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RESEARCH

Comparison of Preeclampsian Pregnancy by Metabolic Components

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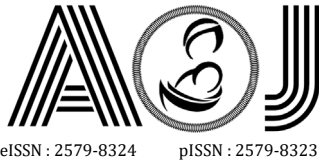
Abstract

In preeclampsia occurring carbohydrate and fat metabolism disorders. Components of the metabolic syndrome such as insulin resistance, obesity, and dyslipidemia contributes to the occurrence of preeclampsia. This was an obser-vational analytic study with Kohort design and has been performed in Obgyn Department of M. Djamil Hospital Padang, primary health care in Koto Berapak, Private Practice Midwife in Lintau from July 2013 to May 2014. 60 samples of second trimester of pregnancy with positive Roll over test. Each subject was examined BMI, fasting blood glucose, LDL, HDL, triglycerides, and insulin levels. Then divided into two groups, positive metabolic components group and negative metabolic components group. Statistical analysis to assess significance using the unpaired t test and chi square on SPSS 18.0 for windows. There was no significant association between metabolic components and preeclampsia ($p > 0.05$). Other metabolic components such as HDL level and insulin resistance were not statistically significant with preeclampsia ($p > 0.05$). HOMA IR examination also showed no significant association with the in-cidence of preeclampsia. However, the subgroup analysis showed a mean insulin levels higher in preeclampsia patients compared with normal pregnancies ($p < 0.05$). BMI showed a significant association with preeclampsia ($p < 0.05$). subgroup analysis showed a mean insulin levels higher in preeclampsia patients compared with normal pregnancies ($p < 0.05$). BMI showed a significant association with preeclampsia ($p < 0.05$). subgroup analysis showed a mean insulin levels higher in preeclampsia patients compared with normal pregnancies ($p < 0.05$). BMI showed a significant association with preeclampsia ($p < 0.05$).

Keywords: Preeclampsia, metabolic syndrome, fasting blood glucose, LDL, HDL, triglycerides, HOMA-IR, BMI

INTRODUCTION

Preeclampsia was defined as a condition of hypertension and proteinuria after 20 weeks of gestation. Preeclampsia is a major pregnancy complication which is increasing in incidence worldwide and is associated with maternal morbidity and mortality. Preeclampsia affects 3%-5% of all pregnancies and causes an estimated 60,000 maternal deaths worldwide each year. In Dr. M. Djamil Padang in the period 1998-2003, the incidence of preeclampsia was 5.5% (663 cases) and eclampsia 0.88% (106 cases) 12,034 deliveries. Data from the medical records of patients treated at the Obstetrics and Gynecology Department of Dr. M. Djamil Padang



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during the period January 1 to December 31, 2010, there were 176 preeclampsia and eclampsia cases, 140 cases of severe preeclampsia, 36 cases of eclampsia, and 3 cases of death due to eclampsia.^{1,2,3,4}

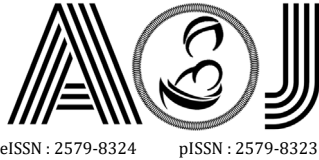
In normal pregnancy there are metabolic changes that are important for fetal growth. Maternal metabolism in the first two trimesters is generally anabolic and catabolic in the last trimester. Since glucose is a material needed more by the fetus, insulin resistance normally occurs during the middle of late pregnancy to increase maternal plasma glucose and amino acid concentrations for diffusion through the placenta.^{5,6}

In pregnancy with preeclampsia, insulin and lipid metabolism disorders occur. Where there are differences in components between normal pregnancies versus preeclampsia. When compared with normal pregnancy, insulin sensitivity and glucose tolerance in preeclamptic patients tend to decrease more. Meanwhile, the levels of free fatty acids and triglycerides were higher in preeclamptic patients compared to normal pregnant patients.⁶

It has recently been reported that metabolic scores are associated with the development of preeclampsia. It remains unclear whether preeclampsia predisposes women to cardiovascular disease in the future via metabolic syndrome, or metabolic predisposition to preeclampsia. However, the risk factors associated with metabolic syndrome are also risk factors for preeclampsia. The components of the metabolic syndrome found in preeclamptic patients are insulin resistance, obesity, and dyslipidemia. This component of the metabolic syndrome is said to contribute to preeclampsia.^{2,7,8,9}

Paretti and colleagues conducted a study in early pregnancy before the onset of preeclampsia. The study found a direct link between insulin resistance and preeclampsia. The fact that there is an increase in insulin resistance in women who previously had preeclampsia and an increase in cholesterol and other components of the metabolic syndrome before pregnancy with preeclampsia makes it possible that insulin is a risk factor for preeclampsia.^{9,10,11,12,13}

Obesity is characterized by low-grade chronic inflammation. This is evidence to support that inflammation has a contribution to cause insulin resistance, dyslipidemia, and oxidative stress. There is a strong association between obesity before pregnancy and preeclampsia. Obesity and overweight contribute to the risk of preeclampsia. Stone and colleagues found that severe obesity and a previous history of preeclampsia were the only risk factors for severe preeclampsia. Eskenazi and colleagues used the same standard criteria for cases of severe preeclampsia and controls. The results of this study show that regardless of parity, women with severe preeclampsia tend to have a high BMI before becoming pregnant. The Danish cohort analysis found that both primiparous and multiparous pregnancies with obesity may develop mild and severe preeclampsia or early onset preeclampsia.⁶



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In pregnancy, all fat fraction increases parallel with increasing gestational age. The increase in lipids is higher in pregnant women with hypertension. VLDL and lipoprotein-rich atherogenic triglycerides are increased in women with preeclampsia. Plasma triglycerides mean and concentration free fatty acids are doubled in preeclampsia. Approximately one-third of women with preeclampsia have plasma triglyceride levels above 400 mg / dl, higher than the 90th percentile measured randomly at 36 weeks' gestation.^{14,15}

Dyslipidemia mediates endothelial cell activation by producing disruptive endothelial factors such as lipid peroxidase, trophoblast components, and lipid changes so that it will induce hypertension in pregnancy. In accordance with the pathogenesis, dyslipidemia in preeclampsia occurs in the first and second trimesters so that it can be used for clinical detection of preeclampsia. In women with preeclamptic pregnancies, high mean concentrations of free fatty acids (oleic, linoleic, palmitic) were found at 16-20 weeks of gestation. Fasting triglycerides increase at 10 weeks of gestation, and the difference becomes more pronounced with increasing gestational age. Early hypertriglyceridemia is associated with an increased risk of early onset preeclampsia (preeclampsia that occurs before 36 weeks of gestation). HDL cholesterol decreases at 20 weeks of gestation and during pregnancy in women who develop preeclampsia.^{6,16}

Total cholesterol and LDL cholesterol do not increase during preeclampsia compared to normal pregnancy. Women with increased total cholesterol during the first trimester are at higher risk for developing preeclampsia. High levels of LDL cholesterol, or non HDL cholesterol, or triglycerides at 4-5 years before the first pregnancy are associated with an increased incidence of preeclampsia. This is consistent with the hypothesis that previous dyslipidemia, which may be a metabolic syndrome, contributes to the development of preeclampsia.^{6,17}

A 2011 cross sectional study in China investigated the association of syndromes metabolic and preeclampsia in women with a history of severe preeclampsia soon after pregnancy. The result is that 27-39% of the 62 women who were sampled in the study suffered from metabolic syndrome.²

Results from a study using a metabolic syndrome score (0, 1, or 2, or more criteria) based on NCEP (National Cholesterol Education Program) criteria that closely matched clinical data (obesity, hypertension before 20 weeks of gestation, and elevated fasting / fasting blood glucose). diabetes mellitus), showing an increase in the score associated with the occurrence of preeclampsia, especially severe disease.⁶

The various metabolic changes that have been described previously, which can be assessed by a metabolic score, are expected to be used in early detection of preeclampsia, so further research is needed.



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Website:<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>**METHOD**

This study was conducted using an observational analytic method with a prospective cohort design at the Obgyn Polyclinic Dr. M. Djamil Padang, Puskesmas Koto Berapak, and Private Practice Midwives in Lintau from July 2013 to May 2014. Of the 60 samples of trimester pregnancy research with a positive Roll over test. Each subject was checked for BMI, fasting blood sugar levels, LDL, HDL, triglycerides, and insulin. Then divided into 2 groups, namely positive and negative metabolic components. Evaluation of blood pressure is carried out every 2 weeks, if hypertension is found, it is followed by examination of urine protein. Patient follow-up was discontinued when a diagnosis of preeclampsia and gestational hypertension was confirmed or the patient gave birth. Statistical analysis to assess significance used unpaired t test and chi square on SPSS 18.0 for windows.

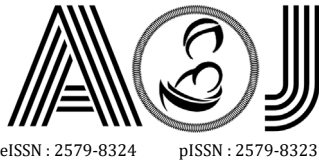
RESULTS**Basic Characteristics of Research Subjects**

The study was conducted from July 2013 to May 2014 with a total of 60 research subjects. The research subjects sampled in the study were divided into 2 groups, a group with a positive metabolic component as many as 30 patients and a group with a negative metabolic component as many as 30 patients. The basic characteristics of research subjects are shown in table 1.

Table 1. Basic Characteristics of Research Subjects

Demographics	Component Metabolic Positive n=30	Component Metabolic Negative n=30	P
Age (years ± SD)	30,32 ± 5,84	28,33 ± 0,01	0,182
Parity (times ± SD)	2,63 ± 1,71	2,13 ± 1,14	0,323
Gestational Age (weeks ± SD)	17,13 ± 5,28	14,40 ± 4,89	0,780
Height (cm ± SD)	150,57 ± 6,26	151,65 ± 5,58	0,482
Weight (kg ± SD)	70,30 ± 86,46	63,10 ± 79,98	0,016
BMI (kg/m ² ± SD)	24, 11 ± 4,42	20,86 ± 2,77	0,001
ANC Systolic BP (mmHg ± SD)	110,67 ± 11,43	112,33 ± 9,35	0,404
ANC Diastolic BP (mmHg ± SD)	73,00 ± 6,51	74,33 ± 6,79	0,372

There was no statistically significant difference in baseline characteristics in the two groups, except for a greater difference in body weight in the group with a positive metabolic component compared to the group with a negative metabolic component. The mean body weight of the group with a positive metabolic component and the group with a negative metabolic component was 70.30 ± 86.46 kg and 63.10 ± 79.98 kg.



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Website:<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>**Metabolic Characteristics of Research Subjects**

Table 2 shows the mean value of each metabolic component in the research subject. BMI examination (22.57 ± 4.02 kg / m²) and blood laboratory tests consisting of fasting blood sugar (70.65 ± 10.53 mg / dl), LDL cholesterol (104.17 ± 48.71 mg / dl), HDL cholesterol (83.25 ± 43.38 mg / dl), triglycerides (118.05 ± 40.57 mg / dl), insulin levels (4.19 ± 1.87 μ U / ml), and HOMA IR (0.73 ± 0.34) were within normal limits, respectively.

Table 2. Metabolic Characteristics of the Subject Research

Metabolic Components	Mean \pm SD
Body Mass Index (kg/m ²)	22,57 \pm 4,02
Fasting Blood Sugar (mg/dl)	70,65 \pm 10,53
LDL cholesterol (mg/dl)	104,17 \pm 48,71
HDL cholesterol (mg/dl)	83,25 \pm 43,38
Triglycerides (mg/dl)	118,05 \pm 40,57
Insulin level (μ U/ml)	4,19 \pm 1,87
IR HOMA	0,34

Subgroup analysis show that the mean insulin levels in preeclamptic patients and patients without preeclampsia were 4.76 ± 0.87 μ U / ml and 4.12 ± 1.95 μ U / ml. These results indicated that the insulin levels of preeclamptic patients were higher than those of patients without preeclampsia and statistically significant (p 0.03).

Clinical Characteristics of Research Subjects

All study subjects were observed until the delivery process. The clinical characteristics of the study subjects are shown in Table 3. Preeclampsia occurred in 6 (10%) patients, while 54 (90%) other patients were not preeclamptic. In the group with a positive metabolic component, there were 18 (30%) patients with a positive metabolic component 1, 10 (16.6%) patients with a positive metabolic component 2, and 1 (1.7%) patients with a positive metabolic component 3 and 4 respectively. Patients with preeclampsia, positive proteinuria 1 were present in 4 (6.6%) patients, positive proteinuria 3 and 4 were present in 1 (1.7%) patients respectively. Vaginal deliveries were present in 51 (85%) patients and 9 (15%) patients with vaginal deliveries.



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Website:<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>**Table 3.** Clinical Characteristics of Research Subjects

Clinical	n (%)
Metabolic Components	
Negative	30 (50)
Positive 1	18 (30)
Positive 2	10 (16,6)
Positive 3	1 (1,7)
Positive 4	1 (1,7)
Preeclampsia	6 (10)
Proteinuria	
Negative	54 (90)
Postive 1	4 (6,6)
Postive 2	1 (1,7)
Postive 3	1 (1,7)
Delivery	
Vaginal	51 (85)
Perabdominam	9 (15)

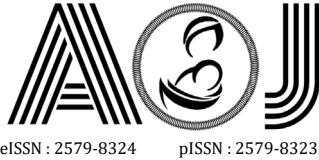
Relationship between Metabolic Components and Preeclampsia

The relationship between the metabolic components in the patient group and the positive metabolic components on the incidence of preeclampsia is shown in Table 4. There was no statistically significant relationship between the metabolic component groups and the incidence of preeclampsia (p 0.195). The sensitivity and specificity of the examination the metabolic components of the incidence of preeclampsia were 83.33% and 53.70%, with positive predictive values and negative predictive values of 16.67% and 96.67%. Based on these values, the likelihood of preeclampsia in patients who are at risk for testing positive metabolic components is 16.67%, while the probability of patients who are at risk of not experiencing preeclampsia on examining negative metabolic components is 96.67%. The positive likelihood ratios and negative likelihood ratios were 1.76 and 0.32.

Table 4. Relationship Metabolic Components with Preeclampsia

		Preeclampsia		p	Sensitivity	Specificity
		Yes	No			
Metabolic component	Positif	5	25	0,195	83,33%	53,70%
	Negatif	1	29			
Total		6	54			

Statistically insignificant associations were also found for other metabolic components such as HDL cholesterol levels and insulin resistance (HOMA IR). There was no statistically significant relationship between HDL cholesterol levels and the incidence of preeclampsia (p 0.904) as seen in table 5. Sensitivity to the incidence of preeclampsia is 16.67% and 85.19%, with positive predictive values and negative predictive values of 11.11% and 90.19%. Based



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on these values, the probability of the incidence of preeclampsia in patients who are at risk for a positive HDL examination is 11.11%, while the probability of patients who are at risk of not experiencing preeclampsia on a negative HDL examination is 90.19%. Meanwhile the positive likelihood ratios and negative likelihood ratios were 1.13 and 0.96.

Table 5. Relationship between HDL Cholesterol and Preeclampsia

		Preeclampsia		p	Sensitivity	Specificity
		Yes	No			
HDL cholesterol level	Positif	1	8	0,904	16,67%	85,19%
	Normal	5	46			
Total		6	54			

Insulin resistance testing (HOMA IR) also showed a statistically insignificant relationship with the incidence of preeclampsia (p 1.00), as shown in Table 6. Sensitivity and specificity of insulin resistance testing (HOMA IR) on the incidence of preeclampsia amounted to 16.67% and 72.22%, with positive predictive values and negative predictive values of 6.25% and 88.6%. Based on this value, the probability of preeclampsia in patients who are at risk for a positive HOMA IR examination is 6.25%, while the probability of a patient at risk of not experiencing preeclampsia on a negative HOMA IR examination is 88.6%. The positive likelihood ratios and negative likelihood ratios were 59.5 and 1.15.

Table 6. Relationship between Insulin Resistance (HOMA IR) and Preeclampsia

		Preeclampsia		p	Sensitivity	Specificity
		Yes	No			
HOMA IR Level	Positif	1	15	1,00	16,67%	72,22%
	Normal	5	39			
Total		6	54			

Assessment of BMI in research subjects showed a statistically significant relationship to the incidence of preeclampsia (p 0.001), with a sensitivity and specificity of 83.33% and 81.48%, as shown in table 7. The positive predictive value and negative predictive value of BMI in predicting the incidence of preeclampsia are 33.33% and 97.78%. Based on this value, the probability of preeclampsia in patients who are at risk for a positive BMI examination is 33.33%, while the probability of patients at risk of not experiencing preeclampsia on a negative BMI examination is 97.78%. The positive likelihood ratios and negative likelihood ratios are 4.50 and 0.21.



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Table 7. Relationship between BMI and Preeclampsia

		Preeclampsia		p	Sensitivity	Specificity
		Yes	No			
BMI	Positif	5	10	0,001	83,33%	81,48%
	Negatif	1	44			
Total		6	54			

Assessment of other metabolic components such as fasting blood sugar levels, LDL cholesterol levels, and levels triglycerides could not be assessed because none of the study subjects with a positive metabolic component had preeclampsia.

The Relative Risk of Metabolic Components to the Incidence of Preeclampsia

Multivariate analysis on the metabolic component shows that BMI is an independent predictor of the incidence of preeclampsia (RR 22 with 95% CI 2.309 - 209.599), as shown in Table 8. BMI check. Based on the ROC curve, it can be seen that the Area Under Curve (AUC) value is 79.6% (95% CI 48.6% - 100%). The clinical and statistical AUC value is satisfactory with moderate interpretation.

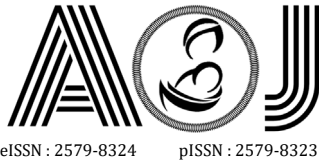
Table 8. The Relative Risk of Metabolic Components to the Incidence of Preeclampsia

Metabolic components	RR	95% CI
HDL cholesterol	1,15	0,118 – 11,182
Insulin resistancy (HOMA IR)	0,52	0,056 – 4,827
BMI	22	2,309 – 209,599

DISCUSSION

This study shows that BMI has a significant relationship with the incidence of preeclampsia in second trimester pregnant patients who are at risk of preeclampsia. Other metabolic components such as LDL cholesterol, HDL cholesterol, triglycerides, and insulin resistance have shown an unrelated relationship significant with the incidence of preeclampsia in pregnant patients in the second trimester who are at risk of preeclampsia. The grouping of patients based on the number of metabolic components with the incidence of preeclampsia also showed no significant association with the incidence of preeclampsia in second trimester pregnant patients who are at risk of preeclampsia.

Several other studies that show results that are in line with this study are research conducted Castano IB et al, 2013 and Yazdani S et al, 2012. In these studies it was found that the risk of preeclampsia would increase in obese women. In a meta-analysis study that assessed the relationship between BMI and preeclampsia showed that the risk of preeclampsia doubled every time an increase in BMI 5 to 7 kg / m². A systematic review conducted by O'Brien et al. 2003 on 13 cohort studies showed a consistent and linear increase



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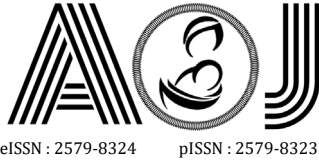
in the risk of preeclampsia with an increase in BMI before pregnancy. Other studies that show different results from this study include systematic review and bivariate meta-analysis by Cnossen JS et al, 2007 which assessed the accuracy of BMI in predicting the incidence of preeclampsia. The study concluded that BMI was a weak predictor of preeclampsia.^{18,19,20,21}

The measurement of BMI is determined by examining body weight and height. In this study, it was found that BMI examination had a significant relationship with the incidence of preeclampsia in at-risk second trimester pregnant patients. This was influenced by the greater body weight in patients in the positive metabolic group compared to patients in the negative metabolic group. The mechanisms by which obesity is associated with the incidence of preeclampsia are not fully understood, but there are several possible explanations mechanisms of the incidence of preeclampsia in obese women. These mechanisms include damage to endothelial function, as well as biochemical and physiological changes that occur in obesity.^{20,22}

Obesity will cause it to happen hyperinsulinemia. Some research maintains a strong association between obesity and hyperinsulinemia. Hyperinsulinemia that occurs in obesity directly predisposes to hypertension through increased renal sodium reabsorption and stimulation of the sympathetic nervous system. Hypertension will cause damage to endothelial function. Some experts also argue that obesity that triggers insulin resistance will cause damage to endothelial function. Damage to endothelial function will cause preeclampsia. This mechanism is supported by subgroup analysis data in this study which shows that the mean insulin levels in preeclamptic patients is higher than the mean insulin levels in patients who do not have preeclampsia.²⁰

Obesity and preeclampsia have similarities in terms of biochemical and physiological changes, including increased oxidative stress, inflammation, hyperlipidemia, endothelial dysfunction and vasoconstriction. These biochemical and physiological changes reinforce the concept that excessive maternal response in obese women manifests as late onset preeclampsia or preeclampsia in term pregnancy. The predisposition to preeclampsia and obesity leads to impaired placentation associated with preterm preeclampsia and causes the exaggerated maternal response seen in preeclampsia in term pregnancy.²²

This study also shows that insulin resistance does not show a significant relationship with the incidence of preeclampsia in pregnant patients who are at risk of preeclampsia in the second trimester. Research conducted by Salamalekis E et al, 2005 showed the same results as this study. Salamalekis E et al. Measured blood glucose and insulin levels in 30 primigravidas at 28 and 34 weeks of gestation measured at 0, 1, and 2 hours after oral glucose tolerance tests (after administration of 75 grams of glucose) in normotensive women and women with preeclampsia. The study found that preeclampsia was not associated with hyperinsulinemia and / or insulin resistance, either during fasting or post prandial.^{23,24}



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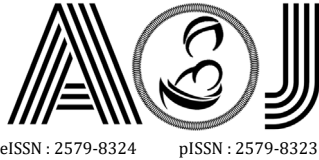
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During pregnancy there is an increase progressive response insulinter to glucose which indicates an increase resistance insulin maternal with increasing age pregnancy hypertension there is hyperinsulinemia which occurs exaggerated in response to an oral glucose tolerance test compared with women with normal pregnancy in the third trimester. Sowers JR et al in 1995 conducted a study to assess the abnormalities of carbohydrate metabolism in women at risk of developing preeclampsia. The study found that hyperinsulinemia or insulin resistance associated with preeclampsia occurred at 18 to 25 weeks of gestation. Hauth JC et al in 2011 found that midtrimester maternal insulin resistance at 22 and 26 weeks of gestation was associated with the incidence of preeclampsia. This explains why insulin resistance that occurred in this study did not show a significant relationship with the incidence of preeclampsia, because the measurement of fasting blood sugar levels and blood insulin levels was carried out at gestational age under 18 weeks.^{25,26}

Another factor that causes this study to not show a significant relationship between insulin resistance and the incidence of preeclampsia is changes in blood insulin levels caused by physiological changes during pregnancy. During normal pregnancy there is variation in insulin resistance to varying degrees. This insulin resistance mainly occurs in the third trimester of pregnancy and returns to pre-pregnancy values after delivery. The occurrence of insulin resistance relative to preeclampsia compared to normal pregnancy indicates failure of metabolic adaptation to pregnancy due to abnormal placentation. Measurement of fasting blood sugar levels and blood insulin levels in this study was carried out in the second trimester of pregnancy where variations in insulin resistance had not occurred optimally.^{27,28}

This study also did not show a significant relationship between HDL cholesterol and the incidence of preeclampsia. Research by Kausar H et al, 2013 assessed predictors of the incidence of gestational hypertension and preeclampsia based on waist circumference, BMI, and lipid profiles in women 6-16 weeks of gestation. This study concluded that the levels of triglycerides, LDL cholesterol, and VLDL cholesterol increase the risk of hypertension in pregnancy while HDL cholesterol reduces the risk of hypertension in pregnancy. Other research by Anjum R et al in 2013 concluded that lipid profile has an important role in regulating blood pressure during pregnancy. Increased levels of triglycerides, LDL cholesterol, total cholesterol and VLDL cholesterol induce hypertension, while HDL cholesterol regulates blood pressure to normal values.^{29,30}

The relationship between changes in serum lipid profiles in preeclampsia is well known. An abnormal lipid profile is associated with cardiovascular disease and has a direct effect on endothelial dysfunction. Changes in lipid synthesis cause a decrease in the ratio of prostaglandin I₂ to thromboxane A₂ which is an important pathogenesis of preeclampsia. Several studies have shown endothelial dysfunction associated with hyperlipidemia. Increased levels of plasma triglycerides, phospholipids, total lipids and decreased HDL



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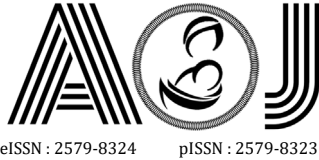
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cholesterol were found in preeclamptic women. High triglyceride levels increase the risk of placental vascular disorders that trigger endothelial dysfunction atherosclerosis and thrombosis. The basic modulator of hypertriglyceridemia is the hormone estrogen which is associated with the condition hyperestrogenemia. Estrogen stimulate biosynthesis of endogenous hepatic triglycerides carrying VLDL cholesterol. Other than that, Hyperinsulinemia and hypertriglyceridemia that occur in pregnancy will modulate the pathogenesis of hypertension in pregnancy. Triglyceride test at gestational age 28 - 32 weeks is a predictor examination of the incidence of preeclampsia. These physiological changes explain why the levels of LDL cholesterol and HDL cholesterol in this study did not show a significant relationship with the incidence of preeclampsia, because the cholesterol level examination was carried out at gestational age under 18 weeks.³¹

The relationship between dyslipidemia and the risk of preeclampsia is biologically consistent with the pathophysiology of preeclampsia. There are at least three hypotheses that explain the mechanisms of dyslipidemia and preeclampsia. First, increased plasma lipids and lipoproteins may induce endothelial dysfunction secondary to oxidative stress. Dyslipidemia is also damaging trophoblast invasion resulting in a cascade leading to preeclampsia. This hypothesis supports the fact that the accumulation of triglycerides in endothelial cells is associated with decreased prostacyclin release. Increased levels of triglycerides are also associated with a shift in the size of LDL cholesterol particles into small diameter particles. The formation of a small variant of LDL cholesterol causes endothelial dysfunction in preeclampsia through stimulation of thromboxane synthesis by endothelial cells and an increase in intracellular calcium in smooth muscle. The second mechanism is the pathological process of preeclampsia through lipoprotein lipase dysregulation which causes a dyslipidemic lipid profile. Third, preeclampsia that occurs through the metabolic syndrome. The metabolic characteristics of insulin resistance syndrome known as hyperinsulinemia and hyperuricemia are also found in preeclampsia. Genetic and environmental factors that play a role in the pathogenesis of the metabolic syndrome and associated vascular disorders are also important in determining the occurrence of preeclampsia.³²

Insulin resistance did not show a significant difference in the incidence of preeclampsia in this study. This can also have an impact on finding no significant differences in HDL cholesterol levels on the incidence of preeclampsia. Insulin resistance increases lipase sensitive hormone activity and adipocyte lipolysis. These changes cause hepatic FFA overload, increase hepatic triglyceride production, increase circulating VLDL cholesterol, and lead to triglyceride deposition. Excessive production of VLDL cholesterol causes lipoprotein changes, in the form of high concentrations of remnant lipoprotein particles and small LDL cholesterol (more easily oxidized) and low levels of HDL cholesterol.⁶



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Assessment of BMI in research subjects showed a statistically significant relationship to the incidence of preeclampsia with a sensitivity and specificity of 83.33% and 81.48%. The positive predictive value and negative predictive value of BMI in predicting the incidence of preeclampsia were 33.33% and 97.78%. Meanwhile, positive likelihood ratio and ratio the negative possibilities are 4.50 and 0.21. This shows that the BMI examination in the second trimester of pregnancy has a good diagnostic value in assessing the incidence of preeclampsia. High sensitivity and sensitivity of BMI can be used to determine the incidence of preeclampsia in pregnant patients who are at risk of preeclampsia in the second trimester.

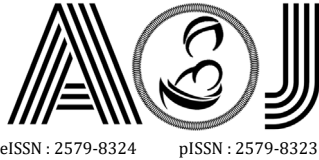
There are limitations in this study where the monitoring of the incidence of preeclampsia in the study sample was only carried out until the patient gave birth so there was no monitoring for the occurrence of post partum eclampsia. In addition, patients with metabolic disorders before pregnancy were excluded from the study so that an assessment of the risk of preeclampsia in women with pre-pregnancy metabolic disorders could not be determined.

CONCLUSION

There was no significant difference in the incidence of preeclampsia based on metabolic components, HDL levels, HOMA IR levels, second trimester pregnant patients who are at risk of preeclampsia. There is a significant difference in the incidence of preeclampsia based on the Body Mass Index (BMI) of pregnant patients in the second trimester who are at risk of preeclampsia. Assessment of other metabolic components such as fasting blood sugar levels, LDL cholesterol levels, and triglyceride levels cannot be assessed.

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