



Stunting and Head Circumference Growth in The First 3 Years of Life

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Abstract

The prevalence of stunting in Indonesia still exceeds WHO recommended standards. Stunting increases the risk of inhibition of brain growth. Head circumference is one of the parameters of brain growth. The study aimed to prove the mean head circumference growth difference between the stunted and non-stunted groups in the first 3 years of life. Another goal was to prove the relationship between zinc intake and zinc levels in toddlers on head circumference. The cohort study involved 50 subjects who were observed from birth to the age of 3 years and were born at Sultan Agung Islamic Hospital and Bangetayu Health Center Semarang City. The mean head circumference growth in the stunting group was lower than in the non-stunting group (4.1 v.s 4.6), $p=0.043$. The mean head circumference of stunted toddlers was smaller than that of non-stunted toddlers (44.9 vs. 47.2), $p=0.000$. There was no relationship between daily zinc intake and zinc levels of toddlers with stunting, $p>0.05$. The growth of the head circumference of stunted toddlers was lower than in the non-stunted group, as well as the head circumference was smaller than in the non-stunted group.

Introduction

The Indonesian Nutrition Status Study (SSGI), 2021 found that the stunting rate in Indonesia is quite high, at 24.4%. It is still above the WHO-recommended figure, which is below 20%. Indonesia's target stunting prevalence rate in 2024 is 14% (Kemenkes RI, 2021; Menpan, 2022). Anthropometric measurement is a measurement used as a sign to determine growth disorders in children. Three parameters that are commonly used to monitor growth in children are weight, height, and head circumference. Head circumference (HC) or occipital frontal circumference (OFC) is often used as a reflection tool for brain growth. A measurement that is often overlooked by parents is the measurement of head circumference. Monitoring head circumference can be used as a simple parameter reflecting brain size and

growth (Nicolaou *et al.*, 2020) its association with cognitive function remains unclear. We sought to understand the relationship among various biological and socioeconomic risk factors, HC and cognitive development. Methods We analysed data across resource-poor settings in Bangladesh, India, Nepal, Peru, South Africa and Tanzania from the Etiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development longitudinal birth cohort study. Participating children were enrolled and followed up between 2009 and 2014. A final sample of 1210 children aged 0-24 months were included in the analyses. The main outcomes were HC for age Z-score and cognitive, gross motor and language scores from Bayley Scales of Infant Development-III tests. Length, weight and HC were measured

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monthly, and cognitive tests were administered at 6, 15 and 24 months of age. To disentangle the associations between risk factors and HC from linear growth and to distinguish the direct and indirect effects of these risk factors on cognitive function, we conducted mediation analysis using longitudinal models to account for all data measured during follow-up. Results Average HC-for-age Z-score (HCAZ).

Based on previous research, low head circumference is significantly associated with stunting (Sindhu *et al.*, 2019). Smaller head circumference at the age of 2 years is associated with cognitive abilities, so it is said that the most optimal brain development occurs in the first 1000 days of life (Qian *et al.*, 2021; Koshy *et al.*, 2021). Other studies have shown that head circumference growth does not predict cognitive or fine motor scores, but predicts better gross motor skills in boys (Dupont *et al.*, 2018).

The fastest child growth occurs in the first 1000 days of life, at this time formation of the brain and other organs occurs. Disorders that occur at this time not detected and not intervened properly will cause long-term effects that can reduce their quality of life. Head circumference measurements need to be carried out every month until the age of 2 years as early detection for disorders that may occur in children's brain development. The growth and development of children are very dependent on the adequacy of nutrition obtained during the first 1000 days of life. A multicenter study by Scharf looked at children from birth to 24 months of age in low-middle-income families in 8 countries. The study concluded that there was a tendency for an increase in cognitive scores to be associated with head circumference compared to body length in children aged the first 24 months (Scharf *et al.*, 2018).

Previous studies have shown that zinc supplementation given to mothers before the 24th week of gestation can prospectively increase the head and chest circumference of neonates (Zhou *et al.*, 2021). Research in Nepal states that zinc supplementation has a beneficial effect on the growth rate of infants (Surkan *et al.*, 2012)(2). Research in India proves that zinc supplementation increases the average body length gain compared to controls

but there is no difference in the increase in head circumference in infants aged 6 months (Miiir, 2017).

The scope of services of RSI Sultan Agung includes residents of the city of Semarang (urban) as well as residents of the Demak area (rural). In 2020 the stunting rate in Semarang City was 3.31% while Demak is 6.05% higher (RepJogja, 2022; Dinkominfo Demakkab, 2022). To support the Indonesian government's efforts to reduce the stunting rate by 14% and to detect the risk of head circumference growth inhibition in stunting cases, it is still necessary to study the effect of stunting on head circumference growth. The results of previous research on the role of zinc on linear growth have not been consistent, so it is still necessary to observe the effect of zinc early in life and at the age of 3 years on the head circumference of toddlers.

Method

This cohort study involved 50 children aged 3 years who were born healthy and at term with a history of births at Sultan Agung Hospital and Bangetayu Public Health Center, Semarang City. The growth of head circumference (HC) was measured when the infant was born and when the infant was 3 years old, the measurement was carried out with an inelastic measuring tape around the head, starting from the midpoint between the eyebrows, placing 1 finger above the eyebrows, circling towards the back to the lower part. Most prominently at the back of the head, back to the starting point of measurement, or the greatest length of the occipitofrontal circumference (Margaret McCarthy & Nugent, 2015) both in utero and early postnatally. Some of these are intrinsic, such as gonadal steroids, while others are externally imposed, such as maternal nutrition or stress. All of these variables can have enduring consequences by imposing epigenetic modifications on the genome that alter set points for activation in adulthood, thereby reflecting early-life programming. In this review, we provide an overview of the most well studied epigenetic processes that occur in the brain. Next, we summarize the studies to date that have implicated gonadal steroids, stress exposure, and nutritional deficits/excess

in changes in neural epigenetic marks, which ultimately alter brain development, but we also note that this field is still in its infancy. Epigenetic regulators include DNA methylation, changes to the chromatin via acetylation and other chemical modifiers, and noncoding RNAs all of which impact the expression of specific genes. In this way gonadal steroids in the developing male fetus direct masculinization of adult brain and behavior, and similarly in utero exposure to a high-fat or calorie-restricted diet impacts glucose metabolism and body fat composition throughout life. Stress early in life changes the sensitivity of the hypothalamic-pituitary-adrenal (HPA). The average annual head circumference growth is calculated based on the difference between the size of the head circumference at birth at the age of 3 years and then divided by 3, the result is cm/year. Determination category of Head Circumference toddlers based on the WHO Z-score curve, it is said that the head circumference is less (small) if $< -2SD$ - $-3SD$, while normal is between $-2SD$ - $+2SD$. None of the children with $LK > +2SD$ or $< -3SD$.

Daily zinc intake, including energy, protein, and calories was measured through a 2 x 24-hour food recall approach. Direct interviews were conducted to ask about food consumed in the last 2 consecutive days. The history of eating for the first 24 hours was recorded, then it was backed up to the previous 1-2 days. All food consumed by toddlers was recorded in detail including the type, portion (volume) of food, and finished or not. The questionnaire was filled out and asked directly to the caregiver who most often took care of children. Calculation of the amount of zinc intake, calories, and protein is calculated using *Nutrisurvey* application. Calculation of the amount of zinc intake, calories, and protein is calculated using *Nutrisurvey* application. Zinc needs of toddlers aged 1-3 years according to nutritional adequacy rate Kemenkes RI., 2019 and RDA (*Recommended Dietary Allowances*) is 3 mg/day, and zinc intake is considered sufficient at 3 mg/day, while daily protein is considered sufficient at 20 g/day (Kemenkes RI, 2019; National Institute of Health, 2022). Examination of blood serum zinc levels in this study was carried out in the GAKI Faculty of

Medicine laboratory, Diponegoro University, Semarang.

Children's height measurements are made with a microtome with an accuracy of 0.1 cm which is permanently mounted on a sturdy wooden ruler for easy portability and stability during measurements. Height was measured by standing barefoot on the wall right in front of the microtome. Body weight was measured using a digital scale and the child stood still on the scale with an accuracy of 0.1 g. Stunting according to the Ministry of the Health Republic of Indonesia based on WHO anthropometry, namely height according to age is below $-2SD$ HAZ score (Kemenkes RI, 2019).

Average height growth is height growth in the first 3 years of life. The difference between birth length and height at age 3 years. The stunting category is HAZ (height for age Z score) $< -2SD$ according to WHO Z-score calculation (Kemenkes RI, 2019). The nutritional status category is based on Weight for Height Z-score (WHZ), normal (well nourished) if it is in the range of $-2SD$ to $+2SD$, while moderately Underweight status is in the range $< -2SD$ to $-3SD$, and in the range $< -3SD$ is included in the category of severely Underweight (Kemenkes RI, 2021). This research was conducted after obtaining ethical approval from the Medical/Health and Bioethics Research Committee of the Faculty of Medicine, Sultan Agung University Semarang, all respondents were given informed consent with parental consent. Statistical analysis using t-test and chi-square test with SPSS application.

Result and Discussion

The characteristics of respondents in this study consisted of gender, socioeconomic status, history of complementary foods, and nutritional status. The characteristics of respondents are shown in the Table 1.

Table 1 shows that the majority of respondents in this study were male respondents as many as 28 (56%), with sufficient socio-economic conditions 41 (82%), and a history of poor complementary foods as much as 29 (58%). The nutritional status of the majority of respondents in this study was normal, with normal WAZ as many of as 45 (90%), normal HAZ of as many as 42 (84%), and good WHZ

of as many as 43 (86%). There are 16% stunting toddlers, but no toddlers with anthropometric WHZ score $< -3SD$. Background of the incidence of stunting is generally related to malnutrition that lasts for a long time even from birth. Factors that can be associated with a lack of nutritional intake for children under five include poverty, family diet, poor nutrition for pregnant/breastfeeding mothers, and especially inappropriate food intake in early life (Menpan, 2022).

Table 1. Characteristics of Respondents.

Characteristic	N	%
Gender		
Male	28	56
Female	22	44
Socio-Economic		
Sufficient Income	41	82
Low Income	9	18
History of weaning food		
appropriate	21	42
inappropriate	29	58
Nutritional status		
WAZ (BB/U)		
Well	45	90
Low	5	10
HAZ (PB/U)		
Non-stunting	42	84
Stunting	8	16
WHZ (BB/PB)		
Normal	43	86
Moderately Underweight	7	14

Source: Results of data processing

Maternal nutrition during pregnancy is very important to note. Based on the review, in the second and third trimesters during pregnancy, the nutritional reserves of the fetus can be used after birth. In the fetal phase, until the child is 3 years old, there is a rapid growth of the brain and central nervous system, and gestational deficiencies of minerals (iodine, selenium, iron, zinc, calcium, magnesium) that occur at this time can cause problems related to brain function such as hyperactivity, autism, speech delays, and memory problems (Farias *et al.*, 2020). Deficiency or excess of nutrients, stress, and gonadal hormones can affect the epigenetic changes in brain development.

It is stated that early life stress changes the hypothalamic-pituitary-adrenal (HPA) sensitivity axis, which cannot be separated from epigenetic changes. Epigenetic factors bridge the interaction between the genome, environment, hormones, and nutrients (Margaret McCarthy & Nugent, 2015).

This study can provide additional information that even though babies are born healthy at term, with normal birth weight, the majority of socio-economic conditions are sufficient with a history of fairly good growth based on data that there are no cases of severe malnutrition. However, there are still toddlers who are stunted and have a small head circumference (Z-score $< -2SD$). Environmental factors after birth have a large enough effect on the growth of head circumference or brain, this can be explained by the concept of epigenetic Environment has a major effect on signal expression from the child's genome, especially the environment in the golden period of brain development in the first 1000 days of life. The biomedical environment, infection, toxic substances, and climate, influence changes in expression signals at the genome level, even though the genome structure does not change. Environmental factors after birth such as nutritional intake, behavior, repeated infections, stimulation of parents/caregivers, experiences of stress, and fulfilment of emotional needs for affection. All of these factors can alter gene expression that create positive or negative effects on brain development (Margaret McCarthy & Nugent, 2015; Bacon & Brinton, 2021).

Table 2. Average Growth and Head Circumference Size Between Stunting and Non-stunted Groups.

Toddler Head Circumference	n	Mean	p*
HC Growth (cm/year)			
Normal	42	4,6	0,043
Stunting	8	4,1	
Average HC of Toddler (cm)			
Normal	42	47,2	0,000
Stunting	8	44,9	

*Independent t-test

The limitation of the study was that food recall was not carried out at the age of under 1 year, especially the period of giving complementary foods at the age of 6 months - 12 months. This is because the fastest growth speed for head circumference is the first 6 months of age and 6 months to 12 months. Second year the rate of brain growth decreases by only about 1 cm every 6 months. Thus, adequate weaning food intake is likely to have a major effect on that period (Jones & Samanta, 2022).

Based on Table 2, the results of the independent t-test showed that the growth of head circumference in the stunting group (4.1cm/year) was significantly smaller than the normal group (4.6cm/year), $p = 0.043$. The mean head circumference of the stunting group was significantly smaller than that of normal toddlers, $p = 0.000$. Another result of this research is that the nutritional status of pregnant women is not related to HC births and HC aged 3 years, HC births are not correlated with HC under five, as well as levels of zinc in newborns (from the umbilical cord) are not significantly related to HC births and HC age 3 years, we do not display data. The results of previous studies proved that the mean umbilical cord zinc levels were lower in the group of babies with birth weight in the range of 2500g - < 2800g compared to the 2800-3900g group (Priyantini, 2021)

Table 3. Correlation between Zinc and Annual Increase in Head Circumference

		Daily Zinc Intake	Toddler Zinc Level
HC growth/ year	r	-0.135	0.027
	p*	0.349	0.854
	n	50	50

* Pearson correlation

Table 3 presents data on daily zinc intake according to the food recall questionnaire and blood zinc levels of toddlers, it turns out that there is no significant correlation between daily zinc intake and zinc levels with annual head circumference growth. Fulfillment of nutritional needs can be done by providing supplementation. Giving oral zinc supplementation early on in neonates with low birth weight can help catch up on

growth, either by increasing insulin-like growth factor-1 (El-Farghali et al., 2015). The results of systematic reviews and meta-analyses of zinc supplementation in children are still diverse, it is said that zinc supplementation in pregnant women does not significantly increase the weight of newborns or the risk of low birth weight.

Zinc supplementation after birth increased height, weight, and WAZ, but did not increase the HAZ or WHZ scores. Zinc supplementation tends to increase height and HAZ scores in children 2 years old (Liu et al., 2018). The low dietary zinc intake observed in Ethiopian children has a significant association with children's health status (Ayana et al., 2018). Another study also stated that daily consumption of multi-nutrient fortified milk-based drinks by toddlers could improve the nutritional status of vitamin A, vitamin D, and selenium, with respect to growth, z-score of body weight, height, and increased BMI (Senbanjo et al., 2022). This study has not proven that daily zinc intake, toddler zinc levels, and newborn zinc levels are related to head circumference growth. However, other results of our study prove that daily zinc intake is associated with stunting in children under five (Priyantini et al., 2023). Analysis of the relationship between the characteristics of toddlers and head circumference category was determined by chi-square test which is shown in table 4.

This study shows that there is a relationship between head circumference and HAZ ($p=0.000$, RR: 22.2), in line with previous research conducted in the semi-urban Vellore settlement which stated that small head circumference was significantly related to stunting. The researcher proved that small head circumference (< -2SD) for infants aged 1 month is at risk of 10.8 times more frequent stunting at the age of 2 years (Sindhu et al., 2019). The growth of head circumference can indicate brain development and is responsible for development of intelligence (Qian et al., 2021). Another study in India proved the correlation of development quotient (DQ) scores with head circumference. The lower the head circumference followed by the lower the DQ score of children aged 6-60 months

Table 4. Relationship Between Head Circumference and Characteristics/Weaning Food/Dietary Intake

	Category Head Circumference		P*	RR
	Normal	Low		
Gender				
Male	21	7	0,563	
Female	18	4		
Socio-Economic				
Sufficient Income	34	7	0,073	
Low Income	5	4		
First Child				
Yes	14	1	0,087	
No	25	10		
Very Early Formula feeding				
Yes	8	5	0,096	
No	31	6		
History of complementary feeding				
Sufficiently qualified	17	4	0,668	
Less qualified	22	7		
Intake of animal protein				
Moderate	28	10	0,190	
Low	11	1		
Daily protein				
Moderate	38	9	0,118**	
Low	1	2		
Zinc intake/day				
adequate intake	28	5	0,103	
insufficient intake	11	6		
WHZ				
Normal	35	8	0,151	
Underweight	4	3		
HAZ				
Normal	37	5	0,000	22,2
Stunting	2	6		
WAZ				
Normal	37	8	0,064**	
Underweight	2	3		

*Chi square test **Fisher test

(Tiwari et al., 2017). It should be noted that the characteristics of our study subjects were term babies with normal birth weight, so in general, there was not much difference in birth head circumference. It is possible that the small head circumference of some toddlers was caused by other factors such as nutritional intake before the age of 3 years, repeated infections, and genetics that we have not completely controlled.

Other results from this study proved that HAZ (stunting) was not related to the adequacy of income and the level of education of the mother (Priyantini et al., 2023). The nutritional

status of children is also influenced by parenting styles, not limited to complementary feeding in the first year of life. As the results of research in Banyumas, that mother's parenting style for toddlers is related to the incidence of stunting (Wati et al., 2022). While, research in Bengkulu proved that family planning (marriage at a young age, birth spacing of 2-5 years, primipara, and several toddlers) was related to the practice of child feeding (PCF) (Simbolon et al., 2022). In contrast, the results of the study in Depok did not prove a relationship between feeding practices and nutritional status (weight

for height) in children aged 6-23 months (Permatasari & Waluyanti, 2019). A systematic review study concluded that larger children's head circumference is associated with better weight growth, higher socioeconomic scores, and taller mother's length (Nicolaou et al., 2020).

Head circumference is a very important measure of brain development (Vandenplas et al., 2019). The results of previous studies have shown that head circumference growth is associated with behavioral traits in early infancy (Dupont et al., 2018). Head circumference discrepancy in the first 6 months of life is related to factors such as gestational age, gestational age, and birth weight (Bouthoorn et al., 2012). The expansion of the human brain in particular the neocortex is one of the most remarkable evolutionary processes and is correlated with cognitive, emotional, and social adaptation abilities. The process of expanding the area determines the growth of head circumference to be normal, microcephaly, or macrocephaly. Brain growth abnormalities may be found as the sole symptom or as part of a syndrome of other neurodevelopmental disorders such as epilepsy, autism, intellectual disability, brain malformations, and body growth abnormalities (Pirozzi et al., 2018). Therefore, measurement of head circumference cannot be ignored, especially at the age of the first 2 years.

Research conducted on children born at term in developed countries with free access to health care showed that higher IQs occur in infants with larger birth weight measurements, as well as greater growth in height and head circumference during the first 5 years of life (Kirkegaard et al., 2020). Weight gain, growth in body length, and head circumference are markers of nutritional status and are independently associated with long-term neurodevelopment. Delayed brain development is not only the result of nutrient intake but also interactions with other factors such as growth hormone, thyroid hormone, susceptibility to recurrent infections, genetics, and epigenetics that occur in the early 1000 days of life (Dauncey, 2014; Skinner & Narchi, 2021).

Conclusion

This study did not show a correlation between zinc intake and the growth of head circumference in children under five but did prove the relationship between growth in head circumference and incidence of stunting. The daily zinc intake of children under five is not associated with the growth of head circumference. Further research is still needed regarding the effect of weaning food aged 6-12 months on the growth of body length and head circumference.

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