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Mob: +92 300 3008585, Fax: +92 41 8815544
E-mail: editorpjn@gmail.com

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Research Article

Maternal Zinc Intake and Its Correlation with Maternal Serum Zinc Levels and Neonatal Birth Weight and Length

[1]Lili Rohmawati, [2]Dina Keumala Sari and [3]Makmur Sitepu

[1]Department of Pediatrics, Faculty of Medicine, Universitas Sumatera Utara/Universitas Sumatera Utara Hospital, Medan, Indonesia
[2]Department of Nutrition, Faculty of Medicine, Universitas Sumatera Utara/Universitas Sumatera Utara Hospital, Medan, Indonesia
[3]Departemen of Obstetric and Gynaecology, Faculty of Medicine, Universitas Sumatera Utara/Universitas Sumatera Utara Hospital, Medan, Indonesia

Abstract

Background and Objective: Poor fetal growth results not only from a deficiency in macronutrients but also from inadequate intake of micronutrients that are vital during pregnancy. One of the micronutrients with an important role in fetal growth is zinc. Zinc deficiency in pregnancy can be detrimental to fetal growth and development. The purpose of this study was to assess maternal zinc intake and its correlation with maternal serum zinc levels and neonatal birthweight and length. **Materials and Methods:** This was a prospective study conducted in Universitas Sumatera Utara Hospital and other hospitals in Medan, North Sumatera, from April to October 2019. Eligible subjects were pregnant mothers with their newborn pairs who fulfilled the inclusion criteria and who were enrolled with a consecutive sampling technique. Maternal dietary intakes were analyzed using a computerized nutrient-intake assessment, the Indonesian Version of the NutriSurvey. Maternal serum zinc levels were measured in the second or third trimester during pregnancy and neonatal birth weight and length were measured upon delivery. **Results:** A total of 70 subjects were recruited. The mean maternal weight during pregnancy was 65.6±10.5 kg and the prepregnancy maternal BMI was 22.7±3.7. The mean maternal serum zinc level was53.3±10.7 µg dL^{-1} and the prevalence of maternal serum zinc levels<56 µg dL^{-1} was 61.4%. Dietary intake was sufficient in regard to energy and fat but was low for zinc. The mean energy, fat and zinc intake levels were 2066±248.4 kcal day^{-1} (96.5±11.4%, 78.3±19.5 g day^{-1} (96.5±24.6%) and 5.8±1.1 mg day^{-1} (58.1±11.1%), respectively. There was a significant difference in dietary intake of protein [(40.7±7.8 vs 61.5±11.9) g d^{-1}; p = 0.001] and zinc [(5.1±0.5 vs 6.9±0.9) mg day^{-1}; p = 0.001] between women with low and normal maternal zinc levels. Maternal zinc intake had a strong positive linear correlation with maternal serum zinc levels and neonatal birth weight and length (r = 0.941; r = 0.573; r = 0.618; p = 0.001, respectively). **Conclusion:** There was a significant positive linear correlation of maternal zinc intake with maternal serum zinc levels and neonatal birth weight and length.

Key words: Birth weight, stunting, zinc, maternal zinc, fetal growth, maternal nutrition

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Corresponding Author: Dina Keumala Sari, Department of Nutrition, Faculty of Medicine, Universitas Sumatera Utara/Universitas Sumatera Utara Hospital, Medan, Indonesia

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Maternal nutrient intakes during pregnancy play a crucial role in influencing fetal growth and birth outcomes. Inadequate maternal dietary intake is related to growth failure during gestation. Poor fetal growth results not only from a deficiency in protein and energy but also from inadequate intake of micronutrients that are vital during pregnancy. One of the micronutrients that plays an important role is zinc. Zinc is very important in maintaining the intact structure of the bio membrane for DNA and RNA synthesis and is an essential micronutrient for fatty acid metabolism during pregnancy[1-3].

It is estimated that over 80% of pregnant mothers worldwide have inadequate zinc intake due to increased demand, low-zinc diets and the consumption of foods that interfere with zinc absorption[4,5]. Zinc deficiency in pregnancy can be detrimental to fetal growth and development[2,6,7]. Some research has found that zinc deficiency in pregnant women will increase the risk of low-birth-weight infants[2,8-10]. Zinc deficiency also affects the metabolism of growth hormone and can be an inhibitory factor in growth regulation. Symptoms of zinc deficiency that can be found are failed growth, retarded bone development and weight loss. It has been shown that maternal serum zinc levels correlate with birth length and head circumference of newborn infants[11]. Some studies also found that mothers of low birth weight neonates had lower serum zinc levels than mothers of normal birth weight neonates and lower maternal serum zinc levels were positively associated with lower birth weight[12].

Zinc is an essential trace element, which means it cannot be produced by the body. There are no zinc deposits in the body and its availability depends on maternal dietary intake. Zinc deficiency can be prevented by adequate consumption of zinc[13,14]. The decrease in maternal zinc levels occurs beginning in the first trimester and zinc levels greatly decrease in the second and third trimesters during pregnancy[15]. The zinc intake in all trimesters of pregnancy was lower than the recommended dietary allowance (RDA). There were significant correlations between the nutrient intake of the mothers and the weight of newborns in all trimesters of pregnancy[16]. Wilson *et al.*[17], in a systematic review, revealed that there may be a relationship between maternal dietary zinc intake and infant birth weight and the development of severe preeclampsia (PE). They further stated that the low maternal zinc status of pregnant women and birth outcome are likely to have a relationship with maternal zinc intake during pregnancy. The purpose of this study was to assess maternal zinc intake and its correlation with maternal serum zinc levels and neonatal birthweight and length.

MATERIALS AND METHODS

This was an observational analytic prospective study conducted in Universitas Sumatera Utara Hospital and other hospitals in Medan, North Sumatera, from April to October 2019. Subjects were recruited with a consecutive sampling technique. Subjects were singleton pregnant mothers in the second and third trimesters with their newborn pairs who fulfilled the inclusion criteria. Pregnant mothers with high-risk conditions, such as severe malnutrition, eclampsia, gestational diabetes, liver diseases, kidney diseases, twin pregnancy, fetal congenital anomalies and stillbirth, were excluded.

Well-trained personnel interviewed the participants using a structured questionnaire to obtain characteristic data. Duration of pregnancy (weeks) and maternal weight (kg) and height (cm) were obtained from medical records. Prepregnancy BMI was calculated using self-reported height and weight. Gestational age (weeks) at delivery was estimated on the basis of the self-reported date of the last menstrual period. Neonatal birth weight (g) and length (cm) were measured prior to delivery by trained nurses and the measurements were performed by Baby Scale® with an accuracy of 0.1 kg and a measure tape with an accuracy of 0.1 cm.

Maternal nutritional daily intake data were obtained from participants using the 24 h food recall method. Dietary intakes of food groups and nutrients were analyzed using a computerized nutrient-intake assessment software program developed by the Indonesian version of NutriSurvey 2007[18].

Maternal serum zinc levels were measured in 6 ml venous blood samples. Blood was preserved at room temperature for 30 min and was subsequently centrifuged for 15 min at 3000 rpm. Maternal serum zinc levels were examined as trace elements by inductively coupled plasma-mass spectrophotometry (Agilent 7700 Series ICP-MS) according to the standard of the Prodia Clinical Laboratory. Normal serum zinc levels were defined with a cut-off value of $\geq$56 μg dL^{-1} according to the 1976-1980 sec National Health and Nutrition Examination Survey data (NHANES II)[19].

Descriptive data and maternal daily nutritional intake are expressed as the Mean±SD and percentage. The independent t-test was applied for bivariate analysis to compare maternal daily nutritional intake with maternal serum zinc levels. Correlation and linear regression tests were performed for maternal zinc intake with maternal serum zinc levels and neonatal birth weight and length. Statistical analysis was performed by SPSS Statistics version 23.0. Statistical significance was considered at a $p<0.05$ and a 95% confidence interval. All patients signed an informed consent form prior to initiation of the study. This study was approved by the Health Research Ethical Committee, Faculty of Medicine Universitas Sumatera Utara (No. 2401/TGL/KEPK FK USU-RSUP HAM/2019).

RESULTS

A total of 79 pregnant mothers with their newborns were enrolled during the study period but 9 subjects were excluded because 2 blood samples were lysed and 7 subjects did not consent for blood extraction. The total number of subjects was 70. Table 1 shows the subject characteristics of this study. The range of the duration of pregnancy was 16-40 (mean 29.9±9.0) weeks. The range of maternal age was 21-35 (mean 28.5±3.5) years. The mean maternal weight during pregnancy was 65.6±10.5 kg and the prepregnancy maternal BMI was 22.7±3.7 kg m^{-1} ^{2}. The range of gestational age of newborns was 37–40 (mean 38.5±0.5) weeks, with a mean birth weight and length of 3223.4±376.7 kg and 48.8±1.5 cm, respectively. The mean maternal serum zinc level was 53.3±10.7 μg dL^{-1} (range 25-87 μg dL^{-1}) and the prevalence of maternal serum zinc levels less than 56 μg dL^{-1} was high (61.4%).

Table 2 shows the amount and percentage of maternal daily nutritional intake during pregnancy. Dietary intake was sufficient in regard to energy and fat. The mean energy intake was 2066±248.4 (range 1227.5-2537.5) (kcal day^{-1}), with an adequacy percentage of 96.5±11.4 (range 57-118) percent; the mean fat intake was 78.3±19.5 (range 48-117) g day^{-1}, with an adequacy percentage of 96.5±24.6 (range 58-149) percent. The mean intake of protein and carbohydrate was 48.7±13.9 (range 29.9-85.5) g day^{-1} and 296.1±45.8 (range 134-375.7) g day^{-1}, respectively. The mean zinc intake was 5.8±1.1 (range 3.5-9.3) (mg day^{-1}), with an adequacy percentage of 58.1±11.1 (range 35-93) percent.

Table 3 shows the comparison of daily maternal nutritional intake with maternal serum zinc levels in individuals with low maternal zinc (<56 μg dL^{-1}) and normal maternal zinc (≥56 μg dL^{-1}). There was a significant difference between dietary intake of protein [(40.7±7.8 vs 61.5±11.9) g day^{-1}; p = 0.001] and zinc [(5.1±0.5 vs 6.9±0.9) mg day^{-1}; p = 0.001].

Table 1: Characteristics of the subjects

Characteristics	N = 70
Duration of pregnancy (weeks)	
Range	16-40
Mean±SD	29.9±9.0
Second trimester, n (%)	32 (45.7)
Third trimester, n (%)	38 (54.3)
Maternal age (years)	
Range	21-35
Mean±SD	28.5±3.5
Maternal weight (kg)	
Range	41.5-99
Mean±SD	65.6±10.5
Prepregnancy maternal BMI (kg m^{-2})	
Range	16.8-32.9
Mean±SD	22.7±3.7
Gestational age of newborn (weeks)	
Range	37-40
Mean±SD	38.5±0.5
Neonatal birth weight (g)	
Range	2600-4100
Mean±SD	3223.4±376.7
Neonatal birth length (cm)	
Range	45-51
Mean±SD	48.8±1.5
Maternal serum zinc levels (μg dL^{-1})	
Range	25-87
Mean±SD	53.3±10.7
Value <56 μg dL^{-1}, n (%)	43 (61.4)
Value ≥56 μg dL^{-1}, n (%)	27 (38.6)

Table 2: Maternal daily nutritional intake

	Amount		Percent (%)	
Nutritional intake	Range	Mean±SD	Range	Mean±SD
Energy (kcal day^{-1})	1227.5-2537.5	2066.0±248.4	57-118	96.5±11.4
Carbohydrate (g day^{-1})	134-375.7	296.1±45.8	36-100	80.9±10.4
Protein (g day^{-1})	26.9-85.5	48.7±13.9	46-142	83.5±22.9
Fat (g day^{-1})	48-117	78.3±19.5	58-149	96.5±24.6
Zinc (mg day^{-1})	3.5-9.3	5.8±1.1	35-93	58.1±11.1

Table 3: Comparison of daily maternal nutritional intake with maternal serum zinc levels

	Maternal serum zinc levels (μg dL^{-1})		
Maternal nutrition intake daily	Low (<56) Mean±SD	Normal (≥56) Mean±SD	p-value
Energy (kcal day^{-1})	2031.2±280.2	2121.4±178.2	0.104
Carbohydrate (g day^{-1})	295.9±43.9	296.4±49.6	0.967
Protein (g day^{-1})	40.7±7.8	61.5±11.9	0.001
Fat (g day^{-1})	78.9±21.7	77.4±15.7	0.748
Zinc (mg day^{-1})	5.1±0.5	6.9±0.9	0.001

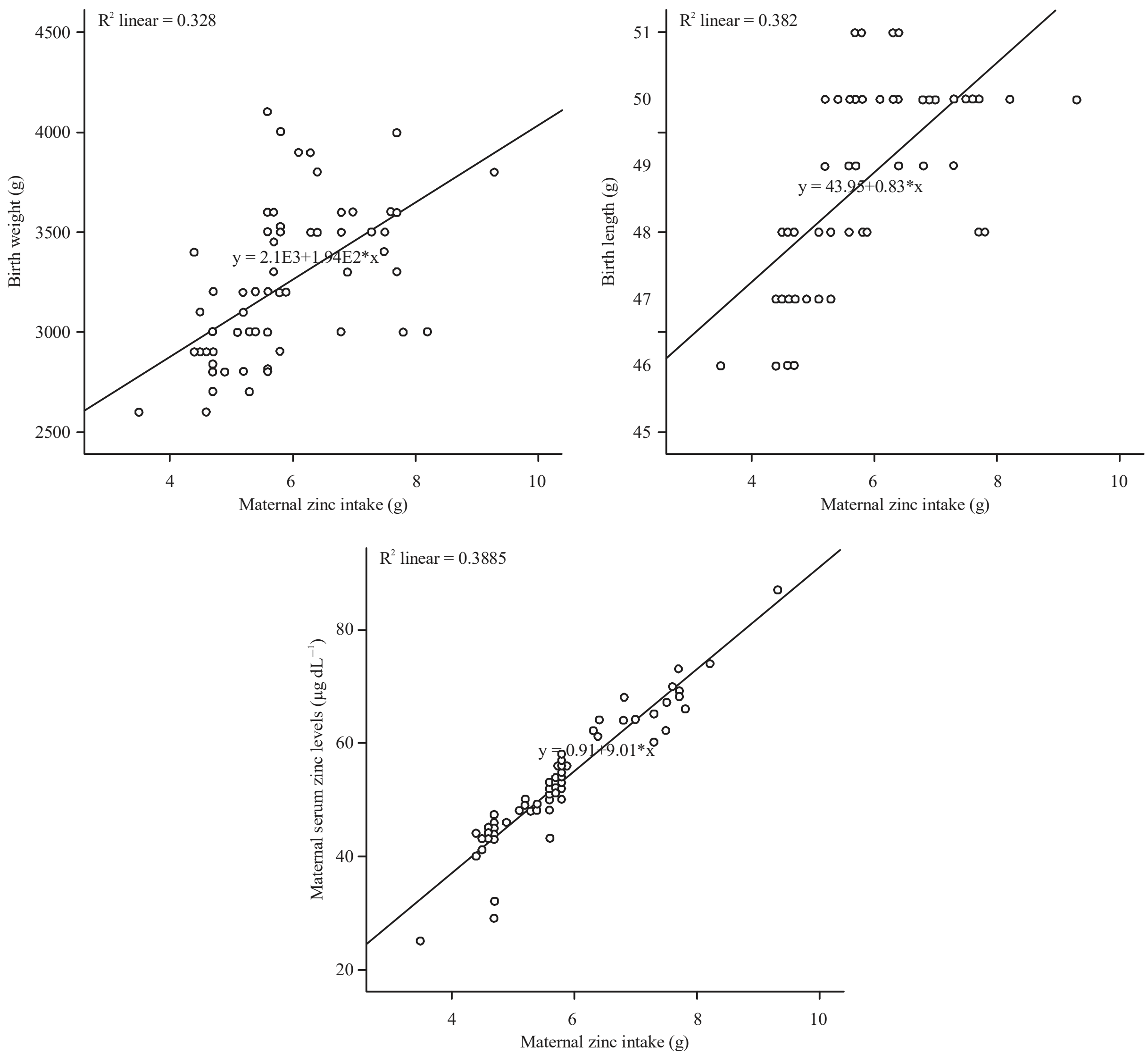

Fig. 1(a-c): Correlation of maternal zinc intake with maternal serum zinc levels and neonatal birth weight and length

Table 4: Correlation of maternal zinc intake with maternal serum zinc levels and neonatal birth weight and length

	Maternal zinc intake		
Variables	r	R^2	p-value
Maternal serum zinc levels ($\mu g\ dL^{-1}$)	0.941	0.885	0.001
Birth weight	0.573	0.328	0.001
Birth length	0.618	0.382	0.001

The linear regression and correlation between maternal zinc intake and maternal serum zinc levels and measurements of neonatal birth weight and length are presented in Table 4 and Fig. 1. Maternal zinc intake had a strong positive linear correlation with maternal serum zinc levels (r = 0.941; $R^2 = 0.885$) and neonatal birth weight (r = 0.573; $R^2 = 0.328$) and length (r = 0.618; $R^2 = 0.382$) (p = 0.001).

DISCUSSION

The need for macronutrients and micronutrients increases rapidly in the second and third trimesters of pregnancy due to the increasing nutritional needs of mothers during pregnancy to facilitate metabolic and physiological changes and fetal growth[1]. In this study, the participants were pregnant mothers in the second and third trimesters (mean 29.9±9.0 weeks) with a mean maternal age of 28.5±3.5 years and a mean prepregnancy maternal BMI of 22.7±3.7 kg m^{-2}. Women who have a normal weight at the start of pregnancy (BMI 18.5-24.9 kg m^{-2}) should aim to gain 11.5-16 kg[4].

Pregnant women require high energy consumption. The energy requirement varies depending on physical activity levels, prepregnancy body mass index (BMI) and metabolic rate. The additional caloric intake in the second and third trimesters of pregnancy is approximately 340 and 452 kcal day^{-1}, respectively, which are needed to facilitate fat reserves and the metabolic processes of new tissues[1]. The additional energy requirement according to the RDA of the Indonesian Ministry of Health is 300 kcal day^{-1} in the second and third trimesters during pregnancy[20]. According to the 2007 Indonesian version of the NutriSurvey, the energy and fat required for pregnant mothers (>4 months pregnant) is 2036.3 kcal day^{-1} and 69.1 g day^{-1}, respectively[18].

In this study, the intake of energy and fat among pregnant women was adequate. The average intake of energy and fat was 2066±248.4 kcal day^{-1} (96.5±11.4%) and 78.3±19.5 g day^{-1} (96.5±24.6%), respectively. Gala *et al.*[21] from Mumbai, India, reported that the average intake of energy and fat of pregnant women was 1578.10±360.82 kcal day^{-1} and 42.11±12.22 g day^{-1}, respectively. They further reported that birth outcome was strongly influenced by maternal diet, particularly energy and protein intake[21]. A study by Bhowmik *et al.*[22] from Ghana, Bangladesh reported that the mean energy and fat intake of pregnant women with a normal BMI was 1487.2±173.3 kcal day^{-1} and 46.0±9.2 g day^{-1}, respectively.

Our study revealed higher energy and fat intake than previous studies. This difference may be caused by the types of food and dietary habits in the study area. Results of this study showed that, pregnant women obtained energy mainly from carbohydrates (rice 3 times/day, sugar); fat mainly from oil (fried foods) and nuts; and protein mainly from eggs, fish, poultry, tempeh and nuts and some participants obtained protein from dairy milk and meat.

During pregnancy, the amount of protein that should be available is as high as 925 g, which is obtained from the mother's tissue, placenta and fetus[23]. According to international guidelines, 21 g of additional protein intake during the second and third trimesters is recommended. The RDA should be increased by 1 g day^{-1} in the first trimester of gestation, 8 g day^{-1} in the second trimester and 26 g day^{-1} in the third trimester[24]. The Indonesian Ministry of Health encourages 20 g day^{-1} of additional protein intake (range 67-100 g day^{-1}) (20). Adequate protein intake of pregnant women according to the 2007 Indonesian version of the NutriSurvey was estimated to be 60.1 g[18]. In this study, the average protein intake was 48.7±13.9 g day^{-1} (83.5±22.9%). A similar study by Gala *et al.*[21] reported that the during pregnancy average protein intake was 45.11±12.87 g day^{-1}. According to Bhowmik *et al.*[22] average protein intake was 46.0±9.2 g day^{-1}. These results were suboptimal compared to the recommended intake.

During pregnancy, maternal zinc intake is required for optimal fetal growth and development[2,25]. In this study, the average intake of zinc among pregnant women was 5.8±1.1 (range 3.5-9.3) mg day^{-1} and the average percentage of adequate intake of zinc was 58.1±11.1 (35-93) percent. Zinc intake is still below the average needs of pregnant women. The recommended zinc intake in pregnant women was 10 mg day^{-1} [18,20,26]. A study by Rahayu *et al.*[27] in Bandung Indonesia found that the average zinc intake of pregnant mothers was 5.1 mg day^{-1}, which was below the Recommended Dietary Allowance (RDA) of the Indonesian Ministry of Health for pregnant women. Gala *et al.*[21] reported an average zinc intake of 4.23±1.18 mg day^{-1} in pregnant women. Low serum zinc levels in pregnant women affect fetal growth and development, resulting in conditions such as growth failure and low birth weight[28,29]. Plasma zinc declines during pregnancy, with a larger decline seen in women with habitual intakes ≤9 mg day^{-1} [23], which is below the recommended minimum daily level, for the last two trimesters of pregnancy[4,20]. Pregnant women needed zinc supplementation, especially those with low zinc levels, as found in this study. Several studies have suggested that zinc supplementation can improve pregnancy and its outcomes[30,31]. A meta-analysis found that giving zinc to pregnant women can reduce the risk of prematurity and low birth weight[32].

The best source of zinc is animal protein because it contains amino acids that increase the absorption of zinc and has high bioavailability. Some foods are good source of zinc but high concentrations of calcium, casein and phytic acid will affect the bioavailability so that the absorption of zinc is reduced[3,4,33,34]. This study showed that pregnant women mainly obtained zinc from fish and seafood, poultry, eggs, tempeh, nuts and rice. Some participants obtained zinc from dairy milk and meat. In this research, we did not analyze foods containing zinc absorption inhibitors.

Maternal serum zinc levels may decrease 35% due to increased demand during pregnancy, especially in the second and third trimesters[35]. Hotz *et al.*[19] reported that mean serum zinc decreased steadily throughout pregnancy from 72±2.7 µg dL^{-1} during the first month to 61±1.7 µg dL^{-1} during the ninth month. A study by Yasoghara *et al.*[36] showed that maternal serum zinc levels decreased progressively prior to pregnancy from 78.1±21.85 to 60.5±14.42 µg dL^{-1}. In this study, we found low maternal serum zinc levels [mean 53.3±10.7 (range 25-87) µg dL^{-1}] at 29.9±9.0 weeks of pregnancy. The proportion of pregnant mothers with low maternal serum zinc levels was 61.4%. A similar study by Seriana *et al.*[11] revealed that term gestational age mothers had low serum zinc levels, which were 36.01±18.34 µg day^{-1}.

Wang *et al.*[10] in China showed that 247 of 3187 pregnant mothers had zinc deficiency (<56 µg dL^{-1}) and the mean maternal serum zinc level was 91.0 µg dL^{-1}. A study from Iran reported that serum zinc levels of subjects decreased significantly and gradually during the first, second and third trimesters[15].

In this study, protein intake was associated with maternal zinc levels. This research showed a significant difference between maternal protein intake of pregnant women with low and normal zinc levels [(mean 40.7±7.8 g day^{-1}, p = 0.001) and (mean 61.5±11.9 g day^{-1}, p = 0.001), respectively)]. We also found a significant difference between maternal zinc intake during pregnancy in women with low and normal zinc levels (p = 0.001). One of the factors affecting the high prevalence of zinc deficiency is the low intake of animal protein sources. It is known that zinc is widely found in protein sources. The zinc requirement can be fulfilled by consuming sufficient protein sources. Pregnancy requires a healthy diet that includes an adequate intake of energy, protein, vitamins and minerals to meet maternal and fetal needs. However, for many pregnant women, dietary intake of vegetables, meat, dairy products and fruit is often insufficient to meet these needs, particularly in low- and middle-income countries[4]. Grieger and Clifton[37] in their review reported that suboptimal dietary intakes (intakes below recommended levels) occur not only in developing countries but also in developed countries. Consumption of whole foods such as fruit, vegetables, low-fat dairy and lean meats throughout pregnancy appears to be beneficial for appropriate birthweight.

Mousa *et al.*[1] reported that some observational studies from the UK and Spain suggest that protein intake increases birthweight independently of energy intake, maternal age, BMI and lifestyle-related variables. A 1-g increase in protein corresponded to a 7-13 g increase in birthweight. Similar findings were reported in a Cochrane review of 12 randomized trials (n = 6705), where an increased birthweight and a decreased risk of stillbirth and small-for-gestational-age (SGA) infants was observed following balanced energy/protein supplementation (<25% energy from protein), with no changes in gestational weight gain[1]. Morisaki *et al.*[38] found that maternal protein intake to have an inverse U-curve relationship with fetal growth. Their results strongly suggest that the effect of protein on birth weight is nonlinear and that a balanced diet ful lling the minimum requirement for all macronutrients was ideal for avoiding fetal growth restriction[38].

In this study, we found that maternal zinc intake had a strong positive linear correlation with maternal serum zinc levels, neonatal birth weight and length (p<0.001). Wijaksono *et al.*[39] also reported a significant strong correlation between maternal serum zinc levels and maternal weight gain during pregnancy and neonatal birth weight. Maternal zinc levels of 0.879% can affect neonatal birth weight[39]. In agreement with this study, Seriana *et al.*[11] reported a significant correlation between maternal serum zinc levels and the length and head circumference of newborn infants.

Research in Yemen by Muftah *et al.*[40] found that maternal malnutrition was significantly associated with babies with low birth weight. Bolaji *et al.*[41] reported that up to 48.4% of pregnant women suffer from zinc deficiency with maternal average serum zinc of 9.0 (±5.3) µmol L^{-1}. The mean zinc levels of mothers of infants with fetal malnutrition were significantly lower than those of mothers of infants without fetal malnutrition[41].

In this research, we also provided education to participants about the adequacy of nutrition among pregnant women. Ota *et al.*[42] reported that nutritional education among pregnant women to increase energy and protein intake and balanced supplementation between energy and protein can decrease the incidence of adverse birth outcomes. According to the WHO[4] recommendation, nutrition education on increasing daily energy and protein intake is recommended for pregnant women to reduce the risk of neonatal low birth weight, especially in undernourished populations. Imbalanced macronutrient intakes, inadequate micronutrient intakes and predominantly plant-based diets were common features of the diets of pregnant women in developing countries. Cohesive public health efforts involving improving access to nutrient-rich local foods and micronutrient supplementation and forti cation are needed to improve the nutrition of pregnant women in developing countries[4]. Furthermore, in accordance with the study from Gala *et al.*[21], maternal diet prior to pregnancy and during pregnancy along with maternal anthropometry, hemoglobin concentrations prior to delivery and gestational age greatly influence birth outcome. Thus, attention has to be given to the nutrition of adolescent girls by providing proper nutrition education and prepregnancy counseling, which will help improve pregnancy outcomes.

This study used the 24 h food recall method. Participants were required to complete the food diary sheet listing every food and drink they had consumed with assistance from well-trained personnel. They should clearly describe the name of the food, the cooking ingredients and method and the seasoning of the food based on household size[4]. The food diary was completed for 2 days to determine the average intake, so the participant's dietary intake could be described. There were some weaknesses that pregnant women may forgot to tell or write the food consumed. In the Ministry of Health Nutrition Handbook and application of the 2007

Indonesian version of the Nutrisurvey, there were some food ingredients that did not exist, so there was a possibility of overestimation and underestimation. The limitation of this study is that it did not assess the factors that affect zinc levels in pregnancy. Further research assessing nutritional intake, zinc analysis in pregnancy and the effect of zinc supplementation in pregnant women on fetal growth and development at the bio molecular level is required.

CONCLUSION

In conclusion, maternal nutritional intake is adequate in terms of energy and fat but is low in zinc intake. There was a significant difference in maternal protein and zinc intake between individuals with low and normal maternal zinc levels. Maternal zinc intake had a positive significant linear correlation with maternal serum zinc levels, neonatal birth weight and length.

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