ORIGINAL PAPER

Is Serum Zinc Level Correlated with Insulin Resistance Among Lactating Mothers in Jakarta?

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Abstract

Introduction: Insulin resistance is a condition that underlies the development of diabetes mellitus. The prevalence of diabetes mellitus keeps rising, including in Indonesia. A higher proportion of diabetes was found in women. Physiological changes during pregnancy can cause insulin resistance that may persist until postpartum period. Lactation and nutrient like zinc may improve insulin resistance. This study aimed to measure the correlation between zinc serum level and insulin resistance of lactating mothers in Jakarta.

Methods: This study used a cross-sectional design, which was conducted in Grogol Petamburan District Community Health Center, West Jakarta and Cilincing District Community Health Center, North Jakarta from February to April 2019. A total of 75 lactating mothers at 3–6 months postpartum were selected using consecutive sampling method. Zinc serum was analyzed using atomic absorption spectrophotometry (AAS) method. Insulin resistance was assessed using the homeostasis model assessment-insulin resistance (HOMA-IR).

Result: Approximately 76% (n = 57) subjects had low serum zinc level. Spearman correlation test between serum zinc level and HOMA-IR was done (r = 0.003, p = 0.977). Also, correlation test between BMI and HOMA-IR (r = 0.563, p <0.001).

Conclusions: No correlation was found between serum zinc level and HOMA-IR however, there was a significant moderate positive correlation between BMI and HOMA-IR.

Keywords lactation, zinc, insulin resistance, HOMA-IR, BMI

Introduction

Rapid advancements of culture, socioeconomic, and technology cause lifestyle changes that come with considerable health consequences like insulin resistance. Insulin resistance is prevalent worldwide, the prevalence of insulin resistance in Venezuela was 46.7% and in Iran was 51%.[1,2] Insulin resistance is the key condition that underlies the development of type 2 diabetes mellitus. Diabetes mellitus is one of the major causes of mortality worldwide. In 2013, 382 million people were affected by diabetes and over 200 million were Asians. Indonesia was included as one of the top ten Asia countries with most diabetes patients.[3] Based on Riskesdas, there was an increase in diabetes patients in Indonesia

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from 2013 to 2018 and the proportion was found higher among women.[4]

In women, physiological changes during pregnancy can cause insulin resistance that may persist until postpartum period.[5] A study by Kirwan et al.[6] showed that by 1 year postpartum, insulin sensitivity only returned to 74% baseline. Lactation can help improve maternal metabolism. A study by Bajaj et al.[7] showed that insulin sensitivity improved significantly in women who were breastfeeding her babies for ≥3 months. However, exclusive breastfeeding rate in Indonesia is still low, below 40%.[8]

Nutrients have also been associated with insulin resistance. Zinc, for instance, has a role in the crystallization and signaling of insulin.[9] A study by Bandeira et al.[9] showed that higher serum zinc level was significantly associated with better insulin sensitivity. Lactating mothers are particularly vulnerable to zinc deficiency because they have relatively greater needs to secrete adequate breastmilk also safeguarding their own healths.[10] A study by Dijkhuizen et al.[11] in 2001, showed that 25% of lactating mothers in Indonesia suffered from zinc deficiency.

Further studies are still needed to assess whether better breastfeeding practice and zinc status can improve insulin resistance, especially in lactating mothers. This study aimed to assess zinc serum level and its correlation with insulin resistance among lactating mothers in Jakarta.

Methods

A cross-sectional study was conducted in Grogol Petamburan District Community Health Center, West Jakarta and Cilincing District Community Health Center, North Jakarta between February and April 2019. This study was part of a larger study on nutritional status, lipid profile, and metabolic status of lactating mothers: specific assessment of zinc, anemia, and insulin resistance with exclusive breastfeeding. This study has been approved by the Committee for Ethics in Research of the Faculty of Medicine Universitas Indonesia (No. 1128/UN2.F1/ETIK/2018 and protocol number 18-10-1241). Subjects were recruited using consecutive sampling method. Both community health centers cover a wide area, so the risk of bias by the sampling method is minimalized. Subjects were included if they were women aged 20–40 years old, at 3–6 months postpartum, were breastfeeding their babies either exclusively or not and gave written consent to participate. Subjects who had diabetes mellitus type 1 or 2, taking diabetes medicine, suffered from a hormonal disease, taking corticosteroid drugs, or smoking were excluded. Subjects with history of gestational diabetes mellitus were not excluded.

Subjects were interviewed for age, number of parity, level of education, occupation, level of physical activity, pregnancy weight gain, postpartum weight changes, and lactation status (exclusive or not). Level of education was classified as low (not graduated or graduated from elementary school and/or not graduated from junior high school), middle (graduated from junior high school and/or not graduated or graduated from senior high school and/or not graduated from college or university), or high (graduated from college or university). Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) Short Form and classified as light, moderate, or vigorous intensity.[12] Postpartum weight change was defined as the difference between currently measured weight with the weight after giving birth, documented in maternal and child health book. History of gestational diabetes mellitus was assessed from the documentation in maternal and child health book. Intakes of energy, protein, and zinc were assessed using a semi-quantitative food frequency questionnaire (FFQ). Weight and height were measured using a Seca 703s weight scale and stadiometer. Body mass index (BMI) was calculated as weight per height squared (kg/m^2) and then categorized using Asia-Pacific BMI criteria. Blood vein samples were obtained in the morning after 10–12 hours of fasting to measure zinc serum, fasting glucose, and fasting insulin. Zinc serum was analyzed using atomic absorption spectrophotometry (AAS) method, level <70 µg/dL was considered low.[10] Insulin resistance was assessed using the homeostasis model assessment-insulin resistance (HOMA-IR). HOMA-IR was calculated from fasting glucose and insulin using HOMA2 calculator software released by the Diabetes Trials Unit, University of Oxford.
This calculator is available at:
http://www.dtu.ox.ac.uk/homacalculator/index.php.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 20 for Windows. The normality of data distribution was assessed using Kolmogorov-Smirnov test, data were considered normally distributed if p-value >0.05. Normally distributed data were described using mean and standard deviation, otherwise median with minimum-maximum values were used. Correlation between variables was analyzed using Pearson or Spearman correlation test. P-value <0.05 was considered significant.

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Results

A total of 75 subjects were recruited and data were analyzed. The characteristics of the subjects can be seen in Table 1.

Table 1. Baseline characteristic of the subjects

Characteristics	Values
Age (years)	27.53 ± 4.28[†]
Parity	2 (1–4)[‡]
First pregnancy, n (%)	31 (41.3)
Multipara, n (%)	44 (58.7)
Education, n (%)	
Low	9 (12.0)
Middle	52 (69.3)
High	14 (18.7)
Occupation, n (%)	
Housewife	70 (93.3)
Working	5 (6.7)
Physical activity, n (%)	
Light intensity	7 (9.3)
Moderate intensity	34 (45.3)
Vigorous intensity	34 (45.3)
Nutritional status based on BMI, n (%)	
Underweight	4 (5.3)
Normal	34 (45.3)
Overweight	15 (20.0)
Obesity	22 (29.3)
Pregnancy weight gain (kg)	12.66 ± 4.41[†]
Postpartum weight changes (kg)	- 8.45 ± 4.65[†]
Lactation status, n (%)	
Not exclusive	25 (33.3)
Exclusive	50 (66.7)

[†]: mean ± standard deviation. [‡]: median (minimum–maximum)

The average age of subjects was 27.53 ± 4.28 years old. Most of the subjects had given birth more than once (58.7%), had a middle level of education (69.3%), were a housewife (93.3%), had moderate to vigorous intensity of daily physical activity (90.6%), were overweight and obese (49.3%), also were breastfeeding their babies exclusively (66.7%). The average weight gain during pregnancy was 12.66 ± 4.41 kg and average weight loss during postpartum was 8.45 ± 4.65 kg. All subjects had no history of gestational diabetes mellitus.

Dietary intakes are shown in Table 2. Data were compared to Recommended Dietary Allowances established for Indonesia in 2013.[13] Most of the subjects had low energy intake (52%), adequate dietary protein intakes (66.7%), and low dietary zinc intakes (77.3%).

Serum zinc, BMI, and HOMA-IR values also their correlations were shown in Table 3. Most of the subjects had low serum zinc levels (76%). The median value of HOMA-IR was 0.54 (0.22–2.21) and most subjects had optimal HOMA-IR value (86.7%) compared to cut-off established by Than et al.[14] from a study in Myanmar. Spearman correlation test was conducted between serum zinc and HOMA-IR. No significant correlation was found (r = 0.003, p = 0.977). Spearman correlation test between BMI and HOMA-IR showed a moderate positive significant result (r = 0.563, p <0.001).

Discussion

Evidence shows that lactation has a beneficial effect on insulin sensitivity. Longer duration and higher intensity or exclusive breastfeeding were associated with better maternal metabolism.[7,15,16] Data from Indonesia Demographic and Health Survey in 2017 (IDHS 2017) showed that only 38% of lactating mothers in Indonesia were breastfeeding their babies exclusively at 4–5 months postpartum.[17] Compared to IDHS 2017, in this study, a higher percentage of lactating mothers who were breastfeeding their babies exclusively (66.7%) were found. This discrepancy might be caused by the difference in study areas. More attention is needed to improve exclusive breastfeeding rates. A good nutrition intake and status of lactating mothers is a requirement to ensure an optimal exclusive breastfeeding practice.[18]

In this study, most subjects had adequate dietary protein intakes (75 g/day for lactating women), however dietary zinc intakes of 77.3%

Table 2. Dietary intakes of subjects

FFQ	Range	Values
Energy (kcal/day)		2543.92 ± 745.59[†]
Low, n (%)	<2500 kcal/day	39 (52.0)
Adequate, n (%)	≥2500 kcal/day	36 (48.0)
Protein (g/day)		87 (41–203)[‡]
Low, n (%)	<75 g/day	25 (33.3)
Adequate, n (%)	≥75 g/day	50 (66.7)
Zinc (mg/day)		10.8 (4.4–45.9)[‡]
Low, n (%)	<15 mg/day	58 (77.3)
Adequate, n (%)	≥15 mg/day	17 (22.7)

[†]: mean ± standard deviation. [‡]: median (minimum–maximum)

Table 3. Correlations between serum zinc and BMI with HOMA-IR

Variables	Range	Values	HOMA-IR	
			r	p
HOMA-IR		0.54 (0.22–2.21)[‡]		
Optimal, n (%)	<1,05	65 (86.7)		
Insulin resistance, n (%)	≥1,05	10 (13.3)		
Serum zinc (µg/dL)		62.33 ± 11.89[†]	0.003[S]	0.977
Low, n (%)	<70 µg/dL	57 (76.0)		
Normal, n (%)	≥70 µg/dL	18 (24.0)		
BMI (kg/m²)		23.56 ± 4.07[†]	0.563[S]	<0.001[*]

[†]: mean ± standard deviation. [‡]: median (minimum-maximum). [S]: Spearman correlation test. [*]: statistically significant

subjects did not meet the requirement of Indonesia RDA (15 mg/day for lactating women).[13] This may be caused by different types of protein consumed. A variety of protein foods are also sources of zinc. Animal proteins like oysters, red meat, and poultry are the best sources of zinc compared to plant-based proteins.[10] The majority of subjects in this study fulfill their daily protein needs mostly from plant-based foods like tempeh and tofu. The contents of phytate in plant-based protein foods will inhibit zinc absorption, reducing its bioavailability.[10] A study by Madanijah et al.[19] suggested that lactating women in Bogor purposively doubled their vegetable intakes because they believed it would increase breastmilk quantity and quality. Also, the socioeconomic status of those mothers might influence their choice of foods. Techniques such as milling, soaking, heating, leavening, and fermenting may reduce phytate and increase zinc bioavailability.[20]

Zinc plays an essential role in the storage and secretion of insulin, activation of PI3K/Akt insulin pathway, and induction of the translocation of glucose transporter-4 (GLUT-4). Zinc is also a cofactor for antioxidant enzymes such as superoxide dismutase. Thus, zinc indirectly reduces reactive oxygen species that may damage pancreatic β-cell.[21,22] In this regard, studies have shown the role of zinc in insulin sensitivity.[22-24] However, in this study, there was no significant correlation between serum zinc and HOMA-IR. Capdor et al.[25] conducted a meta-analysis of zinc supplementation effect on glucose tolerance and insulin level. The supplementation of zinc increase zinc blood level thus resulted in significant improvement of glucose tolerance and insulin level on subjects with underlying chronic disease (diabetes mellitus, metabolic syndrome, obesity) compared with those of healthy subjects.[25] This difference implicates that positive effect of zinc on insulin resistance might be significantly found on those with impaired metabolism, whereas in this study most of the subjects had optimal HOMA-IR values.

A study by Ahn et al.[26] in Korea showed a significant inverse correlation between serum zinc and HOMA-IR in non-diabetic subjects after adjusting for cardiometabolic risk factors (waist circumference, HDL cholesterol, triglycerides) statistically.[26] These results suggest that insulin resistance is influenced by other dominant factors that might overshadow zinc status. Subjects of this

study were women of reproductive age whose estrogen level was still high. Estrogen (17B-ethinyl-estradiol) is considered as a protective factor against insulin resistance. By bonding with estrogen receptor-α, estrogen inhibits lipoprotein lipase (an enzyme catalyzing lipogenesis), thus preventing the accumulation of triacylglycerol (TAG) in adipocyte. In liver, estrogen also inhibits the accumulation of TAG, gluconeogenesis, and inflammatory pathways. This will reduce inflammatory process, thus preserving pancreatic cells. Estrogen also has a direct anti-apoptotic effect on pancreatic β-cells that regulate insulin secretion. In skeletal muscle, estrogen modulates expression of insulin-sensitive glucose transporter (GLUT-4), thereby improving glucose disposal.[27,28] This factor may account for the lack of statistically significant results of this study where the subjects were still metabolically protected by estrogen.

Given the strong role of obesity in the development of diabetes mellitus type 2. We also conducted an analysis of BMI and HOMA-IR. There was a significant moderate positive correlation which shows that higher BMI was associated with worse insulin resistance. Studies by Vashum et al.[29] and Islam et al.[30] showed similar results. Release of chemokines and pro-inflammatory cytokines from adipocytes of obese people may cause chronic low-grade systemic inflammation, eventually causing the development of insulin resistance and diabetes.[30] Most subjects in this study were overweight and obese, therefore a lifestyle improvement should be implemented. For instance, by increasing the level of physical activity and diet modification.

This study has several limitations. First, the recruitment of subjects was limited to two administrative cities of Jakarta that did not fully represent the population of Jakarta. Secondly, dietary assessment using FFQ relied on subjects' memory. This might cause a bias, although a food picture book was used to minimalize it.

In conclusion, most of the lactating mothers in Jakarta had low dietary zinc intakes and low serum zinc levels. No correlation was found between serum zinc level and HOMA-IR, however, there was a significant moderate positive correlation between BMI and HOMA-IR.
Further studies relating to other risk factors that may influence insulin resistance should be conducted.

Lactating women should improve their dietary zinc intakes by increasing their daily intake of animal proteins also by implementing food processing techniques on plant-based proteins to increase the bioavailability of zinc.

Conflict of Interest

Acknowledgment

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Reference

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