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Serum copper levels in adolescents 17 - 19 years old based on stunted and obese status

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ABSTRAK

Latar Belakang: *Individu dengan status gizi stunted memiliki risiko mengalami obesitas saat remaja atau dewasa. Status stunted dan obesitas sering dikaitkan dengan kejadian inflamasi dan potensi stress oksidatif yang dapat ditandai dengan peningkatan kadar serum tembaga.*
Tujuan: *Penelitian ini bertujuan untuk menganalisis kadar serum tembaga pada remaja usia 17-19 tahun berdasarkan status stunted dan obesitas.*
Metode: *Penelitian ini menggunakan rancangan cross sectional. Sebanyak 91 subjek dipilih secara random sampling berdasarkan kriteria inklusi dan eksklusi. Status obesitas diukur menggunakan lingkar pinggang per tinggi (WHtR) dan status stunted diukur menggunakan tinggi badan per umur (TB/U). Pengukuran kadar serum tembaga dianalisis menggunakan teknik ICP-OES dengan nilai normal serum tembaga sebesar 0.7-1.4 mg/L. Analisis data meggunakan uji Anova, uji korelasi Pearson, dan uji T Independen.*
Hasil: *Rerata kadar serum tembaga pada kelompok stunted-obesitas sebesar 0,83±0,21, stunted 1,11±0,28, obesitas 0,72±0,17, dan normal 0,60±0,37. Terdapat perbedaan bermakna kadar serum tembaga kelompok stunted dengan kelompok lain. Kadar serum tembaga memiliki korelasi negatif dengan TB/U (r=-0,337, p=0,001).*
Kesimpulan: *Status stunted, obesitas, dan stunted-obesitas meningkatkan kadar serum tembaga meskipun masih dalam kategori normal. Ada perbedaan bermakna kadar serum tembaga berdasarkan status stunted dan obesitas, serta adanya korelasi negatif kadar serum tembaga dengan TB/U.*

KATA KUNCI: *obesitas; remaja; serum tembaga; stunted; stunted-obesitas*

ABSTRACT

Background: *Stunted have a risk of obesity in the adolescent or adult period. Stunted and obese status were associated with inflammation and oxidative stress that marked by increased serum copper levels.*
Objectives: *This study was to describe difference of serum copper levels in adolescents 17-19 years old based on stunted and obese status.*
Methods: *This study was using cross sectional design. There were 91 adolescents as the sample of this study and selected by random sampling based on inclusion and exclusion criterias. The obese status was measured by waist to height ratio (WHtR) and stunted status was measured by height age of z-score (HAZ). The serum copper levels were analyzed by ICP-OES with normal copper serum value of 0.7-1.4 mg/L. The data were analyzed by Anova test, Pearson correlation, and Independent t-test.*
Results: *The mean value of serum copper level in stunted-obese group were 0.83 ± 0.21, stunted group were 1.11 ± 0.28, obese group were 0.72 ± 0.17, and normal group were 0.60 ± 0.37. There was a significant difference of serum copper level between the stunted with other groups. There was a negative correlation between serum copper level and HAZ (r = -0.337, p = 0.001).*

Conclusions: *Stunted, obese, and stunted-obese status were able to increase serum copper level but still in normal range. A significant difference was found in serum copper levels based on stunted and obesity status, as well as a negative correlation between serum copper level and HAZ.*

KEYWORDS: *adolescents; obese status; serum copper levels; stunted-obese; stunted status*

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INTRODUCTION

Stunted is known as a condition where z-score height for age is < -2SD. Stunted occurs in individuals who are less than three years old. The previous studies stated that stunted children are at risk of growing up to be stunted adult (1). The consequence of other nutritional problems in stunted individuals is obese (1,2). The research conducted in several countries such as Brazil, South Africa and Russia also stated that there was a relationship between stunted and the tendency of obese in the future(35).

Obese with stunted background (stunted-obesity) is associated with the “Barker Hypothesis”. Barker's hypothesis stated that growth disorders can cause reduction in the number and quality of cells and tissues of internal organs, especially endocrine system (6). The problem of endocrine system can affect fat oxidation that cause excessing accumulation of adipose tissue (7). Moreover, stunted-obese is also associated with the "Thrifty Gene Hypothesis". Chronic energy deficiency in individuals causes the body adapting to survive by reducing energy expenditure to a minimum. This gene have tendency of positive energy balance when there is increasing intake on long period resulting in overweight or obese problem(6,8).

Stunted and obese are associated with chronic diseases in adulthood phase. The mechanism that links malnutrition with chronic diseases is oxidative stress (9,10). Oxidative stress is cell damage mediated by free radicals due to excess levels of reactive oxygen than antioxidants (11,12). Excessive levels of reactive oxygen will stimulate chronic inflammation which will lead to various diseases such as cardiovascular disease, neurodegenerative disease (Alzheimer's and Parkinson's), cancer, atherosclerosis, and diabetes mellitus(1214). Excessive production of reactive oxygen can be caused by several factors such as inadequate intake of vitamins and minerals that act as antioxidants, inflammation, and excess accumulation of adipose tissue(15).

Several previous studies have stated that serum copper levels tend to be higher in obese individuals (18,19). High serum copper levels are often associated with excess adipose tissue. Adipose tissue is a pro-inflammatory which is able to release reactive oxigent thereby increasing damage to body cells (18,20,21). Research on serum copper levels associated with a combination of stunted status and obesity is still rare. The purpose of this study was to

Serum copper is one of the most sensitive biochemicals to inflammatory and stress oxidative events (1517). Previous studies stated that serum copper levels tend to be higher in obese individuals(18,19). High serum copper levels are often associated with excess adipose tissue. Adipose tissue is a pro-inflammatory which is able to release reactive oxigent that increasing body cells damage(18,20,21).

The objective of this paper was to determine differences in serum copper levels in adolescents aged 17-19 years based on stunted and obese status.

MATERIALS AND METHODS

This research used a cross-sectional study which was conducted on adolescents aged 17-19 years at Diponegoro University. The sample was selected through the anthropometric screening stage and used a simple random sampling technique. The minimum sample size required was 72 samples that calculated using the independent mean differences formula. The independent variables were stunted and obese status, and the dependent variable was serum copper level.

Anthropometric measurements at the screening stage were body weight, height, and waist circumference with an analysis of height/age and waist-to-height ratio (WHtR). The inclusion criterias were adolescents aged 17 years – 19 years 0 months; z-score HAZ ≤ -2SD for stunted status; waist-to-height ratio ≥ 0.51 for men and ≥ 0.50 for women in obese status; not currently taking drugs, no consumption of supplements (vitamin C, immune system boosters, iron tablets) and hormone therapy that can affect serum copper levels; no smoking; no in a state of illness or have a history of chronic diseases such as hypertension, dyslipidemia, and other chronic diseases; and not menstruating. The exclusion criteria were the subject withdraw from the study, sick during the study, and in the condition where individual was not possible to continue as a sample.

The stages of collecting data were dietary intake interview, blood sampling, and laboratory tests. Dietary intake interview using the SQ-FFQ questionnaire. Blood samples for analysis of serum copper levels were taken through the antecubital vein by specialists from RSUP DR.

Kariadi Semarang in the range 07.00 - 09.30 WIB as much as 5 cc with condition the subject had been fasted for 10 hours before taking blood. Serum copper levels were measured using the ICP OES technique with the PERKER ELMER Optima 8300. Data analysis used the Anova test, Independent T test, Mann-Whitney test, and Pearson correlation test.

RESULTS AND DISCUSSIONS

This research managed 100 research samples with 25 people in each group. Of the 100 people, there were 9 people who disqualified because their serum copper levels were not detected. **Table 1** shows the number of research subjects in each group.

Tabel 1. Distribution research samples based on each group

Group	n(%)
Stunted-obese	26 (28.6%)
Stunted	22 (24.2%)
Obese	26 (28.6%)
Normal	17 (18.6%)
Total	91 (100%)

The findings of stunted-obese adolescents showed that obesity was a risk for stunted individual. Stunted is considered as severe acute malnutrition (SAM). Chronic energy intake deficiency in the past caused stunted individual to adapt by managing energy expenditure to a minimum. This condition can trigger a state of positive energy balance when increasing of intake on the long period, thus supporting of overweight or obese (8). Increasing intake was related to eating patterns that were dominant towards energy-dense foods and low in micronutrients as well as a sedentary lifestyle that triggers the incidence of obesity in stunted individual (22,23).

Table 2 showed stunted-obese group had larger number of female samples (57.69%) compared to male samples (42.31%). This was related to several previous studies which stated that stunted women tend to be more able to catch up on weight gain and subcutaneous fat mass during puberty than to catch up on height (5,24,25). This condition was associated with inflammation in stunted children which was able to suppress the growth hormone IGF-1 that linear growth (height) was disrupted (26).). In addition, female had a lower total energy expenditure when compared to men. Lower total energy expenditure was associated with higher body weight and fat mass (27).

Table 2. Characteristic samples

Category	Groups				
	Stunted-obese n = 26	**Stunted- n= 22**	**Obese n= 26**	**Normal n= 17**	**Total n=91**
Gender					
Female	15 (57.69%)	16 (72.73%)	13 (50.00%)	10 (58.8%)	54 (59.34%
Male	11 (42.31%)	6 (27.27%)	13 (50.00%)	7 (41.2%)	37 (40.66%
Serum copper levels					
Low	8 (30.8%)	0 (0.0%)	11 (42.3%)	13 (76.5%)	32(35.2%
Normal	17 (65.4%)	18(81.8%)	15 (57.7%)	3 (17.6%)	53(58.0%
High	1 (3.8%)	4 (18.2%)	0(0.0%)	1 (5.9%)	6(6.6%

Normal serum copper level is 0.7- 1.4 mg/dl

The results of this research showed that there were 1 stunted-obese subject (3.8%) and 4 stunted subjects (18.2%) who had high serum copper levels. High serum copper levels indicated the presence of inflammation which lead to oxidative stress (15,16). Oxidative stress was damage mediated by excess levels of reactive oxygen (11,16).

Oxidative stress that occur in stunted individuals was triggered by a lack of nutritional intake for a long duration in the past such as protein, vitamins related to antioxidants (vitamin C and vitamin E), and trace elements (selenium, zinc, and copper) which could have an impact on weaking immune system that made it susceptible to chronic infectious and inflammatory diseases (15,29). Chronic inflammation could produce pro-inflammatory chemokines, increase macrophage and neutrophil infiltration, abnormal proliferation of T and B lymphocytes which exacerbate apoptosis, as well as release of oxidants and inflammatory interleukins which lead to oxidative stress which is characterized by damage to cells in the body(20,21).

Oxidative stress in stunted-obese individuals was triggered by change in diet which had impact on increasing intake that supported the accumulation of excess adipose tissue. Adipose tissue was a pro-inflammatory mediator of secreting adipokines. Adipokines played role in increasing reactive oxygen. Increasing reactive oxygen through the mechanism of adipose tissue was a factor that triggers oxidative stress(15).

Table 3 showed a significant difference in serum copper levels by gender (p <0.001). Furthermore, it was known that the female group has a higher average serum copper level than the male group. Copper was a nutrient that had a role in regulating female sex hormones, increasing the release of luteal hormone (LH) and follicle stimulating hormone (FSH) (30). The condition before menstruation also could affect the higher copper serum levels through the mechanism of estrogen (estradiol) stimulation in the synthesis of ceruloplasmin (31). Differences in copper intake and absorption also contribute to differences in serum copper levels(31,32).

Table 3. Serum copper levels based on gender and groups

Category	n	Mean	*p value*
Gender			
Male	37	0.69± 0.27	0.001[a]
Female	54	0.91± 0.30	
Groups			
Stunted-obese	27	0.83±0.21[(2,4)]	< 0.001[b]
Stunted	22	1.11±0.28[(1,3,4)]	
Obese	26	0.72±0.17[(2)]	
Normal	17	0.60±0.37[(1,2)]	

[a]*Independent t- test;* p< 0.05

[b]Uji *Anova*; [1]*Stunted-obese*; [2]*Stunted*; [3]Obese; [4]Normal; p< 0.05

This study showed that there were significant differences between the stunted group with other groups. The stunted group had the highest average (1.11 ± 0.28), stunted-obese group (0.83 ± 0.21), obese (0.72 ± 0.17), and normal (0.60 ±0.37). The highest serum copper level in the stunted group was due to the level of inflammation which might be higher when compared to the other groups.

Furthermore, **Table 4** showed that serum copper levels were negatively correlated with height for age (r = -0.337, p = 0.001). Stunted was a condition of insufficient intake of nutrients in the long term which resulted chronic inflammation. Inflammation in stunted individuals caused abnormal production of growth hormone (IGF-1) and released excess reactive oxygen. Reactive oxigent which continued to regenerate and caused oxidative stress (9,13,16). Therefore, the lower the TB/U that the greater the possibility of chronic inflammation suppressing IGF-1 production and increasing the amount of reactive oxygen released so that oxidative stress events could be characterized by higher serum copper levels.

Table 4. Correlation Serum Copper Levels, HAZ, and WHtR

Serum Copper Levels	HAZ	WHtr
r	-0.337	-0.053
p value	0.001[a]	0.618[a]

[a]*Pearson correlation;*p< 0.05

CONCLUSION AND RECOMMENDATIONS

Stunted, obese, and stunted-obese could increase serum copper levels than normal nutrition status. There was a significant difference in serum copper levels based on stunted and obese status, as well as a negative correlation between serum copper levels and height for age.

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