

## RESEARCH ARTICLE

# Maternal Micronutrient Deficiency during the First Trimester among Indonesian Pregnant Women Living in Jakarta

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## Abstract

*Restricted fetal growth and development is supported by the adequacy of several micronutrients, and mostly by iron, zinc, calcium, folate and B12 vitamin. This study aims to evaluate the maternal micronutrient status from dietary intake and blood sample. A cross-sectional study as part of the micronutrient intervention study was carried out in 143 healthy pregnant women during their first visit to the two maternity clinics in Jakarta Indonesia (August 2013 – July 2014). Twenty-four hour dietary recall and semi-quantitative food frequency questionnaire were used to collect micronutrient intake data, while standard laboratory procedures were applied to analyze micronutrient status from the blood sample. The dietary assessment data showed insufficiency of iron, zinc, calcium, vitamin D, folate and vitamin B12 intake (less than its RDA) among 88.8%, 95.1%, 97.9%, 100%, 90% and 78.3%, respectively. In relation iron status, 11.2% of the subjects were anemic and 20.3% had low ferritin level. Zinc deficient was found among 35% of the subjects. Deficiency of calcium and vitamin D were found among 25.2% and 90.2% of the subjects, respectively. Furthermore, deficiency of both folate and vitamin B12 were found to be 2.8%. Nutrition counseling and education, and the provision of multi-micronutrient fortified food as well as multi-micronutrient supplement specifically designed for mothers should be started in the earliest time, i.e. starting from the peri-conception period.*

**Keywords:** Indonesia, micronutrient, pregnancy

## Defisiensi Mikronutrien Maternal Selama Trimester Pertama pada Ibu Hamil di Jakarta

### Abstrak

*Pertumbuhan dan perkembangan janin didukung oleh kecukupan beberapa mikronutrien, terutama oleh zat besi, seng, kalsium, folat dan vitamin B12. Tujuan penelitian untuk mengevaluasi status mikronutrien ibu dari asupan makanan dan sampel darah. Penelitian cross-sectional ini bagian dari penelitian intervensi mikronutrien dan melibatkan 143 wanita hamil sehat yang melakukan kunjungan pertama ke dua klinik bersalin di Jakarta Indonesia (Agustus 2013 - Juli 2014). Recall diet dua puluh empat jam dan kuesioner semi-kuantitatif frekuensi makanan digunakan untuk mengumpulkan data asupan mikronutrien, sedangkan analisis mikronutrien dari sampel darah menggunakan prosedur standar laboratorium. Hasil analisis menunjukkan insufisiensi besi, seng, kalsium, vitamin D, folat dan vitamin B12 (lebih rendah dibandingkan RDA) yaitu 88,8%, 95,1%, 97,9%, 100%, 90% dan 78,3%. Kaitannya dengan status besi, sebanyak 11,2% subjek anemia dan 20,3% memiliki tingkat feritin rendah. Kekurangan seng ditemukan sebanyak 35% subyek. Kekurangan kalsium dan vitamin D ditemukan sebanyak 25,2% dan 90,2%. Sedangkan kekurangan folat dan vitamin B12 keduanya ditemukan sebanyak 2,8%. Konseling gizi, edukasi, dan penyediaan makanan yang diperkaya mikronutrien serta suplemen mikronutrien khusus ibu hamil harus mulai sedini mungkin yaitu mulai dari periode peri-konsepsi.*

**Kata kunci:** Indonesia, mikronutrien, kehamilan

## Introduction

Restricted fetal growth and development is caused by the interrelated factors, i.e. hormonal adaptation and epigenetic gene regulation. Nutrition is fundamentally needed to start a pregnancy or during the periconceptional period because it has the potential effect to number of cells differentiation in the developing vital organs during the embryonic stage. The impact on vital organ functions, i.e. renal, cardiovascular, pancreas, body composition and pulmonary functions, increase the infants cardio-metabolic risk in his adult life. Thus, nutrition could have an impact on the overall outcome of the pregnancy itself and on the nature of adult diseases.<sup>1</sup>

The hormonal adaptation and epigenetic gene regulation leading to cardiometabolic functional programming are supported by the adequacy of several micronutrients, and mostly by iron, zinc, calcium, folate and vitamin B12. Iron, beside its function for haematopoiesis, it is also linked to the changes in renal morphology and hypertension in the offspring. Zinc has a structural, regulatory and catalytic function as cofactor for numerous metalloenzymes, and may contribute to the elevated arterial blood pressure and kidney lesions in alter life. Calcium is commonly known being responsible for bone mineralization. However, inadequate maternal calcium intake may also play a role in hypertension programming. Folate is crucial for synthesis of nucleic acids and cellular division. Moreover, folate and vitamin B12 together were linked to the increased of adipose tissue and insulin resistance.<sup>2</sup>

Indonesia as one of the developing countries faces maternal nutrition problem, i.e. high proportion of low birth weight baby (10.2%), high prevalence of anemia (ranged from 10-40%), although the compliance of iron pills intake among pregnant women was reported up to 89%.<sup>3</sup> There is no information yet regarding to micronutrient status in relation to the increasing cardiometabolic risk for the later life of the offspring. This study aims to evaluate maternal micronutrient status from dietary intake and blood sample among Indonesian pregnant women during their first visit to the maternity clinic in Jakarta.

## Methods

A cross-sectional study as part of the main study entitled "Effect of Probiotic and Micronutrient-enriched Milk on Maternal Micronutrients' Status and Digestive Health among Indonesian Pregnant Women: a Randomized Double-Blind Placebo-Controlled Study" was carried in two maternity clinics in Jakarta Indonesia during August 2013 – July 2014. Apparently healthy pregnant women living in Jakarta with a singleton uncomplicated pregnancy was recruited after signing the informed consent. By using 50% as the proportion of any micronutrient deficiency, 95% degree significance and 90% degree of reliability, then 100 subjects were needed as the minimal sample for this study.

We performed general pregnancy examination to measure weight, height, and blood pressure. Twenty-four hour dietary recall and semi-quantitative FFQ (food frequency questionnaire) were used to collect micronutrient intake data. The average of these two approaches was used to present the micronutrient intake of the study. Standard laboratory procedures were applied to analyze each of micronutrient concentration from the blood sample.

All data was managed and analyzed descriptively by using Statistical Program for Social Sciences (SPSS) version 20, and presented as tables and figures.

## Results

This study recruited 143 subjects. Table 1 shows the general characteristics of the subjects. The age was varied between 17 to 39 years old, in which the age of 20-35 years is recommended to have a safe pregnancy. Most of the subjects were graduated from high school (91%) and more than 50% was working. The subjects visited the maternity clinic at their 10 weeks of pregnancy in average.

Using the measurements of weight and height during their first trimester, the body mass index as the indicator to plan a healthy body weight increment throughout the pregnancy was varied from as low as 17.3kg/m<sup>2</sup> (thin) to as high as 38.2kg/m<sup>2</sup> (obese). Nausea (70.6%) was the most reported complaint found among the subjects as compared to the other complaints related to pregnancy.

**Table 1. General Characteristics of the Subjects (n = 143)**

Variables	Value
Age, year*	29 (17 - 39)
Education Level, n (%):	
Less than High School	13 (9.0)
High School	56 (39.2)
Higher Education	74 (51.8)
Working Status, n (%):	
Housewife	61 (42.7)
Working	82 (57.3)
Gestational age, week	10.5 ± 2.5
Body weight, kg*	57 (39 – 94.7)
Height, cm*	156 (140 - 168)
Body mass index, kg/m <sup>2</sup> *	23.3 (17.3 – 38.2)
Blood pressure, mmHg:	
Systolic*	110 (90 - 144)
Diastolic*	70 (56 - 90)
General complaints related to pregnancy, n (%):	
Nausea	101 (70.6)
Vomit	55 (38.5)
Constipation	5 (3.5)
Diarrhea	11 (7.7)

\*median (minimum and maximum value), otherwise in mean ± SD;

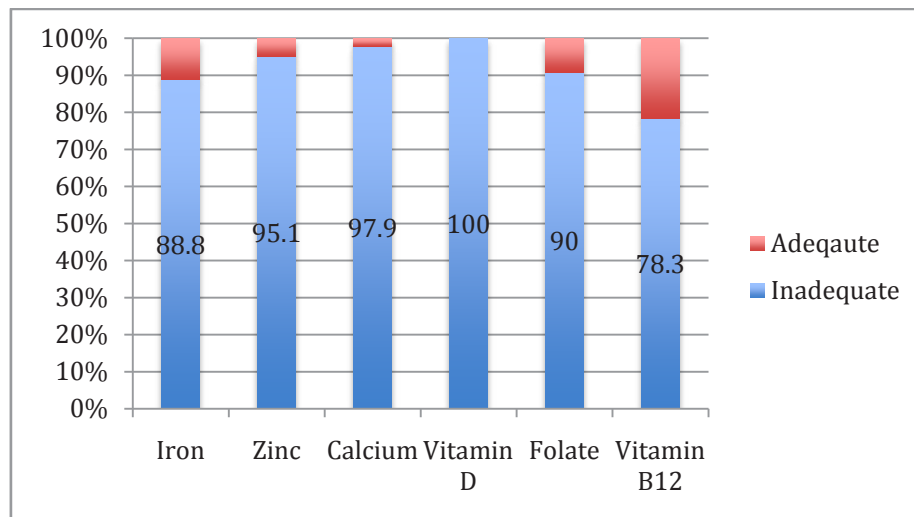
Table 2 shows the dietary intake of iron, zinc, calcium, folate and vitamin B12 of the subjects as compared to the Indonesian RDA, and all are presented as its median. In general, it revealed that 50 percent of the subjects had lower intake as compared to its RDA.

**Table 2. Dietary Iron, Zinc, Calcium, Vitamin D, Folate and Vitamin B12 Intake of the Subjects as Compared to the Indonesian RDA for First Trimester of Pregnancy (Recommended Dietary Allowances) (n = 143)**

Dietary Intake	Value	RDA
Iron, mg*	10.3 (2.7 – 67.8)	12
Zinc, mg*	2.3 (0.5 – 55.6)	12
Calcium, mg*	433.3 (126.8 – 1916.7)	1200 - 1300
Vitamin D, µg	1.1 (0 – 11.1)	15
Folate, µg*	297.3 (19.6 – 1052.1)	600
Vitamin B12, µg*	1.4 (0.1 – 27.9)	2.6

\*median (minimum and maximum value)

However, Figure 1 shows in detailed the inadequacy of the dietary intake of iron, zinc, calcium, vitamin D, folate and vitamin B12 intake (less than its RDA) among 88.8%, 95.1%, 100%, 97.9%, 90.9% and 78.3%, respectively.



**Figure 1. Dietary Iron, Zinc, Calcium, Vitamin D, Folate and Vitamin B12 Inadequacy in the First Trimester of Pregnancy (n = 143)**

Based on the biomarker of each nutrient under study, except for calcium, Table 3 shows that there

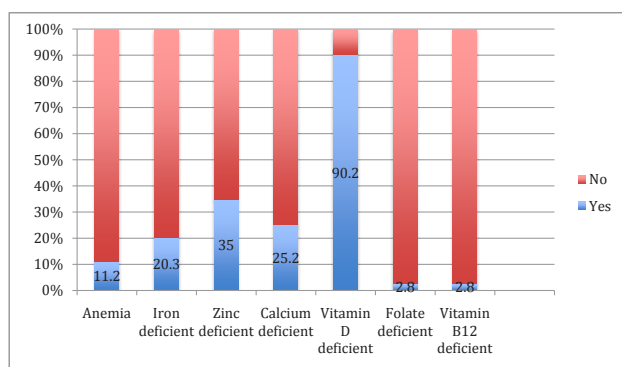
are impacts of the inadequate dietary intake to the micronutrients' concentration in the blood sample.

**Table 3. Iron, Zinc, Vitamin D, Folate and Vitamin B12 Concentration of the Subjects as Compared to the Reference Value for First Trimester of Pregnancy (n = 143)**

Variables	Value	Reference Value (Ref)
Hemoglobin, mg/dL	12.4 ± 1.0	≥11
Ferritin	65.1 (5.8 – 483.7)	>30
Zinc, µg/dL*	61 (30 - 102)	57 – 88
Calcium, mg/dL	9.0 ± 0.3	8.8 – 10.6
Vitamin D, ng/mL	11.1 (4.3 – 29.2)	18 - 27
Folate, ng/mL*	19.2 (10.7 – 34.9)	2.6 – 15
Vitamin B12, pg/mL*	448 (202 - 997)	118 - 438

\*median (minimum and maximum value)

Figure 2 shows that in relation to iron status, 11.2% of the subjects had hemoglobin values of less than 11g/dL (anemia) and 20.3% had ferritin level of less than 30ng/mL (iron deficient). Zinc deficient had the highest prevalence (35%), while only a quarter (25.2%) of the subjects had deficiency of calcium as compared to approximately 90% with vitamin D deficiency. Folate and vitamin B12 deficiency were both found among 2.8% of the subjects.



**Figure 2. Deficiency of Iron, Zinc, Calcium, Vitamin D, Folate and Vitamin B12 in the First Trimester of Pregnancy (n = 143)**

## Discussion

Although most of the subjects had proper education, this study indicated that some women still did not plan their pregnancy safely in accordance to the recommended age and nutritional status. When a pregnancy occurs to woman less than 18 years old or so called teenage pregnancy, then she might be at a higher risk of developing pregnancy-induced hypertension, anemia and prolonged or

obstructed labor. In addition, the newborn may die, be born too soon, too small, or with a low birth weight.<sup>4</sup> Accordingly, pregnant women with advanced age (35 years or older) are predisposed to have adverse pregnancy outcomes, including maternal near miss, maternal death, and severe maternal outcome. Additionally, perinatal outcomes may be adversely affected, including preterm birth, stillbirths, early neonatal mortality, perinatal mortality, low birth weight, and neonatal intensive care unit admission.<sup>5</sup>

Based on body mass index measurement, it revealed in this study that some of the subjects started their pregnancy with undernutrition status (BMI<18.5kg/m<sup>2</sup>), and some with over-nutrition status (BMI>25.0kg m<sup>2</sup>). Both maternal under- and over-nutrition are all linked to abnormalities of fetal growth and their postnatal obesity risk, in which obesity is among those adult diseases that have roots in the fetal programming.<sup>6,7</sup>

Regardless to their nutritional status, this study focused more to some nutrients status (i.e. intakes and biomarkers), namely iron, zinc, calcium, vitamin D, folate and vitamin B12. Those micronutrients are mostly needed during the peri-conceptual period to plan a healthy pregnancy outcome. In this study, approximately more than 80% of the subjects had inadequate dietary intake of all those nutrients. These findings resulted to some evidence on their biomarkers. Approximately 10% and 20% of the subjects started their pregnancy with low hemoglobin (anemia) and iron deficiency, respectively. This is in line with the widely known fact that pregnant women are in high risk for iron deficiency and anemia. The amount of dietary iron, its bioavailability and the changes in iron absorption during pregnancy are factors determining iron absorption leading to iron deficiency and anemic conditions.<sup>8</sup> Iron deficiency limits oxygen delivery to cell that will affect fetal organogenesis. Relating to cardiometabolic risk programming, Stephane et al<sup>9</sup> confirms that in a perinatal iron deficiency there was an adverse effect to blood pressure control through altered intra-renal hemodynamic properties. However, Welten et al<sup>10</sup> shows that the variation of maternal hemoglobin levels during pregnancy were not associated with fetal cardiometabolic risk programming in childhood.<sup>11</sup> Despite on these evidences, this study shows that almost 90% of the subjects had inadequate dietary iron intake that needs further intervention to prevent its negative outcomes.

Zinc deficiency status has the highest prevalence (35%) in this study as compared to the other nutrients under study. Together with magnesium, zinc is important for insulin sensitivity, storage and secretion, and altered zinc metabolism has been implicated in the development of type 2 diabetes and its complications. On the other hand, maternal iron or zinc deficiency results in an increase in the relative weight of the kidneys and a reduction in nephron number in the offspring. In addition, in animal model, moderate maternal zinc restriction resulted in a largely irreversible reduction in the glomerular filtration rate, an increase in systolic blood pressure, and fibrosis in a number of the structures within the renal cortex.<sup>11</sup> In this study, 95% of the subjects had inadequate dietary zinc intake that also needs further intervention along with iron supplementation program, because both food sources for iron and zinc are mostly animal based which is expensive and cannot be affordable for all pregnant women.

In this study, 25.2% of the subjects had calcium deficiency. Dietary calcium intake during pregnancy had an inverse association with systolic blood pressure in children at one month old and diastolic blood pressure at 6 and 12 month of age, but not at 3 years old. In addition, blood pressure of 9-year old children did not differ by maternal calcium intake in pregnancy. This suggests that the effect did not persist beyond infancy.<sup>11</sup> Further intervention should also be applied for calcium supplementation because in this study almost all of the subjects had inadequate calcium intake.

Vitamin D status manifests at different life stages. During preconception it will affect the IVF success, and while during pregnancy it involves in bone development process by enhancing dietary calcium absorption, it has an effect on immune function within both the innate and adaptive immune systems that may be important to specific aspects of placental function and nephrogenesis. While during the perinatal period, the early life immunomodulation is likely to also be affected by vitamin D status.<sup>12</sup> There is evidence addressing the role of vitamin D in the promotion of long-term metabolic health, i.e. obesity, diabetes mellitus (type 1 and type 2), and cardiovascular diseases.<sup>13</sup> Vitamin D adequacy depends on both endogenous, UV-induced synthesis, and exogenous sources, i.e. diet and supplements. In this study, all subjects had inadequate dietary vitamin D intake. Accordingly, approximately 90% of the subject had vitamin D deficiency. Again, it is worthy to provide vitamin D supplementation during pregnancy to prevent its negative impact.

Gestational folate or vitamin B12 status may be a predictor of insulin resistance via epigenetic mechanism in which higher maternal erythrocyte folate concentrations at 26 week and low vitamin B12 status at 18 week of gestation are associated with higher adiposity and insulin resistance among children at 6 year of age. However, folic acid supplementation during pregnancy did not affect fasting glucose, HbA1C, or HOMA among 6- to 8- year old offspring.<sup>11</sup> In this study, only 2.8% of the subjects had folate or vitamin B12 deficiency that were not in line with the high prevalent of dietary folate and vitamin B12 intake inadequacy, i.e. 90% and 78.3%, respectively. However, it is recommended to provide folic acid and vitamin B12 supplementation to prevent neural tube defect (NTD) and anemia as the outcomes of the pregnancy.

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