

## ORIGINAL ARTICLE

## Zinc deficiency as risk factor for stunting among children aged 2-5 years

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### ABSTRACT

#### BACKGROUND

Stunting is a nutritional problem in the form of linear growth disturbance caused by low intake of macro- and micronutrients. The prevalence of stunting in children aged 2-5 years in Semarang is higher in well-to-do families (67.2%) than in poor families (32.8%). The purpose of this study was to analyze the role of low adequacy levels of vitamin C, iron, zinc and low food expenditure as risk factors of stunting among children aged 2-5 years.

#### METHODS

This was a case-control study with a sample of 71 cases (stunting) and 71 controls (no stunting). The collected variables were adequacy levels of vitamin C, iron, zinc and level of food expenditure. Nutrient intake data were obtained with the semiquantitative food frequency questionnaire (FFQ), while data on food expenditure were obtained through a food expenditure questionnaire. Data analysis was performed using simple and multivariate logistic regression method.

#### RESULTS

The results of the simple logistic regression showed that low levels of vitamin C (OR=2.97; 95% CI=1.41 – 6.31), iron (OR=2.87; 95% CI=1.44 – 5.71) and zinc (OR=9.24; 95% CI=2.02 – 42.12) were risk factors of stunting. Multivariate analysis showed that the risk factor that most affected stunting was a low level of zinc (OR=6.39; 95% CI=1.34 – 30.33). A low level of food expenditure was not proven to influence the incidence of stunting.

#### CONCLUSIONS

A low level of zinc was the risk factor that most affects stunting in children aged 2-5 years. Preventive strategies to prevent stunting and promote healthy eating is recommended.

**Keywords:** Stunting, risk factors, zinc, iron, children 2-5 years

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## INTRODUCTION

Stunting is one of the nutritional problems in the form of linear growth disturbance due to low nutrient intakes and chronic infectious diseases.<sup>(1)</sup> Stunting in the underfives is usually less realized since the difference in height of children with stunting and normal children at such an age is not too apparent. Based on the criteria of the World Health Organization (WHO), stunting is indicated by a height-for-age z-score of less than -2 standard deviations (SD).<sup>(2)</sup> In Indonesia, according to data from the Basic Health Research (*Riset Kesehatan Dasar*, RISKESDAS), the prevalence of stunting increased from 35.6% in 2010 to 37.2% in 2013, comprising 28% ultrashort and 19.2% short underfives.<sup>(3)</sup> The prevalence of stunting in the underfives in Central Java in 2014 reached 33.9%. On the other hand, data from the Semarang City Health Service show that according to the results of the Monitoring of Nutritional Status survey (*Pemantauan Status Gizi*) based on the height-for-age index in Semarang City the prevalence of stunting in the underfives is 4.03% and in children aged 2-5 years 20.37%.<sup>(4)</sup>

An important component that plays a role in growth is the intake of the micronutrients vitamin C, iron and zinc. A study in Egypt on vitamin C intake in pregnant women showed that the vitamin C concentration in the blood of pregnant women has a significant positive impact on neonatal anthropometrics and placental weight.<sup>(5)</sup> Vitamin C is required in the growth process through its role in collagen synthesis. In a person with vitamin C deficiency, the latter will inhibit the formation of structural proteins and collagens, thus inhibiting the growth process.<sup>(6)</sup> In this connection, few studies have been conducted on vitamin C as a risk factor of stunting in the underfives.

A study on the relationship between iron intake and stunting incidence carried out by Hidayati<sup>(7)</sup> found a difference in iron intake of children with stunting and of those without stunting in urban slums. Iron deficiency is

associated with decreased immune function, which is measured by changes in several components of the immune system. However, a study in Vietnam on the effect of iron and zinc supplementation in infants showed no significant effect on stature.<sup>(8)</sup>

A study conducted at Puskesmas Klungkung found that low serum zinc concentration was a risk factor for short stature.<sup>(9)</sup> On the other hand, the study of Taufiqurrahman<sup>(10)</sup> showed that zinc was not a risk factor for stunting incidence in the underfives in the province of West Nusa Tenggara (*Nusa Tenggara Barat*, NTB). The study by Gibson<sup>(11)</sup> on children 6-12 years of age reported a significant difference between serum zinc concentration of male children of short stature and that of male children of normal stature, but no difference in female children. The study by Mozaffari-Koshravi<sup>(12)</sup> showed that zinc supplementation only affected the height of male children aged 2-5 years .

In addition, the economic factor of household poverty results in an inability to meet food requirements.<sup>(13,14)</sup> Candra<sup>(15)</sup> states that a budget of less than Rp 25,000.00 per day results in the inability of the household to have access to a sufficient quantity and quality of food for meeting daily requirements and is a risk factor for stunting in the underfives, with an OR of 2.43. However, a different study in Semarang found that per capita income was not correlated with the level of consumption of energy and protein in children aged 2-5 years.<sup>(16)</sup> Semarang is the capital of Central Java and has a community of diverse economic status. According to data obtained from the Health Service of Semarang City, there are 32.8% underfives with stunting from low households and 67.19% underfives with stunting from well-to-do households.<sup>(4)</sup> This shows that stunting is higher in children of well-to-do households at a ratio of 2:1 as compared with children of low households, pointing to a disparity, since in well-to-do households there should be fewer children with stunting.

The present study was conducted in children aged 2-5 years since this age group has passed

the first thousand days of life and has been weaned of exclusive breastfeeding, thus being at highest risk of low parenting. The majority of previous studies on stunting used the variables of energy and protein macronutrient intakes, with significant results. In contrast, the present study used the variables of vitamin C, iron and zinc micronutrient intakes and the level of food expenditure. In view of the inconsistent results of previous studies and the fact that several variables had not been investigated, it was considered necessary to conduct a study with the objective of analyzing low intakes of vitamin C, iron, and zinc, and a low level of food expenditure as risk factors for stunting in children aged 2-5 years.

## METHODS

### Research design

The study was of observational case-control design and was conducted in the catchment area of Puskesmas Bangetayu, Genuk District, Semarang City, from August until September 2016.

### Research subjects

The subjects of this study were children aged 2-5 years who met the inclusion criteria and were domiciled in Genuk District, Semarang City, at a ratio of cases to controls of 1:1. The cases were children aged 2-5 years who had stunting and a height-for-age z-score (HAZ) of  $<-2SD$ , while the controls were children aged 2-5 years with a height-for-age z-score of  $\geq -2SD$ . The respondents in this study were the mothers of the children who had been selected as study subjects. The inclusion criteria in this study were children aged 2-5 years who resided in Genuk District, had a growth curve card (*Kartu Menuju Sehat, KMS*), were living with their own parents and agreed to be included in the study sample. The exclusion criteria in this study were children of premature birth, those with physical defects, were out of town at the time the study was conducted, and withdrew from the study sample.

The study sample was calculated using OR values of several previous study variables<sup>(10,15)</sup> thus obtaining a minimal sample size of 71 subjects for each group after correction for possible dropouts (10%). Recruitment of the subjects was by consecutive non-random sampling.

### Anthropometric measurements

Height was measured with a stadiometer to an accuracy of 0.1 cm. Stunting was categorized as a height-for-age z-score of  $<-2SD$  and normal stature as a height-for-age z-score of  $\geq -2$ .<sup>(2)</sup>

### Nutrient intake measurements

The level of adequacy for vitamin C, iron and zinc were determined using the semi-quantitative FFQ. Nutrient adequacy level was determined by the Nutrisurvey 2007 program, then calculated on the basis on the Indonesian Recommended Daily Allowances (IRDA) for 2013. The level of adequacy for vitamin C, iron and zinc were categorized as adequate if the intake was  $\geq 77\%$  IRDA and low if the intake was  $<77\%$  IRDA.<sup>(17)</sup>

### Level food expenditure

The household food expenditure is the amount used for the food consumption of all household members for one month divided by the number of household members. The level of food expenditure was categorized as low if the food expenditure was  $<Rp437,520.00$  per capita, and high if the food expenditure was  $\geq Rp437,520.00$  per capita.<sup>(18)</sup>

### Statistical analysis

Simple and multivariate logistic regression was used to analyze the data at a significance level  $\alpha$  of  $<0.05$ .

### Ethical clearance

This study was carried out after obtaining approval from the Ethics Commission, Faculty of Medicine, Diponegoro University, Semarang No. 852/EC/FK-RSDK/VIII/2016.

Table 1. Characteristics of the study subjects by stunted and non-stunted children

Characteristic	Stunted (n=71)	Non-stunted (n=71)	P
	Mean ± SD / Median	Mean ± SD / Median	
Age (months)	42	44	0.387 **
Weight(kg)	12.4	14.1	0.000 **
Height (cm)	89.6 ± 0.65	97.38 ± 0.87	0.000 *
Z-score (SD)	-2.17	-0.83	0.000 **
Income (Rp)	1,900,000	1,900,000	0.939 **

\* Independent t-test; \*\* Mann-Whitney test

## RESULTS

The majority of study subjects were female (55.63%). Table 1 lists the characteristics of the study subjects, i.e. age, weight, height, z-score and monthly income. There were no differences in age and monthly income of the study subjects ( $p > 0.05$ ) in the group of cases and the group of controls. With regard to weight, height and z-score of the study subjects, there was a difference ( $p < 0.05$ ) between the group of stunted and the group of non-stunted.

Table 2 shows that the proportion of children with a low level of adequacy for vitamin C was greater in the group of stunted (42.3%) than in the non-stunted group (19.7%) (OR=2.97; 95% CI=1.41 – 6.31). Likewise, the proportion of children with a low level of adequacy for iron was greater in the group of stunted (69%) than in the non-stunted group (43.7%) (OR=2.87; 95% CI=1.44 – 5.71). In addition, the proportion of children with a low

level of adequacy for zinc was greater in the group of stunted (21.1%) than in the non-stunted group (2.8%) (OR=9.24; 95% CI=2.02 – 42.12). Finally, the proportion of children with a low level of food expenditure was greater in the group of stunted non-stunted (81.7%) than in the group (74.6%) (OR=1.51; 95% CI=0.67 – 3.38).

Multivariate analysis performed on 3 variables, i.e. levels of adequacy for vitamin C, iron and zinc. The results of the multivariate logistic regression analysis presented in Table 3 showed that the variable with the most important role on stunting incidence was a low adequacy level for zinc.

A low adequacy level for iron had a 2.13-fold significantly higher risk for stunting incidence than a adequate adequacy level for iron (OR=1.20; 95% CI=1.03-4.37). A low adequacy level for zinc had a 6.39-fold significantly higher risk for stunting incidence than a adequate adequacy level for zinc (OR=6.39; 95% CI=1.34-30.33).

Table 2. Simple logistic regression analysis of several variables for the stunted and non-stunted children

Level of adequacy	Nutritional status of children		P	OR (95% CI)	
	Stunted (%)	Non-stunted (%)			
Vitamin C (mg)	Low	30 (42.3)	14 (19.7)	0.004	2.97 (1.41 - 6.31)
	Adequate	41 (57.7)	57 (80.3)		
Iron (mg)	Low	49 (69)	31 (43.7)	0.002	2.87 (1.44 - 5.71)
	Adequate	22 (31)	40 (56.3)		
Zinc (mg)	Low	15 (21.1)	2 (2.8)	0.001	9.24 (2.02 - 42.12)
	Adequate	56 (78.9)	69 (97.2)		
Level of food expenditure	Low	58 (81.7)	53 (74.6)	0.310	1.51 (0.67 - 3.38)
	High	13 (18.3)	18 (25.4)		

Table 3. Multivariate-adjusted odds ratios for stunting across iron and zinc intakes

	OR	95% CI	P
Level of adequacy for iron	1.20	1.03 - 4.37	0.039
Level of adequacy for zinc	6.39	1.34 - 30.33	0.019

## DISCUSSION

A low adequacy level for vitamin C was a risk factor for stunting in children aged 2-5 years. The results of this study was in agreement with the study in Cairo on children aged 2-5 years, which showed that mean vitamin C intake was significantly lower in children with stunting than in controls.<sup>(19)</sup> Differing results were found in a study on primary school students in Tehran, Iran, showing no significant differences for micronutrient intakes (vitamin C, iron and zinc) between children with stunting and those without stunting.<sup>(20)</sup> These differing results was caused by a difference in age, in which the subjects of the Tehran study were primary school students with a mean age of  $82 \pm 4$  months. Differing nutrient intakes and environments may also lead to differing study results.

Vitamin C is important for the synthesis of collagen, fibers and structural proteins. Collagen is required for the formation of bones and teeth and wound repair. Vitamin C is required in the growth process through its role in collagen synthesis, through hydroxylation of proline and lysine into hydroxyproline, an important material for collagen synthesis, and a protein affecting the structural integrity of the cells in all connective tissues, such as cartilage. Normal collagen cannot be formed without the presence of vitamin C.<sup>(6)</sup> Children with vitamin C deficiency will experience inhibition the formation of structural proteins and collagens thus inhibiting the growth process.

A low adequacy level for iron was a risk factor for stunting in children aged 2-5 years. These study results are in line with the results of a study conducted in Kepulauan Nusa Tenggara reporting that iron and zinc were the strongest variables on stunting incidence in the underfives (24-59 months).<sup>(10)</sup>

Iron deficiency is associated with decreased immune functions, as measured with changes in several components of the immune system that occur in iron deficiency.<sup>(21)</sup> The consequence of the changes in immune functions is lowered resistance toward infectious disease.<sup>(22)</sup> Underfives with iron deficiency are more susceptible to microorganisms, because iron deficiency is closely associated with damaged functional capacity of the immune defense mechanism that is important for the entry of infectious disease.<sup>(23)</sup>

Iron plays a role in the immune system. The immune responses by the T lymphocytes will be disturbed upon decreased production of cells, which is caused by decreased DNA synthesis. DNA synthesis is caused by disturbances of ribonucleotide reductase which requires iron for its ordered functioning, so that iron deficiency may cause disorders of the immune system. Children with immune system disorders are more susceptible to infectious diseases, thus affecting nutritional status.<sup>(24)</sup>

A low adequacy level for zinc is a risk factor for stunting in comparison with respondents with a adequate adequacy level for zinc. Our study results are in agreement with the study conducted by Hidayati,<sup>(7)</sup> stating that low zinc intake carries a 2.67-fold higher risk for stunting incidence in children. Kenneth<sup>(25)</sup> revealed in a study on children in Peru that children who received zinc supplementation had weights which were 0.41 kg higher in comparison with children who did not receive zinc and proved that zinc deficiency may inhibit growth.

Zinc plays an important role in the structure and function of biomembranes, and zinc is an important component of several enzymes that regulate cell growth, protein and DNA synthesis, energy metabolism, regulation of gene transcription, hormone concentrations and

metabolism of growth factors.<sup>(26)</sup> Zinc commonly plays a role in the synthesis of growth hormones. A growth hormone that plays a role in growth is insulin-like growth factor-1 (IG-F) which functions to increase cellular growth. Zinc also plays a role in human immune functions.<sup>(27)</sup> Marasmic infants who receive zinc supplementation show increases in defensive responses. Children in developing countries who received zinc supplementation showed decreases in the incidence and duration of acute and chronic diarrhea.<sup>(28,29)</sup>

A low level of food expenditure was not a risk factor for stunting. In the present study the mean income in the group of cases was Rp 2,023,267.00 and in the group of controls Rp 1,938,014.00. On average the group of controls allocated a greater amount of funds for food than did the group of cases, so that the types and amounts of nutrients consumed by the group of controls was more diverse and considerable in comparison with the group of cases. Thus the proportion of total nutrients seen in this study in the group of controls was higher than in the group of cases. The results of this study are in line with the study in Semarang, where the per capita income was not associated with level of energy and protein consumption in children aged 2-5 years.<sup>(16)</sup>

A low food expenditure in households results in a diet with low diversity, nutritiousness, and balance, which affects dietary consumption patterns.<sup>(30,31)</sup> Low availability of foods may result in low realization of nutrient intakes in households.<sup>(32)</sup> A decrease in the quality of household food consumption that is characterized by limited purchases of foods that are sources of proteins, vitamins and minerals will lead to undernutrition.<sup>(33)</sup>

The low adequacy level for zinc is the most important variable affecting stunting in children aged 2-5 years. Iron and zinc play a role in the immune system.<sup>(23)</sup> The immune responses by T lymphocytes will be disturbed upon a decrease in the production of cells, which is caused by decreased DNA synthesis, so that iron and zinc

deficiencies may cause disorders of the immune system.<sup>(26)</sup> Children with disorders of the immune system are more susceptible to infectious disease, thus affecting nutritional status.<sup>(29)</sup>

A limitation of this study was the use of a retrospective case control design, with the possibility of recall bias in data collection, particularly on the variables of food intakes. In this case the recall capacity of the respondents will considerably affect the study results. In future, studies may be conducted using other less biased instruments, such as biochemical assessment, so that the obtained results may be more valid. The public health implication of this study is to recommend vitamin C, iron and zinc intakes in children. Finally, stunting is a heterogeneous multi-factorial disorder and besides dietary factors, other variables, such as hereditary factors and metabolic conditions must be considered.

## CONCLUSIONS

A low adequacy level for zinc is the most influential factor for stunting incidence in children aged 2-5 years. This study demonstrates the necessity of continued coordination of interventions to reduce multiple micronutrient deficiencies for optimal growth of children aged 2-5 years.

## CONFLICT OF INTEREST

There was no conflict of interest in this study (financial, personal, political, intellectual or religious).

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## CONTRIBUTORS

SB contributed to drafting the manuscript and the study design. SB, AM, AR contributed to data collection, analysis and interpretation. SB and AM contributed revising manuscript critically for important intellectual content. All authors read and approved the final manuscript.



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