The Comparison of Low-Density Lipoprotein and High-Density Lipoprotein Between Severe Preeclampsia and Normal Pregnancy in Dr. Hasan Sadikin General Hospital Bandung

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Abstract

Objective: This study aims to distinguish level of (LDL/HDL) and Low Density Lipoprotein/High Density Lipoprotein ratio in severe preeclampsia patient compared to normal pregnancy.

Method: The study design was comparative cross-sectional study with consecutive sampling method that compared the laboratory results of LDL, HDL and ratio LDL/HDL that met the inclusion criteria. Subjects of this study were severe preeclampsia and normal pregnancy patient that fulfilled the inclusion criteria (n=60) in Dr. Hasan Sadikin General Hospital Bandung during August-September 2017.

Result: It is revealed that the differences in level of LDL and LDL/HDL ratios in both groups were significant with p value $\leq 0,05$. But there were no differences in HDL level. Increased level of LDL/HDL ratio in pregnancy was related to increased risk of preeclampsia with cut-off point $> 2,632$. If the increased level of LDL/HDL above cut-off point then the incident of severe preeclampsia increased 21,36 times.

Conclusion: It was concluded that level of LDL and LDL/HDL ratios in severe preeclampsia were higher than in normal pregnancy. The increased LDL/HDL ratio of > 2.632 increased the risk of severe preeclampsia by 21.36 times.

Key words: Preeclampsia, LDL, HDL, LDL/HDL ratio

Perbandingan Rasio *Low Density Lipoprotein/High Density Lipoprotein* antara Preeklamsi Berat dan Kehamilan Normal di RSUP Dr. Hasan Sadikin Bandung

Abstrak

Tujuan: Penelitian ini adalah untuk mencari perbedaan rasio *Low Density Lipoprotein/High Density Lipoprotein* (LDL/HDL) pada preeklamsi berat dibandingkan dengan kehamilan normal sebagai faktor risiko timbulnya preeklamsi.

Metode: Rancangan penelitian kasus kontrol membandingkan LDL, HDL, dan rasio LDL/HDL penderita preeklamsi berat dan kehamilan normal (n=60) bulan Agustus-September 2017 di Rumah Sakit Dr. Hasan Sadikin Bandung.

Hasil: Hasil penelitian didapatkan perbedaan kadar LDL dan rasio LDL/HDL pada kedua kelompok secara bermakna dengan nilai $p \leq 0,05$. Namun tidak didapatkan perbedaan yang bermakna pada kadar HDL. Peningkatan kadar LDL dan rasio LDL/HDL berhubungan dengan peningkatan risiko terjadinya preeklamsi dengan nilai *cut-off* $> 2,632$. Bila terjadi peningkatan rasio LDL/HDL diatas nilai *cut-off* maka risiko terjadinya preeklamsi berat sebesar 21,36 kali.

Simpulan: Kadar LDL yang tinggi dan nilai *cut-off* rasio LDL/HDL $> 2,632$ meningkatkan risiko terjadinya preeklamsi berat 21,36 kali

Kata Kunci: Preeklamsi, LDL, HDL, Rasio LDL/HDL

Introduction

Preeclampsia is a syndrome characterized by hypertension and proteinuria or organ dysfunction that occurs in pregnancy in >20 weeks gestational age.

Other manifestations include visual disturbance, headache, epigastrium pain, thrombocytopenia, and abnormal liver function which are caused by mild to severe microangiopathy on target organ.¹ Maternal mortality due to severe preeclampsia in the developing countries is higher than in the developed countries. Among other countries in South East Asia, the incidences of preeclampsia in Indonesia is still considered high, which is 3.4-8.6%.^{2,3}

The exact pathophysiology of preeclampsia is not fully understood yet. Many theories have attempted on explaining it such as abnormality of placenta vascularization, endothelial dysfunction, immunologic intolerance, cardiovascular adaptation, genetic and nutrition deficiency, and also inflammation theory.^{1,4,5}

In the last two decades, endothelial dysfunction is considered as the cause of preeclampsia. Dyslipidemia can cause endothelial damage by increasing macrophage and oxidized LDL. Oxidized LDL will be phagocytized by macrophage forming foam cells and increasing accumulation of monocytes which will stimulate cytokines production and cause endothelial damage.^{5,6,7,8} Increase of small LDL will cause the risk of endothelial damage due to its nature of being easily oxidized which will trigger inflammatory reaction on endothelium. The decrease of HDL will aggravate the reaction due to the decrease of free cholesterol transported back to liver. Increased LDL/HDL ratio in pregnancy will also cause the risk of endothelial dysfunction.

Endothelial dysfunction will cause imbalance production between vasodilator and vasoconstrictor which will cause massive

vasoconstriction and therefore preeclampsia syndrome.^{6,9,10,11,12}

The current study was to compare the values of LDL level, HDL level, and LDL/HDL ratio in women with severe preeclampsia and normal pregnancy.

Method

The study was conducted in Department of Obstetrics and Gynecology Dr. Hasan Sadikin Bandung General Hospital, in collaboration with the Department of Clinical Pathology during August to September 2017. In total of 30 women with severe preeclampsia and 30 women with normal pregnancy were selected for the study using a consecutive sampling. The diagnosis of severe preeclampsia was referred to guideline of diagnosis and therapy of Obstetrics and Gynecology in Dr. Hasan Sadikin Bandung General Hospital

Patients included were women with normal pregnancy of >20 weeks gestational age, pregnancy with a single alive fetus by ultrasonography, no history of hypertension prior to pregnancy, no degenerative disease such as diabetes mellitus, and no cardiac abnormality. Patients were excluded from the study if the blood sample was lytic or damaged and if the administration data was incomplete. Laboratory examinations of LDL and HDL levels were performed using Cobas Integra 400 plus with spectrophotometry and calorimetric enzymatic methods. Afterwards, the results were noted in study's tables to be statistically analyzed.

Statistical analysis for the categorical data was conducted using Chi-Square. Saphiro Wilks test was performed for normality test on the numerical data. Since the data was abnormally distributed, Mann-Whitney test was then commenced. Lambda correlation test was performed to find the correlation between two numerical variables.

Result

Sixty subject were involved in this study. A description of the study population's characteristic is illustrated in Table 1. The characteristics between two groups showed no significant differences ($p>0.05$). The age of the subjects were mainly 20-34 years old. The subjects were mostly primigravida.

Table 2 demonstrates the comparison of LDL, HDL, and LDL/HDL ratio between two study groups. HDL levels between two groups did not show any significant differences ($P>0.05$). Nevertheless, there were significant differences in LDL levels and LDL/HDL ratios ($p<0.05$). The mean LDL level and LDL/HDL ratio in severe preeclampsia group were higher than the

Table 1 Characteristics of Two Study Groups

Characteristics	Group		<i>p</i> value*
	Severe preeclampsia (n = 30)	Normal pregnancy (n = 30)	
Age (years)			
<20	3	6	0.43
20 – 34	23	22	
≥ 35	4	2	
Mean (SD)	27.7 (6.4)	25.5 (6.1)	
Range	18 – 38	17 – 37	
Parity			
G1	12	12	1.00
G2	10	10	
≥ G3	8	8	
Median (range)	2 (1-5)	2 (1 – 3)	

*) analyzed using Chi-square test

Table 2 Comparison of LDL Level, HDL Level, and LDL/HDL Ratio between Two Study Groups.

Variable	Group		<i>p</i> value*
	Severe preeclampsia (n=30)	Normal pregnancy (n = 30)	
HDL (mg/dl)			0.09
Mean (SD)	47.3 (12.1)	54.1 (13.9)	
Median	48	53	
Range	20 – 78	36 – 99	
LDL (mg/dl)			
Mean (SD)	181.7 (47.7)	124.9 (30.2)	<0.001
Range	98 – 274	74 – 216	
Ratio LDL/HDL			
Mean (SD)	4.1 (1.7)	2.3 (0.5)	<0.001
Median	3.7	2.3	
Range	2.0 – 9.1	1.2 – 3.2	

*) analyzed using Mann-Whitney test, except for LDL using unpaired t test

Table 3 Correlation between LDL/HDL ratio cut-off value and severe preeclampsia Using Receiver Operating Characteristics (ROC) Curve

LDL/HDL ratio cut-off value	Groups		<i>p</i> value	OR (CI 95%)
	Severe preeclampsia (n = 30)	Normal pregnancy (n = 30)		
> 2.632	26 (86.7%)	7 (23.3%)	<0.001	21.36 (5.53 – 82.43)
≤ 2.632	4 (13.3%)	23 (76.7%)		

control group.

The correlation between cut-off value of LDL/HDL ratio and incidence of severe preeclampsia has been evaluated in Table 3. The odd ratio (OR) obtained from the correlation was 21.36. Therefore, a pregnant woman whose LDL/HDL ratio was >2.632, had a risk to suffer severe preeclampsia 21.36 times higher than a pregnant woman whose LDL/HDL ratio was ≤2.632.

Discussion

In the current study, we noted that there were no significant differences of subjects' ages between two groups. Women whose age was in high risk of developing complication (< 20 years old and ≥ 35 years old) in two groups were 9 people (15%) while the age group of women who developed severe eclampsia was dominated by the age 20-34 years old (90%). This might be caused by the higher educational degree and older age of marriage in women. Therefore, women tended to get pregnant in older age which caused the prevalence of severe preeclampsia shifted to older age group. Woman's age of > 35 years old is a predisposition factor for preeclampsia because older age is associated with increased incidence of chronic hypertension and bigger risk of developing gestational hypertension. Older age can also cause thickening of intima layer. Lipid profile, especially cholesterol and phospholipid also progressively increases with age.^{5,13} This current study also stated that most subjects from the severe preeclampsia group were multigravida. This result is

not in accordance with previous theories stating that preeclampsia mostly happened in primigravida. This difference might be caused by various factors including multifetal pregnancy, extreme pregnancy age, et cetera.

The HDL level in current study did not show any significant differences between two groups. This result is consistent with previous study by Villa, et al. which compared lipoprotein serum levels in 31 pregnant women and reported that there were no significant differences between two groups.¹⁴

In the current study, the cut-off points of LDL/HDL ratio obtained from the ROC curve, was 2.632, that could be used as predictor of severe preeclampsia. Therefore, the risk to develop severe preeclampsia was 21.36 times higher compared to pregnant women with LDL/HDL ratio ≤2.632. This result is in accordance with prior study by De, et al.¹⁵

The results from the analysis obtained from normally distributed data concluded that the level of LDL and LDL/HDL ratio in severe preeclampsia were higher than in normal pregnancy. It was also concluded that the increased LDL/HDL ratio of >2.632 increased the risk of developing severe preeclampsia by 21.36 times.

There were some limitations in the current study. For first, the subjects were not fasting prior to blood sampling. Than, this study also included all range of age so the LDL and HDL levels obtained in this study were still affected by age, specifically for age >35 years old.

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