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The Relationship Of Serum Zinc (Zn) Level, Insulin Like Growth Factor-1 (IGF-1), And Hemoglobin (Hb) With Placenta And Anthropometry Of Newborn

Halisah[1], Armiyati Nur[1] , Nurpudji Astuti Taslim[2] , Sitti Maisuri Chalid[3] , Aidah Juliaty[4] , Nasrudin Andi Mappaware[5] , Mardiana Ahmad[6] , Firdaus Hamid[7] , Ema Alasyri[4] , Aminuddin[2] , Kiki Uniatri Thalib[8] , Siti Suharni Hermanses[8,9] , Fasiha[9], Ismiyanti.H Achmad[9] , Mustardianto[10]

[1]Doctoral Program, Graduate School of Medicine, Hasanuddin University, Makassar, Indonesia.

[2]Department of Clinical Nutrition, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia.

[3]Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia.

[4]Department of Pediatrics, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia.

[5]Faculty of Medicine, University of Muslim Indonesia, Makassar, Indonesia.

[6]Midwifery Department, Graduate School, Hasanuddin University, Makassar, Indonesia.

[7]Microbiology Department, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia.

[8]College of Health Science Andini Persada, Mamuju, Indonesia.

[9] Department of Midwifery Maluku Health Polytechnic

[10]Jenderal Achmad Yani University, Indonesia.

ABSTRACT

Background: Zinc is an essential micromineral as a cofactor of more than 300 metalloenzymes that play an important role in cell regeneration, metabolism, growth, and repair of body tissues. Efforts to prevent fetal growth and development disorders begin in pregnant women, through integrated interventions, including specific nutrition interventions and sensitive nutrition. One of the specific nutritional interventions that can be given to pregnant women besides iron (Fe) is zinc supplementation.

Research purposes: To see the relationship between serum zinc levels, insulin like growth factor-1 (IGF-1) and Hemoglobin to pregnancy outcomes (anthropometry of infants and placenta).

Method: The subject population is normal pregnant women, 20-26 weeks of gestation, height 150 cm, age 19 years, family income below the Regional Minimum Wage of West Sulawesi Province.

Result: The results of statistical tests showed a significant relationship between serum zinc (Zn) levels, pregnant women and infant anthropometry with a significance value of $p < 0.05$, but there was no significant relationship between chest circumference and foot size. Levels of insulin like growth factor-1 (IGF-1) on anthropometry of infants found a significant relationship on body weight, head circumference, chest circumference, abdominal circumference, with $p < 0.05$

Conclusion: The provision of zinc supplementation for pregnant women is important because it can stimulate the growth and development of the fetus in the womb, especially for adolescent pregnant women who are chronically deficient in energy and of short stature.

Keywords: Zinc, Pregnancy Outcome

Introduction

The nutritional status and health of a pregnant woman are indicators of determining perinatal growth and neonatal well-being. Therefore, efforts to prevent impaired fetal growth and development are initiated in pregnant women, through integrated interventions, including specific nutrition interventions and sensitive nutrition. One of the specific nutritional interventions that can be given to pregnant women besides iron (Fe) is zinc (Zn) supplementation.[1].

Zinc is an essential micromineral as a cofactor of more than 300 metalloenzymes that play an important role in cell regeneration, metabolism, growth, and repair of body tissues. Every day the body experiences zinc excretion so that daily zinc intake is needed to maintain normal zinc in the body because the body does not have a special mechanism to store zinc. Zinc is said to be a micronutrient because it is needed in the body in small amounts, only 20 milligrams per day. However, although it is needed in small amounts, if not met, zinc deficiency results in decreased immunity, increased morbidity due to infectious diseases, impaired growth and motor and cognitive development. In pregnant women, severe zinc deficiency can cause spontaneous abortion and congenital abnormalities, while moderate zinc deficiency will cause low birth weight (LBW) babies. Zinc is used for bone formation. Insufficient zinc intake in pregnant women stimulates the baby's susceptibility to zinc deficiency, this is due to zinc intake which accumulates during pregnancy until delivery. [2].

In developed countries, there are about 82% of pregnant women consuming foods with less zinc sources, causing health problems [3]. The results showed that from 68 samples of pregnant women, zinc consumption of all respondents was not according to needs, namely 39.7% in the poor category and 60.3% very less. Based on the results of serum zinc examination, all respondents experienced zinc deficiency with a low category of 58.8% and very low 41.2%, and found that plasma zinc levels were higher in normal infants compared to infants with Intrauterine growth restriction (IUGR)[4]. On examination of pregnancy outcome 4.4% had low birth weight and 41.2% babies were born short. However, the description of the prevalence of zinc deficiency specifically in developing countries is not known, due to the lack of proper consensus as an indicator of zinc status and the lack of data on various aspects of zinc status [5].

Methods

Quasi experiment which was held in September 2020 - June 1, 2021 in the city of Mamuju Regency. The subject population is normal pregnant women, 20-26 weeks of gestation, height 150 cm, age 19 years, family income below the Regional Minimum Wage of West Sulawesi Province. This study was approved by the Research Ethics Commission of the Hasanuddin University Medical Faculty Makassar, and written consent was obtained from all respondents who were willing to participate in the study. This study has also been registered with Clinical Trials No.NCT05100550. Pregnant women who met the inclusion criteria were given informed consent. Pregnant women who were identified with a history of zinc treatment before the study, suffering from pre-eclampsia, multiple pregnancies, and other complications that could affect the condition of the mother and fetus were excluded.

Method of collecting data

Consecutive sampling method was used to select the sample, determine the intervention and control groups separated by area of the Puskesmas. Data collection for newborns was carried out by anthropometric measurements of the baby's weight using a weighing scale SECA 703, the length of the baby's body using the SECA 207 Length board, measuring head circumference, chest circumference and abdominal circumference with a measuring tape and foot length using a big black stainless steel ruler.

To measure the weight of the placenta using a digital scale, the diameter of the placenta uses a meter, the maximum and minimum diameters of the placenta are calculated, then the average middle value is taken. The thickness of the placenta is measured using a needle at 5 points in 3 different places, namely one needle in the central area. In the placenta, two needles in the area midway between the center and the edge of the placenta and two other needles in the area at the edge of the placenta were then taken the average of the mean values. Serum zinc (Zn) levels were examined using the Colori metric and elisa test methods for the examination of IGF-1. A statement of consent was given to subjects who met the criteria and agreed to participate after being notified of the benefits of the study. Subjects were given treatment with zinc supplement tablets as much as 20 mg/day for 12 weeks along with providing education about the benefits and impacts of zinc deficiency for pregnant women using the family approach method as many as 4 meetings through home visits as well as observing adherence to taking zinc supplements during education implementation. All blood samples were centrifuged in the laboratory to separate the serum and then stored at a temperature of 2-8 degrees Celsius, the collected samples were examined for serum zinc and IGF-1 levels at the Laboratory of RSPTN Hasanuddin University Makassar.

Data analysis

IBM SPSS Statistics for Windows, Version 23.0 (IBM Co., Armonk, NY, USA), was used to analyze the data. Subjects were pregnant women who were given education accompanied by zinc supplementation. We used univariate analysis to describe the frequency, mean, standard deviation, and range of mothers sampled in this study. Correlation test of serum zinc, IGF-1, hemoglobin levels to anthropometry of infants and placenta was studied using bivariate analysis.

Results

The results of statistical tests showed a significant relationship between serum zinc (Zn) levels, pregnant women and infant anthropometry with a significance value of $p < 0.05$, but there was no significant relationship between chest circumference and foot size. Levels of insulin like growth factor-1 (IGF-1) on anthropometry of infants found a significant relationship on body weight, head circumference, chest circumference, abdominal circumference, with $p < 0.05$. However, there was no significant relationship between body length, foot length, placenta diameter and placenta thickness. Based on the results of statistical tests on hemoglobin (Hb) levels of pregnant women on infant anthropometry, it was found that there was a significant relationship with weight and head circumference of newborns with $p < 0.05$. However, there was no significant relationship between hemoglobin (Hb) levels of pregnant women and body length, chest circumference, abdominal circumference, and foot length, with $p > 0.05$ (Table 1).

Table 1. Relationship of serum zinc (Zn) levels, insulin-like growth factor-1 (IGF-1), Haemoglobin (Hb) with infant anthropometry

Variable	Zink		IGF-1		Hb	
	p	r	p	r	p	r
Newborn anthropometry						
Weight	0.003	0.404**	0.033	0.273*	0.003	0.374**
Body length	0.005	0.353**	0.104	0.210	0.062	0.240
Head circumference	0.009	0.332*	0.001	0.399**	0.046	0.257*
Chest size	0.054	0.248	0.017	0.304*	0.334	0.126
Belly circumference	0.040	0.263*	0.008	0.338**	0.237	0.154
Foot length	0.237	0.154	0.059	0.243	0.237	0.154

p= Spearman Rho test

The results of statistical tests showed a significant relationship between serum zinc (Zn) levels, pregnant women with weight, diameter and thickness of the placenta with a significance value of $p<0.05$. Insulin-like growth factor-1 (IGF-1) levels were found to have a significant relationship with the weight of the placenta with $p < 0.05$, but not related to the thickness and diameter of the placenta.

Based on the results of statistical tests on hemoglobin (Hb) levels of pregnant women against placental anthropometry, there was no significant relationship with $p>0.05$ (Table 2).

Table 2. Correlation of serum zinc (Zn) levels, Insulin-like growth factor-1 (IGF-1), Haemoglobin (Hb) with placental anthropometry

Variable	Zink		IGF-1		Hb	
	p	r	p	r	p	r
Anthropometry of the placenta						
Placenta weight	0.040	0.263	0.004	0.365**	0.095	0.216
Placenta Diameter	0.348	0.122	0.295	0.136	0.103	0.211
Thick of placenta	0.013	-0.316	0.179	-0.174	0.241	-0.153

p= Spearman Rho test

Discussion

The results of this study found a relationship between blood serum zinc levels of pregnant women and pregnancy outcomes. Zinc is one of the trace minerals or micro-minerals that are essential for all forms of life, including plants, animals and microorganisms [6]. More than 300 different zinc dependent enzymes have been identified in all phyla. Zinc has a known action on these metalloenzymes due to its participation in its structural, catalytic and regulatory action [7]. Zinc deficiency is always accompanied by changes in smell and taste and by anorexia and weight loss. A metalloenzyme responsible for taste sensation has been identified and is associated with human hypogeusia or dysgeusia, a disorder that can be completely corrected by zinc therapy[7]. These changes can occur even in individuals who consume foods with low amounts of zinc [8]. Zinc stimulates the appetite of pregnant women so that it affects the pattern of nutrient consumption which has an impact on the growth and development of the fetus in the womb.

The relationship between zinc, GH and animal growth proves that zinc can be directly involved in the synthesis and action of GH. The first published report on this topic was from La Bella et al. which showed that zinc at a concentration of 6x10m5 M stimulated GH secretion when bovine pituitary extract was used [9]. Normal levels of IGF-1 in serum is a marker that GH levels in the blood are normal and vice versa. IGF-1 is produced in the liver under regulation by GH. Growth Hormone stimulates IGF-1 synthesis in the liver and vice versa, IGF-1 levels will require a back response to GH production in the pituitary. Several studies have shown a correlation between IGF-1 levels and blood insulin levels[10]. Normal levels of IGF-1 in serum is a marker that GH levels in the blood are normal and vice versa. IGF-1 is produced in the liver under regulation by GH. Growth Hormone stimulates IGF-1 synthesis in the liver and vice versa, IGF-1 levels will require a back response to GH production in the pituitary. Several studies have shown a correlation between IGF-1 levels and blood insulin levels [11]. In acute conditions, IGF-1 suppresses insulin and glucagon production in the human body [9] Insulin-like Growth Factor 1 (IGF-1) is a polypeptide hormone produced mainly by the liver in response to growth hormone (GH) stimulation.[10]. IGF-1 stimulates the synthesis of 1,25-(OH)2D in the kidneys to increase the absorption of calcium and phosphate in the mother's body which will then be sent to the fetus through the placenta for growth and fetal bone formation. [12]. IGF-1 also gives a positive signal to the Mammalian Target of Rapamycin (mTOR) which is a placental nutrient sensor in trophoblast cells. IGF-1 stimulates several nutrient transporters in the placenta, including glucose, protein and fatty acid transporters which are needed for the growth and development of the fetus during pregnancy. IGF-1 is one of the main regulators of fetal growth through its effects on the mother's body metabolism and stimulation of the placenta, if the concentration of IGF-1 is reduced it can result in impaired nutrient transport from mother to fetus so that fetal growth and development is not optimal [13].

Several previous studies have reported that maternal serum IGF-1 levels can affect birth weight, but there is still controversy regarding the role of IGF-1 on fetal growth, this is because IGF-1 cannot cross the placenta and the effect of IGF-1 may be through the stimulation of placental function and an increase in the supply of nutrients to the fetus[10]. Maternal IGF-1 can affect fetal growth through its stimulatory action on nutrient transporter activity in the placenta [14]. The placenta plays a very important role in the growth and development of the fetus so that disturbances in placental function can cause overgrowth or IUGR [15]. Maternal hormones such as insulin, IGF-1 and mTOR signaling in the trophoblast are the main regulators of amino acid transport in the placenta, where amino acids are needed by the fetus for the process of forming tissues and organs[11]. Glucose is also one of the important nutrients in fetal growth, the production of fetal blood sugar is very minimal, making the fetus completely dependent on the supply of glucose from the maternal circulation through the placenta. Low blood sugar levels during pregnancy can lead to an increased incidence of neonates with Small for Gestational Age (SGA)[16].

The interaction between iron and zinc takes place indirectly, the role of zinc in the synthesis of transferrin protein, which is an iron transport protein, and because zinc deficiency also reduces the immune system and can interfere with iron metabolism. In pregnant women with normal Hb and normal birth weight due to adequate blood supply of nutrients for oxygen to the placenta which will affect the function of the placenta to the fetus so that the baby is born with a normal birth weight [17].

Can be concluded that the provision of zinc supplementation for pregnant women is important because it can stimulate the growth and development of the fetus in the womb, especially for adolescent pregnant women who are chronically deficient in energy and have poor posture.

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