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CRP and IGA Levels in Wasting Children Under Five Based on Zinc and Retinol Level

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Abstract. The effect of zinc deficiency may have play role on immune response that takes place during the critical growth period. Disorder of immune system may lead to the increased risk of infectious diseases. Immunoglobulin A (IgA) has a function as the first time barrier againts microorganisms and cell proliferation within immune system, which also highly influenzed by zinc. In children with malnutrition, including zinc, disorder, the production of secretory Ig A within their digestive system is also disturbed. The objective of this study was to analyze the difference of CRP and IgA levels on normal zinc levels and low zinc levels in wasted children underfives in Peneleh Puclic Health Center Surabaya City. Crossectional comparative design was done in 28 wasting children. Underfive children were randomized to observed CRP and IgA level. At the end of the study there were no significant differences in serum CRP level ($p > 0.05$)between children with low serum zinc levels and normal zinc levels (P=1.000). Children with higher serum zinc levels had higher blood levels of IgA (p=0.005). There were significant differences in IgA level (p =0,001) between children with normal zinc level and low zinc level. The result suggested that normal zinc levels may play role to perform antibody (IgA) for wasted underfive children to protect infection diseases than low zinc levels in wasted children under five.

Keywords: Serum CRP levels, Serum Ig A levels, Serum zinc levels, Wasting children

1. Introduction

Zinc deficiency is a one of micronutrient problem remains a public health problem in many developing countries including Indonesia. But the prevalence of zinc deficiency in Indonesia to date has not been available overall data on a national scale. The prevalence of small-scale zinc deficiency is known based on studies carried out in several places. Data from the survey are still scattered with relatively small sample and give an indication of a micronutrient problem faced.

Study in East Nusa Tenggara in 1996 found 71% of pregnant women with zinc deficiency (serum zinc <7 g / dl). Study in Central Java also showed relatively high prevalence of zinc deficiency which is equal to 70-90%. Study in Central Java, West Java and Lombok (West Nusa Tenggara) between the years 1997-1999, found zinc deficiency in infants ranging from 6% - 39%. And the last survey in nine provinces, found that the prevalence of zinc deficiency in children under five on average 31.9% with a range of 11.7% (West Sumatra) to 46.6% (NTB) (Herman, S., 2008).

Zinc deficiency also affect on the development of immune responses that occurred during the critical period of growth (Beach, et al, 1980; Prasad 1998). Immune function in experimental study (Prasad, 1998), indicating that T cell function becomes less good when there is moderate zinc deficiency in humans. Immune system disorder increase the risk of infectious disease because zinc in immune function also play an important role especially in Cell Mediated Immunity (CMI), and in Thymic Dependent Lymphocytes (T-cells).

Immunoglobulin a serves as a means of defense (barrier), first on microorganism and cell proliferation in the immune system is also highly influenced by zinc, in children with nutritional disorders including acquired disorders of zinc production in secretory immunoglobulin A in their digestive tract. Decreased levels of Ig A result in the inclusion of gram-negative bacteria into the intestinal wall and enable the septismia. Manifestations of sepsis such as fever, leukocytosis and tachycardia quite sensitive, but not a specific indicator of infection because in some of these markers can not be used as a marker of infection (Povoa, et.al, 2004).

Zinc has an important role in the immune system that is a potential mediator of the body's defense against infection. There are two types of work in immune system that is innate immunity and adaptive immunity as a barrier.

In this system seems to playing a part was Ig A, Ig A in which the emergence occurs about 1-3 days after infection occurs. Infections can impair a child's nutritional status. This occurs because the infection can decrease food intake, disrupt the absorption of nutrients, causing a direct loss of nutrients and increase the demand. Acute phase of infection and inflammation can cause low serum zinc levels and decrease in hepatic methalotionein where plasma protein itself bound by C-Reactive Protein (CRP). The presence of infection causes the immune system weakens, so the ability to protect the body be reduced and make pathogens including viruses enter the body and cause disease.

2. Research Method

Study Design and population: The study was done at Peneleh village in the Peneleh health district, which is located in Surabaya city, Indonesia. The village has a government health centre where the children were examined. Children aged from 24 to 60 month were recruited by eligibility criteria were 1) wasting(WH/ (-3 SD) – (-2 SD) have blood drawn and interviewed by signing an informed consent was elected as many as 101 sub-population of wasting children under five. 2) serum zinc <13.00 and ≥ 13.01 μmol / L in order to obtain 2 groups of children under five are 55 wasting children with normal zinc levels (≥ 13.01 μmol / L) 46 wasting children low zinc levels (<13.00 μmol / L). By using simple random sampling method for comparation analysis, 14 wasting children under five with normal zinc levels and 14 wasting children under five with low zinc levels.

Data was collected through interviews and direct observation, 2x24-hour recall and examination of CRP levels, levels of IgA and levels of zinc. blood serum zinc levels checked by using the AAS method (Atomatic Absorbent Spectofotometer) expressed in μmol / L, CRP levels checked by using Latex Test is expressed in mg / l and IgA levels were measured using ELISA method is expressed in mg / ml. The difference in levels of CRP and IgA levels of wasting among children under five levels of zinc based on independent t-test was used to test for the scale of the data interval / ratio, Chi-square test for nominal scale data and the Mann-Whitney test for ordinal data with data scale.

The amount of food is the average amount of food consumed inputs for 2x24 hours by using a food recall, and then converted into nutrient values with the guidelines of Food Composition List (DKBM) and subsequently compared with Nutrient Adequacy Score (RDA) in 2004.

3. Research Results

3.1. Serum CRP Levels

Tabel 1: Serum CRP levels and serum zinc levels in wasting children

Infection Disease (the 1st last month)	Low serum zinc levels		Normal serum zinc levels	
	n	%	n	%
No infection disease	6	43	7	50
Infection disease	8	57	7	50
Total	**14**	**100**	**14**	**100**

There was no significant differences between serum CRP levels in low serum zinc levels and normal serum zinc levels (p =1.00).

3.2. Infection Status and Serum Zinc Levels

Tabel 2: Infection status and serum zinc level in wasting children

Serum CRP levels	Low serum zinc levels		Normal serum zinc levels	
	n	%	n	%
High (≥6mg/L)	13	93	13	93
Low (<6 mg/L)	1	7	1	7
Total	**14**	**100**	**14**	**100**

There was no significant differences between infection status in low serum zinc levels and normal zinc levels (p = 1.000)

3.3. Serum IgA levels

Status of immunity was measured by using the parameters of Immunoglobulin A (Ig A) with cutt of points 70-350 mg / dl.

Tabel 3: Serum IgA Level and status serum zinc levels in wasting Children

Serum IgA Levels	Low serum zinc levels	Normal serum zinc levels
Average	139 ± 80	314 ± 187
Range	80 - 324	90 - 601

There were significant difference between serum Ig A levels in normal serum zinc levels than low serum zinc level (p <0,05).

Table 4: Daily Intake Energy Levels in Wasting Children Read phonetically

Daily Intake Energy Level (kCal)	Low serum zinc levels	Normal serum zinc levels
Mean	822 ± 282	845 ± 287
Range	487 - 1407	428 - 1484

There was no significant differences between daily energy intake between low serum zinc levels and normal zinc levels p = 0.833 (p> 0.05).

Table 5: Daily Intake Protein levels in Wasting Children

Daily Intake Protein Level (gram)	Low serum zinc levels	Normal serum zinc levels
Mean	30 ± 12	32 ± 13
Range	14 - 55	13 - 65

There was no significant differences between daily protein intake in low serum zinc levels and normal zinc levels in wasting children p = 0.733 (p>0.05)

Independent T test, did not showed significant differences between daily intake zinc levels in low serum zinc levels and normal serum zinc levels in wasting children p = 0.309 (p> 0.05). Although zinc intake in the children with normal zinc levels and low zinc level were deficit.

Table 6: Daily Intake Zinc Levels in Wasting Children under five

Daily Intake Zinc Levels (mg)	Low serum zinc levels	Normal serum zinc levels
Mean	3 ± 1	3 ± 1
Range	2 - 5	2 - 7

4. Discussion

4.1. Serum CRP Levels and Serum Zinc Level

The results showed no differences between serum CRP levels in low serum zinc levels and normal zinc levels in wasting children under five(p = 1.000)(p> 0.05). There was no significant differences between infection status in low serum zinc levels and normal zinc levels p <0.05 (p = 1.000).

This acute phase response affected the status of micronutrients in the body such as the status of zinc, where the effects of an infection on zinc metabolism was decline in serum zinc levels. Nutrient deficiency also disrupt the immune system and causes the body becomes resistant to infection. During the pain condition, levels of zinc in the plasma will decrease, although not so heavy. Zinc levels will decline due to a fever of 35% (Pakarek, 1969 in Thurnham, 2009).

Malnutrition often have a correlation with disease. Infectious diseases can affect nutritional status in several ways such as reducing nutrient intake of people with anorexia due to the inflammatory response, reduces the absorption of food caused by damage to the intestine, increased nutrient requirements due to increased metabolism, redistribution of nutrients, or activation of inflammatory / immune response, or loss of substance endogenous nutrients that may be caused by diarrhea (Thurnman, I in Hughes, 2004).

These findings suggest that a higher percentage of neutrophils with less bactericidal activity in many children with sickle cell disease and zinc deficiency may be a factor in the higher incidence of infections noted in these patients, and zinc might play a role in the formation, release, and activity of neutrophils(Carpeintery,U.et all,1983)

The zinc supplemented group had decreased incidence of infection compared with the placebo group. After zinc supplementation, red blood cell, hemoglobin (Hb), hematocrit, (Hct), plasma zinc, and antioxidant power increased; plasma nitrite and nitrate (NOx), lipid peroxidation products, DNA oxidation products, and soluble vascular cell adhesion molecule-1 decreased in the zinc supplemented group, compared with the placebo group. Zinc supplemented patients exhibited significant decreases in lipopolysaccharide-induced tumor necrosis factor-alpha (TNF-alpha) and IL-1beta mRNAs, and TNF-induced nuclear factor of kappaB-DNA binding in MNCs, compared with the placebo group (Bao Bin. Et all.2008).

Serum zinc levels were found significantly lower (i<0.001) in VL patients than non-endemic controls. The serum zinc levels in VL endemic controls were also significantly lower (P<0.001) than nonendemic controls, but these values were not statistically significantly different from VL patients. However, all samples from Bihar (VL patients and controls) had lower serum zinc levels than non-endemic controls from Delhi (Mishra.J,et all,2010.)

In order to investigate activation of the acute phase response, CRP was determined in the low serum zinc levels and normal serum zinc levels in wasting children. There was no difference between low serum zinc levels and normal zinc levels in wasting children.Wasting children, or low weight for height, is a strong predictor of mortality among children under five. It is usually the result of acute significant food shortage and/or disease.

Plasma CRP is produced in the liver in response to an infection or injury to the tissue and inflammatory processes. Inflammatory process is a process the body's reaction to the presence of infectious disease. CRP levels in the body will increase rapidly even up to 100 times around 6 hours after the inflammatory process occurs. Because the half-life is short, the CRP levels will also decrease rapidly when the inflammatory process to subside.

4.2. Serum IgA Levels and Serum Zinc Levels

There were significanty higher in serum Ig A levels in normal serum zinc levels (314 ± 80 mg/dl) than low serum zinc levels (139 ±187 mg/dl) in wasting chidren underfive.

Although in both groups of wasting children have the same infection, but wasting children with normal serum zinc levels still have a better immunity than low serum zinc levels. High levels of IgA in normal serum zinc levels in wasting children, it would protect from infection or desease.

4.3. Recommended Daily Allowance

Daily energy intake 822 ± 282 kCal (62% RDA) or deficit of calories according to age. Daily protein intake 30 ± 12 grams (90 %RDA), daily zinc intake 3 ±1 mg (36% RDA) in low serum zinc

levels in wasting children under five. Daily energy intake 845 ± 287 kCal (68 % RDA) or deficit of calories according to age. Daily protein intake 32 ± 13 grams (98% RDA), daily zinc intake 38 ±1 mg (38% RDA) in normal serum zinc levels.

There was no significant differences between daily energy intake in low serum zinc levels and normal zinc levels $p = 0.833$ ($p > 0.05$), did not showed significant differences between daily protein intake in low serum zinc levels and normal zinc levels in wasting children $p = 0.733$ ($p > 0.05$), did not showed significant differences between daily intake zinc levels in low serum zinc levels and normal serum zinc levels in wasting children $p = 0.309$ ($p > 0.05$).

Protein is essential in any muscle building plan, amino acids which are the building blocks of all proteins. They are used to replenish the damaged muscle tissue that is caused from strenuous exercise. The amount of protein and timing is very important when it comes to protein consumption. But not 100% of the calories from protein, energy daily intake must be balance (Gibson, 2005).

Needs of energy is different individually, different in each child and is determined by basal metabolism, age, physical activity, ambient temperature and health. Lack of energy in a long time and not addressed will cause the child has malnutrition. Least enough food for human consumption, can be qualitatively estimated from the size of the contribution of protein to energy value. When the adequacy of energy and protein met then the adequacy of other nutrients in general has also met or not trouble enough. At the macro nutrient deficiency conditions (calories and protein), it will usually be followed also by the lack of micronutrients (vitamins and minerals).

Daily protein intake to support growth and optimal child development must consider aspects of the quality and quantity. Protein needs of the children included high because children are still in a phase of rapid growth while the excess dietary protein is not stored as a reserve but will be discarded because of metabolism to produce the calories.

In addition to protein and vitamins, there are minerals that have a role in the immune system is zinc. According to the Adhi and Adriani (2008), states that the decreased levels of zinc affect the body's immune system against infection. Underfive children with low zinc levels, immunity decline marked by high frequency of illness, especially infectious diseases. Serum zinc concentration in humans decreased if suffering from an infection resulting in immune deficiencies. In addition, zinc deficiency can cause delayed growth and decreased appetite (Pudjiadi, 2001).

Consumption of zinc are less likely simply due to lower infection attack the body's immune defense. In addition, decreased appetite who may have an impact quickly on changes in body weight. As a result, it is clear that c-reactive protein is protein found in the blood the evels of which rise in response to inflammation. This condition is an both of low serum zinc levels and normal serum zinc levels, but in normal serum zinc levels wasting children more survive by produce IgA more higher than low serum zinc levels.

In conclusion, data suggest the significance. However, further studies are necessary not only to establish the suggestion can be given after analyzing the results of the overall research and low level of consumption among children under five malnutrition that affects the levels of zinc, it is advisable to energy intake, fat and zinc are very low, needs to be improved by providing nutrient-dense foods such as oysters or shredded snack oyster as a source of zinc and zinc supplementation conducted in conjunction with high-dose vitamin A administration.

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