)
Age group, n			
7 months	2	4	
8 months	3	6	
9 months	1	11	
10 months	8	9	
Mean age (SD), days			270.39 (31.78)
Sex, n			
Male	8	14	
Female	6	16	
Mean hemoglobin (SD), g/dL			11.37 (1.11)
Mean ferritin (SD), $\mu\text{g/L}$			40.59 (36.24)

Of the 14 infants with ID, 8 infants had high risk and two infants had low risk of impaired neurological development. Of 30 non-iron deficient infants 4 infants had high risk and 16 infants had low risk (Table 2). The relationship between infant iron status and neurological development was analyzed by Spearman's rho, revealing a moderate significant inverse association ($r = -0.547$; $P < 0.0001$).

risk of impaired neurological development. Other studies have reported a similar relationship between iron deficiency and neurological development in infants.¹⁴⁻¹⁷

A limitation of our study was that we did not assess other factors that may have affected iron status and neurological development, such as upbringing, genetics, quality of food, and maternal iron status.

Table 2. Distribution of infants based on iron status and neurological development

Iron status	Neurological development			Total, N
	Low risk, n	Moderate risk, n	High risk, n	
Deficient	2	4	8	14
Non-deficient	16	10	4	30

Discussion

Iron deficiency usually occurs in the second year of life, due to decreased iron intake and rapid growth in the first year. Normal infants need to absorb approximately 0.8 mg/day of dietary iron (0.6 mg for growth and 0.2 mg to replace ongoing losses).⁸ Though anemia is a common manifestation of iron deficiency, other effects of iron deficiency on various tissues, organs, and systems are usually under recognized. Impaired brain development, as well as cognitive, behavioral, and psychomotor impairment are the most worrisome manifestations of iron deficiency. Studies have demonstrated that some of these impairments occurring during periods of brain growth spurts (<2 years age) may be irreversible.⁹

The prevalence of ID in our subjects was 32%, similar to that of a cross-sectional study by Apriyanti *et al.* in children aged 6-59 months.¹⁰ We noted that eight males and six females had ID. Gender differences in ID reportedly only affect adolescents, as females are at higher risk due to menstruation and rapid growth.¹¹ The highest prevalence was found in the 10-month age group (8/14), perhaps as a result of inadequate iron in the diet, being bottlefed with non-iron fortified formula, or maternal iron status.^{12,13}

The relationship between infant iron status and neurological development was analyzed using Spearman's rho, with $r = -0.547$ with $P < 0.0001$. This finding was statistically significant. The lower the serum ferritin levels (iron deficiency), the higher

In conclusion, lower serum ferritin level (iron deficiency) is significantly associated with higher risk of impaired neurological development. Hence, we recommend iron supplementation and some brain stimulation for infants with moderate to high risk of impaired neurological development. However, further study should be performed including analyzing several factors that can affect iron status and neurological development, such as upbringing, genetics, quality of food, and maternal iron status.

Conflict of Interest

None declared.

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