Research Article

The Levels of Zinc, Selenium, Iron and Copper in Preterm Pregnancy do not Differ with those of Healthy Pregnancy

Kadar Seng, Selenium, Besi dan Tembaga pada Kehamilan Prematur tidak Berbeda dengan Kehamilan Sehat

Noroyono Wibowo, Fitriana

Department of Obstetrics and Gynecology
Faculty of Medicine Universitas Indonesia
Dr. Cipto Mangunkusumo General Hospital
Jakarta

Abstract

Objective : To compare zinc, selenium, iron and copper levels in maternal serum of healthy and preterm pregnancy.

Methods : This was a cross-sectional study with preterm and healthy pregnant woman who will carry delivery in Dr. Cipto Mangunkusumo National Hospital and Budi Kemuliaan Hospital Jakarta from January to April 2017. This study was conducted by comparing the levels of each micronutrient in both groups of subjects.

Results : From January to April 2017, there were 53 subjects divided into 30 normal pregnant women and 23 preterm pregnant women. The levels of zinc, selenium iron and copper in preterm pregnancy were 42 μg/dL, 72,39 μg/L, 74 μg/L, and 2144,52 μg/dL. Levels of zinc, selenium, iron and copper in normal pregnancy were 42 μg/dL, 67,27 μg/L, 70,5 μg/L, and 2221 μg/dL. There was no difference in micronutrients level in both groups.

Conclusions : This study concluded that there was no difference in zinc, selenium, iron and copper levels in healthy and preterm pregnancy.

Keywords : copper, iron, pregnancy, selenium, zinc.

Abstrak

Tujuan : *Membandingkan kadar seng, selenium, besi dan tembaga pada serum maternal ibu hamil normal dan preterm.*

Metode : *Penelitian dilakukan dengan uji potong-lintang dengan subjek penelitian ibu hamil baik preterm maupun aterm yang akan melaksanakan persalinan di RSUPN Dr. Cipto Mangunkusumo dan RS Budi Kemuliaan Jakarta pada Januari hingga April 2017. Penelitian dilakukan dengan membandingkan kadar masing-masing mikro nutrien pada kedua kelompok subjek.*

Hasil : *Dalam jangka waktu Januari hingga April 2017 didapatkan 53 subjek penelitian yaitu 30 ibu hamil normal dan 23 ibu dengan kehamilan preterm. Seluruh subjek dimasukkan dalam analisis data. Kadar seng, selenium, besi dan tembaga pada ibu dengan kehamilan preterm secara berurutan adalah 42 μg/dL, 72,39 μg/L, 74 μg/L, dan 2144,52 μg/dL. Sedangkan kadar seng, selenium, besi dan tembaga pada ibu hamil normal secara berurutan adalah 42 μg/dL, 67,27 μg/L, 70,5 μg/L, dan 2221 μg/dL. Tidak ada perbedaan bermakna kadar mikro nutrien pada kedua kelompok subjek.*

Kesimpulan : *Penelitian ini menyimpulkan bahwa tidak ada perbedaan kadar seng, selenium, besi dan tembaga pada ibu hamil normal dan ibu dengan kehamilan preterm.*

Kata kunci : *kehamilan, seng, selenium, besi, tembaga.*

Correspondence author : Noroyono Wibowo. wibowonoroyono@yahoo.com

INTRODUCTION

Nutritional needs in pregnant women increase more than the healthy population. Nutritional needs in pregnant women consist of the macronutrients consist of protein, carbohydrates and fats and micronutrients like minerals and vitamins. Nutritional disorders, both overnutrition and undernutrition may cause amenorrhea, infertility and miscarriage and impaired fetal growth.[1]

Maternal nutrition status during pregnancy plays a vital role in determining the outcome of pregnancy. Nutrition has been known to play a role in the pathogenesis of pregnancy complications such as preterm birth, impaired fetal growth, preeclampsia, anaemia and gestational diabetes mellitus.[2,3] Maternal malnutrition, either over-nutrition, undernutrition, or micronutrient deficiency can cause intrauterine inflammation.[4] Some micronutrients such Vitamins A, B6, B12, C, D, E, folic acid, zinc, and docosahexaenoic acid (DHA) affect immune system function and reduce oxidative damage in the placenta. Zinc, vitamin A and D act as immune system regulators and have anti-inflammatory effects.[2]

A prospective study found that dietary iron intake was associated with significantly increased risk of type 2 diabetes. Furthermore, serum ferritin levels were associated with the risk of diabetes, hypertension, metabolic syndrome, cardiovascular risk factors, and inflammation.[5] Iron deficiency affects 1.6 billion people worldwide, and pregnant women are at the highest risk. Anaemia during pregnancy is associated with labour complications, premature birth, low birth weight, decreased iron infant status, impaired maternal and infant interactions, and increased maternal and infant mortality.[6]

Zinc levels are lower in women in developing countries. This is related to 2,5 times more likely to deliver babies weighing less than 2000 g.[1] Selenium deficiency causes reproductive obstetric complications among others male and female infertility, miscarriage, preeclampsia, fetal growth restriction,[(7)] preterm labour,[7-9] and gestational diabetes.[7]

Preterm pregnancy is considered as abnormal pregnancy outcomes. Preterm labour is delivery before 37 weeks of complete gestation. Preterm labour is still a problem worldwide. The 2010 WHO report states that Indonesia is ranked fifth in the country with the highest preterm delivery of 675,700 per year.[10,11]

Preterm labour, impaired fetal growth and preeclampsia is known as "the Great Obstetric Syndrome". This all three diseases known as multifactorial diseases. In their pathophysiology known that there is implantation failure resulting in placental dysfunction. As a result, there will be Toll-like Receptor (TLR) activation followed by bonded to MyD88 forms Nuclear Factor Kappa Beta (NFκB). This activation will form pro-inflammatory cytokines such as IL, IL-1β and TNF-α. Placental dysfunction also causes oxidative stress. NFκB's aberrant and premature activities and oxidative stress cause preterm labour.[5,6,12,13]

Micronutrient levels in pregnant women are examined from maternal serum. Some studies have not come to a consistent conclusion about the relationship between micronutrient levels and preterm pregnancy. In addition, there is no similar research has been conducted in Indonesia. In this study, researchers want to know the differences in micronutrient levels in both normal pregnant women and preterm labour. The micronutrient levels assessed in this study are zinc, selenium, iron and copper.

OBJECTIVES

The objective of this study is to determine the average rate of micronutrients of zinc, selenium, iron and copper in normal labour and preterm labour. This study also wanted to know the difference between the mean level and the relationship in each group. The authors hypothesised that there were significant mean differences between the two groups.

METHODS

This was a cross-sectional study conducted for 4 months, from January until April 2017, at Emergency Room RSUPN Dr. Cipto Mangunkusumo and RS Budi Kemuliaan Jakarta. Subjects were collected using consecutive method sampling. The minimum subjects are 31 subjects in each group. The inclusion criteria for this study are mothers who will give delivery with full-term pregnancy (27-42 weeks) or had preterm labor at 28-36 weeks of gestation without premature rupture of membranes, no complications found during pregnancy, no nutritional problems and no other treatment unrelated pregnancy. The exclusion criteria in this study are multiple pregnancies, the subjects have another medical condition, and there are congenital abnormalities in the fetus.

Subjects who met the study criteria were asked their willingness to follow the study. After anamnesis and physical examination, the data are collected in research status. Right before the patient gave birth, 5 cc of blood venous was taken by an intravenous puncture for micronutrient examination. Micronutrient examination is done at Prodia Laboratory. Blood samples were centrifuged at 3000 rpm followed by ICP-MS analysis.

Data were analyzed with SPSS version 20.0. Data with normal distribution will be reported in average and standard intersections, whereas if abnormal data distribution will be reported in the median with minimum and maximum value. Then, bivariate analysis was done unpaired T-test if the distribution of the date is normal and Mann-Whitney test if the data distribution is not normal. The relationship between the two groups was assessed from the p-value in the comparison of the two group's average.

RESULTS

There were 53 mothers from RSUPN Dr. Cipto Mangunkusumo and RS Budi Kemuliaan who met the criteria, participate in research as the subject of research. A total of 23 samples were mothers with preterm birth and 30 samples were mothers with normal pregnancies. The mean age of mothers is 27 years old with the youngest age is 16 years and the oldest age is 46 years.

Micronutrient Examination

There was no significant correlation between micronutrient levels and maternal pregnancy status in maternal serum examination. The mean values of zinc in both groups were similar and no significant difference was found between iron levels in both groups. The selenium level in preterm is 5,13 µg/L higher than the normal group. The copper levels in full-term pregnancy are 76,47 µg/L higher than preterm, but there is no statistical difference between the two groups.

Table 1. Micronutrient Levels in Full Term and Preterm Pregnancy

Variable	Group	n	Result	*P-value*
Zinc [µg/dL; median (min-max)]	Preterm Term	23 30	42 (16-64) 42 (24-59)	0,962*
Selenium [µg/L; mean ± SD]	Preterm Term	23 30	72,39 ± 18,25 67,27 ± 20,37	0,347#
Iron [µg/dL; median (min-max)]	Preterm Term	23 30	74 (22-234) 70,5 (24-292)	0,846*
Copper [µg/L; mean ± SD]	Preterm Term	23 30	2144,52 ± 658,47 2221,,00 ± 542,61	0,645#

* Mann-Whitney test
# Unpaired T-Test

This study includes 53 subjects where 23 subjects with preterm labor and the other are full-term labor. The subjects were less than minimum number of subjects needed, 62 subjects, 31 subjects each group. The research conducted over productive age, ranged from 16 to 46 years old.

Zinc is transferred passively from mother to fetus through the placenta. During pregnancy, there is an increase in zinc binding capacity. Higher levels of zinc on the umbilical cord allow the transfer of zinc from the maternal to the fetus. This decrease of maternal zinc levels during pregnancy is considered as physiological adjustment during pregnancy due to changes in blood volume.[14] Zinc is needed during early pregnancy for organ formation and tissue development. In previous studies it was found that there was a positive correlation between gestational age and zinc levels on the umbilical cord. Meanwhile, maternal serum maternal serum levels were inversely related to gestational age.[14,15]

In this study was found that both in preterm and full-term pregnancy, the mean level of Zinc was 42 µg/dL. This level was slightly below the normal levels.[16] There was no significant difference between zinc levels in both groups. Based on a study conducted in 2000 in India, it was concluded that zinc levels in pregnant women in Indonesia are very low. The zinc levels found in maternal serum examination were 633,5 µg/L. They also concluded that zinc levels in pregnant women were higher than zinc levels in non-pregnant adult women.[17]Other study conducted in Iran stated that the level of zinc in full-term pregnancy were 654,76 µg/L.[18]

The relationship between gestational age and zinc levels in maternal blood has been widely studied. In research conducted by Khadem et al, found a significant difference between zinc levels in full-term and preterm pregnancy. Level of zinc tend to be higher in the early pregnancy.[18,19]

A study conducted in India found that zinc levels in full-term neonates were found to be significantly different than in preterm born neonates. It was found that zinc levels in maternal serum of normal pregnant women were significantly lower than in preterm pregnant women. There was a positive relationship between maternal age and serum zinc on the umbilical cord and inversely related to zinc levels in maternal serum.[15]

This study concluded that there was no correlation between zinc level and gestational age. In contrast, a study conducted in Iran concludes that there was a statistically significant difference between zinc levels in the third trimester compared to the first and second trimesters. There was no significant difference between zinc levels in the first and second trimesters.

Some confounding factors to zinc level in maternal blood serum were not included in this study. Confounding factors may affect maternal zinc levels such as dietary nutritional intake, smoking, alcohol consumption and gastrointestinal disorders.[20]

The average selenium levels were 69,49 μg/L. The mean difference between both groups is 5,13 μg/L. The selenium levels in preterm pregnancy were higher than full-term pregnancy. However, there was no statistically significant relationship between both groups. Levels of selenium in pregnancy found in this study were 2 times higher than the level of selenium in normal pregnant women.

A study conducted in Spain showed the level of selenium in maternal blood serum ranged between 57,3 to 117,9 μg/L. The study also concluded that selenium level in maternal serum was higher than other tissue such as umbilical cord, placenta, nails and hair.[21] Other study showed that selenium level in full-term pregnancy was higher, with an average of 111 μg/L.[22] Another study conducted in Canada stated that the selenium level in pregnant women was 120 μg/L.[23] All of this study show that selenium level in maternal serum in this study was lower than the other.

Several studies support the conclusion of this study. There was no significant relationship between gestational age and maternal selenium levels. [21,22,24] A study conducted in Israel concludes that there was a significant increase of selenium levels in the umbilical cord along with increasing gestational age. This result was hypothesised due to an increased need for selenium by the placenta.

Similarly, a study by Iranpour et al. found no significant association between gestational age and plasma selenium levels but found a significant difference in mean selenium levels in the full term pregnancy with preterm in the umbilical cord. Although there was no significant difference, the levels of selenium in maternal blood full-term pregnancy were higher than in the preterm, in contrast to the results found in this study.[25] Other studies conducted in Israel suggest that selenium levels at the third trimester of pregnancy are lower than the first trimester.[22]

Iron levels in maternal serum group of preterm pregnant women in this study were 74 μg/L and 70,5 μg/L in a full-term pregnancy. The iron levels in both groups of subjects were within the normal range according to the CDC. Iron levels in full-term pregnancy the study were slightly below the lower limit of normal serum iron levels in normal women. However, there were no significant differences found. A similar conclusion also concluded by a study conducted in Jordan. The serum iron levels found in this study were also similar to the Jordanian study which is 74 μg/L.[26] Several other studies also concluded that there is no relationship between gestational age and iron content. A study conducted in India found that the iron level in full-term pregnancy were only 35,4 μg/L.[27]

From a study conducted in India, it was found that iron levels in the umbilical cord were significantly higher than maternal serum iron. Although the maternal serum iron levels were lower than normaly values, the haemoglobin and iron levels of infants were still within normal range.[28] There was a significant association between iron levels in maternal serum and iron levels in neonates. This is due to that iron is actively transported to the fetal tissue as needed. Some other things to consider in determining iron levels in pregnant women is the dietary intake of iron, Hemoglobin levels, and environmental factors such as smoking.

Copper cannot move passively diffusive from the maternal serum to the fetus. Copper from maternal serum is deposited in the placental tissue and then transferred to the fetal tissue actively according to the needs of the fetal tissue. Increased levels of copper during pregnancy occur due to increased bonding with proteins. This increase occurs physiologically because estrogen will induce ceruloplasmin synthesis during pregnancy.14 In anaemic pregnancies, ceruloplasmin is a compensatory mechanism. Ceruloplasmin bound to copper and transported through the placental tissue to maintain copper levels in the neonate.[29]

Copper levels in this study were 2144 µg/L in the preterm group and 2221 µg/L in the full term pregnancy. There was no significant difference between copper levels in both groups. The levels of copper in this study were above the normal average according to the National Academy of Science.[30]

In a study conducted in Jordan it was found that there was a significant difference between copper levels in the first trimester and the second and third trimesters. The results of this study showed that there was an increasing level of copper levels according to gestational age.[31]Another study conducted in India it was found that there was a relationship between gestational age with copper levels in the umbilical cord, but no relationship between gestational age and copper levels in maternal blood serum.[32]

CONCLUSION

In this study, it can be concluded that iron, selenium and copper levels in preterm and healthy pregnancy are within normal range, but zinc levels in preterm and healthy pregnancies are lower than the normal range. There is no significant difference between zinc, selenium, iron and copper levels in preterm and healthy pregnancies. However, due to a small number of subjects, we suggest to do further study with larger number of samples and examine the micronutrient levels in the placental tissue and umbilical blood cord to understand the mechanism of micronutrient transfer.

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