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ORIGINAL ARTICLE

Analyses of Nutrients and Body Mass Index as Risk Factor for Preeclampsia

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Abstract

Background Little is known about the pathogenesis of preeclampsia. Many factors are identified as risk factors for preeclampsia including nutrients and obesity. The aim of this study was to assess whether nutrients and body mass index (BMI) are risk factors for preeclampsia.

Methods This was a case–control study at the Department of Obstetric and Gynecology in Dr. M. Djamil Hospital, Padang, Indonesia. A total of 140 patients were enrolled in this study with 70 cases and 70 controls. All subjects completed an interview for their nutritional status and prepregnancy BMI after delivery. The nutritional status

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was assessed by Food Frequency Questionnaire and then analyzed by Nutrisurvey Program. The independent samples *t* test was used for nutritional status, and Chi-square test was used for BMI. For nutrients, logistic regression procedures were employed to calculate potential risk factors associated with preeclampsia.

Results Prevalence of abnormal BMI was more common in the preeclampsia group compared with those without preeclampsia 19 (27.1%) versus 12 (17.1%) but not found as a significant risk factor in this study ($p = 0.222$). Deficiency of vitamin E (OR 1.76, 95% CI 10.2 ± 30.5), zinc (OR 99.4, 95% CI 1.37 ± 7219), fat (OR 59.1, 95% CI 3.14 ± 500), calcium (OR 109, 95% CI 0.29 ± 40,041), vitamin C (OR 19.5, 95% CI 2.52 ± 151) were associated with increased risk of preeclampsia. Excess of carbohydrate was associated with increased risk of preeclampsia (OR 52.9, 95% CI 0.801 ± 3495).

Conclusions Deficiency of vitamin E, zinc, fat, calcium, and vitamin C, and excess of calories and carbohydrate were associated with increased risk of preeclampsia.

Keywords Body mass index · Nutrition · Preeclampsia · Risk factor

Introduction

Preeclampsia is an important problem in obstetrics because it is still a major cause of maternal mortality compared to bleeding and infection. Preeclampsia leads to maternal and perinatal morbidity. Preeclampsia is also associated with high rates of preterm delivery, small for gestational ages, and perinatal death [1]. Little is known about the pathogenesis of preeclampsia. Many factors are identified as risk factors for preeclampsia including parity, multiple pregnancies, age, family history of preeclampsia, obesity, history of systemic disease, and nutrition.

Since preeclampsia is characterized by reduced perfusion of the placenta, oxidative stress, and endothelial dysfunction, nutrition has long been hypothesized to have a role in the etiology of preeclampsia [2]. Oxidative stresses are proposed as the linkage between the two stages of preeclampsia. Nutrients can affect oxidative stress by increasing or decreasing free radicals or antioxidants or by providing substrate for the formation of free radicals. Several nutrients, particularly omega-3 ($n - 3$) fatty acids, antioxidants, and folic acid, have an important roles in modulating endothelial function. It has also been suggested that nutrients such as trace elements, fatty acids, and folic acid can contribute to insulin resistance, a risk factor for preeclampsia. In many studies, decrease in serum magnesium levels has been considered as the cause of pathogenesis of preeclampsia. Minerals have an important influence on the health of pregnant women and growing fetus. Among them, serum or placental zinc (Zn) concentrations have been reported to be low in PE women. Furthermore, decreased levels of zinc, selenium, and copper have been observed in patients with preeclampsia [3]. In another side, the nutrients with antioxidants among high risk women showed a protective effect [4]. Folic acid has been hypothesized as a protective agent of preeclampsia.

Maternal obesity and insulin resistance are also believed to be important risk factors for the development of placental endothelial dysfunction and preeclampsia. Prevention of preeclampsia has remained elusive, owing largely to their complex nature. Currently, maternal obesity in prepregnancy is one of the strongest modifiable risk factors. Recent studies have shown a relation between obesity in prepregnancy and the risk of preeclampsia. The reason for obesity being associated with an increased risk of preeclampsia was explained by increased levels of serum triglycerides and very low-density lipoprotein particles in obese women. This lipid alterations have been suggested to promote oxidative stress caused by ischemia–reperfusion mechanism or activated neutrophils, which leads to endothelial cell dysfunction [1].

The hypothesis about nutritional status and body mass index (BMI) prepregnancy associated with preeclampsia has intrigued us to study the risk factor for preeclampsia in Dr. M. Djamil Hospital, Padang, Indonesia.

Methods

This was a case–control study at the Department of Obstetric and Gynecology in Dr. M. Djamil Hospital, Padang, Indonesia, between January and December 2013. Pregnant women after 20 weeks gestations were included. A total of 140 patients were enrolled in this study with 70 cases and 70 controls. Cases were those diagnosed with preeclampsia; meanwhile, controls were normotensive pregnant women without any other comorbidity.

After providing written informed consent, all subjects completed an interview for their nutritional status and prepregnancy BMI after delivery. The nutritional status was assessed by Food Frequency Questionnaire (FFQ) and then analyzed by Nutrisurvey Program. Calories, protein, fat, carbohydrates, calcium, phosphorus, zinc, sodium, potassium, magnesium, vitamin A, folic acid, vitamin B1, vitamin B2, niacin, vitamin B6, vitamin B12, vitamin C, and vitamin E were assessed. Maternal BMI was categorized into two groups: normal BMI and abnormal BMI. Normal BMI was defined as 18.5–24.9 kg/m^2. The independent samples *t* test was used for nutritional status, and Chi-square test was used for BMI. Odds ratio (OR) with 95% CI was calculated. A p value <0.05 was considered statistically significant. For the nutrition variable, if the p value <0.25 then continued by logistic regression backward to assess the risk factor.

Results

Most of the subjects had normal weight, both in case and control groups. Table 1 shows that prevalence of abnormal BMI was more common in the preeclampsia group compared with those without preeclampsia 19 (27.1%) versus 12 (17.1%). BMI was not found as a significant risk factor in this study ($p = 0.222$).

As shown in Table 2, the mean level for most of the variables, except calories, fat, and vitamin B1, was lower in subjects with preeclampsia than those without preeclampsia. The difference for most of the subjects was also statistically significant with $p < 0.05$, except for vitamin B1 and vitamin B2. Table 3 shows the risk factors for preeclampsia obtained by logistic regression analyses. The nutrients that were significantly associated with increased risk of preeclampsia were deficiency of vitamin E, zinc, fat, calcium, and vitamin C. Excess of calories and carbohydrate also significantly associated with increased risk of preeclampsia. Meanwhile, vitamin A and vitamin B1 were protective factors.

Discussion

The reason for obesity being associated with an increased risk of preeclampsia was explained by increased levels of serum triglycerides, very low-density lipoproteins, and formation of small low-density lipoprotein particles in obese women. This lipid profile was also found in women with preeclampsia. These lipid alterations have been suggested to promote oxidative stress, caused by ischemia–reperfusion mechanism or activated neutrophils, which leads to endothelial cell dysfunction [1]. Moreover, dyslipidemia also can cause atherothrombosis and induce the aggregation of the thrombocytes than can lead to coagulopathy which is a characteristic of preeclampsia. Obesity is accompanied by oxidative stress. The origin of oxidative stress is proposed to be secondary to increased free fatty acids and inflammation. It is also suggested that diet can contribute to oxidative stress. Obese individuals have lower blood concentrations of antioxidants. This could be due to reduced dietary intake of antioxidants, but increased consumption by reactive oxygen species is also possible [5].

In this study, we found no relationship between BMI with preeclampsia. As mentioned before, dyslipidemia is the important factor that can lead into preeclampsia. But our study did not assess profile lipid of the subjects. Furthermore, central obesity has a higher risk of preeclampsia. Central obesity is characterized by visceral fat. Visceral fat produces C-reactive protein (CRP), PAI-1, and leptin that contributes to oxidative stress. People with central obesity have a higher risk to get preeclampsia. In this study, we did not assess the central obesity of the subjects. Measures of body composition, including percent body fat, may very likely identify the obese woman at risk of preeclampsia more accurately.

Our study found that carbohydrate intake in preeclampsia group was significantly higher than the non-preeclampsia group. The subjects that have higher carbohydrate will have lower protein level. Meanwhile, protein is needed in the process of trophoblast invasion so the protein-energy malnutrition increases the risk of preeclampsia. We also found that intake of proteins in preeclampsia was significantly lower in the preeclampsia group.

Folic acid and vitamin B12 are also a protector factors against preeclampsia. Those micronutrients play an important role in suppressing the metabolism of homocysteine, whereas the excess of homocysteine was a causative factor of endothelial damage and became one of the causes of preeclampsia. In addition, folic acid- supplements preconception enhance the placentation process and can prevent preeclampsia. Three earlier cohort studies assessed the effect of folic acid containing multivitamins (including folic acid) and gestational hypertension (including preeclampsia), and all showed a protective effect of folic acid supplementation on preeclampsia [2, 6, 7].

Table 1 Asssociation between body mass index and the risk of preeclampsia

BMI	Preeclampsia	%	Non-preeclampsia	%	p*	OR	CI 95%	
							Min.	Max.
Abnormal BMI	19	27.1	12	17.1	0.222	1.801	0.797	4.067
Normal BMI	51	72.9	58	82.9				
	70	100	70	100				

BMI body mass index, *OR* odds ratio, *CI* confidence interval

* p value were obtained by Chi-square

Table 2 Differences of mean nutritions level in preeclampsia and non-preeclampsia group

	Preeclampsia Mean (95% CI)	Non-preeclampsia Mean (95% CI)	p*
Calorie (Kcal)	1269.22 (745.2–2214)	1171.15 (649.1–2447.6)	0.048
Protein (g)	42.37 (23.03–95.42)	54.9 (24.2–200.6)	0.000
Fat (g)	26.8 (4.65–58.9)	32.4 (10.79–93.12)	0.009
KH (g)*	219.5 ± 56.8	163.49 ± 46.5	0.000
Calcium (mg)	234.7 (63.7–758.3)	9362.9 (63.7–922.4)	0.000
Phosphor (mg)	589.4 (296.5–1444.5)	714.6 (324.6–2353.4)	0.006
Fe (mg)	9.4 (2.84–23.9)	11.06 (2.84–35.6)	0.005
Zinc (mg)	4.8 (2.39–12.87)	5.5 (2.4–16.5)	0.005
Natrium (mg)	299.3 (76.9–970.24)	533.3 (105.9–1847.60)	0.000
Kalium (mg)*	595.4 ± 237.2	732.15 ± 367.8	0.010
Magnesium (mg)	181.1 (97.1–370.14)	210.0 (97.1–554.5)	0.010
Vitamin A (μg)	544.9 (174.9–1567.4)	763.9 (174.9–3354.5)	0.000
Folic acid (μg)	108.6 (56.8–421.6)	163.5 (56.83–497.9)	0.000
Vitamin B1 (mg)	0.7 (0.27–2.15)	0.65 (0.27–2.01)	0.085
Vitamin B2 (mg)	0.94 (0.25–2.45)	1.1 (0.25–2.7)	0.046
Niacin (mg)	4.3 (0.6–11.9)	5.8 (2.1–23.7)	0.000
Vitamin B6 (mg)	1.1 (0.66–2.14)	1.22 (0.67–3.8)	0.009
Vitamin B12 (mg)	1.1 (0.15–9.15)	2.8 (0.27–21.1)	0.000
Vitamin C (mg)	43.4 (8.4–136.8)	68.2 (19.2–262.7)	0.000
Vitamin E (mg TE)	1.9 (0.2–4.4)	3.6 (1.8–8.2)	0.000

CI confidence interval

* p value was obtained by independent samples t test

A recent large cohort study from Denmark also showed that regular use of folic acid in pregnancy was related to a reduced risk of preeclampsia among normal-weight women [8]. But in this study, we did not found the folic acid and vitamin B12 as a protective agent of preeclampsia. The different result maybe caused by supplementation that has been done generally. In other side, the no supplementation subject was rare so that selection bias/confounding become difficult to control.

The previous study showed that vitamin B6 deficiency is associated with cardiovascular disease. This is related to the function of B6 for the establishment of pyridoxal 5 phosphate which is an essential coenzyme in many metabolism processes. The coenzyme deficiency will lead to the diseases such as preeclampsia. Another micronutrients that play a role in the occurrence of preeclampsia is magnesium. In a study, obtained serum magnesium levels in patients with preeclampsia were significantly lower than normal pregnancy. This indicates that magnesium as one of the predictors of preeclampsia. Magnesium also allegedly acted as a coenzyme intracellular and functions to maintain contraction and vascular tone [2].

Serum zinc, calcium, and magnesium levels have been compared between preeclamptic and healthy pregnant women in various studies. Some results showed that copper, zinc, and calcium levels were significantly lower in preeclamptic patient, whereas magnesium concentrations showed no significant differences between the two groups [9]. Our study is consistent with that study, whereas we found zinc and calcium deficiency as a risk factor for preeclampsia (OR 99.46, 95% CI 1.37, 7219; OR 31, 95% CI 1.21, 841).

Our study found that vitamin E and A deficiency increase the risk of preeclampsia (OR 19.57, 95% CI 2.5, 151, OR 1768, 95% CI 10.22, 305,890). Antioxidants are important in maintaining cellular integrity in a normal pregnancy by inhibiting peroxidation reaction and thus protecting enzymes, proteins, and cells from destruction by peroxides. Antioxidant defense mechanisms include cellular and extracellular enzymes such as free radical scavengers, including vitamin C and E, and metabolites such as bilirubin and uric acid. Vitamin C and E are antioxidants derived from the diet. Vitamin C scavenges free radicals in the aqueous phase, and the lipid-soluble vitamin E acts in vivo to prevent the formation of lipid peroxides and thus protect cell membranes. There is evidence of oxidative stress in women with established preeclampsia, including increased plasma concentration of 8-epi-prostaglandin $F_{2\alpha}$, lipid peroxides, and decreased concentrations of antioxidants such as vitamins C and E [10].

Table 3 Results of multivariate logistic regression analysis

	OR	*p*	95% confidence interval
Calorie	3.87	0.028	2.39 ± 6,268,293
Protein	0.049	0.650	0.27 ± 12,994
Fat	59.182	0.138	3.14 ± 500
KH	52.9	0.063	0.801 ± 3495
Calcium	109	0.119	0.29 ± 40,041
Fe	9.84	0.149	0.441 ± 219
Zinc	99.4	0.035	1.37 ± 7219
Natrium	0.62	0.731	0.041 ± 9.37
Kalium	0.005	0.054	0.000 ± 1.08
Magnesium	0.015	0.528	0.000 ± 7321
Vitamin A	0.002	0.055	0.000 ± 1.14
Folic acid	42.9	0.193	0.15 ± 12,383
Vitamin B1	0.000	0.009	0.000 ± 0.014
Vitamin B2	3.75	0.550	0.049 ± 285
Niacin	2.39	0.068	0.571 ± 1E + 007
Vitamin B6	0.299	0.591	0.004 ± 24.3
Vitamin B12	4.511	0.243	0.36 ± 56.4
Vitamin C	19.5	0.004	2.52 ± 151
Vitamin E	1.76	0.004	10.2 ± 30.5

OR odds ratio

Conclusions

Deficiency of vitamin E, zinc, fat, calcium, and vitamin C, and excess of calories and carbohydrate were associated with increased risk of preeclampsia.

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Compliance with Ethical Standards

Conflict of interest Yusrawati, Nicko Pisceski Kusika Saputra, Nur Indrawati Lipoeto, Rizanda Machmud declare that they have no conflict of interest.

Human and Animal Right Statements All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the Research Ethics of the Dr. M. Djamil Hospital (Project Number PE.10.2014).

Informed Consent Informed consent was obtained from all patients for being included in this study.

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