Original article

Stunted and ferritin levels in children aged 0-24 months: Does gender influence the incidence?

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Abstract. *Background and aim:* Stunted remains a global nutritional problem in developing countries, such as Indonesia. Iron deficiency is common among stunted individuals due to the depletion of iron reserves, which induces hypoxia in hepatic cells and inhibits protein synthesis, including insulin-like growth factor 1 (IGF-1). Serum ferritin, the storage form of iron, is a sensitive marker for detecting iron reserves. This study aims to assess growth faltering, stunted, and ferritin levels in children under two years old. *Methods:* This study used a cross-sectional approach using secondary data from medical records of children under two years old who visited the Nutrition and Metabolic Diseases outpatient clinic at Husada Utama Hospital between July 2018 and June 2020. Data were analyzed using SPSS version 21.0 (IBM, UK), including normality and homogeneity tests, independent sample t-test (or Mann-Whitney U test), chi-squared test, and Fischer's exact test. Bivariate analysis was conducted to determine relationships between variables. *Results:* Among the subjects, 52 children (44.83%) were undernourished. The incidence of stunted or severe stunted was higher in males than in females (44.83% or 26 children vs. 25.86% or 15 children). Ferritin levels were significantly lower in males compared to females (29.69 + 24.80 μg/dl vs. 53.38 + 95.36 μg/dl, $p = 0.011$). A weak negative correlation was observed between low ferritin levels and male sex ($r = -0.184$, $p = 0.048$). Male children had a 2.450-fold higher risk of low ferritin levels (95% CI [0.994-6.042], $p = 0.052$) and a 2.329-fold higher risk of stunted (95% CI [1.064-5.097], $p = 0.034$). However, no significant correlation was observed between stunted and low ferritin levels ($r = 0.066$, $p = 0.478$). *Conclusions:* A correlation was found between sex and low ferritin levels, with males at a higher risk for both low ferritin levels and stunted among children aged 0-24 months old.

Key words: ferritin, stunted, growth faltering, iron reserve

Introduction

Stunted is the most common form of undernutrition affecting children under five years old (1). It is a result of chronic malnutrition (2), which remains a global nutritional problem, particularly in developing countries such as Indonesia. Chronic malnutrition begins with weight faltering, which has significant short- and long-term impacts on growth and development (3), including reduced intelligence quotient (IQ) by 2.71 points (3), diminished learning ability, impaired adaptation, and increased disease susceptibility (4). Iron is essential for multiple metabolic processes, including oxygen transport, DNA synthesis, and electron transport (5). For humans, iron is needed to produce red blood cells (6) and contributes to immune function (7), acting as a mediator and acute-phase reactant in immune responses (8). Iron is also involved in energy production and cellular metabolism through its participation in enzymes, cytochromes, NADPH, and flavoproteins, particularly in oxidative phosphorylation and ATP synthesis. Through its role in energy production, iron supports cell proliferation and growth by improving oxygenation, hemoglobin (Hb) levels, and the production of growth factors, including insulin-like growth factor 1 (IGF-1) (9). In oxygen transport, iron binds oxygen to porphyrin ring molecules in hemoglobin, facilitating its movement from the environment to terminal oxidases. In addition, iron in the form of myoglobin aids oxygen diffusion in tissues (8). Iron is also involved in bone growth and remodeling, which are critical during infancy and childhood due to bones being highly metabolical active tissue. It contributes to collagen I production, a crucial component of bone, and acts as an enzyme (hydrolase) with catalytic activity in osteoclasts (10). Moreover, iron in the form of cytochrome P450 plays a role in vitamin D activation, while other iron-containing proteins support mitochondrial activity and osteoclast function. Through its indirect influence on gonadal steroids, iron also affects the activity of growth factors such as IGF-1 in the bones (11). Health problems such as iron deficiency anemia (IDA) are common in stunted populations due to the depletion of iron reserves (12,5). The depletion of iron reserves induce hypoxia in hepatic cells and inhibits protein synthesis, including IGF-1 (13). This explains why iron deficiency can impact growth, as IGF-1 is involved in both iron metabolism and protoporphyrin synthesis (1, 5). Serum ferritin, the storage form of iron, is a sensitive marker for detecting iron reserves. When iron levels drop, ferritin levels decrease accordingly (5, 13). Regular ferritin assessments are crucial for preventing stunted during childhood, particularly in children over two years old. This study aims to assess growth faltering, stunted, and ferritin levels in children under two years.

Methods

This study used a cross-sectional approach using secondary data from medical records of children under two years who visited the Nutrition and Metabolic Diseases outpatient clinic at Husada Utama Hospital between July 2018 and June 2020. Subjects included in this study did not have congenital diseases such as cerebral palsy, growth hormone deficiency, cardiovascular diseases, thyroid disorders, malignancies, or chronic renal failure. Only complete medical records were used as the data source for this study. The minimum required sample size for this study was 116, based on the following sample size formula.

$$n1 = n2 = \frac{(za\sqrt{2PQ} + Z\,b\sqrt{P1Q1 + P2Q2})^2}{(P1 - P2)^2}$$

Undernutrition was defined according to the WHO Child Growth Standards, with undernutrition indicated by a z-score of -2.0 SD or less on the WHO growth curve (14).

Data analysis

All data including body weight, body length, ferritin levels, weight-for-age z-score (WAZ), length-for-age z-score (LAZ), and weight-for-length z-score (WLZ) were analyzed using SPSS version 21.0 (IBM, UK). Statistical tests performed included normality and homogeneity tests, independent sample t-test (or Mann-Whitney U test), chi-squared test, and Fischer's exact test. Bivariate analysis was conducted to determine relationships between variables. This study was approved by the Health Research Ethics Committee of Airlangga University with a certificate number 30/EC/KEPK/FKUA/2020 on November 16, 2020.

Results

A total of 116 subjects were recruited for this study, comprising 58 males (50%) and 58 females (50%) aged one to 24 months, divided based on sex. The characteristics of the subjects are summarized in Table 1. The incidence of undernutrition remained prevalent, affecting 55 children (44.83%). There were no significant differences between males and females in terms of age, body length, WAZ, WAZ categories, LAZ, WLZ, WLZ categories, one-month weight increment, one-month length increment, and ferritin levels ($p > 0.05$). However, males had significantly higher body weight compared to females (8.82 + 1.33 kg vs. 8.16 + 1.18 kg, $p = 0.005$). The incidence of stunted or severe stunted was more common in males than

Table 1. Characteristics of the subjects.

Characteristic	Total (n = 116)	Male (n = 58) Mean + SD	Female (n = 58) Mean + SD	p
Age, month	13.66 + 5.43	13.72 + 5.34	13.60 + 5.57	0.905[1]
Age categories				
0-12 months old	52 (44.83)	27 (46.55)	25 (43.10)	0.852[2]
13-24 months old	64 (55.17)	31 (53.45)	33 (56.90)	
Infections				
No infection	104 (89.66)	52 (89.66)	52 (89.66)	0.261[3]
Urinary tract infection	9 (7.56)	3 (8.62)	6 (10.34)	
Pulmonary infection	1 (0.86)	1 (1.72)	0 (0)	
Urinary tract and pulmonary infection	2 (1.72)	2 (3.45)	0 (0)	
Body weight, kg	8.49 + 1.29	8.82 + 1.33	8.16 + 1.18	0.005[1*]
Body length, cm	73.43 + 5.20	73.82 + 5.55	73.03 + 4.84	0.419[1]
WAZ	-1.11 + 1.44	-1.17 + 1.19	-1.05 + 1.66	0.827[4]
WAZ categories, n (%)				
Severely underweight	5 (4.31)	2 (3.45)	3 (5.17)	0.468[3]
Underweight	20 (17.24)	8 (13.79)	12 (20.69)	
Normal weight	87 (75)	47 (81.03)	40 (68.97)	
Overweight	2 (1.72)	0 (0)	2 (3.45)	
Obese	2 (1.72)	1 (1.72)	1 (1.72)	
LAZ	-1.18 + 2.35	-1.50 + 1.73	-0.88 + 2.82	0.139[4]
LAZ categories, n (%)				
Severely stunted	12 (10.34)	5 (8.62)	7 (12.07)	0.031[3*]
Stunted	29 (25)	21 (36.21)	8 (13.79)	
Normal stature	70 (60.34)	31 (53.45)	39 (67.24)	
Tall	5 (4.31)	1 (1.72)	4 (6.90)	
WLZ	-0.71 + 0.98	-0.64 + 1.01	-0.78 + 0.95	0.423[1]
WAZ categories, n (%)				
Wasted	10 (8.62)	5 (8.62)	5 (8.62)	1.000[3]
Severely wasted	2 (1.72)	1 (1.72)	1 (1.72)	
Good nutrition	104 (89.66)	52 (89.66)	52 (89.66)	
One-month weight increment (kg)	0.37 + 0.28	0.35 + 0.33	0.39 + 0.22	0.520[1]
Weight faltering, n (%)				
Weight faltering	48	28	20	0.187[2]
Adequate weight gain	68	30	38	
One-month length increment (cm)	1.12 + 1.30	1.16 + 1.19	1.08 + 1.42	0.731[1]
Growth faltering, n (%)				
Growth faltering	63 (54.31)	29 (50)	34 (58.62)	0.456[2]
Adequate length increment	53 (45.69)	29 (50)	24 (41.38)	
Ferritin, μg/dl	41.53 + 70.38	29.69 + 24.80	53.38 + 95.36	0.011[4]
Ferritin category, n (%)				
Low level	27 (23.28)	18 (31.03)	9 (15.52)	0.078[2]
Normal	89 (76.72)	40 (68.97)	49 (84.48)	

[1]Independent sample t-test; [2]Fischer's exact test; [3]Chi-square test; [4]Mann-Whitney U test; [*]Significant if $p < 0.05$.

Table 2. Comparison of ferritin levels between male and female children.

	Ferritin μg/dl	Male n = 58	Female n = 58	r (phi)	p
Mean + SD	41.53 + 70.38	29.69 + 24.80	53.38 + 95.36	-	0.011[1]
Low level	27 (23.28)	18 (31.03)	9 (15.52)	-0.184	0.048
Normal	89 (76.72)	40 (68.97)	49 (84.48)		

[1]Mann-Whitney U test.

Table 3. Correlation of ferritin levels with stunted/severely stunted children.

	Ferritin μg/dl	Stunted n = 41	Non-stunted n = 75	r (phi)	p
Mean + SD	41.53 + 70.38	34.17 + 32.19	45.56 + 84.21	-	0.289[1]
Low level	27 (23.28)	8 (19.51)	19 (25.33)	-0.066	0.478
Normal	89 (76.72)	33 (80.49)	56 (74.67)		

[1]Mann-Whitney U test.

in females (44.83% or 26 children vs. 25.86% or 15 children). In addition, ferritin levels were significantly lower in males compared to females (29.69 + 24.80 μg/dl vs. 53.38 + 95.36 μg/dl, p = 0.011).

Table 2 summarizes ferritin levels in children aged 0-24 months old. A weak negative correlation was observed between low ferritin levels and sex (r = -0.184, p = 0.048). Male had a 2.450-fold higher risk of low ferritin level (95% CI [0.994-6.042], p = 0.052) at the age of 0-24 months. In addition, males had a 2.329-fold higher risk of being stunted (95% CI [1.064-5.097], p = 0.034).

Table 3 summarizes the correlation between stunting and ferritin levels in the children. No correlation was observed between stunting and low ferritin levels (r = 0.066, p = 0.478).

Discussion

Undernutrition, which includes stunting, wasting, and being underweight (15), remains a global health problem, contributing to almost half of all child deaths worldwide (16). It has both short- and long-term consequences, such as growth failure and impaired intellectual development, and can also lead to chronic illness in adulthood (17). This study revealed that males had higher body weights than females, possibly due to females having a greater fat mass and lower fat-free mass which impacts their energy intake and calorie needs (18). Brogan et al. (2010) similarly found a distinct difference in body weight gain between males and females during the first year of life, with males generally having higher body weights. However, after 12 months, females tended to have higher body weights (19). These differences in body weight gain suggest that males have a higher risk of being obese compared to females (18). This study also found that stunting was more prevalent in males than in females, which is consistent with another study that associated the male sex with stunting (p = 0.047) (20). Several studies have shown that the male sex is a risk factor for stunting (21, 22), with a study suggesting that males had a 2.62-fold higher risk of stunting than females (23), which is consistent with the findings of this study. Boys, in general, are more susceptible to various forms of undernutrition, including wasting, stunting, and being underweight (24). The difference in growth between males and females begins in utero, with males experiencing poorer outcomes than females. Female newborns are physiologically more developed than male newborns and can better withstand unfavorable conditions, functioning similarly to 4-6-week-old male infants. In addition, male newborns are more vulnerable to infections due to weaker immune responses and lower antibody production. Leptin, which plays a role in maintaining the immune response, is also higher in females than males. Interestingly, the sex difference in stunting tends to disappear after the age of 30 months in males (25). This study found that ferritin levels were significantly lower in males than in females. Antunes et al. (2012) found that males were 3.3 more likely to have low ferritin levels (95% CI [1.7-6.3], $p < 0.001$) (26), which is consistent with this study. Higher weight gain in males likely contributes to their increased vulnerability to iron deficiency anemia (IDA) (26). A multi-country trial also found that males at five (108.7 g/l vs. 111.4 g/l, $p = 0.004$) and 11 (106.2 g/l vs. 111.0 g/l, $p = 0.001$) months of age had significantly lower hemoglobin (Hb) and serum ferritin levels (14.3 g/l vs. 21.1 g/l, $p = 0.001$) compared to females, increasing their risk of IDA by 3.3-fold (27). Woodhead et al. (1991) observed that preadolescent girls absorbed iron more efficiently than boys (45% vs. 35.2%), possibly due to hormonal (28). Cord serum ferritin levels were also higher in female infants (166 + 110 μg/l vs. 123 + 77 μg/l) (29), while hepcidin levels were higher in male infants (38.3 ± 9.06 μg/l vs 34.3 ± 8.16 nmol/L, $p = 0.003$), contributing to a higher risk of iron deficiency in male infants (30). Another study also revealed that males had a greater risk of iron deficiency, which is significantly associated with developmental delays in motor skills, language, and adaptive behavior (31). This study revealed a correlation between male sex and low ferritin levels. Blood analyses at the age of four, six, and nine months showed that male infants had significantly lower Hb, mean corpuscular volume (MCV), and ferritin levels compared to females, with males having a 10-fold risk of IDA by the age of 9 months. However, the sex difference in ferritin levels may be influenced by race, hormone differences, such as insulin and leptin, genetics, and maternal factors (32). Another study suggested that differences in iron metabolism during the first year of life, lean body mass increment, and genetic factors may explain the higher risk of IDA in males (26). A study in Nepal involving young children aged 6-59 months found that those under two years had a higher risk of IDA, with stunting increasing the risk of anemia by 1.55 times (95% CI [1.11- 2.17] underweight status increasing the risk by 1.69 times (95% CI [1.14-1.93]) (33). Other research found that stunting increases the risk of anemia by 2.72 times (95% CI [2.063-3.582]) (34). However, this study found no significant correlation between stunting and low ferritin levels. A study found a negative correlation between BMI-for-age z-score and iron status, suggesting that adiposity may reduce iron levels. BMI-for-age z-score correlated with soluble transferrin receptor or sTfR ($r = 0.209$, $p < 0.001$) and serum ferritin or SF ($r = 0.214$, $p < 0.001$). Waist circumference and fat mass also correlated with sTfR and SF in children aged 6-12 years old (35). Another study found severely stunted children had a 3.6-fold higher risk of reduced Hb levels, indicating a 40% higher risk of anemia (95% CI [-5.7; -1.5], $p = 0.001$) (36). Other factors of stunting may include poverty and infection. In this study, the lack of a significant correlation between stunting and low ferritin levels may be due to socioeconomic factors, as this study was conducted in a private hospital serving a middle-to-upper socioeconomic population, where children may have better access to high-quality diets.

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